PROGRAM BOOK AND CONFERENCE ABSTRACTS.

The 11th Annual Indonesia Society for Cancer Chemoprevention Conference and Congress

Virtually on November 9th-21st, 2020

HOST ISCC

CO-HOST WAOCP.org APOCP.org

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THE 11th ANNUAL ISCC CONFERENCE AND CONGRESS NOVEMBER 9-21, 2020
Jakarta, Indonesia

Hosted by:

Indonesian Society for Cancer Chemoprevention

CO-HOST by:

Asian Pacific organization for Cancer Prevention (APOCP)

West Asia organization for cancer Prevention (WAOCP)

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WELCOME REMARKS FROM THE ORGANIZING COMMITTEE

Distinguished guests and invited speakers, respected colleagues, ladies and gentlemen,
It is a great honor for me to welcome all of you to this virtual event from Yogyakarta, the city known as the center of education and culture of Indonesia.
On behalf of the Organizing Committee, I would like to warmly welcome you to the 11th Annual ISCC Conference and Congress, "Accelerating the Cutting-Edge Transformative Research in Cancer Chemoprevention for Comprehensive Outcomes". This event is hosted by Indonesian Society for Cancer Chemoprevention (ISCC) in collaboration with the Asian Pacific Organization for Cancer Prevention (APOCP) and West Asia Organization for Cancer Prevention (WAOCP), and supported by Faculty of Pharmacy Universitas Gadjah Mada and Nara Institute of Science and Technology (NAIST) Japan.
ISCC has hosted the annual conference and congress since 2010. This year's event consists of Lecture Series, Scientific Presentation, Poster Competition, Workshops, and ISCC Congress. Aiming to disseminate the information and update on the research and technology; to facilitate idea and technology sharing; and to develop networking and communication in the world in the field of cancer chemoprevention; the Conference covering eight topics as follow: Pharmaceutics and Applied Materials for Drug Delivery; Pharmacology, Toxicology, and Microbiology; Pharmacy Practices and Clinical Pharmacy; Medicinal and Pharmaceutical Chemistry; Pharmacognosy and Ethnobotany; Cancer Chemoprevention and Immunomodulation; Cancer Biomarker and Diagnostic; and Bioinformatic and Computer-Aided Drug Design.
Although this year the Conference is firstly held virtually, the Committee is delighted with the positive response from the academicians, indicated by the abstract submission that we have received. We received 68 abstracts to be presented in the Conference; not only from our own Indonesia, but also from Malaysia, Japan, Germany, and Canada. Each of the abstract was reviewed by reviewers who are experts on the subjects. We are glad to announce that the abstracts will be published by WAOCP. To follow it up, the full papers will be next submitted to the journal targets depending on the topic. The journal targets are including 3 Scopus-indexed journals: Indonesian Biomedical Journal, Indonesian Journal of Pharmacy, Indonesian Journal of Biotechnology; and 1 DOAJ-indexed journals: Indonesian Journal of Cancer Chemoprevention.
The committee has also received 50 abstracts for the undergraduate student poster competition from more than 10 universities in Indonesia, and also from Malaysia. The poster will be then judged by three reviewers and the winners will be announced at the Closing Ceremony. Additionally, the poster will be displayed in ISCC's social media platform as well.
We are very grateful for the contribution of our 21 invited speakers that come across the globe from the U.S., Japan, Iran, Taiwan, Singapore, Malaysia, and Indonesia. Through the lecture series covering the topics within our Conference, we strongly believe that the invited speakers will enrich the Conference by showing emerging trends not only in the basic research of cancer chemoprevention but also its transformation for a comprehensive cancer treatment. We hope that the lecture series will be both informative and encouraging the advancement of cancer chemoprevention research and technology.

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Equally important, we are indebted for the commitment of our 6 speakers for the 4 workshops. Molecular docking and bioinformatic workshops aim to open the possibility in using the online resources for cancer chemoprevention researches, despite the limited facility access in this current pandemic situation. Moreover, 2 scientific writing workshops with speakers from Indonesian and NAIST, Japan will encourage and improve writing productivity and quality, respectively.

Organizing a conference is indeed a team effort, so does the ISCC Conference and Congress 2020. I want to thank all the organizing committee members for the hard work. I also wish to acknowledge the members of the scientific committee including the reviewers, who had the tremendous task of reviewing the submissions we received. The Committee also thanks to Stem Cell and Cancer Research (SCCR) Sultan Agung Islamic University Semarang, PT. Neura Integrasi Solusi (Neurabot), PT. Biogen Scientific, and PT. Kairos Jaya Sejahtera for their sponsorship.

We confident all the participants will be advantaged from these two-weeks of intellectual discussions and, more essentially, networking among our peers.

Yogyakarta - Indonesia, November 2020
Chairman of the Organizing Committee,
Dr. apt. Muthi Ikawati, M.Sc.

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FOREWORD BY THE CHAIRPERSON OF INDONESIAN SOCIETY FOR CANCER CHEMOPREVENTION

Assalamu'alaikum wr. wb.

Dear colleagues,
First of all, on behalf of the chairman of Indonesian Society for Cancer Chemoprevention (ISCC), it is my pleasure to welcome all the participants to The 11th Annual ISCC Conference and Congress. This year, the event occurred through hybrid meeting due to COVID-19 pandemic, however the online implementation does not diminish the value and quality of all research related to cancer chemoprevention. This is our concern commitment to develop together effectively the newest science and technology to combat cancer under chemoprevention paradigm.
This year, our annual conference is held in collaboration with the Asian Pacific Organization for Cancer Prevention (APOCP) and West Asia Organization for Cancer Prevention (WAOCP) with the theme of "Accelerating the Cutting-Edge Transformative Research in Cancer Chemoprevention for Comprehensive Outcomes". This topic is become the hot issues in cancer treatment in the world. Fortunately, the invited speakers, covering this topic and the related fields already prepared the updated recent information to be shared in this agenda through 21 lecture series and 4 workshops. We hope that all of the newest knowledge presented in this conference would be useful for our comprehensive understanding to improve our profession, academic and research activities. Moreover, we hope this conference can provide the latest information and encourage the advancement of research and technology for scientists, academicians, and professionals related to cancer treatment around the world.
We would like to thank the Ministry of Research and Technology, the President of APOCP, the Dean of the Faculty of Pharmacy UGM, the speakers, the committee, the sponsors and all of the participants.
Thank you very much for your kind attention, I hope you can expand your knowledge and networking through our conference.
Wassalaamu'alaikum wr wb.

President
Indonesian Society for Cancer Chemoprevention
Prof. Dr. apt. Edy Meiyanto, M.Si.

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Class I: Pharmacology, Toxicology, and Microbiology Pharmacognosy and Ethnobotany

Topic	Code
New animal model for chronic pain behaviour study assessment in pharmacology: zebrafish for developing chronic pain drugs	42-A-P
Antibacterial activity of ethanolic extract of bitter herbs (*Andrographis paniculata*) and peppermint leaves (mentha piperitae l.) against *Klebsiella pneumoniae* and *Staphylococcus epidermidis*	54-A-P
The effect of volume of *Curcuma longa* juice on characteristics and antibacterial activities of nanosilver biosythesis	55-A-P
Revealing *Alpinia galangal* L. potency as an antigenotoxic agent	70-A-P
Cinnamon as a potential tissue-protective supplement to chemotherapy–a review	92-A-P
A review of awar-awar's leave (*Ficus septica Burm* F.): prospect as an antigenotoxic agent	107-A-P
Effects of *Zingiber officinale* Rosc. extract and DFA III in the bone density and blood lipid profiles of ovariectomized rats	137-A-P
Antimalaria activity of flavonoid-rich fraction of ethanolic extract of kembang bulan leaves (*Tithonia diversifolia*) *in vivo*	50-A-P
A Review: revealing the potency of banana peels (*Musa acuminata* Cavendish Subgroup) as a phytoestrogen-rich nutraceutical	111-A-P
Bioactivity, chemical composition, and toxicity of *Myristica fragrans* Houtt. essential oil	143-A-P

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Class II: Pharmaceutics and Applied Materials for Drug Delivery Pharmacy Practices and Clinical Pharmacy

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Class III: Cancer Chemoprevention and Immunomodulation

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Class IV: Bioinformatic and Computer Aided-Drug Design Cancer Chemoprevention and Immunomodulation

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The potency from vitiver (*Vetiveria zizanoides*) as co-chemotheraphy and immunomodulator in cancer patients.	149-A-P

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Class V: Cancer Biomarker and Diagnostic Medicinal and Pharmaceutical Chemistry

Topic	Code
In silico and *in vitro* studies of kaempferol againts DENV-2	33-A-P
Purified ethanolic extract of *Arcangelisia flava* leaf cytotoxicity and selectivity assay on several cancer cell lines	35-A-P
Combination of extract *Curcuma xanthorrhiza*, *Curcuma longa* L. and *zingiber officinale* var. rubrum suppressed the expression of cyclooxygenase-2 on lipopolysaccharide-induced RAW 264,7 cells	36-A-P
The mechanism of alpha mangostin compounds to inhibit the MCF7 growth by inhibit the over expression receptor estrogen and Akt: western blot assay and molecular dynamic simulation	49-A-P
Molecular docking and molecular dynamic simulations of alpha mangostin as an inhibitor for GSK3-Beta in triple negative breast cancer	99-A-P
Curcumin-like structure (CCA-1.1) induces senescence through mitotic arrest against 4T1 cells	139-A-P
Recent advances in amelioration of doxorubicin toxicity and enhancement of its antitumour activity	146-A-P
Natural bioactive cyclopeptides from microbes as promising anticancer drug leads: a mini-review	148-A-P
Conditioned medium of Wharton's jelly mesenchymal stem cells (WJMSCs) as a potential therapy for COVID-19	154-A-P
The prospect of citrus product for complementary colon cancer therapy	147-A-P
Structural characterisation and non-specific immunomodulatory in vitro activity of bioactive compounds from red betel (*Piper crocatum*, Ruiz. & Pav.) leaves	151-A-P
Chemical composition and cytotoxic activity of oily fractions of hexan extract of *Micromelum minutum*	153-A-P

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LECTURE SERIES

Oral Presenations

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LECTURE SERIES

Poster Presenations

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Code: A-O-1

PD-1: Its Discovery, Involvement in Cancer Immunotherapy, and Beyond

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Abstract

In the early 1990s, a novel gene was discovered in Kyoto University, Japan, in search for the molecular mechanisms involved in self-nonself discrimination by the immune system. In 1989, a UK team showed that self-reactive (potentially harmful) immature T lymphocytes (T cells) in the thymus undergo programmed cell death (apoptosis). This observation led the Kyoto University researches to assume that, if they are able to discover the genes strongly associated with the deaths of immature T cells, some of them would become good candidates for the key molecules playing pivotal roles in self-nonself discrimination. Only one gene was discovered at that time in a challenging screening experiment in molecular biology, and the gene (or its product) was named programmed death-1 (PD-1), with a hope that it would be somehow involved in the apoptosis-inducing processes of self- reactive immature T cells. However, it turned out, several years later, that the novel molecule had nothing to do with the induction of programmed cell death/apoptosis. Very interestingly, the wonderful developments in cancer immunotherapy in the recent years strongly suggest that, while PD-1, induced to be expressed on the surface of activated T cells, forces T cells to ignore cancer cells as one of the authentic 'self' components (i.e., prevents T cells from attacking cancer cells), the antibody-mediated blockade of PD-1's function makes activated T cells aware of the 'nonself' nature of cancer cells and unleashes their cytotoxicity.
Therefore, although PD-1 was not directly involved in the cell death-inducing processes (despite its ominous name), it could still be playing crucial roles in self- nonself discrimination, as initially expected in the early 1990s.

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Code: A-O-2

Natural Products in Cancer Chemotherapy and Prevention

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Abstract

Natural products continue to play an important role in drug discovery. About two-thirds of recently approved pharmaceuticals are natural products, natural product-derived- or nature-inspired chemical entities. Plants, marine animals, algae, and microorganisms are prolific sources of bioactive natural products. Some of these natural products have been used to treat cancers, whereas others have great potential to be developed as new cancer chemotherapeutic or preventive agents. Despite their enormous potential, the number of new natural products identified in recent years has significantly declined. Traditional approaches to natural products discovery are no longer sufficient to provide new bioactive compounds. Many of the compounds isolated have been identified previously. This high frequency of re-discovery of natural products has led to the process perceived to be less efficient, labor intensive, time consuming, and expensive. The trend has called for new ways of drug discovery and development, e.g., the application of contemporary approaches such as molecular genetics, chemoenzymology, genome mining, and synthetic biology. These approaches have changed the way drugs are discovered or developed. Using these methodologies, we have identified or produced numerous novel analogs of natural products. Some of them have excellent pharmacological profiles against cancer cells while others have good chemopreventive activity

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Code: A-O-3

Medicinal Chemistry for Cancer Chemoprevention

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Abstract

Cancer is the second leading cause of mortality in the world. While great strides have been made in treating and controlling cancer progression, there are still gaps and room for significant improvement. Sometimes several unwanted side effects occur during chemotherapy. Chemoprevention is the use of any compound, natural or synthetic, that eliminates carcinogenicity or tumor progression through various mechanisms. Conventional mechanisms include activating free radical scavenging enzymes, controlling chronic inflammation, and lowering specific signaling pathways. In recent times, epigenetics has provided a better understanding of the chemical protection potential of many factors. Natural treatments, such as using herbal products to treat cancer, can reduce harmful side effects. Several herbal products are currently used to treat cancer. However, some herbal products have shown promising anticancer properties in the laboratory but have not been evaluated in humans. More research is needed to determine how effective these herbal products are in treating cancer in humans. Phytochemicals have shown promising results in recent years as anticancer agents with their potential mechanisms of action, and it is a great challenge, especially for medicinal chemists, to design and synthesize ideal chemical protective agents.

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Code: A-O-4

Drug Development Targeted on Cancer Metabolism

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Abstract

Cancer cells arise from normal counterparts by a series of oncogenic mutations, which confer various tumor-specific features, including unregulated cell proliferation, impaired cell differentiation, resistance to cell death and senescence, reduced genomic stability, and cancer-specific metabolism. A number of molecularly targeted drugs against these oncoproteins have been developed and dramatically improved 5 years' survival of cancer patients. However, these drugs turned out not to be an ultimate cure, and more novel drugs need to be searched for. Novel molecular targets include enzymes that confer cancer-specific metabolism (e.g. Warburg effect).

It is well known that the relatively high levels of reactive oxygen species (ROS), which were produced during the metabolic process within cells, contribute to tumor-specific properties such as accelerated proliferation and a high rate of mutation. But extremely high levels of ROS provoke oxygen stress-mediated cell death and senescence, and, therefore, tumor cells have their own mechanism to control intracellular levels of ROS (ROS-metabolic enzymes).

We previously showed that curcumin, a phytopolyphenol mainly found in turmeric (Curcuma longa), targeted multiple ROS-metabolic enzymes that were overexpressed in leukemia cells. Curcumin increased intracellular ROS levels, irreversibly arrested cell cycle, induced cellular senescence and cell death in various human tumor cells, and, furthermore, effectively suppressed tumor formation in a xenograft mouse model. Currently, we developed and analyzed curcumin derivatives with improved characteristics. Because the control of intracellular ROS levels is currently one of the most promising tactics for tumor suppression, we believe that novel curcumin derivatives will be a good source for developing a novel type of anti-cancer drugs.

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Code: A-O-5

Reprogramming Cancer Stem Cells: A New Approach in Anti-Cancer Technology

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Abstract

Cancer stem cells have been demonstrated as small subpopulation of cells inside cancers those can self-renew and also differentiate to produce all the other cells of a cancer. According to the cancer stem cell hypothesis, cancer-causing mutations likely occur in normal adult stem cells. While another hypothesis, differentiated cell may acquire mutations and give rise to a new line of cancer cells. This process can repeat ad infinitum, and some mutations may confer new traits such as dedifferentiation or self-renewal ability.

In breast cancer stem cell model, cluster of differentiation (CD)44^+ normal mammary stem or progenitor cells might acquire cancer-causing mutations, resulting $CD44^+$ cancer cells that can self-renew and differentiate into all tumor cell types, including $CD24^+$ cancer cells. Additional mutations may occur in any of these cells, leading to differentiation, dedifferentiation, or the acquisition of new characteristics. Despite CD44, there are lots of biomarkers expressed by breast cancer stem cell, including ATP-binding cassette (ABC)G2, CD10, epithelial cellular adhesion molecule (EpCAM), CD29, CD133, aldehyde dehydrogenase (ALDH)1, C-X-C chemokine receptor type 4 (CXCR4), Notch4, wingless-related integration site (Wnt), hedgehog and many others. These biomarkers have been suggested to be reprogrammed , so that the genetic mutations and deviations could be corrected. Some of potential targets for reprogramming breast cancer stem cell have been suggested including CD44, EpCAM, CD29, CD133, CD 24, stem cell antigen (Sca) and CXCR4.

Plasticity of Cancer stem cell could be regulated by several factors including mutations, tumor microenvironment, epithelial-mesenchymal transition (EMT), and epigenetic modulation. The mutations could be resulted in oncogenes, tumor suppressor genes and transcription factors. There are several factors playing important roles in tumor microenvironment, such as growth factors, interleukins, and matrix metalloproteinase (MMP)s. While due to epigenetic modulation, there are DNA methylation, histone modification, and chromatin remodeling.

Therefore, to reprogram cancer stem cell, there are several possible approaches. Some reports suggested classic transcription factors for the induced pluripotent stem cell (iPSC), other suggested microRNAs and small molecules. Also, secretome and exosome were suggested to modify cancer microenvironment. The new microenvironment could change the cancer stem cell, some reports have shown the changes of cell metabolism including mitochondria; membrane potential. Finally, by reprogramming, the cancer stem cells were expected to be "tamed" and modified as new lines of normal stem cells. Nevertheless, the complexity of realizing this therapy approach needs further research.

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Code: A-O-6

Cancer Bioinformatics

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Abstract

Of 71 anti-cancer drugs for solid tumors approved by the FDA between 2002 and 2014, the median gains in progression-free and overall survival are ~2 months. A review of 277 randomized controlled trials for systemic therapies for solid cancers published 2011-2015 show that only one third of these trials with statistically significant meet the meaningful overall survival benefit. These observations suggest two potential unmet clinical needs: (1) the existence of drug resistance (either intrinsic or acquired), and (2) the importance of patient stratification. In other words, it is imperative to implement a companion diagnostic biomarker along with drug discovery pipeline. To address these two questions, we have accessed several big data to identify compounds (old drugs) for anti-cancer drug discovery. Firstly, resistance to chemotherapy or targeted therapy, such as EGFR inhibitor, is a major problem for systemic lung cancer treatment. Such resistance may be explained by cancer stem-like cell (CSC) theory. By using the Connectivity Map dataset, we have identified phenothiazine-like antipsychotic drugs which may reverse the CSC-associated gene expression. Further, the in vitro and in vivo experiments have validated its anti-CSC effects. This study demonstrated a novel platform for screening potential anti-CSC drugs, which may overcome the drug resistance. Secondly, synthetic lethality (SL) has emerged as a novel anti-cancer strategy. SL is an interaction between two genes such that simultaneous perturbations of the two genes result in cell death or a dramatic decrease of cell viability, whereas a perturbation of either gene alone is not lethal. The successful application of SL concept in the drug development is the approval of olaparib (a PARP inhibitor) by FDA in 2014 for the treatment of advanced ovarian cancer with *BRCA1/2* mutations. We have first built a big data approach to simulate this clinical trial results. Then, we evaluated several old drugs, which have been used in oncology, and mapped their corresponding SL pairs. Finally, we have analyzed several big data to reveal potential drugs for colon cancer treatments. Examples will be illustrated. In conclusion, this systematic analysis strategy could rapidly place old drugs with biomarkers for clinical study.

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Code: A-O-7

Cancer Burden in Asia

Alireza Mosavi Jarrahi

Editor-in-Chief, Asian pacific Journal of cancer Prevention.
President Asian Pacific Journal of Cancer Prevention.
Medical School, Shahid Beheshti University of Medical sciences.

Abstract

Asia accounts for 60% of the world population and half the global burden of cancer. Large segments of Asian population are being in a state of epidemiologic transition toward chronic and degenerative diseases. The aim of this study is to utilize the new findings on cancer epidemiology and present the burden of cancer in Asia. Data on incidence and mortality were retrieved for different sources for different region of Asia. Information on risk factors and their attribute on cancer burden is estimated. The age adjusted incidence and mortality for different cancer site and their economic burden was estimated and mapped to different population of Asia. It is estimated that close to 9000,000 cases of cancer occur in Asia in year 2019, this figure corresponds to an average age standard rate of 165 per 100000 populations. Breast cancer remains the leading cause of mortality and morbidity among the female and lung cancer among men. Sedentary lifestyle contributes to a large portion of cancer in western part of Asia while viruses specially HPV contribute to cancer burden in eastern part of Asia. The Different risk factors and their attributable risk are documented and indicating large diversity in different population of Asia. Cancer burden is very divers in Asian population and factors contributing to this diversity implicate specific prevention and control measures across different population of Asia.

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Code: A-O-8

Development of Boron Agents for BNCT

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Abstract

Boron neutron capture therapy (BNCT) has been attracting growing interest as one of the minimally invasive cancer therapies. BNCT uses the nuclear reaction between low-energy thermal neutron (0.025 eV) and boron-10 (^{10}B), and the generated α-particle and lithium nuclei are high linear energy transfer (LET) particles (2.4 MeV) that are sufficiently powerful to kill cells. Therefore, selective delivery of ^{10}B atoms to tumor is essential for effective BNCT. Mercaptoundecahydrododecaborate ($Na_2[B_{12}H_{11}SH]$) and L-p-boronophenylalanine (L-BPA) have been used in BNCT for many years. L-BPA, in particular, has been widely used for the treatment of not only melanoma but also brain tumor and head and neck cancer because it can be taken up selectively by tumor cells through an amino acid transporter (LAT-1). BNCT has long been limited to use in the treatment of patients due to the thermal neutron sources available only from reactors. In 2009, however, the world's first accelerator for BNCT was developed in Japan, and since then it has become possible to perform BNCT in hospitals. In fact, the phase I/II clinical studies of accelerator-based BNCT for brain tumor and head and neck cancer patients were initiated since 2013. Finally, in March 2020, accelerator-based BNCT system as a new medical device combined with L-BPA-based boron delivery agent (Boropharan [^{10}B]) were approved by the Ministry of Health, Labour and Welfare of Japan for the treatment of locally unresectable recurrent or unresectable advanced head and neck cancer. However, the development of new boron carriers is still an urgent requirement for patients who are not able to be treated with L-BPA. Boron drugs used in BNCT must minimize their effect on normal tissues and maintain the ^{10}B-boron concentration in tumor tissues at which an antitumor effect can be anticipated during neutron irradiation. We developed maleimide-functionalized *closo*-dodecaborate (MID). MID was readily conjugated with the serum albumin (BSA) and this MID-BSA accumulated into tumor selectively due to enhanced permeability and retention (EPR) effect. Further, the conjugation of cyclic RGD peptide, a ligand of integrins which are overexpressed on many cancer cells, resulted in longer accumulation in tumor compared to MID-BSA. Significant tumor growth inhibition was observed in U87MG human glioblastoma xenograft model mice subjected to thermal neutron irradiation.

Keywords : boron neutron capture therapy, accelerator, L-BPA, maleimide-functionalized *closo*-dodecaborate, cyclic RGD peptide.

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Optimization System Beam Shaping Assembly of Cyclotron 30 MeV for Boron Neutron Capture Therapy

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Abstract

Cancer is a global disease that must be considered for treatment. Boron Neutron Capture Therapy is one of the applications of nuclear technology using the principle of nuclear radiation interaction. By optimizing the neutron output needed in cancer therapy, it is also necessary to optimize the design of the BNCT system using Beams Shaping Assembly (BSA). The objectives of this study is knowing the parameter values of the BSA design used with a target of 7Li. This research is based on simulation using the PHITS program by modeling the geometry and BSA components that function as collimators from the 30 MeV neutron accelerator generator with a current of 2 mA. The independent variable of this research is the material of BSA components used in the system. The results of this study indicate a BSA design with 37 cm MgO2 as a reflector, 20 cm MgF2 as a moderator, Bismuth as a neutron thermal filter, and Li-polyethylene as a gamma filter. So that in this design the IAEA parameters are appropriate for the Boron Neutron Capture Therapy system.

Keywords: BNCT, BSA, Neutron Flux, Lithium Targe

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Exploration of Targets and Molecular Mechanisms of Citrus Flavonoids against Breast Cancer Chemoresistance using Integrative Bioinformatics Analysis

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Abstract

Chemoresistance is still a major hurdle of successful chemotherapy for breast cancer. Cancer stem cells, the side population of the breast tumors, are considered to be responsible for chemoresistance, leading to relapse and metastasis. Citrus flavonoids have been studied as co-chemotherapeutic agents against breast cancer, including hesperidin, hesperetin, and nobiletin. Our research group was developed citrus flavonoids as co-chemotherapeutic agents against breast cancer, including hesperidin, hesperetin, and nobiletin. We explored the targets and molecular mechanisms using a bioinformatics approach. Target mining was conducted with COMPARE and STITCH, while chemoresistance and breast cancer stem cells regulatory genes were collected from PubMed. Protein-protein interaction networks and hub gene selection were conducted with STRING and Cytoscape. Gene Ontology and KEGG pathway enrichment analysis were conducted with DAVID. Physiological assays were carried out to validate hesperetin targets, including cytotoxicity, mammosphere- and colony-forming assays, cell cycle, apoptosis, and gene expression analysis. The results of our study contributed to speeding up the finding of targets for the further development of citrus flavonoids against chemoresistance of breast cancer.

Keywords: bioinformatics, breast cancer, chemoresistance, citrus flavonoids, target identification.

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Code: A-O-11

The utilization of 3D model of breast cancer cells for drug screening

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Abstract

Developing resistant of breast cancer (BC) cells against chemotherapeutic agents elicit to discovering novel anti-cancer drugs. Therefore, a reliable cancer drug screening is required. The 3-dimensional (3D) cell culture is the best method for this purpose. The 3D spheroid and organoid in a scaffold are interestingly to be developed. There are various methods available. This 3D cell culture method has many advantages compared to conventional 2D cell culture methods, because it has characteristics resemble tumor cell microenvironment *in vivo*. However, generating BC multicellular spheroid (MCS) is challenging. Hence, agarose coated 96-well plate is a low cost and reproducible techniques for auto-generating MCS in HCC-1954 and BT 474 breast cancer cells. Moreover, the 3D cell culture has higher cell viability and lower cell death. 3D cell culture also has higher resistance to doxorubicin, whereas 2D cell culture is more sensitive to apoptosis as seen by the expression of PARP-1 cleavage in 2D cell culture upon doxorubicin treatment. Furthermore, organoid breast cancer cells can be developed in an apple scaffold. This is an important alternative method for evaluating a radio-contrast agent when an *in vivo* model is unavailable. In conclusion, both 3D spheroid and organoid models are important tools for drug screening.

Keywords: drug resistant; organoid; spheroid

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Mesenchymal Stem Cell-Secretome as a New Therapeutic Paradigm: Opportunities and Challenges in Cell-Free Therapy

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Abstract

Mesenchymal Stem Cells (MSCs) have been shown to offer a new therapeutic approach for the treatment of several diseases. Their therapeutic effects are primarily mediated by paracrine factors mechanism through a release of tons of anti-inflammatory cytokines and large-scale growth factors, known as MSC-secretome. Regarding exert therapeutic effects, the MSCs-secretome could also modulate the target cell functions by delivering this secretome as the cargos containing molecules medicinal product. Structurally, the MSC-secretome consist of the soluble molecules such as cytokines and growth factors, and the exosomes that are the nanometer-sized membrane-bound microvesicles containing mRNA, miRNA, lipid signalling. Here, we discuss recent findings related to the role of MSC-secretome to improve several diseases in pre-clinical models and clinical conditions. We also explore the characteristics of MSC secretome, the biologically active substances contained in those secretome and their fate in controlling the excessive inflammatory milieu as well as in regenerating the damaged tissue. We summarize in particularly, the recent clinical trials performed to evaluate the safety and efficacy of the MSC secretome. Overall, this paper provides a general overview of MSC-secretome as a novel cell-free therapeutic paradigm with no risk of tumour formation and lower immunogenicity compared with the parent MSCs.

Keywords: MSCs-secretome, soluble molecules, exosome, anti-inflammatory cytokines, growth factor

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Novel Epigenetic Roles of Tumor Suppressor p53 in Maintaining Homeostasis and Quality of Embryonic Stem Cells

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Abstract

Embryonic stem cells (ESCs) can generate any type of cells and are thus of substantial interest in regenerative medicine. ESCs must have strict mechanisms to maintain pluripotency and genomic stability. However, these mechanisms are poorly understood. The tumor suppressor p53 appears to contribute to the differentiation of ESCs and inhibits induced reprogramming of somatic cells, consistent with its pro-differentiation role in ESCs. On the other hand, loss of p53 causes aneuploidy and genetic instability in ESCs, and p53 also supports pluripotency depending on the context, suggesting that p53 is important not only for preventing cancer but also for ESC homeostasis and quality. These data suggest that p53 activity must be tightly controlled in ESCs to maintain the undifferentiated state while enforcing genomic stability. It is unclear how p53 is regulated to achieve these different functions. Recently, we reveal the strategy of p53 in ESCs to regulate its target gene expression, depending on the needs in ESCs. We showed that a subset of p53 target genes, including p21 which are associated with differentiation, are epigenetically silenced by H3K27 trimethylation (H3K27me3) in ESCs, despite p53 binding to them. Histone modifications together with p53 binding poise these genes for future expression, thereby enabling the maintenance of an undifferentiated state and a robust response to differentiation signals. On the other hand, another set of p53 target genes that do not have H3K27me3 marks undergo p53-mediated transcription in ESCs, which potentially contributes to the genomic stability and maintenance of ESCs. Our study showed that p53 is active in ESCs and revealed a unique epigenetic strategy in ESCs for p53's target gene choice to keep the quality of ESCs while poising other p53 target genes for preparing future differentiation signals.

Keywords: p53, epigenetics, tumor suppressor, ESC, differentiation.

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Challenges of Natural Product Formulation for Cancer Prevention and Therapy

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Abstract

The developing and application of nanoformulation based-natural product has emerged for the variety human diseases treatment, especially for the cancer therapy. This approach may improving conventional cancer therapeutic methods, which are including surgery, chemotherapy, immunotherapy, and radiotherapy. A large number of these treatments are associated with the inhibition growth or proliferating to death of the healthy cell or tissues, structural deformities, systemic toxicity, long-term side effects, tumor cell's drug resistance to the psychological problems. The recent use of natural nano-medicine in cancer treatment is progressed and transformed rapidly. The nanotherapeutics have promisingly overcome the limitations of the original drug delivery system, i.e., low solubility and bioavailability, multidrug resistance, and so on. Particularly, these innovative techniques are being intentionally studied in different model systems, which will reduce the side effects and improve the proximity to the therapy purposes. The propose method can specifically targeted to the tumor cells, enhancing the precisely, tolerability and efficacy of cancer therapeutic modalities which in turn improves patient response and survival. Ultimately, the integration of phytotherapy and nanotechnology in the clinical setting may improve the pharmacological response and clinical outcome to the patients.

Keywords: natural product nanoformulation, anticancer

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Biotechnological Approaches to Utilize Natural Resources as a Potential for Cancer Prevention

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Abstract

Indonesian has a long experience in using many medicinal plants for health purposes so called *Jamu*. This has been developed from household production into modern industrial prospective. The biological activities for traditional use of medicinal plants have been continuously proven by scientific researches. This include the use of medicinal plants for cancer prevention and treatment. In addition, the secondary metabolites from many groups of compounds which are responsible for biological activities have been also reported. However, the level of active compounds from medicinal plants are usually low. This become one of bottlenecks for development of medicinal plants. The biotechnological approaches have been applied to solve this problem. In our laboratory, some compounds which is a potential to be used for cancer prevention and treatment have been investigated and enhanced using this approach. The wide range of techniques from classical one such as plant cell culture with several modification to genetic engineering techniques were applied. Some of results are presented here. Suspension cultures of *Phyllanthus niruri* produced cubebin dimethyl ether and urinatetralin, which are potential for anticancer. Feeding 0.5 mM ferulic acid or 0.5 mM caffeic acid, being early precursors of lignan biosynthesis, resulted in an increase up to 0.7 mg g-1 DW of cubebin dimethyl ether (control value 0.1 mg g-1 DW) and up to 0.3 mg g-1 DW of urinatetralin (control value 0.2 mg g-1 DW) Another cytotoxic lignan, justicidin B was produced by transgenic hairy root culture of *Linum leonii* up to 5-fold compared to callus cultures. The transgenic roots was stimulated by the gene from *Agrobacterium rhizogenes* which was transformed into the plants. The treatment of cell suspension cultures of Linum flavum L. with Na_2EDTA enhanced the production of anticancer agent 6-methoxypohophyllotoxin (6-MPT) production a concentration dependent way, in a range of 0.1-5 mM. This effect is due to the inhibition of coniferyl alcohol glucosyltransferase (CAGT). The CAGT gene was also successfully cloned and determined its sequence. Recently, we have produced several bioflavonoids which are very potential for cancer prevention due to their strong antioxidant activities. Rutin, nicotiflorin, quercetin, quercetrin, hesperidin and kaempferol among others as dominant among others from cassava (*Manihot utilissima*), *Kelor* (*Moringa oleifera*) which contains rutin, nicotiflorin,; *Euphorbia hirta* which quercitrin; and orange peel (*Citrus sinensis*). We have established the approaches for enrichment of flavonoid glycosides from these plants. Further development of prospective methodologies for the production of bioflavonoid such as using combinatorial biosynthesis including the engineering of flavonoid biosynthetic pathway will be also discussed.

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Natural Product for Cancer Prevention and Therapy

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Abstract

Research on natural materials for cancer is still in great demand by researchers, especially on the properties and mechanisms of action from these natural substances. The terms chemopreventive and chemotherapy from natural material for cancer have been used by researchers to determine their effects both for prevention and treatment. The physiological characteristics of cancer include uncontrolled growth, immortal, new cancer formation, and create new blood veins, so the development targets of anticancer are proliferation inhibition, apoptosis inducement, and angiogenesis inhibition. Chemopreventive agents are compounds that can prevent and inhibit the growth of cancer cells. Chemopreventive research using medicinal plants has recently grown. Several plants that have been studied as anti-cancer agents as both induce apoptosis and proliferation inhibition to include *Nerium indicum* Mill., *Tithonia diversifolia* (Hemsley) A Gray, and *Phaleria macrocarpa* (Scheff.) Boerl, which will be discussed in this session. This paper will discuss the herbal medicine development stage, the development target of anticancer drugs, and examples of herbal research for cancer.

Keywords: Natural resources, cancer, proliferatif, chemoprevention, therapy

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Structural Modification of Natural Product for Cancer Drug Development

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Abstract

The Indonesia archipelago is rich natural resources and is number two after Brazil as mega diversity in the word, but until now almost raw material medicine (drugs) still import. There are 8000 species that have been as herbal medicine (jamu) but the product of herbal medicine standardized (OHT, 64) and fitopharmaca (26). Drug discovery mainly from natural product resources as like medicinal plants, marine resources, animals and microbes. The challenge for discovery takes time, high cost and technology also need multidiscipline. The problem also many drugs is all still import, and some drugs already resistant, and any side effect. Based on this situation, they still need to find and develop new drugs, from various sources. Some drugs as artemisinin, quinine, campotechine, and taxol produced from plants, lovastatin from Aspergillus terreus. Indonesia has many natural sources as medicinal plants and as raw materials for produce lead compounds. We need to choose plants that have major compounds (active), easy to isolate also can use commercial drug to develop to get more active compounds for some diseases target. One of the main fail discovery drugs is ADME and effectivity problem. For this solution, we need to structure modification, optimization to increase activity and make some analogs base on Lipinski Rule, to control lipophilicity (Log P) and energy interaction between ligand and receptor. Some major compounds as like quinine, cinnamic acid, and citronella oil, UK3A and others can use to make some derivatives or analogs to increase activities as candidate drugs. For synthesis derivatives, we use with simple reaction and with 1-3 steps. Sone derivatives and analogs gave potential lead compounds as anticancer to develop as candidate drugs

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Ethics and Law in Biomedical Research

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Abstract

Ethical and legal aspects in biomedical research still focus on the protection of research subjects based on the protocol of the Declaration of Helsinki. Apart from the translational research aspect “from bench to bedside”, bioethically and in the current pandemic context there is a balance between the consideration of ethical, legal and social implications, including the issue of dual use research concern with the “incentive policy" of emergency use authorization universally. Moreover, in relation to the field of cancer diseases which can be a comorbid, routine treatment must be carried out which requires a telemedicine breakthrough by health service facilities in the new normal era or a combination of therapy with adjuvant immunomodulators in Covid-19 patients. In Indonesia, a legal certainty foundation is needed for the national solidarity trial to protect all parties involved, including cancer research. Besides, it is necessary to distinguish ethical and legal norms for researchers and research institutions.

Keywords: ethics, legal, ethicolegal, biomedical research, dual use, Covid-19

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Mitochondrial Protecting and Targeting Agents; Prospect for Chemoprevention

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Abstract

The mitochondria have emerged as a novel target for anticancer chemotherapy. This tenet is based on the observations that several conventional and experimental chemotherapeutic agents promote the permeabilization of mitochondrial membranes in cancerous cells to initiate the release of apoptogenic mitochondrial proteins. Interestingly, several putative cancer chemopreventive agents also possess the ability to trigger apoptosis in transformed, premalignant, or malignant cells in vitro via mitochondrial targeting. In addition, Genomic, functional and structural mitochondrial alterations have been associated with cancer. Some of those alterations may provide a selective advantage to cells, allowing them to survive and grow under stresses created by oncogenesis. Due to the specific alterations that occur in cancer cell mitochondria, these organelles may provide promising targets for cancer therapy. The development of drugs that specifically target metabolic and mitochondrial alterations in tumor cells has become a matter of interest in recent years, with several molecules undergoing clinical trials. This review focuses on the most relevant mitochondrial alterations found in tumor cells, their contribution to cancer progression and survival, and potential usefulness for stratification and therapy.

Keywords: Mitochondria, apoptosis; cancer, chemoprevention, Metabolic remodeling, Oxidative stress

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Phytochemicals for the Management and Prevention of Oral Squamous Cell Carcinoma: Current progress and challenges

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Abstract

Cancer is a multifactorial disease characterized by uncontrolled growth and spreads of cells to the distant sites in any part of the body. Oral squamous cell carcinoma (OSCC) is the most frequently occurring oral cancer which can results in major mortality and morbidity due to its poor prognosis. Indeed, the incidence of oral cancer has increased worldwide counting Asia countries including South East Asia. OSCC is usually treated with either radiotherapy or surgery, and often combined with adjuvant chemotherapy. A number of chemically synthesized agents such as cisplatin, 5-FU, and hydroxyurea have been conventionally used as the drugs of choice for treatment of OSCC either as single agent or in combination chemotherapy regimens. These anti-neoplastic agents are effective at killing cancer cells by disturbing the cell-cycle progression of cancer cells. However they are also generally toxic to normal cells as well. Moreover, the use of chemically synthesized drugs has not significantly improved the overall survival rate over the past few decades due to development of drug resistance by the cancer cells. In light of this, there is a need to pursue more selective active agents that have fewer side effects, are cost-effective, and have a minimum level of disease resistance. Naturally occurring compounds from medicinal plants serve as vital resources for novel anti-cancer drugs. The merit of phytocompounds with chemotherapeutic and chemopreventive potential have been comprehensively investigated due to their minimal adverse effects and are relatively non-toxic. Increasing knowledge of the molecular mechanisms underlying cancer progression has led to the development of a vast number of chemotherapeutic drugs, including those of phytochemicals. However, these advances have so far not improved the phytocompound-based drug development for OSCC treatment. To date only few phytochemicals have been tested in clinical phase trials to determine feasibility and toxicity against OSCC. Other anticancer drug candidates are still in preclinical trial stages. This review aims to briefly discuss the current state and challenges in drug development using phytochemical for OSCC chemotherapy and chemoprevention. Pharmacologic action and molecular or specific targets of anticancer phytochemicals which are evaluated at preclinical and clinical level are also highlighted.

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Abstract
Pharmaceutics and Applied Materials for Drug Delivery

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Antimicrobial activity test of nanosilver biosynthesis using turmeric juice (*Curcuma longa* L.) and that effect on physicochemistry properties of gel

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Abstract

Silver is one of the antibacterial agent, that have no reports of any bacterial resistance. The antibacterial ability of silver can be developed in the form of nanosilver. Turmeric can be used as a bioreduction in nanosilver synthesis. The development of nanosilver in the topical can be used as an active ingredient in gel preparations. The purpose of this study is to determine the antimicrobial activity of nanosilver biosynthesis against gram-positive and gram-negative bacteria and determine the effect of nanosilver biosynthesis concentration on the physical and chemical properties of gel. Nanosilver biosynthesis of turmeric rhizome juice was characterized using spektrophotometry UV-VIS, Transmittan Electrone Microschope, and antimicrobial activity against *S.aureus* and *P.aeroginosa*. Nanosilver dispersed into hydrogel using polymer of carbopol 940. Gels are made in five formulas with concentration variations of nanosilver biosynthetic solutions of 5, 10, 15, 20, and 25 g. The gel was evaluated for physical and chemical properties including organoleptic, pH, viscosity, spreadability during storage for 12 days at room temperature. The characterization results show turmeric rhizome juice was capable of producing nanosilver with a maximum absorption characteristic at 407-428 nm, spherical shape with an average particle size of 16.71 nm. The results showed nanosilver biosynthesis has wide spectrum antibacterial activity. Based on research results, variations concentration of nanosilver affected the physicochemistry properties of gel, where the greater the active substance can decrease pH, viscosity, and spreadability. The five formulas fullfill the pyhysicochemistry properties by do not change significantly during 12 days of storage at room temperature. Further research need tobe done the antibacterial activity of gel.

Keywords: nanosilver, bioreduction, turmeric, antibacterial, gel.

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Code: 19-A-P

Black pepper: a comprehensive review on its potency as an anti-aging and chemopreventive agent

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Abstract

Black pepper (*Piper nigrum* L.), frequently used as a functional spice, has been expanded as a potential for medicinal purposes. Despite innumerable studies about its beneficial biological effects, the potency as an anti-aging and chemo-preventive agent would be a challenge. Several example of black pepper constituents that show pharmacological properties are piperine, chavicine, β-caryophyllene, and sabinene. This current article provides a review of its major constituents, the anti-aging and chemoprevention potency of black pepper. We screened the relevant studies from scientific journals via electronic research using Google scholar, PubMed, and Medline. All collected information were summarized into tables and graphs to support the narrative explanation. Comprehensively, black pepper and its constituents exhibit the anti-aging through various mechanisms: anti-senescence, anti-oxidant, ROS level modulation, and suppression of aging-related enzymes. Moreover, some mechanisms involved in cancer prevention activities are through cell cycle regulation, antiangiogenic and anti-metastasis effect, apoptosis induction, and suppression of carcinogenesis. While in combination with doxorubicin, it was proven to be synergist on several cancer cells. Besides, the immunomodulation effects of piperine have been investigated in enhancing and supressing certain cytokines on splenocyte cells. These studies prove that black pepper could be considered for developing pharmaceutical, nutraceutical, and cosmeceutical products.

Keywords: Black pepper, piperine, cancer, anti-aging, chemoprevention.

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Evaluation of Radical Scavenging Properties of *Holothuria scabra* Extract using DPPH Assay

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Abstract

Oxidative stress is a mechanism contributing to the initiation and progression of carcinogenesis. As a consequence of the increasing necessity for more effective and less toxic therapeutic in cancer, natural marine products have become attractive as a source material for drugs development. Several previous studies have shown that sea cucumber extract has activity as an antioxidant. Therefore, we evaluated the antioxidant activity of sea cucumber, *i.e. Holothuria scabra* extract from Indonesian marine. Measurement of the antioxidant activity of sea cucumber H. scabra methanol extract was carried out using the 2,2–diphenyl–1–picrylhydrazyl (DPPH) inhibition assay technique. The result showed that the higher of the extract concentration, the higher the inhibition percentage of DPPH. Analysis using statistics showed that the antioxidant activity of the extract was increased in a dose-dependent manner; IC_{50} 7448 + 132 (ppm) with R2 0.99. The study indicates that *H. scraba* extract has antioxidant activity, even though less potent compared to herbal medicine in general. Further research to elucidate the active compound is warranted to evaluate the extract of natural antioxidant sources.

Keywords: anticancer, antioxidant, carcinogenesis, DPPH, *Holothuria scabra.*

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Nutraceutical and Cosmetics Opportunities of *Citrus* Pectin for Tissue Protective and Immunomodulator: A Review

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Abstract

A natural polysaccharide, pectin, is the main water-soluble component of Citrus's peel. Pectin exhibits biomedical activities, including anticancer, antioxidant, immunomodulator, and anti-aging. This review discusses the opportunities and characteristics of citrus pectin to be developed as nutraceuticals and cosmetics. Relevant evidence from scientific journals was retrieved from Google Scholar, Medline, and PubMed. Several information was grouped into categories covering common natural ingredients of nutraceuticals and cosmetics, pectin extraction and preparation, antioxidant of pectin, pectin formulation, and pharmacological and immunomodulatory properties of pectin. Pectin from citrus peel can be prepared using various extraction systems, including water, organic solvents, and hydrodynamic-cavitation. The isolation of pectin from crude citrus-peel extract involves a degradation, hydrolysis, and separation process using an organic solvent. Pectin exhibits antioxidant and anti-inflammatory activities, which may also have a vital role in reducing free radical formation. Citrus-pectin showed aging-suppressive effect in animal models. Pectin also performs immunomodulatory and ROS scavenging properties which are potential to protect tissue damage. Overall, pectin has a worthy quality to be developed as a biomaterial for nutraceuticals or cosmetics products combined with other antioxidant and immunomodulator agents for tissue protective purposes.

Keywords: Citrus Pectin, immunomodulator, tissue protective, nutraceutical, cosmetics.

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Code: 37-A-P

Improvement of Cytotoxic Activity of Cantigi Extract on T47D Breast Cancer Cells Using Gelatin Nanoparticles

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Abstract

Biological activity improvement of extracts can be carried out by various methods. A previous report showed that a plant extract with an antibacterial activity loaded into gelatin nanoparticles (GNPs) provided activity improvement. This study aimed to evaluate whether Cantigi (*Vaccinium varingiaefolium* Blume Miq.) leaves extracts loaded into GNPs were able to provide cytotoxic activity (CA) improvement on T47D cells compared to the crude extracts. The leaf powder was successively extracted using hexane, ethyl acetate, and ethanol 95%. The CA of the extracts was then examined on T47D cells by MTT method. The most active extract was loaded into GNPs, characterized, and examined on T47D cells. The GNPs were manufactured by varying temperature and mixing speed. The ethyl acetate extract was the most active (IC_{50} of 75.15±3.72 μg/mL), however this result was less active than the ethyl acetate extract-loaded GNPs (IC_{50} of 18.77±0.68 μg/mL). Increase in temperatures (40 to 60^{o}C) caused increase in particle size (PS), entrapment efficiency (EE), and CA of the GNPs. Meanwhile increase in mixing speeds (500 to 1000 rpm) caused decrease in PS, EE, and CA of the GNPs. The ethyl acetate extract-loaded GNPs provided better CA than the crude extract.

Keywords: Cantigi (*Vaccinium varingiaefolium* Blume Miq.), crude extract, cytotoxic activity, ethyl acetate extract loaded GNPs, T47D cells.

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Code: 41-A-P

Hyptolide inhibits cell growth and promotes apoptosis on highly metastatic breast cancer cells

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Abstract

Hyptis pectinata is a herb popularly used in Indonesia for the treatment of inflammations, pain, bacterial infections and cancer. In the present study, hyptolide a major compound isolated from Hyptis pectinata extract was assayed against highly metastatic breast cancer MDA-MB-231 cells. The cytotoxic activity of hyptolide was carried out using MTT assay. Cell cycle and apoptosis assay was done using flow cytometry with PI and Annexin-V PI staining, respectively. The results demonstrated that exposured of hyptolide performed cytotoxic effect in a dose-dependent manner on MDA-MB-231 breast cancer cells with IC_{50} value of 58 µg/mL. The cytotoxic effect in the treatment hyptolide was through Sub G0 phase cell cycle arrest and apoptosis induction. Hyptolide possesses cytotoxic effect by induced cell cycle arrest and apoptosis in highly mestatic breast cancer cells. These results indicate that hyptolide has cytotoxic activities and maybe the potential to be used in drug design in an attempt to develop new compounds for chemotherapeutic agent with fewer side effects.

Keywords: cytotoxic, cell cycle, apoptosis, hyptolide, MDA-MB-231.

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Code: 47-A-P

The Effect of Polymers on Physicochemical Properties and Drug Release from Ibuprofen Solid Dispersion Transdermal Patch

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Abstract

Ibuprofen is a drug that has effectiveness as an analgesic, anti-inflammatory, and antipyretic drug. Ibuprofen showed common side effects such as gastrointestinal disorder when used orally. The transdermal patch formulation of Ibuprofen has been known to prevent these side effects. In this study, We used various types of polymers for transdermal patch formulations. This study aims to determine the effect of various types of polymer on transdermal patch Physicochemical properties (pH, moisture content, etc) and the release flux value of ibuprofen. Transdermal patches were prepared in six formulas using a combination of HPMC: S-CMC and PVP K-30 polymers: Carbopol 940 with a ratio of 1: 0; 0.5: 0.5; and 0: 1, respectively. The ibuprofen patch is prepared by the fusion method. Physicochemical characterization of transdermal patch formulas was organoleptic, weight uniformity, thickness, folding endurance, patch surface pH, and %moisture content. The results of the PH data analysis showed that all formulas met the requirements of PH. The largest PH was F1. The results showed that all transdermal patch formula met the physicochemical characteristics requirement of transdermal patch preparations. Ibuprofen transdermal patch in-vitro release rate (flux) of F1 and F5 shows the highest flux release and F2 has the lowest flux release.

Keywords: transdermal patch, ibuprofen, physicochemical properties, drug release.

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Code: 52-A-P

In vitro releasing modelling of meloxicam with *DDSolver*

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Abstract

Dissolution is a process of releasing drug compounds from dissolved subtance in solvents which is closely related to absorption and bioavailability, therefore the kinetics and mechanism of drug release need to be evaluated. Meloxicam who will be tested for release kinetics is pure meloxicam and modified meloxicam in the form of SNEDDS (*Self Nanoemulsifying Drug Delivery System*). The purpose of modification of meloxicam drugs in the form of SNEDDS to increase the solubility of meloxicam which is very low in water that is 4,4 µg/mL. In the SNEDDS meloxicam formulation, *Sunflower seed oil* was used as an oil, Cremophor RH 40 as a surfactant, and PEG 400 as a co-surfactant. From this formula, percent transmittance test, emulsification time, thermodynamic stability, and robustness to dilution were characterized, and the best formula was obtained to be used for the in vitro dissolution test with *DDSolver*. The result showed that the best formula for SNEDDS meloxicam contained *Sunflower seed oil*, Cremophor RH 40, and PEG 400 with a ratio of 1:7:2 which the results of the characterization of the percent transmittance of 99.71%±0.06; emulsification time of 30.00%±7.00 seconds. The thermodynamic stability test showed that preparation didn't experience precipitation, phase separation, cracking, creaming, or coalescence. Meanwhile, the robustness to dilution test using *One-way* ANOVA give significant result (p>0.05) with a normal and homogeneous distribution marked with p>0.05. Evaluation of drug release model with DDSolver showed that the release of pure meloxicam (β=0.99) and SNEDDS meloxicam (β= 1.00) followed Weibull equation. The dissolution curve is exponential and the release mechanism of both pure and SNEDDS modification occurs by diffusion mechanism.

Keywords: Meloxicam, SNEDDS, *DDsolver*, modelling of drug release.

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Code: 67-A-P

The Potency of Chitosan-Based Nanoencapsulation in Anti-Tuberculosis Agents for Reducing the Resistance Rate of Mycobacterium Tuberculosis

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Abstract

Tuberculosis (TB) is the deadliest infectious disease that remains a world health problem. The situation exacerbated by the presence of Mycobacterium tuberculosis (MTB) resistant strains that are resistant to certain drugs from the therapy regimen. It is necessary to develop more new effective drug to overcome resistance problems. Unfortunately, the development of new drugs needs a lot of time and money. Chitosan is a non-toxic biodegradable material that has been widely applied as carrier in drug delivery systems (DDS). DDS modification is one of the strategies to increase drug efficacy through increased bioavailability, targeted drug delivery also controlled drug release. This narrative review discusses the application of chitosan-based nanoencapsulation on anti-tuberculosis agents that have potential to reduce MTB resistance rate through literature study. The decrease in resistance rate can occur through several mechanisms, namely disrupting the permeability of MTB cell walls, inhibiting efflux pump action, overcoming overexpressing drug targets and penetrating through biofilm barriers. Apart from decreasing the rate of cellular resistance mechanism, DDS modification may also improve patient adherence by reducing the frequency of drug administration and possible side effects. These will manifest in a more controlled th-erapy thus the possibility of developing resistance towards MTB may be suppressed.

Keywords: chitosan, nanoencapsulation, mycobacterium tuberculosis, resistance.

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The Potency of Gallic Acid from *Jatropha Curcas* L as an Anti-Aging Agents: A Review

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Abstract

Reactive oxygen species (ROS) might be produced by some exogenous factors and endogenous metabolic processes in the human body. The excessive generation of ROS leads to pathophysiological processes and premature aging (senescence). This review aims to reveal the potency of *Jatropha curcas* L., locally known in Indonesia as "jarak", as an anti-aging and increase its value through formulation in a sheet mask that can be used as a daily skincare routine**.** Numerous literature from journals published from 2005 to 2020 were retrieved from Google Scholar, PubMed, Scopus, and other databases. Based on literature studies, jarak contains gallic acid, which acted as an antioxidant by reducing the level of ROS as well as anti-melanogenic by inhibiting the tyrosinase enzyme. Furthermore, jarak can prevent premature aging through various pathways such as lowers the oxidative stress markers like lipid peroxidation, DPPH radical, and protein carbonyls, reduces nitric oxide levels and mitochondrial permeability transition pore (MPTP) formation. In addition, gallic acid acts as a specific inhibitor of MPTP opening by blocking cyclophilin D interaction with adenine nucleotide translocator on the mitochondrial membrane. All of the evidence demonstrated that jarak potentially could be developed as an anti-aging agent.

Keywords: Reactive Oxygen Species (ROS), senescence, *Jatropha curcas* L., gallic acid, anti-aging.

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The Effects of Binahong (*Anredera cordifilia* (Ten.) Steenis) Leaves on the Proliferation and Migration of Human Dermal Fibroblasts in High Glucose Conditions

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Abstract

Diabetes mellitus causes several complications including diabetic wounds. Binahong (*Anredera cordifolia* (Ten.) Steenis) contains a chemical content that functions as an antibacterial, anti-obesity, antiviral, anti-inflammatory, anti-ulcer, and antidiabetic. This research aims to study the effect of ethanolic extract of binahong leaves on the proliferation and migration of human dermal fibroblast (HDF) in high glucose conditions. HDF cells were cultured on a 96-well plate with a density of 10,000 cells/well in triplicate groups. Several concentration variations of binahong extract were used as follows: 0.5%, 1%, 2%, and 4%. HDF was cultured in the standard Dulbeco Minimal Essential Medium (DMEM) as the negative control and in the high glucose DMEM as the positive control. After 24 hours of treatment, the cell proliferation was then measured with CCK-8 assay the to obtain the optical density (OD). The migration assay was conducted by scratch assays**.** The binahong leaf extract could affect cell's proliferation ability in the high glucose DMEM similar to the proliferation ability in the standard DMEM. The highest effects of proliferation ability and migration were found at the 4% concentration group; while the proliferation ability was decreased in the above concentration group. It can be concluded that binahong leaf extract can increase the proliferation and migration of HDF in high glucose conditions.

Keywords: proliferation, migration, human dermal fibroblast (HDF), diabetic, binahong (*Anredera cordifolia* (Ten.) Steenis).

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Abstract
Pharmacology, Toxicology and Microbiology

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In silico and *in vitro* studies of kaempferol againts DENV-2

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Abstract

Nowdays, there is a lack of specific antiviral therapy against dengue virus (DENV) in current use. Dengue is one of the most prevalent diseases in Indonesia that lead to a spectrum of disease, ranging from a mild into severe spectrum of disease. Therefore, research regarding the development of anti-viral to DENV is essential. Flavonoids are natural biomolecules that are known to be effective antivirals. Kampferol is a natural flavonol, a class of flavonoid. The aim of this study was to evaluate the activity of kaempferol, against DENV-2 *in vitro*. Various concentration of Kaempferol was added to DENV-2 strain New Guinea C (NGC) and infected to Vero cell line to calculate the inhibitory concentration (IC_{50}). Also determined the toxicity of Kaempferol that correspond with cytotoxic concentration (CC_{50}) value was determined by MTT assay. Selectivity index (SI) value was defined as the ratio of CC_{50} to IC_{50}. Kaempferol showed no cytotoxic effects against vero cells with CC_{50} values of 68.28 µg/mL and exhibited strong antiviral activity with IC_{50} of 22,24 µg/mL, hence a significant SI value of 3.01. Kaempferol exerts in silico potent antiviral activity against non structural NS3, NS5 and envelope E with free energy value – 9.11; -6.29; -6.76 kkal/ mol. Further studies need to be conducted in order to evaluate the inhibitory activity of kaempferol against DENV by *in vivo* studies.

Keywords: kaempferol, dengue virus, *in vitro*, *in silico.*

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Code: 42-A-P

New Animal Model for Chronic Pain Behaviour Study Assessment in Pharmacology: Zebrafish for Developing Chronic Pain Drugs

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Abstract

Rodents, such as mice and rats, were commonly used as a model in the majority of pharmacology studies. In many cases, used rodents as models showed unsatisfied results such as in the behavioural experiment. Higher individual variation caused behavioural studies neeeded more number of subject to produce validity of data. It makes a big issue in pain research, especially chronic pain. Research zebrafish as a model for the assessment of chronic pain behavior in pharmacology. The information was searched from the various database such as google scholar, Science Direct, and PubMed. All of the sources were extracted from 2010 until 2020. Many kinds of research in pain had been evaluated using zebrafish as a model. Even through chronic pain models using zebrafish are not clear yet, some studies revealed that it was possible to do a chronic pain experiment using zebrafish. The chronic pain model in zebraish is not entirely different compared to rodents. Chronic pain can be induced by chronic inflammation, neuropathy, drug use, or disease. For finding a new drug in chronic pain using zebrafish as a model, the researcher needs to estabilish the method and completes with another physiology or biochemistry to quantify the result and minimize the bias**.**

Keywords: chronic pain, pain behaviour, rodents, zebrafish, pain-killer.

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Code: 54-A-P

Antibacterial Activity of Ethanolic Extract of Sambiloto Herbs (*Andrographis Paniculata*) and Pepermint Leaves (*Mentha Piperitae* L.) Against *Klebsiella Pneumoniae* and S*taphylococcus Epidermidis*

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Abstract

The increasing number of resistant bacteria has prompted the exploration of new antibacterial agents. New exploratory efforts for antibacterial agents can be started by utilizing plants. Plants that can be used as antibacterial agents are sambiloto and peppermint. This study aimed to determine the antibacterial activity of sambiloto herbs (*Andrographis paniculata*) extract dan peppermint leaves (*Menthae piperita* L.) extract against *Klebsiella pneumoniae* and *Staphylococcus epidermidis.* Extraction was done by maceration method using 96% ethanol. Antibacterial activity was measured using the disk diffusion method with concentration of 25%, 12.5%, and 6.25 % w/v. Ethanol extract of sambiloto herbs with a concentration of 25% had a greater inhibition zone in *Klebsiella pneumoniae* of 11.83±0.41 mm (*p* value<0,05 in Kruskal Wallis test) than in *Staphylococcus epidermidis* ATCC 12228 of 11.33±1.69 mm. Ethanolic extract of peppermint leaves with a concentration of 25% showed a greater inhibition zone in *Klebsiella pneumoniae* of 13.11±1.83 mm, compared to *Staphylococcus epidermidis* ATCC 12228 at 9.83±1.42 mm. Both extracts possessed antibacterial activity against *Klebisella pneumoniae* and *Staphylococcus epidermidis* ATCC 12228. Ethanol extract of sambiloto herbs contained alkaloids, flavonoids, saponins, and terpenoids, while ethanol extracts of peppermint leaves content were steroids, phenols, and flavonoids. All of these properties are known to have antibacterial activity.

Keywords: antibacterial, *Klebsiella pneumoniae*, peppermint, *Staphylococcus epidermidis*, sambiloto.

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Code: 55-A-P

The Effect of Volume of *Curcuma Longa* Juice on Characteristics and Antibacterial Activities of Nanosilver Biosythesis

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Abstract

Nanosilver has potensially as antibacterial. Silver ion can be done as nanosilver by green synthesis method using plant extracts. In this study, turmeric juice was chosen as a substance that converts silver ion into a nanosilver. This research was conducted to determine the effect of volume variations of the mixture between turmeric juice and AgNO3 solution on characteristics of nanosilver and antibacterial activity. Nanosilver biosynthesis was prepared by mixing turmeric juice and 1.0 mM AgNO3 solution at a ratio of 1:42; 3:40; 5:38; 7:36; and 9:34 mL. The mixture stirred for 24 hours at room temperature, then analyzed using spectrophotometry UV-VIS and antibacterial activity against *Staphylococcus aureus* and *Staphylococcus epidermidis*. The best mixture formula of nanosilver biosynthesis was done by Transmission Electron Microscope, Fourier Transform-IR, Scanning Electron Microscope, and antibacterial activity against *Pseudomonas aeruginosa*. Biosynthesis nanosilver with ratio of tumeric juice-AgNo3 solutiom of 5:38 mL was the best formula that has yellow-brown colours, maximum wavelength peak at 407 nm. It was indicated formation of nanosilver, and an average inhibition diameter among the other formulas against *Staphylococcus aureus* bacteria was 14.86±0.39 mm and *Staphylococcus epidermidis* bacteria was 13.97±0.76 mm. The FTIR spectra of the 5:38 mL ratio formula show successfully biosynthesis nanosilver process in exist of –C–N–, –C–O–C–, or –C–O, and –OH groups with peaks at 816, 1030, 1237, 1323, 1383, and 3411 cm^{-1} which are compounds in turmeric rhizome juice and act as capping agent. TEM and SEM analysis showed that nanosilver biosynthesis has round shape with particle size of 17.98 nm. Inhibition zone against *P.aeruginosa* is 13.55±0.01 mm. There is a relationship between the volume ratio of turmeric rhizome juice and $AgNO_3$ solution to the antibacterial activity.

Keywords: indicate 5 keywords separated by commas, add a full stop at the end of keywords.

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Code: 70-A-P

Revealing *Alpinia Galanga* L. Potency as an Antigenotoxic Agent

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Abstract

Genotoxicity is the effect of a substance that causes genetic material damage. Galangal (*Alpinia galanga* L.), a spice plant used as a cooking spice, has the potential to counteract genotoxic effects, which has been revealed from several studies on its activity as an antioxidant, anti-inflammation, and anti-aging. Although there have been many studies about galangal pharmacological activity, its potential as an antigenotoxic agent has not been widely studied. This study aims to provide information about the potency of *Alpinia galanga* L. as an antigenotoxic agent. This study reviewed numerous research about the genotoxic mechanism from *Alpinia galanga* L., and its constituents' activity. The result then compiled into an overview of the antigenotoxic and chemoprevention potential of galangal and its chemical constituents, namely 1'-S-1'-acetoxychavicol acetate, 1'-S-1'-acetoxyeugenol acetate, β-farnesene, chavicol, galangin, and isocoronarin D. These constituents performed the activity as antigenotoxic mainly through antioxidants effect. There are many antioxidant mechanisms possessed by compounds in galangal, some of which are scavenging of free radicals, inhibition of radicals production, inhibition of enzymes that activate genotoxin, inhibition of transcription factor that activate carcinogen, and activating antioxidant response elements.. Comprehensively, galangal and its constituents exhibit activity leading to antigenotoxic effects through antioxidant activities.

Keywords: *Alpinia galanga* L., antigenotoxic, antioxidant, chemoprevention.

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Code: 107-A-P

A Review of Awar-awar's Leave (*Ficus septica* Burm F.): Prospect as an Antigenotoxic Agent

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Abstract

Ficus septica belongs to the Moraceae family and has been empirically used as a medicinal plant in Indonesia for its anti-inflammatory properties. With massive DNA damaging exposure in the environment, genotoxic or DNA damage can simply occur. Some constituents from *Ficus septica* were found to show activities as antigenotoxic. This review provides an overview of how *Ficus septica*'s constituents played a pivotal role as antigenotoxic agents. Related research articles were retrieved from Google Scholar, ScienceDirect, and PubMed. The information was divide into several points including chemical constituents of *Ficus septica*, *Ficus septica* utilization, anti-inflammatory and antioxidant activities related to antigenotoxic, and the prospect of *Ficus septica* for antigenotoxic purpose. *Ficus septica*'s leaves contain several chemical compounds namely antofine, thylophorine, ficuseptine-A, genistin, kaempferitin, and vanillic acid which showed antigenotoxic potency. Antofine, thylophorine, and ficuseptine-A suppress nitric oxide production, a pro-inflammatory marker that induces genotoxicity. Meanwhile, genistin, kaempferitin, and vanillic acid are antioxidants that act as ROS scavenger and protect DNA from damage. The finding of these studies comprehensively proves that *Ficus septica* has the potency to be developed as an antigenotoxic agent. However, further research related to its development is still needed.

Keywords: *Ficus septica*, antigenotoxic, DNA damage, nitric oxide, ROS.

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Code: 137-A-P

Effects of *Zingiber Officinale* Rosc. Extract and DFA III in the Bone Density and Blood Lipid Profiles of Ovariectomized Rats

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Abstract

Zingiber officinale Rosc. performs various biological activities, including estrogenic and anti-dyslipidemic, thus, can be developed as anti-osteoporosis caused by the deficiency of estrogen. DFA III, a functional oligosaccharide, also possess anti-osteporosis potencies. This study aimed to investigate the anti-osteoporosis activity and improvement of the blood lipid profile of ginger rhizome extract (GE) and DFA III in ovariectomized (OVX) rat models. This study was conducted using 30 young adult female rats (*Rattus Novergicus*). The rats were divided into six treatment groups (n = 5: sham-operated; OVX; OVX + estradiol; OVX + GE 750 mg/kg BW; OVX + DFA III; and OVX + GE + DFA III). Blood sampling was carried out at the beginning and at the end of the treatment to measure blood lipids (total cholesterol, triglycerides, and HDL). The mammary glands and bones were isolated after daily treatments for 14 days. Although in this study design GE did not increase the bone density and improve blood lipid profiles in ovariectomized mice, administration of GE and/or DFA III had a positive effect on the body weight in ovariectomy conditions. To investigate more clear effects, the treatment time may be extended.

Keywords: *Zingiber officinale* Rosc., DFA III, osteoporosis, ovariectomy, blood lipids

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Abstract
Pharmacy Practices and Clinical Pharmacy

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Survey of Knowledge, Attitude, and Practice of Antibiotic Use among Tertiary Students in Jember

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Abstract

At the individual level, knowledge and belief can influence health attitude and practice, including the use of medications such as antibiotics. The purpose of this study was to explore knowledge, attitude, and practice of antibiotics use among tertiary students in Jember, East Java, Indonesia. Data for this, cross-sectional study was collected from a conveniently selected sample presenting in the city square and three malls in Jember. A total of 320 students (females n=256, 80.0%) from seven universities agreed to participate by signing the informed consent form, with the majority of them were in the third semester (n=86, 26.8%). The results show that amoxicillin was the most frequently cited antibiotic (n=173, 54.1%). Statistically significant relationships were found between three domains (knowledge-attitude p=0.001, knowledge-practice p<0.001, and attitude-practice p<0.001). Across five socio-demographic variables examined, the type of study programs was found to have a statistically significant correlation with knowledge, attitude, or practice. Non-health science students tended to have a lower score for each domain. In conclusion, albeit the use of antibiotics was prevalent among tertiary students in Jember, irrespective of methods of acquisition, the non-health science students were prone to incorrect knowledge, attitude, and practice.

Keywords: antibiotics use, tertiary students, knowledge, attitude, practice.

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Abstract
Medicinal and Pharmaceutical Chemistry

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Code: 36-A-P

Combination of Extract *Curcuma Xanthorrhiza, Curcuma Longa* l and *Zingiber Officinale* var. *Rubrum* Suppressed the Expression of Cyclooxygenase-2 on Lipopolysaccharide-induced RAW 264,7 cells

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Abstract

The enzyme cyclooxygenase-2 (COX-2) has an important role in the inflammatory process. Ginger (*Curcuma xanthorrhiza*), turmeric (*Curcuma longa L*), and red ginger (*Zingiber officinale var. Rubrum*) are known as anti-inflammatory agents. This study aims to determine the anti-inflammatory effect of the combination of ginger, turmeric, and red ginger extracts on COX-2 expression in RAW 264.7 cells induced by lipopolysaccharide. This study was an experimental post-test only with a control group design. The RAW 264.7 cells were cultured into six groups; A (control group without LPS), B (control group with LPS), C (control group without primary antibody), D (125 μg/mL), E (250 μg/mL), and F (500 μg/mL). All the cells were fixed with ethanol and tested by immunocytochemistry. The data were analyzed by one-way ANOVA and Post Hoc test LSD. The expressions of COX-2 in A (29,00±2,42), B (71,81±2,01), C (12,81±1,37), D (46,16±2,30), E (45,07±3,53), and F (38,55±1,19). The most substantial differences shown by the mean of the treatment group F were 500 μg/mL (p=0.00). A combination of extracts of ginger, turmeric, and ginger red can reduce the effects of inflammation on RAW 264.7 cells induced by lipopolysaccharide at a concentration of 500 μg/mL.

Keywords: ginger, turmeric, red ginger, antiinflammatory, cox-2.

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Code: 49-A-P

The Mechanism of Alpha Mangostin Compounds to Inhibit the MCF7 Growth by Inhibit the Over Expression Receptor Estrogen and Akt: Western Blot Assay and Molecular Dynamic Simulation

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Abstract

α-mangostin is a yellow xanthone compound that isolated from Mangosteen pericarp (*Garcinia mangostana* L) which has been shown to have anti-inflammatory, antifungal, antimicrobial and anti-cancer activities. The purpose of this study was to determine the activity of α-mangostin compounds as anti-breast cancer against ERα, to know the cytotoxic activity of alpha mangostin, and to determine the mechanism of α-mangostin in inhibiting the growth of over-expression of ERα. The results of this study with molecular docking methods (molecular docking), showed that the free energy in α-mangostin against ERα was -8.55 kcal/mol while in tamoxifen -11.37 kcal/mol. Molecular dynamic results showed that DG of α-mangostin using MMGBSA was -42.704kcal/mol. The examination results of α-mangostin cytotoxic activity with resazurin method obtained IC50 values of 0.044 μg/mL, while the tamoxifen control 0.1 μg/mL. The test with western blot method, it was found that the Akt protein in the $2xIC_{50}$ band had decreased, whereas in ERα MCF7 breast cancer cells did not experience inhibition of proliferation. It can be concluded that α-mangostin could be a potential ERα inhibitor and breast anticancer based on molecular dynamics and cytotoxic testing. Based on western blot testing, α-mangostin can inhibit the proliferation of breast cancer from Akt but not to ERα.

Keywords: α-mangostin, breast cancer, receptor estrogen alpha, MCF7, molecular dynamic.

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Code: 99-A-P

Molecular Docking and Molecular Dynamic Simulations of Alpha Mangostin as an Inhibitor for Gsk3-Beta in Triple Negative Breast Cancer

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Abstract

Triple negative breast cancer (TNBC) is breast cancer subtype does not expression of estrogen receptor, progesterone or human epidermal growth factor receptor 2 (HER2), which has clinical features that include high invasiveness, high metastatic potential and poor prognosis. TNBC lacks receptors and hence cannot be treated using targeted therapies and needs to be adequately responded properly by exploring the potential of Indonesian herbal plant as anti triple negative breast cancer drug candidates. In this research, molecular docking and molecular dynamic simulations of alpha mangostin on Glycogen Synthase Kinase 3β target have been performed. Molecular docking and molecular dynamic simulations were employed to identify the molecular interactions of alpha mangostin against Glycogen Synthase Kinase 3β (GSK3β) (PDB ID: 4ACC). The results showed that alpha mangostin weaker binding affinity than native ligand (-8.22 kcal/mol), with native ligand has the strongest binding affinity of -8.92 kcal/mol. According to the binding site analysis, the hydrogen bounds of native ligand showed on Asp133 and Arg141, while alpha mangostin alpha mangostin only showed on Asp133. On the other hand, it mostly docked on the similar sites with native ligand Ile62, Phe67, Val70 and Thr138 concluded that native ligand and alpha mangostin suggest a similar mechanism. Molecular Dynamics simulation using Molecular Mechanics Poisson-Boltzmann and Surface Area (MM-PBSA) calculation method showed that alpha mangostin has a better affinity with a value of ΔGTotal -114.463 kcal/mol compared to native ligand was amounted to ΔGTotal -75.158 kcal/mol. Alpha mangostin showed a valuable potential as anti triple negative breast cancer agent through GSK3β inhibition.

Keywords: alpha mangostin, glycogen synthase kinase3β, molecular dynamic, triple negative breast cancer.

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Code: 139-A-P

Curcumin-Like Structure (CCA-1.1) Induces Senescence through Mitotic Arrest Against 4T1 Cells

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Abstract

Triple-negative breast cancer (TNBC) remains as the deadliest cancer type due to the lack of treatment options. Hence, several attempts have been made to develop new anticancer for TNBC therapy. This study intended to challenge curcumin analog (CCA)-1.1, which is derived from pentagamavunone-1 structure, against the 4T1 cell line. The cell viability, cell cycle profile, apoptosis induction, intracellular ROS level, and senescence induction were determined *in vitro* using trypan blue exclusion, propidium iodide (PI) staining, Annexin-PI staining, DCFDA diacetate staining, and SA-β-*gal* method. CCA-1.1 showed cytotoxic activity on 4T1 cells, giving IC_{50} value of 3 ⎡M, while less toxic on non-cancerous 3T3-L1 cells. CCA-1.1 induced rapid cell death and inhibited cell cycle progression at the mitotic phase. Instead, of causing apoptosis, CCA-1.1 induced mitotic catastrophe. Furthermore, CCA-1.1 itself increased the intracellular ROS level and induced senescence, possibly through catastrophic cell death. In summary, our preliminary study strengthens the potency of CCA-1.1 for its anticancer activities against TNBC cells and prospective to be pharmaceutically developed as a novel candidate for cancer therapy.

Keywords: curcumin analog (CCA-1.1), mitotic arrest, senescence, 4T1.

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Code: 146-A-P

Recent Advances in Amelioration of Doxorubicin Toxicity and Enhancement of its Antitumour Activity

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Abstract

Doxorubicin, a member of anthracycline antibiotics, is a widely used chemotherapeutic for treatment of various cancers. However, its clinical efficacy is hampered by serious adverse events, such as cardiotoxicity. Therefore, various strategies have been tested to ameliorate the adverse effects of doxorubicin. This mini review provides an overview of the recent advances that have been investigated to minimise the toxicity of doxorubicin, while also improving its antitumour activity. Review of the literature within the last five years revealed a variety of approaches that have been investigated, which include structural modifications to produce analogues with enhanced activity, utilisation of a drug delivery carrier, and combination therapy with other compounds. Structural modifications to doxorubicin enabled the characterisation of structure-activity relationship that can assist in developing more effective analogues. Employment of a delivery carrier, such as encapsulation in liposomes, was shown to improve the pharmacokinetics profile of doxorubicin. Similarly, combination therapy with other compounds, such as curcumin, demonstrated enhanced antitumour activity and lowered doxorubicin toxicity. The various strategies to minimise doxorubicin toxicity and enhance their antitumour potency have their own advantages and limitations, as well as different potential applications in the clinical setting.

Keywords: doxorubicin, antitumour, anticancer, antibiotic, drug delivery.

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Natural Bioactive Cyclopeptides from Microbes as Promising Anticancer Drug Leads: A Mini-Review

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Abstract

Natural products from microbes are a rich source of bioactive molecules to serve as drug leads, predominantly in the field of cancer therapy. Peptides are among the most important nature-derived biomolecules. Owing to their great diversity and favorable characteristics, cyclopeptides from natural sources become a promising candidate for the development of therapeutics including anticancer drugs. This mini-review aims to identify bioactive cyclopeptides from microbial natural products that have demonstrated considerable antitumor activities. Selected examples are given from the literature search for the potent anticancer cyclopeptides isolated recently from fungi and bacteria from both terrestrial and marine origin. Most of the important information from those literatures are extracted and discussed herein. This mini-review provides a look into the mode of action of the anticancer (cyclo)peptides. Naturally cyclic peptides with natural and unnatural amino acids isolated from fungi, actinomycetes, marine cyanobacteria, as well as from microbes associated with marine organisms are described. Cyclopeptides can potentially be used as anticancer drugs. In particular, marine microbial cyclopeptides have remarkable delivered chemical templates for pharmacologically or clinically potent anticancer lead compounds to the attention of the pharmaceutical industry.

Keywords: bioactive molecules, cyclopeptides, natural products, microbes, anticancer drugs.

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Code: 153-A-P

Chemical Composition and Cytotoxic Activity of Oily Fractions of Hexan Extract of *Micromelum Minutum*

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Abstract

Micromelum minutum (Rutaceae) has been extensively surveyed with the isolation of some bioactive compounds. Phytochemical investigation on the leaves of Indonesian *M. minutum* gave three coumarins and a flavonoid from ethyl acetate extract. In continuation of our study we investigated the chemical composition and cytotoxic activity of oily fractions of the hexan extract. The ground dried leaves of *M. minutum* were macerated with hexane to give viscous extract. Fractionation of the hexan extract using vacuum liquid chromatography gave 2 oily fractions, F2 and F3. The chemical constituent of F2 and F3 was analyzed using GCMS, while their cytotoxic activity was evaluated using MTT assay against MCF-7 and 4T1 cells. The GC-MS analysis showed that F2 contains terpenoids with β-element as the major component, while F3 contains terpenoids and fatty acids with longipinokarveol as the major component. F2 and F3 showed to have cytotoxic activity against MCF-7 with the IC_{50} of 34 and 84 µg/mL and against 4T1 with the IC_{50} of 61 and 111 µg/mL, respectively. The oily fractions of the hexan extract of the leaves of *M. Minutum* contain terpenoids and fatty acids and have cytotoxic activity against MCF-7 and 4T1 cell lines.

Keywords: *Micomelum minutum*, hexan extract, oily fraction, chemical constituent, cytotoxic activity.

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Conditioned Medium of Wharton's Jelly Mesenchymal Stem Cells (Wjmscs) as a Potential Therapy for COVID-19

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Abstract

COVID-19 presents a serious and urgent healthcare. Several studies showed that Conditioned Medium (CM) from human Wharton's Jelly Mesenchymal Stem Cells (hWJMSCs-CM) contains variety important proteins including cytokines, growth factors, angiogenic factors. MSCs have antimicrobial effects through direct and indirect mechanisms, the secretion of antimicrobial peptides and proteins (AMPs). This research was done to measure the level of indoleamine 2,3-dioxygenase (IDO), Fibroblast Growth Factor-7 (FGF-7), Antibacterial Protein LL-37 (LL-37), Interleukin 1 Receptor Antagonist (IL-1ra) in hWJMSCs-CM. hWJMSCs-CM were harvested from different condition namely various period of starving incubation and non-starving incubation. The level of IDO, FGF-7, LL-37, IL-1ra in hWJMSCs-CM were measured by ELISA method. hWJMSCs secreted IDO (5.86 – 13.12 ng/mL), FGF-7 (46.74 – 72.13 pg/mL), LL-37 (1.70 – 4.14 ng/mL), IL-1ra (1.35 – 8.32 pg/mL). Longer period and starving incubations significantly increased proteins secretion. hWJMSCs-CM secrete IDO, FGF-7, LL-37, IL-1ra potentially serve as an adjuvant therapy for COVID-19.

Keywords: COVID-19, Conditioned Medium Wharton's Jelly Mesenchymal Stem Cells, IDO, LL-37, IL-1ra.

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Abstract
Pharmacognosy & Ethnobotany

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Influence of Extraction Solvents on Efflux Pump Inhibitory Activity for Drug-Resistant of Curcuma (*Curcuma Longa* L.)

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Abstract

Traditional antibiotics are increasingly suffering from the emergence of multidrug resistance amongst pathogenic bacteria. This reason leading to a range of novel approaches to control microbial infections being investigated as potential alternative treatments. Multidrug efflux pumps play an important role in bacterial multidrug resistance by actively excreting antibiotics. To evaluate the influence of extraction solvents of the curcuma (*Curcuma longa* L.) on efflux pump inhibitory activity of *Salmonella enterica* serovar Typhimurium. The *S.* Typhimurium efflux pump resistance was detected by inhibitors of pumps efflux (EPIs). Antibacterial activities of ethyl acetate, acetone, and ethanol 96% extracts exhibited against *S. Typhimurium* with minimum inhibitory concentration values 0.1% combined with gold antibiotic standard. Only two extracts were found to increase the sensitivity of tested antibiotic. The ethanol 96% extract of *C. longa* increases sensitivity of ampicillin and tetracycline, while acetone extract and the drug chloramphenicol and ciprofloxacin showed synergistic effects. Our study highlights the potential of these extracts of the curcuma as drug EPIs.

Keyword: Bacteria, Efflux pumps inhibitors, Multi Drug Resistance.

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Code: 50-A-P

Antimalarial Activity of Flavonoid-Rich Fraction of Ethanolic Extract of Kembang Bulan Leaves (*Tithonia Diversifolia*) *In Vivo*

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Abstract

Malaria is a disease caused by *Plasmodium* sp which infects humans through the bites of Anopheles mosquitoes. The kembang bulan plant [*Tithonia diversifolia* (Hemsley) A. Gray] is one of the plants that had antimalarial activity. The active compounds in the leaves of the kembang bulan which are against malarial disease are flavonoids. This research was conducted to determine the activity of the flavonoid-rich fraction of the ethanol extract of the kembang bulan leaves as an antimalarial. The antimalarial activity test was carried out *in vivo* using Balb/C mice infected with *P. berghei*. The results showed that the flavonoid-rich fraction had antimalarial activity with an ED_{50} value of 0.538 mg/kg BW. The flavonoid-rich fraction of ethanolic extract of kembang bulan leaves had antimalarial activity.

Keywords: antimalarial, *Tithonia diversifolia*, flavonoids.

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Code: 92-A-P

Cinnamon as a Potential Tissue-Protective Supplement to Chemotherapy– A Review

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Abstract

Chemotherapy is a widely used chemical-based cancer treatment. The usage of these potent chemicals is commonly followed by undesired effects, one of which is cytotoxicity. Prolonged exposure to cytotoxic chemicals might contribute to tissue injury in cancer patients. Overcoming tissue injury induced by chemotherapy is a major concern in cancer treatments until right now. This review brings an insight into cinnamon's potency as a tissue-protective supplement to cancer treatments using chemotherapy. Original articles about cinnamon pharmacological activities from 2005 to 2020 were retrieved from PubMed, Scopus, and ScienceDirect databases. Cinnamon was reported to have tissues and cellular healing on injured renal, liver, lungs, reproductive organs, and blood damages of animal models caused by some reactive chemicals, carcinogens, or chemotherapeutic agents. Its antioxidant properties were predicted as the underlying cause of these noticeable effects as well as the modulation of intracellular signaling, including MAPK cascades and cytokines expression. Cinnamaldehyde, the primary compound, was one of which possesses these antioxidant properties. The tissue-protective abilities of cinnamon indicate that it is a promising agent to develop as a supplement to chemotherapy treatment.

Keywords: cinnamon, tissue-protective, chemotherapy, supplement, cinnamaldehyde.

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Code: 111-A-P

A Review: Revealing the Potency of Banana Peels (*Musa Acuminata Cavendish Subgroup*) as a Phytoestrogen-Rich Nutraceutical

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Abstract

Lack of estrogen can be treated by Hormone Replacement Therapy (HRT), but high cost and unwell-secured therapy. One alternative therapy is by utilizing natural ingredients containing phytoestrogens, for example, is banana. Cavendish is the most commercialized banana cultivar, which accounts for around 47 percent of global production. The consumption of this banana produces byproduct, banana peels, which has not been widely used. Banana peels extract (BPE) contains bioactive compounds that are useful for improving the quality of life. This review aims to reveal the prospect of banana peels as phytoestrogen-rich nutraceutical at an affordable price. This study was conducted by data from FAO and review literature collected through an international database such as journals from Pubmed, Science Direct, and Semantic Scholars with several keywords. Based on literature studies, BPE was reported to contain flavones, flavanone, flavanol, and polimethoxyflavone, potentially as a phytoestrogen. BPE also rich in carotenoid and phenolic compounds with anti-aging and antioxidant activity. Phytosterols in BPE is also known to reduce cholesterol serum levels, which can help prevent hyperlipidemia due to a lack of estrogen. The findings of these studies proved that banana peels have great potential to be developed as economical phytoestrogen and antioxidant-rich nutraceutical.

Keywords: *Musa acuminata Cavendish Subgroup*, banana peel extract (BPE), phytoestrogen, antioxidant, nutraceutical.

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Code: 143-A-P

Bioactivity, Chemical Composition, and Toxicity of *Myristica Fragrans* Houtt. Essential Oil

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Abstract

Myristica fragrans Houtt., known as nutmeg, is an indigenous plant of Indonesia. It is commonly used for its culinary and medicinal properties. Nutmeg oil has unique pungent fragrance and warm taste. It is widely used in Tibetan, Chinese, Ayurvedic and Indonesia traditional medicine due to its pharmacological activities. This review gives information about medicinal properties, chemical diversities and toxicity of nutmeg oil. The data was compiled from recent literature (2000–2020) on nutmeg oil biological activities, chemical composition, and toxicity. Several reports on GC/MS analysis of nutmeg oil showed that there were 27–37 components detected at various concentrations. The main compounds detected were sabinene, 4-terpineol, α-pinene, and myristicin. The reported pharmacological properties such as antiinflammation, antioxidant, anticonvulsant, fumigant, antiparasitic, anticancer, and antimicrobial agent. Intake of the essential oil in large amounts could result in toxic effects including tachycardia, nausea, vomiting, agitation, or hallucinations, which is attributed to myristicin, safrole, and elemincin Nutmeg oil had the potential to be developed into medicinal product with diverse pharmacological properties.

Keywords: *Myristica fragrans*, nutmeg oil, chemical composition, bioactivity, toxicity.

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Abstract
Cancer Chemoprevention and Immunomodulation

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Anti-Migratory Activity of a New Curcumin Analog, CCA-1.1, Towards T47D Breast Cancer Cells

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Abstract

Chemoprevention-curcumin analog 1.1 (CCA-1.1), a novel curcumin analog, has been proven to have antiproliferative effects against T47D cells covering the cytotoxic activity in correlation with cell cycle inhibition, apoptosis induction, ROS generation, and senescence induction. This study investigates the anti-migratory effect of CCA-1.1 on T47D breast cancer cells. Molecular docking analysis is used to assesses the binding activity of CCA-1.1 to MMP-2 and MMP-9. Then, cell migration and MMPs expression after CCA-1.1 treatment on T47D cells were measured using the scratch wound healing and gelatin zymography assay, respectively. We found that CCA-1.1 possessed a higher binding affinity than PGV-1 to MMP-2 and MMP-9 proteins. Furthermore, CCA-1.1 also inhibited the migration of T47D cells and suppressed these MMP-2 and MMP-9 expression induced by Dox. CCA-1.1 has potency as an anti-migratory agent and may anti-metastatic agent.

Keywords: New curcumin analog (CCA-1.1), T47D cells, breast cancer, MMPs, anti-migration

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Code: 17-A-P

Considering the Potential Application of Galangal as Co-Chemotherapy and Anti-Aging

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Abstract

Galangal (*Alpinia galanga* L.) is a medicinal plant belongs to the Zingiberaceae which exhibits numerous biological activities including anticancer. Galangal extracts as well as its active compounds such as Acetoxychavicol acetate, Galangin, 4'-hydroxycinnamaldehide, and Acetoxyeugenol acetate possess anticancer activities in melanoma 4A5 cells, myeloid leukemic cells, MCF-7 cells, and 4T1 cells. This review aims to reveal the reversal effect of galangal concerning its pro-oxidant and anti-oxidant properties. Relevant information was collected from scientific journals via electronic search using Medline, PubMed, and Google Scholar. Galangal indicates pro-oxidant properties by raising the amount of ROS that results in 4T1 cancer cell senescence. This property of Galangal works synergistically in combination with the well-known chemotherapeutic agent doxorubicin. Galangin, one of the Galangal components, on the other hand, exhibits anti-oxidant properties as a radical scavenger in reactive oxygen species (ROS), contributing to the elimination of free radicals and oxidative stress, as well as the prevention of genotoxic. Meanwhile, galangal did not interfere with the ROS level of doxorubicin-treated fibroblast cells. Galangal also reduces its senescence induction, leading to its potency as a co-chemotherapy and anti-aging agent in innovative products.

Keywords: Galangal, Galangin, Co-chemotheraphy, Anti-oxidant, Anti-aging

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Code: 18-A-P

Citrus Peel Extract as Tissue Protective and Immunomodulator: A Review

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Abstract

Citrus peel possesses a variety of biological activities such as anticancer, antiinflammation and antioxidant effects, but to promote health, there is a need to explore further in immunomodulatory effects. In this review, we provide the beneficial effects of citrus peel constituents on immune response covering the immunomodulatory effect and tissue-protective effect. Information on the expected effects obtained through PubMed, Google Scholar and Science Direct, to sustain the narrative explanation, all the data is then summarized into tables and graphics. Citrus peel products are rich in phenolic compounds and pectin, exhibit the immunomodulatory effects such as anti-inflammatory, antimicrobial and antiviral infection, and cancer immunotherapy. The tissue-protective effects including antioxidant, upregulating anti-aging genes, reducing the harmful effects of chemotherapy drugs and reducing stress as the neuroprotective effect. In this review, we summarized that citrus flavonoids and pectin had potential benefits as immunostimulant immunosuppressant for infectious diseases, cancer and protection against the cytotoxic agent. Citrus peel flavonoid can be developed as food products and nutraceutical products.

Keywords: Citrus peel extract, hesperidin-diosmin, immunomodulator, tissue-protective, antiviral.

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Code: 25-A-P

Cytoprotective Activity of Ethylacetate Fraction of *Zanthoxylum Acanthopodium* DC. Fruits

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Abstract

Free radicals produce from metabolism or enviromental which interact continously with biological system. *Zanthoxylum acanthopodium* DC. fruits have been used as traditional medicine for treat various diseases. The aim of this study was to evaluate antioxidant and cytoprotective activities of ethylacetate fraction (EAF) of *Zanthoxylum acanthopodium* DC. fruits. *Zanthoxylum acanthopodium* DC. fruits powder was macerated with n-hexane and continue with ethylacetate. Phytochemicals were analyzed using LC-MS/MS method. Antioxidant activity was determined with DPPH method. Total phenol and flavonoid were determined with colorimetric method. Cytoprotective activity were determined by MTT asay and flow cytometry assay on Vero cells which induced with H_2O_2 0.8 mM. Phytochemicals were found phenolics (tyrosol dan hymecromone), alkaloids (mexiletine, berberine, evodiamine, 2-(3,4-Dimethoxy-1-phenanthryl)-N,N-dimethylethanamine, sedamine), lignans (savinin) and flavonoids (quercetin, quercetin 3-*O*-α-L-arabinopyranoside, quercetin-3-glucoside and isoquercetin). Antioxidant activity from DPPH assay measured as IC_{50} was 156.48±0.04 µg/mL. EAF was found to contain high levels of phenolic (90.67±0.93 mg GAE/g), total flavonoid (77.56±0.02 mg QE/g). EAF at 100 µg/mL were showed highest viability (87.03±1.36%) and ROS expression (76.57%) on Vero cells.. EAF of *Zanthoxylum acanthopodium* DC. fruits has cytoprotective activity.

Keywords: cytoprotective, *Zanthoxylum acanthopodium* DC., fruits, ethylacetate.

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Code: 27-A-P

The Role of Polyketide Isolates of Soursop Leaves (*Annona Muricata* L.) on *Rb* Protein Expression in Hela Cells by Immunocytochemistry Staining

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Abstract

Cancer is characterized by the loss of control function in the cell cycle regulation, apoptosis, and cell homeostatic function. Cervical cancer occurs in the cervix caused by infection with the human papilloma virus. Retinoblastoma functions as suppress tumor growth. This study aims to determine the cytotoxicity effect of polyketide isolates of soursop leaves on HeLa cells and also to see Rb protein expression in HeLa cells with immunocytochemistry staining. The cytotoxic activity test of polyketide isolates of soursop leaves was carried out using the MTT method at several concentration series 5; 10; 20; 40; 80; 160; 320; 640 µg/mL to obtain an IC_{50} value. Subsequently, immunocytochemistry observations were carried out on HeLa cells to detect Rb protein expression.Polyketide isolates of soursop leaves had cytotoxic activity with IC_{50} values of 78 µg/mL. The treatment of of polyketide isolates of soursop leaves showed the existence of pRB indicated by brownish red color both in the nucleus and cytoplasm of HeLa cells. Polyketide isolates of soursop leaves has cytotoxic activity on Hela cell line. The polyketide isolates of soursop leaves was able to suppress the proteins that degrade the pRb protein, namely the E7 protein produced from the HPV virus.

Keywords: polyketide, soursop., HeLa cells, retinoblastoma.

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Code: 35-A-P

Purified Ethanolic Extract of *Arcangelisia flava* Leaf Cytotoxicity and Selectivity Assay on Several Cancer Cell Lines

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Abstract

Our previous studies showed that ethanolic extract of *Arcangelisia flava* leaf is cytotoxic and selective against breast and colon cancer cell lines. This research was conducted to determine the purified ethanolic extract of *A. flava*'s leaf (PEEAfL) cytotoxicity and selectivity on several cancer cell lines, such as HeLa, MCF-7, WiDr. Vero cells were used as normal cell to analyze the selectivity of PEEAfL as they are representing the normal cells. The cytototxicity assay was done using MTT method. The cytotoxic activity was analyzed using IC_{50}, while the selectivity assay was determined using selectivity index (SI), the ratio of the IC_{50} on normal cell line and that on cancer cell line. The IC_{50} value of PEEAfL on HeLa, MCF-7, WiDr, and Vero cells were 1,322±373; 2,080±417; 374±67; 2,010±110 μg/mL, respectively. The SI value of PEEAfL on WiDr was 5.37. The PEEAfL was considered to be cytotoxic and selective on WiDr only. Yet, the molecular mechanisms have not been determined.

Keywords: the purified ethanolic extract of *A. flava*'s leaf, cytotoxicity assay, selectivity assay.

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Code: 40-A-P

Hsp-70 Expression in Tumor-Associated Macrophages Induced by *Typhonium Flagelliforme* Tuber Extract

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Abstract

One of the apoptotic resistance mechanisms in breast cancer stem cells (bCSCs) is designed by the existence of tumor-associated macrophages (TAM), type-2 macrophages. TAM enhances the apoptotic resistance of CSCs by decreasing extremely the low levels of inducible nitric oxide (iNO) and a reactive oxygen intermediate (ROI). On the other hand, Hsp-70 expression may modulate TAM to upregulate those molecules. *Typhonium flagelliforme* tuber-extract (TFTe) have an apoptotic activity through increasing iNO and ROI levels of cancer cells, however, the role of TFTe to increase the Hsp-70 expression of TAM leading to apoptosis improvement remains unclear. TAM was produced by co-culturing the human breast cancer-derived peripheral blood mononuclear cells (PBMCs) with the bCSC. TAM was assigned into two treatment groups consisting of: one treatment group (treated by TFTe at 0.89μg/mL) and the control group (medium administration only). The expression of Hsp-70 was analyzed by the immunocytochemistry. This study showed a significant increase of Hsp-70 expression in TAM. TFTe may promote the increase of Hsp-70 expression in TAM.

Keywords: *Typhonium flagelliforme*, TAM, bCSC, Hsp-70, apoptosis.

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Code: 48-A-P

Chemopreventive Effects of Ethylacetate Extract of *Vernonia Amygdalina* Delile. Leaves on DMBA-Induced Female Rats

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Abstract

Vernonia amygdalina Delile. (Asteraceae) is used in traditional medicine to treat diabetes mellitus and some research provides its activity to treat breast cancer. This study was carried out to investigate the potency of ethylacetate extract (EAE) of *Vernonia amygdalina* Del. leaves to suppress DMBA-induced breast cancer development. *Vernonia amygdalina* Del. leaves in a powder form were extracted by maceration method with n-hexane and continued with ethylacetate solvent. EAE was administered in three doses, namely 50, 100, and 200 mg/kg BW. Body weight of rats were weighed every week. Tumor development was examined by palpation every week and terminated at week 16th after the end of DMBA induction. Tumor tissue were analyzed with Hematoxylin and Eosin staining. The results showed that EAE treatment at dose 50, 100, and 200 mg/kg BW reduced tumor incidence. The 200 mg/kg BW dose exhibited of tumor multiplicity. EAE performs chemopreventive effect to suppress breast cancer development at the dose 200 mg/kg BW.

Keywords: *Vernonia amygdalina* Del. leaves, ethylacetate, breast cancer.

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Code: 51-A-P

Arcangelisia Flava Leaf Ethanolic Extract Generates Synergistic Cytotoxic Activity with Doxorubicin against Cancer Cells

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Abstract

Yellow wood (*Arcangelisia flava*) is a native Indonesian plant. According on several studies, *A. flava* has a cytotoxicity effect and selectivity on several cancer cells. The aim of this study was to determine the cytotoxic activity of *A. flava* leaf ethanolic extract (AfLEE) and doxorubicin combination on several cancer cells. The cytotoxicity test was done using MTT assay on single and combination of AfLEE and doxorubicin on T47D breast cancer cells, HeLa cervical cancer cells, and WiDr colon cancer cells. The IC_{50} value of single cytotoxicity test was used as the basis for the combination test. Of the combinatory cytotoxicity test at the concentration under IC_{50}, CI was used as the parameter. The results showed AfLEE had cytotoxic effect on T47D, HeLa, and WiDr cells with IC_{50} values of 310±6; 442±66; and 449±18 µg/mL, respectively; while the IC_{50} value of doxorubicin were 0.175±0.011; 7.479±3.967, and 5.781±0.599 µg/mL, respectively. Of the viable cell that significantly different from the combinatory test showed that AfLEE and doxorubicin combination indicate synergistic activity. This study showed that AfLEE generates synergistic activity when used in combination with doxorubicin.

Keywords: *Arcangelisia flava* leaf ethanolic extract, combinatory cytotoxicity test, synergism, doxorubicin, cancer cells.

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Code: 61-A-P

A Review on Date's (*Phoenix Dactylifera*) Potency as Nutritional Adjuvant in Cancer Therapy

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Abstract

Administration of antineoplastic agents can generate various side effects to cancer patients ranging from mild to severe effects. In addition, both cancer and antineoplastic agents can also generate metabolic disorders. Therefore, application of nutritional adjuvant as complementary cancer therapy may improve the effectiveness of cancer treatment. With regard to this issue, date (*Phoenix dactylifera*) which has been known to contain nutrients and numerous bioactive compounds may play a role as a potential nutraceutical for cancer therapy. This review had been performed to analyze the potency of date as a nutritional adjuvant in cancer therapy. We performed the literature review by searching and collecting the important articles with the keywords related to the therapeutic effects of date products especially in metabolic disorder, chemoprevention, anti-inflammation as well as anti-oxidant. Date contains various nutritional components including carbohydrates, dietary fibers, vitamins, fatty acids and amino acids which will contribute to improve metabolic disorder. On the other hand, its bioactive compounds such as polyphenols, carotenoids, sterols and tannins play as anti-oxidant sources. In addition, the anti-inflammatory effect is attributed to the major flavonoids contents such as apigenin, quercetin and luteolin. Date also shows chemoprevention activities which mediated by its anti-oxidant, anti-inflammation and immunomodulatory effects. This review suggests that date possesses prospective application as nutritional adjuvant in cancer therapy either to improve metabolic disorders or to alleviate the side effects. However, combination effects of date with antineoplastic agents are crucial to be investigated to clarify its potency as nutritional cancer adjuvant.

Keywords: chemoprevention, date, metabolic disorder, nutritional adjuvant, *Phoenix dactylifera*.

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Code: 64-A-P

The Potency of Awar-Awar (*Ficus Septica* Burm. F.) Leaves as an Anti-Metastatic Co-Chemotherapy agent for Breast Cancer Patient: an Overview

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Abstract

Breast cancer contributes to woman deaths worldwide. Ninety percent of the death cases were occured due to cancer cell metastasis. Doxorubicin as a first-line chemotherapy agent for breast cancer also induces metastasis as one of the side effects. Awar-awar (*Ficus septica* Burm. F.) is a common plant that easily found in Indonesia and known for its various anti-cancer activities. This review focuses to discuss the potency of awar-awar as an anti-metastasis. Various literatures were searched by inputting relevant keywords within the topic through several databases then discussed in related categories. Awar-awar leaves contain phytochemical compounds including phenanthroindolizidine alkaloids. The leaf extracts and phenanthroindolizidine alkaloids exhibited cytotoxic activities on several breast cancer cells through apoptotic induction, cell cycle modulation, and inhibition of the expression of anti-apoptotic protein Bcl-2. When combined with doxorubicin, both the extract and the chemotherapeutic compound exhibited synergistic effects. Awar-awar leaves extracts and its phenanthroindolizidine alkaloid content also can inhibit metastasis in breast cancer cells by decreasing the expression of VEGF, an angiogenesis growth factor, MMP-9 and Rac-1 which are involved in cell metastasis. Hence, awar-awar leaves are potential to be developed as an anti-metastatic co-chemotherapy agent for breast cancer.

Keywords: breast cancer, awar-awar (*Ficus septica* Burm. F.), phenanthroindolizidine alkaloids, co-chemotherapy, metastasis.

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Knowledge, Awareness on Breast Cancer and Practice of Breast Self-Examination among Staff Nurses in Sultan Ahmad Shah Medical Centre (Sasmec@Iium), Kuantan, Pahang: Preliminary Findings

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Abstract

Knowledge insufficiency and late detection may contribute towards the growing number of incidence and mortality rate of breast cancer in Malaysia. The aim of this study was to identify the socio-demographic and level of knowledge, awareness and practice on breast cancer among staff nurses of SASMEC@IIUM, Kuantan, Pahang. A cross-sectional study was conducted using self-developed questionnaires with good validity (CVI=88.3%) and reliability (Cronbach Alpha=0.87) among 50 nurses conveniently to assess their level of knowledge, awareness, and practice on breast cancer. Data was analyzed descriptively using SPSS version 23.0. Among 50 nurses, 82% were female and Malays, 66% were married, while 16% had family history with breast cancer. Almost 56% had post-basic education and mean clinical experience of 6.6 (±6.28) years. The mean knowledge score on risk factors of breast cancer is 10.82 (±3.17), slightly lower than the 50th percentiles (11.00) and moderate knowledge score on sign and symptoms of breast cancer, [mean (SD)= 8.18 (±1.69)]. In terms of awareness and practice on breast self-examination, the score was moderate [mean (SD)= 74.04 (±25.07)] consequently [mean (SD)= 66.62 (±26.85)]. Overall, the knowledge of risk factors on breast cancer is still lower in comparison to knowledge of sign and symptoms. This consequently support the moderate score found on awareness and practice towards breast self-examination. Therefore, more awareness campaign and internal training should be conducted by the organization managerial to improve the healthcare professionals' knowledge, awareness and practice on breast cancer as the front liners.

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Code: 68-A-P

The Prospect of *Syzygium Cumini* L. (Skeels.) Seeds as a Cancer Immunotherapy and Co-Chemotherapeutic agent

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Abstract

Chemotherapeutic agents are efficacious in eradicating cancer cells, but their long term of usage, somehow, induces immunosuppression. The extract of seeds from *Syzygium cumini* L. (Skeels.), known in Indonesia as "duwet", and its compounds reported for having immunomodulatory activities. No reports review the potency of duwet seeds as cancer immunotherapy or co-chemotherapy agents. This article aims to summarize the prospect of duwet seeds as a cancer immunotherapy and as a co-chemotherapeutic agent. Literatures from international journals and other sources published from 2005 up to recent were retrieved from diverse databases. Several keywords used in this literature study were combined with the Boolean search technique using AND, OR, and Notation to search the literature. Based on literature studies, the extract and compounds of duwet seeds can modulate the immune system through various molecular pathways. Moreover, the extract and compound contents of duwet pips showed a cytotoxicity effect on several cancer cells. Duwet seeds greatly potential to be developed as cancer immunotherapy and co-chemotherapeutic agents. Further research using cancer animal models treated with duwet seed extract and in combination with anticancer agents is needed to further validate the potency.

Keywords: immunotherapy, chemotherapy, duwet (*Syzygium cumini*), immunomodulator, combination.

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Code: 69-A-P

A Review: Potency of S*wietenia Macrophylla* as a Phytoestrogen for Menopausal Women

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Abstract

Menopause is a condition of aging in the reproductive organs that causes estrogen hormone deficiency. The condition causes various physiological function disorders, such as cardiovascular disease, hyperlipidemia, osteoporosis, and menopausal syndrome. Phytoestrogen is one of the alternatives that can be used in menopausal therapy. Mahogany (*Swietenia macrophylla*) contains compounds that may have the potential to adapt as phytoestrogens. This review was conducted to explore mahogany's potency as a potential agent for preventing hyperlipidemia dan menopausal syndrome in women. A literature search was conducted with relevant keywords across Google scholar, PubMed, and Science direct. Mahogany has shown to have several bioactivities, including hypoglycemic, anti-inflammatory, and antioxidant activity. In addition, this review found that mahogany leaves and seeds exhibited hypolipidemic activity based on in vivo studies with mice. Mahogany's estrogenic effect was due to the phytoestrogen 7-hydroxy -2-(4-hydroxy-3-methoxy-phenyl)-chroman-4-on (7HMK), the unique compounds contained in mahogany seeds. In conclusion, Mahogany possesses hypolipidemic activity and estrogenic-like effect, and thus potential to be developed as alternative herbal supplements to prevent hyperlipidemia and menopausal syndrome.

Keywords: Mahagony (*Swietenia macrophylla)*, hyperlipidemia, menopause, phytoestrogen.

DOI:10.31557/APJCB.2020.5.S1.1-159

Code: 71-A-P

The Potential of *Pangium Edule* as a Antisenescence and Natural Antioxidant: A Review

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Abstract

Unbalance between endogenous antioxidants and Reactive Oxygen Species (ROS) can lead senescence that triggers premature aging. Kluwak seeds (Pangium edule Reinw) contain various compounds which are potent antioxidants such as: vitamin E, vitamin C, flavonoids, and β-carotene. This article aims to reveal the potential of kluwak as an antisenescence agent and natural antioxidant. Several keywords use in this literature study were combined with the Boolean search technique using AND, OR, and NOT notation to search the literature. Based on literature studies, kluwak extract and compounds have antioxidant activity through DPPH radical scavenging activity which works synergistically to prevent premature aging which is made in topical preparation because it can act directly on skin and it has a fairly fast onset when compared to oral preparations. Kluwak has a big potential to be developed as an antisenescence agent and natural antioxidant. It can be served in topical preparation such as hydrogels which have advantages in giving cooling effect on the skin, keeping skin moisturized longer, and is not causing irritation. Further research was carried out by looking at the antioxidant activity and antisenescence effect in vitro and formulate the topical hydrogel of kluwak's seed extract.

Keyword: kluwak, antioxidant, senescence, polyfenol, hydrogel.

DOI:10.31557/APJCB.2020.5.S1.1-159

Code: 72-A-P

Revealing the Potential of Cangkring Stem Bark (*Erythrina Fusca* Lour) as A Immunomodulator and Co-Chemotheraupethic agent

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Abstract

Chemotherapy is one of the most effective treatment in cancer therapy. However in clinical practice, chemotherapy promotes side effect that harmful to the immune system, by causing immunosuppression such as doxorubicin. The function of cancer chemotheraphy is destroying cancer cell whether has side effect such as immunosuppression. Therefore adjuvant chemotherapy is one alternative to reduce the side effects of immunosuppression against chemotherapy. Cangkring is a natural product that has activity as antioxidant and toxicity in several cancer cells but selective for normal cells. Thus, cangkring has prospect as co-chemotherapy to alleviate side effect of chemotherapy.This article aims to reveal the potential of cangkring stem bark (*Erythrina fusca* Lour) to modulate the immune system. This article is prepared by searching for literature from accredited international journals. Based on previous study, cangkring stem bark contains pterocarpan, isoflavonoids that have inhibitory effect on nitric oxide and cytokine production on immune cells, as well as antioxidant activity. These results indicate that cangkring bark has the potential as an immunomodulatory adjuvant in cancer chemotherapy patients.

Keywords: cancer; co-chemotherapy; adjuvant immunomodulators; *Erythrina fusca*; immune system.

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Code: 76-A-P

The Potency of *Jatropha curcas* Seed Meal as an Anticancer agent through Metastatic Inhibition

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Abstract

Jatropha (*Jatropha curcas*) is often used as biodiesel because of the oil content in the seeds. The production of jatropha oil produces a by-product in the form of jatropha seed meal known not only to contain compounds with cytotoxic activity but also to contain phorbol esters which act as co-carcinogens and tumor promoters. This review aims to find the potential of jatropha seed meal as an anticancer agent, particularly antimetastatic, through literature studies. We did a literature study to obtain data related to compounds with anticancer activity and methods of removing phorbol esters. This review covers literature from 2009 to 2020 collected from search engines such as PubMed, ScienceDirect, and Google Scholar. Based on our review, Jatropha seed meal contains isoamericanol A, rutin, myricetin, daidzein, and gallic acid which have anticancer activities. The activities including inhibition of cell invasion and migration, cell cycle arrest induction, and reduction of the MMP-9's activity. Overall, a jatropha seed meal is potential as antimetastatic agent. A comprehensive study is needed to explore the possibility of developing it as supportive agent in combination with a chemotherapeutic agent. Future implementation of jatropha seed meal formulation in a capsule is beneficial to increase its acceptability and stability.

Keywords: *Jatropha curcas*, jatropha seed meal, cancer, metastatic, capsule.

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Code: 100-A-P

Potential Roles of Citrus Peel as Adjuvant to Alleviate Cancer Associated Cachexia: A Review

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Abstract

Cachexia is characterized by an on-going loss of skeletal muscle mass with or without loss of fat mass. Cancer cachexia can be generated by the tumor metabolisms and or the administered chemotherapeutic drugs. On the other hands, citrus peel enriched with flavonoids which show multiple benefits for human beings. Recently, information regarding the nutritional and therapeutic properties of citrus peel extract shows its potential application as chemopreventive, antiproliferative and co-chemotherapeutic agents. This review was carried out to analyze the prospects of citrus peel as adjuvant to improve cancer cachexia. We searched for *in vitro-in vivo* assays from published journals regarding the evaluation of either citrus peel or its active ingredients which may be implicated in cancer cachexia. Citrus peel has been reported to alleviate cachexia based on *in vitro* and *in vivo* models. In *in vitro* experiments, citrus peel extract (CPE) has been reported to increase food intake through the activation of orexigenic OX1R-expressing neurons. While, *in vivo* experiments against tumor-bearing rat has reported the effect of CPE in the attenuation of muscle atrophy through the suppression of pro-cachexic factors. Furthermore, hesperidin and naringin are citrus peel flavonoids which may related with anti-cachexic effects. This review suggests the prospect of citrus peel as the nutritional adjuvant against cachexia even though its clinical effects to improve cachexia shall be investigated.

Keywords: cachexia, cancer, citrus peel, flavonoids, muscle athropy.

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Code: 126-A-P

Revealing the Potential of Kluwak (*Pangium Edule* Reinw) as a Co-Chemotherapeutic agent

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Abstract

The side effect of doxorubicin and chemoresistance in cancer therapy encourage the development of co-chemotherapy enhancing agent from herbal materials. This study aims to explore the potential activity of kluwak seed (*Pangium edule* Reinw) as an anticancer agent by collecting literatures of compounds in kluwak with anticancer activity. Relevant evidence from scientific journals was retrieved from Google Scholar, Science Direct, and PubMed. Several informations were grouped into categories covering active compounds in kluwak and anticancer activity of compounds in kluwak. Based on the literatures study, Kluwak seed known to contain compounds with antioxidant activities such as: tocotrienols, vitamin C, flavonoids (quercetin and catechins), and β carotene. The compounds contained in kluwak seed work synergistically as an anticancer agent through various molecullar mechanisms, including: inhibit cell invasion and migration and induce apoptosis especially in cancer cell. All of the evidences demonstrated that kluwak seeds potentially can be develop as co-chemotherapeutic agent. However, further research related to it's development is still needed.

Keywords: cancer, co-chemotherapy, *Pangium edule* Reinw, antioxidant, anticancer.

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The Prospect of Citrus Product for Complementary Colon Cancer Therapy

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Abstract

Citrus fruit is a rich-beneficial nutrient for human digestion health, especially its flavonoid compounds from the citrus peel that gained increased attention due to its broad range of biomedical activities, including anticancer activities in colon cancer. This review provides an overview of the anticancer potential of compounds from citrus peel and the future possibility of citrus-related product development. Relevant data from research articles from Google Scholar were collected and synthesized. Citrus peels contain flavonoids, such as hesperidin, naringin, neohesperidin, narirutin, eriocitrin, diosmin, and rutin. The citrus peel extract reported a selective antiproliferative effect towards several colon cancer cells covering cancer growth inhibition, cell cycle arrest, apoptosis, anti-senescence, and inhibiting cancer cell invasion. Also, dried citrus peel reduces the levels of oxidative-stress-related markers, reactive carbonyl species, and ACF formation in the colon cancer animal model. ADME study of citrus peel-extract possesses good bioavailability, which subsequently challenges the utilization of citrus peel to provide an inexpensive and environment-friendly material for the production of novel nutraceuticals. Taken all together, those pieces of well-established evidence have confirmed that citrus peel exhibit remarkable opportunities to be developed as complementary product for colon cancer therapy.

Keywords: citrus, flavonoids, colon cancer, antiproliferative, nutraceuticals.

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Code: 149-A-P

The Potency from Vitiver (*Vetiveria Zizanoides*) as Co-Chemotheraphy and Immunomodulator in Cancer Patients

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Abstract

Vetiveria zizanioides (VZ) an aromatic plant commonly known as "akar wangi." Vetiver oil has sedative properties and is traditionally used in aromatherapy to relieve stress, anxiety, nervous tension, and long-term insomnia. However, no review discusses the vetiver as an immunomodulatory agent. This review aims to reveal the prospect of VZ as an immunomodulatory agent. This study collected literature through an international database such as FAO's statistical data and journals from Google Scholar, Pubmed, and Science Direct, with several systematic keywords. The articles reviewed with carried out by synthesizing data and information and arrange a review. VZ contains compounds such as cedr-8-en-13-ol, β-guaiene, cycloisolongifolene, khusimene α-amorphene, β-vatirenene. Some studies shown that VZ has activity as antioxidant, anti-inflammatory, antinociceptive, cytotoxic, antibacterial, antimalarial, anti-tuberculosis hepatoprotective. A study shows VZ enhances the phagocytosis activity of murine peritoneal macrophages both in vivo and in vitro. The presence of antioxidant and anti-inflammatory activities indicates that VZ has a prospect as an immunomodulator. This review results indicate that VZ has a potential prospect to be an immunomodulatory agent.

Keywords: *Vetiveria zizanioides*, phagocytosis, immunomodulatory, antioxidant, and antiinflamation.

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Code: 151-A-P

Structural Characterisation and Non-Specific Immunomodulatory *in Vitro* Activity of Bioactive Compounds from Red Betel (*Piper Crocatum*, Ruiz. & Pav.) Leaves

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Abstract

Red betel (*Piper crocatum*, Pav. & Ruiz) leaves is a component of traditional medicine that is widely used to maintain health. However, there is no scientific report about the compounds responsible for this activity. The aim of this study was to isolate and identified active compounds from red betel leaves that could be improved the immune system. Preliminary study indicated that the ethanolic extract of red betel leaves has an immunomodulatory effect on the non-specific immune response of rats [50 ug/mL (116 latex), 25 ug/mL (115 latex), 5 ug/mL (99 latex) per 100 macrophages]. The ethanolic extract was then portioned, fractionated with bioassay guided isolation. Activation of macrophage *in vitro* (phagocytic assay) was used to guide the isolation of active compounds. The structure identification of active compounds was determined using spectroscopic methods. The active compounds in the active fraction were separated and purified then resulted two compounds (compound 1 and 2). Based on spectral data, it was identified that compound 1 was 2-allyl-4(1'-hydroxy-1'-(3",4",5"-trimethoxyphenyl)propan-2'-yl)-3,5-dimethoxycyclohexa-3,5-dienone and compound 2 was its acetyl derivative. Compound 1 and 2 (5 ug/ml) have immunomodulatory activity compared to Imboost (Echinaceae product) as positive controls.

Keywords: bioactive compounds, characterisation, *Piper crocatum, Ruiz. & Pav.*, immunomodulatory, macrophages.

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Abstract
Cancer Biomarker and Diagnostic

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Code: 141-A-P

Detection of Global DNA Hypomethylation as a Cancer Biomarker

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Abstract

Epigenetic changes show equal or even greater importance than DNA mutation in cancer development. Epigenetic alterations, such as regional DNA hypermethylation of CpG islands in promoter regions of tumor suppressor genes or global DNA hypomethylation occurs in early carcinogenesis and tumor development. Besides their relevance, hypomethylated DNA in cancer provides more sensitive markers than cancer-linked DNA hypermethylation acting as a promising biomarker for early cancer detection, diagnosis, prognosis and therapy monitoring. This review will highlight various methodologies utilizing global DNA hypomethylation as biomarker for clinical testing, including conventional methods and the advanced methods as alternatives to traditional ways. While such methodologies are used as the gold standard for DNA methylation analysis; however, its clinical is still challenging because there is still no method available for the easy and cost-effective read-out of DNA methylation on intact DNA. Present trends in development of simple and cost-effective for the diagnosis of global DNA hypomethylation as future cancer diagnostic are also discussed.

Keywords: cancer, epigenetic, DNA hypomethylation, biomarker, diagnostic.

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Abstract
Bioinformatic and Computer Aided-Drug Design

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Code: 26-A-P

Prediction of Anti-SAR-Cov-2 activity from *Chrysanthemum cinerariifolium* (Trev.) Compounds

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Abstract

Coronavirus or COVID-19 is a pandemic affecting millions of people around the world. Therefore the aim of this study is to predict the potential compounds resulting from metabolite profilling UPLC QToF MS/MS ethanol extract 96% *of Chrysanthemum cinerariifolium* (Trev.) leaves as anti SARS-CoV-2. The method used is molecular docking from the Molegro Virtual docker version 6.0. The selected protein targets were the SARS-CoV-2 protease and receptor (PDB: 6LU7), PD-ACE2 (PDB: 6VW1), and the Spike glycoprotein (PDB: 6LXT). Furthermore the comparative drugs used in this study were ramdesivir and chloroquine. The results showed that four compounds exhibted higher antiviral activity than the native ligands remdesivir and chloroquine. Furthermore, antiviral activity was shown by the similarity of amino acid bonds with native ligands and comparative drugs. It was predicted that the compounds in *C.cinerariifolium* leaves have the potential to inhibit SAR-CoV-2 development.

Keywords: COVID-19, *in silico*, *C.cinerariifolium*, SARS-CoV-2 protease, PD-ACE2, and Spike glycoprotein.

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Code: 34-A-P

Design of Boronhafagama Moleculer as Tyrosin Kinase Inhibitor for Anticancer

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Abstract

Tyrosine kinase is an effective treatment target for various types of cancer. Azranaphthyridine tyrosine kinase inhibitors have been developed for leukemia, but have genotoxic side effects. This research aims to design the boronhafagama molecule (chemical name 1- (4-hydroxynaphthalen-1-yl) -5- (4-hydroxyphenyl) -3-oxa-1,5-diaza-2,4-diborapentane-2,4- diol) with better safety and efficacy than azanaphthyridine. The molecular design was based on molecular docking with PLANTS software, while the design of synthesis used raw materials: p-amino phenol, Boron trioxide (B2O3) and p-amino naphthol. Design Methods. Validation of 5LMA.PDB, by redocking ref_ligand azanaphthyridine in the receptor (tyrosine kinase). RMSD is valid if the value is <2 Angstroms. The new boronhafagama molecule interacts with tyrosine kinase and docking scores compared to azanaphthyridine docking scores. Results and Discussion: In this proposal, an in silico test was carried out between the azanaphthyridine/native ligand and the boronhafagama novel molecule to tyrosine kinase (PDB:5LMA) with RMSD = 0.3847 Å. The results of the in silico test showed that the Docking Score (DS) of the boronhafagama novel molecule was -106,561 (2); while the azanaphthyrine compound was -106,217 (10). The results of the in silico test show that the novel boronhafagama molecule has potential as an anticancer by inhibiting tyrosine kinase receptor.

Keywords: boronhafagama, tyrosin kinase, anticancer, inhibitors, azanaphthyridine.

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Immunoinformatics Reveals Novel Viral T-Cell Epitopes from Kaposi's Sarcoma Oncovirus for Potential Vaccine Design Specific to Indonesian Population

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Abstract

Kaposi's sarcoma (KS) is the most common cancer found in HIV-positive individuals, caused by co-infection of Kaposi's sarcoma-associated Herpesvirus (KSHV). Recent study showed that KSHV is detected in HIV infected patients in Indonesia. However, currently there is no KSHV vaccine available. The present study aimed to elucidate novel viral T-cell epitopes from known KSHV proteome available in public database specifically for the most frequent Human Leukocyte Antigen (HLA) alleles found in Indonesian population for both Major Histocompatibility Complex (MHC) class I and II. Immunoinformatics approach was used to assess candidate T-cell epitopes. All KSHV proteomes available in viprbrc.org were downloaded. All possible 8-mers to 10-mers peptides were generated. MHC class I epitopes were then predicted using NetMHCpan, NetCTLpan, and NetMHCstabpan. For MHC class II, all possible 13-mers to 25-mers peptides were generated. NetMHCIIpan was then used to perform epitope prediction. In the case of MHC-I, 799 predicted epitopes were obtained. From these epitopes, 75 epitopes are found in all KSHV strains used in this study. For MHC-II, only 234 epitopes (out of 23,960 predicted epitopes) are found across all KSHV strains. In this study, a list of potential KSHV-derived T-cell epitopes for the most frequent HLA alleles in Indonesia were obtained. These epitopes should be validated further using molecular docking and molecular dynamics simulation. In addition, to complete the epitope prediction, B-cell epitope prediction could also be performed. A list of *bona fide* epitopes then might be used to build multi-epitope vaccine constructs. Finally, *in vitro* and *in vivo* studies should be performed for experimental validation.

Keywords: immunoinformatics, Kaposi's sarcoma, KSHV, T-cell, epitope.

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Computational based Evaluation of Triterpenoid from Indonesian Endemic Vegetables as Inhibitor A-Glicosidase

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Abstract

Diabetes mellitus is a metabolic disorder which characterized by elevated blood sugar levels abnormally. This sugar abnormality can occurs due to *α*-glucosidase enzyme activity in hydrolyzing carbohydrates. Therefore, inhibiting the activity of α-glucosidase enzyme was chosen for target therapy. In this study, molecular docking was conducted to select potential natural compound candidates from Indonesian vegetables which posses as alternative inhibitor of α-glucosidase activity. The docking protocol was validated by the RMSD value of crystal versus docking calculation. A number of 137 chemical compounds were generated from 13 vegetables and docked into α-glucosidase enzyme. The *α*-glucosidase enzyme was collected from pdb database with codename 3A4A. Chemical compound which has lower affinity will be chosen. Docking protocol showed an acceptable RMSD value of 1,223 and AMD89 has the best affinity. AMD89 5*β*,19-epoxy-3*β*,25-dihydroxycucurbita-6,23(E)-diene, triterpenoid from *Momordica charantia L.* show affinity value of -11,3 kcal/mol. It was more lower then *α*-glucosidase native ligand (-4,4 kcal/mol). Therefore, 5*β*,19-epoxy-3*β*,25-dihydroxycucurbita-6,23(E)-diene may bind strongly with α-glucosidase. Although the 5*β*,19-epoxy-3*β*,25-dihydroxycucurbita-6,23(E)-diene was previously reported. This study successfully revealed the potency of Indonesian vegetable, *Momordica charantia L.* as bioactive candidate for blood sugar level management.

Keywords: Diabetes mellitus, *α*-glikosidase, triterpenoid, molecular docking, *Momordica charantia L*.

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Code: 45-A-P

Molecular Docking Analysis of Anti-Covid-19 Compounds from *Saussurea Lappa* Plant

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Abstract

During these current pandemic COVID-19 cases were still increasing, yet there is no cure for COVID-19. One of the potential antivirus is *Saussurea lappa* which has antivirus activity against Hepatitis B virus. The objective of this study was to examine the potential antivirus activity of 17 compound from *Saussarea lappa* against SARS-CoV-2. Molecular docking process was carried out using Molegro Virtual Docker Software to find potential anti-virus candidates from 17 *Saussarea lappa* compounds. The target docking proteins were spike and 3CLMpro protein. These two proteins were collected from protein data bank with codename 6ZB5 for spike and 6LU7 for 3CLMpro. The molecular docking protocol was conducted with three replications. The docking protocol was validated by the RMSD value of crystal versus docking calculation. It wasshowed that RMSD value obtained from 3CLMpro and spike protein was respectively 4.17987 Å and 4.84479 Å. Compounds from *Saussurea lappa* that have the best rerank score were Lappadilactone compound for 3CLMpro protein (-115,708) and the Cynaropicrin for spike protein (-107,976). Both of them showed the greatest affinity. Lappadilactone and Cynaropicrin from Saussurea lappa had potential COVID19 by its binding on protein 3ClMpro with Lappadilactone and Spike with Cynaropicrin.

Keywords: Molegro Docking, *Saussarea lappa,* Anti-Covid-19, Spike, 3CLMpro.

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Code: 46-A-P

Evaluation of Lipid Lowering Indonesian Vegetables*: In Silico* Study

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Abstract

Indonesia is an agricultural country that produces a lot of vegetables including endemic species. However, the usages of these endemic vegetables are fading and less variation available in the market. The need of health benefit evaluation can bring the endemic vegetable back in to the kitchen. These evaluations can provide not only in the drug discovery (lipid lowering medicament) but also a domino effect will ended up in increasing economic value of underutilised Indonesian vegetables. In this study, a molecular docking protocol was employed to predict and select compounds from Indonesian vegetables database as an anti-hyperlipidemia drug candidate. The docking protocol was validated by the RMSD value of crystal versus docking calculation. From 13 species of vegetables, 137 total compounds were collected and docked into lipase-procolipase enzyme. This enzyme was collected from protein database with codename 1LPA. The protocol produced an acceptable RMSD value of 1.348 Å. The docking experiment resulted AMD71 (24-Methylenecycloartanol) from *Sechium edule* as the best potent lipase inhibitor with affinity value of -10.2 kcal/mol which was higher than lipase-procolipase's native ligand (-5.5 kcal/mol). The study successfully revealed the potency of Indonesian veggie, *sechium edule*, as bioactive containing food source in lipid level management.

Keywords: *Sechium edule,* anti-hyperlipidemia, Indonesian vegetables, lipase-procolipase, molecular docking.

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Code: 53-A-P

Introducing a Two-Dimensional Graph of Docking Score Difference Vs. Similarity of Ligand-Receptor Interactions

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Abstract

Observation of molecular docking results is generally performed by analyzing the docking score and the interacting amino acid residues separately either in tables or graphs. Sometimes it is not easy to rank the test ligands' docking results, especially if there are many. This study aims to introduce a new way to analyze docking results with a two-dimensional graph between the difference in docking score and the similarity of ligand-receptor interactions. Molecular docking is performed with one reference ligand and several test ligands. The docking score difference is obtained between the test and the reference ligands as the graph's x-axis. Meanwhile, the similarity of ligand-receptor interactions is obtained from the ratio of amino acid residues and types of interactions between the test and the reference ligands, which are the y-axis. Docking result analysis is more straightforward because two critical parameters are presented in one graph. The area formed on the upper left of the graph if a straight line is drawn between the test ligands with the smallest docking score difference and the highest ligand-receptor interaction similarity is the potential test ligand area. This graph can be used to support the analysis of the docking results.

Keywords: Analysis, docking, docking score, interaction, two-dimensional graph.

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Code: 58-A-P

CEP55 Inhibitor: Extensive Computational Approach Defining a New Target of Cell Cycle Machinery Agent

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Abstract

Centrosomal protein 55 (CEP55) is a pivotal protein for cytokinesis during cell division. The altered expression of CEP55 could cause mitotic failure related to tumorigenesis. However, there are no specific CEP55 inhibitors have been developed yet. This study aimed to provide a comprehensive information about CEP55, conduct functional domain analysis of CEP55 across species, and perform a computational approach for potential inhibitors of CEP55. The CEP55 expression were analyzed using the Oncomine and TCGA databases. Evolutionary analysis of the CEP55 was performed using MEGA-X software. Molecular docking was used to screen the binding affinity of several natural products on CEP55–ALIX binding interaction. High CEP55 expression was observed in eleven different types of cancers and associated with the worse outcomes of cancer treatments. Phylogenetic and evolutionary analyses revealed that the amino acid residues essential for CEP55 binding and localization were mostly conserved across vertebrates. From seventeen plant-based compounds, flavanol group, epigallocatechin gallate and catechin possessed superior binding affinity to disrupt ALIX–CEP55 interaction by the substitution of gallic ester or hydroxyl groups on the C3 position of flavonoid ring. This study provides comprehensive information about CEP55 gene and insights for designing potent inhibitors against CEP55 signaling.

Keywords: anticancer, evolutionary analysis, molecular docking, CEP55 inhibitor, natural product.

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Abstract
Drug discovery and Pharmaceutical Science

(Poster Competition)

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Code: 63-A-P

Guttaflow Bioseal as Monocone Obturation Technique in Curved Root Canals. A Scanning Electron Microscopy Study

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Abstract

The obturation quality of GuttaFlow Bioseal (GFB) in curved root canals is not clearly investigated. This study evaluated the volumetric percentage of obturated root canals (VPORC), extrusion of root filling material beyond the apical foramen (ERFM) and duration of obturation procedure (DOP) in curved root canals**.** Access cavity was prepared on twenty mandibular first molars. The degree of root canal curvature in mesiobuccal and mesiolingual root were determined according to Schneider's method. Samples were prepared using HyFlex CM rotary files and divided into two groups (n=10); Group 1 [gutta-percha (GP) cone and GFB] and Group 2 [GP cone and RoekoSeal Automix]. DOP was recorded and obturation radiograph was taken. Mesial roots were sectioned horizontally to obtain the apical, middle and coronal regions and observed under scanning electron microscope (SEM) at 70x magnification. SEM images were transferred to SketchAndCalc Area Calculator software. VPORC and ERFM in both groups showed no statistically significant difference irrespective of root canal curvature. DOP in severe canal curvature between Group 1 and Group 2 revealed statistically significant difference. VPORC and ERFM were not affected by the status of root canal curvature. DOP with GFB in severe canal curvature was slightly longer.

Keywords: GuttaFlow Bioseal, scanning electron microscope, monocone obturation, curved root canals, mandibular first molars.

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Code: 73-A-P

Pengujian Potensi Aktivitas Antibakteri Penyebab Jerawat Dalam Ekstrak Bunga Marigold

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Abstract

Today there are many faced skin problems by many people, one of which is acne. One of the bacteria that causes acne is Propionibacterium Acnes. One of the antibacterial compounds that can inhibit the growth of Propionibacterium Acnes bacteria in treating acne is the terpenoid fan flavonoid compound. Marigold plants or commonly called kenikir (Tagetes erecta L.) are ornamental plants with yellow to orange flower crowns that have many uses such as anti-nematodes and as fungicides. Marigold also contains α terpinolene and limonene which function as antibacterial. The bioactive content contained in this plant is terpenoids, alkaloids, and polyethylene. Terpenoids and flavonoids are believed to be antibacterial. The results obtained from research conducted on 100% concentration of terpenoid and flavonoid compounds in marigold flowers with a yellow color were considered more effective in inhibiting the growth of acne-causing bacteria because the inhibition zone created was larger.

Keyword: marigold, flavonoid, terpenoid.

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Code: 74-A-P

Calophyllum Inophyllum as an Alternative Treatment for Rheumatoid Arthritis and Extra-Articular Manifestation in Salivary Gland

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Abstract

Rheumatoid arthritis (RA) is an autoimmune disease characterized by systemic and chronic inflammation. RA can manifest in the temporomandibular joint (TMJ) and its surrounding salivary glands within the oral cavity area, 80% of RA patients involves the TMJ among several affected joints. The current RA treatment utilizes disease-modifying antirheumatic drugs (DMARDs), or corticosteroids. The mentioned treatment focuses on treating inflammation. Meanwhile, Indonesia is a country abundant with natural resources that can be developed into an alternative cure for RA and its following manifestations. One plant that fulfills that potential is the *Calophyllum inophyllum*, also known as nyamplung, due to its anti inflammatory properties. The purpose of this review is to provide information on the potential antiinflammatory and anti arthritis activities to treat RA and its manifestations. This review is compiled through an article search throughout various scientific databases with the publication year within 2000 and 2020. Our search results in the statement that Calophyllum inophyllum extract has an anti inflammatory activity by lowering pro-inflammatory cytokine levels. In addition, the extract also has anti arthritis properties. Nyamplung plant extract has the potential to be an alternative treatment for RA in TMJ and its extra-articular manifestations.

Keywords: rheumatoid, salivary gland, inflammatory, arthritis, Calophyllum inophyllum.

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Code: 78-A-P

Discovering the Undiscovered

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Abstract

Current researches in drugs discovery for pharmaceuticals science are involving many steps such as researching the chemicals subtances, collecting compounds, synthesizing chemicals, clinical testing, and designing product appearance. Drug discovery provides new and innovative products. This finding can't be happen without the research and development team. The goal of the discovery of new drugs is to find products that can overcome health problems or new types of diseases. Drug discovery is also based on scientific knowledge in the fields of pharmacology, pharmacognomy, and other fields. The discovery of this drug cannot be done instantly. It usually takes about 10-17 years to produce a drug that has quality efficacy and minimal side effects. The discovery process started from targeting, invitro functions, invivo validations, and the bioinformatics which took 2-3 years. Then it goes through the discovery and screening process with a period of 6-18 months. Followed by the drug optimization process which takes 1-3 years, the bioavailability with 1-2 years, the development process which is a clinical trial level 1 and 2 with 5-6 years. It ends with drug registration process that takes 1-2 years. After going through all the processes, the new medicinal product will be distributed to the market.

Keyword: drugs discovery, pharmaceutical science, reasearches, processes, and time required.

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Code: 82-A-P

Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open-Label Non-Randomized Clinical Trial

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Abstract

Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19 patients. We evaluate the effect of hydroxychloroquine on respiratory viral loads. French Confirmed COVID-19 patients were included in a single arm protocol from early March to March 16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. Presence and absence of virus at Day6-post inclusion was considered the end point. Six patients were asymptomatic, 22 had upper respiratory tract infection symptoms and eight had lower respiratory tract infection symptoms. Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported in the litterature for untreated patients. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination. Despite its small sample size, our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

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Non-Pharmacological Therapy Using Hyperbaric Oxygen Therapy against Cancer: A Review

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Abstract

The atomic bombs released in Hiroshima and Nagasaki in 1945 had a detrimental effect for Japan's situation, in particular from health sector. Studies showed that cancer rates in Japan was increased for the following years, leading to a treatment necessity. One of the methods used to treat cancer is Hyperbaric Oxygen Therapy (HBOT). To assess the feasibility of HBOT in radiotherapy treatment for cancer. We examined the paper published from Pubmed, Medline, and Cochrane Library from 2010 to 2020 and found 50 articles investigating the relationship between cancer and HBOT. HBOT remains among the best treatments used today. The side effects are rather low. Therefore, continuing HBOT will be accepted and can be achieved with the full pressure modification and air breaks insertion. In certain cancer types, such as breast cancer, pancreatic cancer, and gastric cancer, both recent and older research studies have shown that HBOT can inhibit and decrease the cancer growth. However, cervical and bladder cancers tend to be non-responsive to HBOT. For some cancer types, HBOT will be a safe and efficient therapy. Nonetheless, to evaluate any HBOT potential to cure other forms of cancer, further research is needed.

Keywords: Hyperbaric Oxygen Therapy, Cancer, Radiotherapy, Growth Cancer, Pressure.

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Code: 94-A-P

Silica-Nanoparticles in Slow Release Supplement: Preparation and Characterization

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Abstract

The nanosilica was prepared from bamboo leaves ash by calcination method in 800^{o} C for an hour. The result was 350 g silica from 500 g of its ash. The SEM shows a homogeneous surface of SiO2 and the EDX consists of 56.73% Si. The FTIR test indicates the Si-O-Si functional groups. The XRD shows 2θ = 21.6 which corresponds to JCPDS No. 39- 1425 and 18-1170. The supplement was vitamin C tablet which prepared into slow release supplement model, by mixing of three component: generic ascorbic acid, magnesium stearate, and nanosilica in certain composition. Some assessments were carried out to determine the tablet's characteristic: the size, homogeneity, and hardness. Physical testing of the slow-release vitamin C tablet was found to meet the requirements of tablet by Indonesian Farmakope. *In vitro* assessment was represented by dissolution test in simulation solutions of stomach by 0.1M HCl and the intestine by citric acid. The result showed that the dissolution of the samples were slower than the control tablets. This indicates that the addition of silica-nanoparticles affect the characteristics of slow release supplement.

Keywords: *silica, nanoparticles, slow realease supplement*.

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Code: 95-A-P

The Application of Water Spinach as Natural Sedative for National Defense Strategy against Universal War

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Abstract

Water spinach (*Ipomoea aquatica*) is a vegetable with sedative activity. It is highly potential to disguise into the enemy's territorial center, as one of CBRNE (Chemical, Biological, Radiological, Nuclear, Explosives) agent. This plant spreads the compounds through water to give sedative effect for enemies. It is very easy to use, but effective as a warfare. The aim of this study is to elucidating sedative effect of water spinach based on clinical research conducted in Indonesia. This study is a literature review to describe sedative effect of water spinach. The study showed that respondents who consumed water spinach have a sedative effect due to the influence on the central nervous system. Moreover, water spinach causes reduction in muscle tone which indicated by decreasing activity. Quercetin in water spinach presume trigger the inhibition of format reticularis in the central nervous system, GABA receptors and ligand-gated ion channels. Hence, the impulse delivery is inhibited and generated slow motoric activity. Water spinach has sedative effect due to quercetin activity in central nervous systems. However, we need further research to confirm its sedative effect.

Keywords: Water Spinach, Sedative, CBRNE agents, Central Nervous System, Quercetin.

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Code: 96-A-P

Antibacterial Pimple Patch from *Ficus Carica* L. Leaf Extract

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Abstract

Acne is often complained by many people, especially women. It is caused by excessive production of oil (sebum) on the skin due to the presence of *Propionibacterium acnes.* Tin leaves (*Ficus carica* L.) contain flavonoids that has antibacterial activity to cleanse the facial skin from acne. Patch can overcome lumps, gives antibacterial effect and effective to treat inflamed acne. The aim of this study is to provide new ideas to create pimple patch using flavonoids from *Ficus carica* L. This is a literature study to describe a new idea for making pimple patch. Expected pimple patch from extract leaves *Ficus carica* L. containing flavonoid that help to kill *Propionibacterium acnes* and relieve the inflammation. The process is beginning by extraction using ethanol as the desired compound separation method, dissolved into chispheric polymers that are added *Ficus carica* L. leaf extract mixed into the pimple patch, and then added glycerine as a plasticizer. Hence, it is expected to have a safer and sterile antibacterial effect because of its safety compared to synthetic drugs. *Ficus carica* L. could potentially be developed into pimple patch to create an anti-bacterial activity.

Keywords: Acne, *Ficus Carica* L., pimple patch, antibacterial.

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Code: 97-A-P

Potential SDS, Saponin in *Sapindus Rarak* as Shark Repellent to Optimize the Performance of the Navy Soldiers

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Abstract

Marine may potentially cause harm to humans, especially those who dive. More than a dozen incidents of humans have died from shark attacks. During World War II, many US soldiers died from shark attacks. Indonesia, a maritime country, urgently needs to anticipate shark attacks for the navy soldiers. The army uses saponin-based compounds to be used as shark repellent. Indonesia has high saponin flora, *Sapindus rarak* (SR). Currently, it is only used to wash batik. Whereas SR has potential to be developed for shark repellent due to SDS inside for supporting national security and defense. Aim of this study is proposing new shark repellent from SR to support our navy soldiers. Literature review was conducted to explore extraction, fractionation, and formulation of SR, and its impact in shark. Saponins from SR that are looking for are SDS groups in granular and aerosol form, which function as shark repellents. Saponins will foam when spread on the surface of the sea. Oxygen level in water is reduced and the sharks are not easy to take oxygen. Saponins will have an impact on shark's respiratory epithelial and blood cells. Saponin from *Sapindus rarak* has activity as shark repellent.

Keyword: integrity state, navy soldier, shark repellent, *Sapindus rarak*, saponin.

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Code: 98-A-P

Application Virtual Reality Care in Clinical Farmacy: A Review

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Abstract

Virtual Reality (VR) is a technology that allows users to be in a computer generated environment in a controlled system and this VR has entered the medical world. virtual reality is widely used in health care, pharmacy, and clinical research. This task focuses on the literature review for the effectiveness of VR in pharmacies. The aim of this study to describe a task the pharmacist group in the future using virtual reality care to support's people lives. This study is a literature review to describe pharmacist jobs in the future with the VR care. Pharmacist and patient can corporate together to detect changes in patient behavior, which will be programmed into a virtual center to demonstrate how their new daily goal might change their physical appearance and well-being. Awards and social networking in virtual world will motivate patients to continue to make positive decisions regarding their health. VR care benefical in pharmacy, in particular make drugs and pharmacotherapy. VR care can increase quality of life the patient's in the future.

Keyword: virtual reality, pharmacist, patients, care, pharmacotherapy, technology.

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Code: 104-A-P

In Silico Study and Antiproliferative Effect of Pinostrobin and Pinostrobin Acetate on T47D Breast Cancer Cells, and its Selectivity on Normal Cells

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Abstract

Past evidence showed that pinostrobin isolated from temu kunci (*Boesenbergia pandurate* Roxb. Schlecht) possess biological activity against cancer cell. Pinostrobin was modified to pinostrobin acetate by considering hydrophobic, electrophilicity, and steric properties using Topliss model to increase its cytotoxic activity. The specific objective of this research is to investigate the biological activity of pinostrobin and pinostrobin acetate by in silico study and the antiproliferative effect on human breast cancer cell lines (T47D), and its selectivity on normal cells. In this study, ADMET study was conducted using pkCSM online program. The molecular docking of the pinostrobin and pinostrobin acetate were evaluated on EGFR (1M17.pdb) using MVD v5.0. The antiproliferative activity then evaluated using re-rank score (RS). The cytotoxicity test were evaluated on human breast cancer cell lines (T47D) using MTT assay. The selectivity test were evaluated on normal cell lines (Vero). The antiproliferative activity and selectivity test then evaluated using IC_{50}. The pkCSM online program predicted that pinostrobin and pinostrobin acetate more absorbed and less toxic than 5-Fluorouracil (5-FU)**,** the docking showed that the re-rank scores of pinostrobin and pinostrobin acetate are smaller than 5-FU. From the docking result, we can predict that the compounds have a higher biological activity. But, in vitro studies showed that these compounds, pinostrobin and pinostrobin acetate are less potent compared to the commercial anticancer drug 5-Fluorouracil, with respective IC_{50} were 2523 µM, 252 µM, and 95 µM (5-FU). Although in vitro studies in antiproliverative effect of pinostrobin and pinostrobin acetate are less potent compared to 5-Fluorouracil, it can be concluded that the modification compounds of pinostrobin can be further developed as a potential breast anticancer drug.

Keywords: docking, pinostrobin, modified structure, MTT assay.

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Code: 109-A-P

Polymeric Nanoparticle of Alpha-Mangostin Conjugated to Trastuzumab Formulation as a New Drug Delivery Model in Treating Breast Cancer

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Abstract

Breast cancer is the most typical form of cancer among women. There have been 2.1 million women worldwide who suffer from breast cancer every year and around 10-30% of breast cancer sufferers are diagnosed with HER-2 positive. However, recent drugs targeted to HER-2 are low efficacy, high costs and has more adverse effects. Therefore, in this review we aimed to collect information related to make a polymeric nanoparticle of alpha-mangostin conjugated to trastuzumab formulation as an alternative therapy in treating breast cancer patients diagnosed with HER-2 positive. A literature search was conducted using PubMed and Scopus databases. Results showed that alpha-mangostin associated with β-cyclodextrin in nanopolymeric formulation could enhance solubility and cytotoxicity level, with minimum inhibitory concentration (IC_{50}) 8.86 and 9.96 μg/mL, respectively. Conjugating drug with specific antibody as like as ado-trastuzumab emtasine using trastuzumab as antibody for HER-2 could increase efficacy and safety profile. By conjugating to trastuzumab, the specificity of alpha-mangostin against breast cancer cells could be increased as like as ado-trastuzumab emtansine formulation. Thus, the polymeric nanoparticle of alpha-mangostin conjugated to trastuzumab formulation as a new drug delivery model would able to be an answer to public unrest in facing breast cancer.

Keywords: breast cancer, HER-2, alpha mangostin, trastuzumab, nanopolymeric.

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Code: 110-A-P

Evidence-based Recommendation for Mental Illness Improving during COVID-19 Isolation and Lockdown Policy

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Abstract

Since the WHO designated COVID-19, the virus have infected more than 43 millions people among the world. While in Indonesia total cases reach 392,934 (Data collect until October, 27 2020). Social distancing and isolation were done to suppress the spread of the virus. This situation causes mental disorders in the form of high stress levels, anxiety, depression, OCD, and other serious psychological conditions. We provide Evidence-based recomendations for solving the psycological condition obtacles impacted by COVID-19 for global and especially Indonesian cases. We use systematic reviews and extract data that discuss mental problems during Covid-19. We identified 27 articles from Science Direct and PubMed database, than selected all articles and resulted 15 articles. Lockdown causes most of the people to stay in a place continuously, it can lead to mental problems. We suggest new habits to work in a standing state for a certain period of time, use social media to provide education and facts about COVID-19, and practical guidance for early management of the psychosocial aspects of COVID-19 which are innovative in providing mental recovery in Indonesia. The results give new innovations for the government to suppress the mental illness problem during COVID-19 outbreaks.

Keywords: covid-19, mental illness, new working, lockdown, mental recovery.

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Code: 114-A-P

Berbagai Manfaat Daun Bidara (Ziziphus Mauritiana Lamk) Bagi Kesehatan Di Indonesia: Meta Analisis

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Abstract

Khasiat daun bidara (Ziziphus mauritiana Lamk) telah disebutkan dalam Al-Quran dan Hadist Nabi Muhammad SAW,Studi meta analisis ini bertujuan untuk mengetahui berbagai manfaat daun bidara (Ziziphus mauritiana Lamk) yang telah dibuktikan secara ilmiah melalui penelitian di Indonesia. Melakukan penelusuran literatur menggunakan aplikasi Google Scholar dan melalukan analisis terhadap literatur yang masuk dalam kriteria inklusi. Dari hasil penelusuran ditemukan 22 artikel dan hasil penelitian yang menyimpulkan tentang maanfaat daun bidara. Manfaat terbesar daun bidara adalah sebagai antimikroba, selain itu juga terdapat banyak manfaat lain seperti analgetik antipiretik dan antiinflamasi, antikanker, serta dalam berfungsi sebagai pelindung sel-sel tubuh seperti ginjal, hati dan otak.

Keywords: Bidara.

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Code: 115-A-P

Oyster Mushroom's (*Pleurotus Ostreatus*) Prospect as the Immunostimulatory agent

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Abstract

Pleurotus ostreatus or oyster mushroom is a famous edible mushroom from the Pleurotaceae family which contains a high nutritional profile like proteins, carbohydrates, macro and microelements with less fat. The constituents of *Pleurotus ostreatus* have activity related to antioxidants and immunomodulators. The antioxidant activity of *Pleurotus ostreatus* is derived from the amounts of phenolic compounds and flavonoids contained that inhibit free radicals. Several constituents found in *Pleurotus ostreatus* that have antioxidant activity are 1-octen-3-ol, 3-octanone, ascorbic acid, and gallic acid. Besides, *Pleurotus ostreatus* contains beta-glucan and alpha glucan. Based on a previous study, beta-glucan and alpha glucan have immunostimulatory activity through activate immune cells such as macrophage, neutrophil, monocyte, dendrite cell, and Natural Killer cell. Based on that findings, *Pleurotus ostreatus* has the prospect to be studied further for its immunostimulatory activity. For the application, a study showed the benefits of *Pleurotus ostreatus* developed as an innovative nutraceutical product.

Keywords: *Pleurotus ostreatus*, glucan, immunostimulator, nutraceutical, antioxidant.

DOI:10.31557/APJCB.2020.5.S1.1-159

Code: 118-A-P

The Potential of Brazilin and Brazilein from Secang (*Caesalpinia Sappan*) as anti Senescence agent by Inducing Antioxidant Activity

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Abstract

Senescence is known to be triggered by external factors, mainly oxidative stress. To answer the problem, anti senescence agents in the form of antioxidants are needed. Secang (*Caesalpinia sappan*) is an herbal plant known to have various active compounds especially from homoisoflavonoid group such as brazilin and brazilein which acted as an anti senescence agent by inducing antioxidant activity. This article reviewed the potency of secang as an anti senescence agent. Various literature from journals published in 2000-recent were retrieved from PubMed, Google Scholar, and other databases. Based on the literature study, brazilin have shown to have antioxidant activity by elevating superoxide dismutase (SOD) enzyme which decrease Reactive Oxygen Species (ROS) and lower oxidative stress by increasing the expression of SOD-3 gene. Other mechanisms involve inducing heme oxygenase-1 (HO-1) enzymes to further reduce ROS. Furthermore, brazilein have shown antioxidant activity by scavange OH·, which is one of ROS. Thus, in regards to its antioxidant activity, secang has the potential to be developed as an anti-aging agent therapies targeting senescent cells.

Keywords: Antioxidant, brazilin, brazilein, anti senescene, *Caesalpinia sappan.*

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Code: 120-A-P

The Potency of Bran in Rice (*Oryza Sativa* L.) as an Anti-Aging through its Radical-Scavenging Activities

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Abstract

Aging is a process of slowly diminishing the ability of tissues to repair themselves and maintain their normal function, so that they cannot survive infection and repair existing damage. Prevention of aging that is caused by extrinsic factors such as chemicals and pollution is a strategy people are paying attention to nowadays. Rice bran is interesting to study because it is easy to find, cheap, and rich in nutrients that are beneficial to health. Some of them act as antioxidants, an activity contributes to aging prevention. Especially vitamin E which is a typical compound found in rice bran with many benefits, which is one of the reasons we chose rice bran to be studied. The purpose of this study is to review potential compounds in rice bran and its mechanism which supports anti-aging properties. The method used in this research is through literature study by citing secondary data from several journals and related sources, such as NCBI, PubMed, and ScienceDirect. Compounds in bran including vitamin E, γ-oryzanol, and carotene, can act as antioxidants to prevent aging. These compounds act by control intra-ovarian reactive oxygen species (ROS) and fibroblast; scavenging radicals by electron transfer, allylic hydrogen abstraction, and addition reactions; protecting cells from lipid peroxidation in oxidative states; and reduces glutathione disulfide (a parameter of oxidative stress) in Graves' orbitopathy. All of the evidence demonstrated that rice bran potentially can be developed as an anti-aging agent.

Keywords: aging, rice bran (*Oryza sativa* L.), antioxidant, reactive oxygen spesies (ROS), radicals.

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Code: 121-A-P

Robusta Coffee (*Coffea Canephora*) Beans Extract: A Review on its Potential Cosmeceutical and Nutraceutical Applications

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Abstract

Aging is a natural process characterized by a progressive decrease of tissues physiological integrity, leading to dysfunction and increased susceptibility to death. This damage is a major risk factor for human pathology, including cancer, diabetes, cardiovascular disorders, and neurodegenerative diseases. Robusta coffee is the most popular beverage and commonly cultivated in Indonesia. This review discusses the future possibility of Robusta coffee beans being developed as an active ingredient for innovative cosmeceutical and nutraceutical products. Relevant journals were obtained from Google Scholar, PubMed and Scopus. The information was grouped into categories covering chemical compounds, extraction method, antioxidants activity, formulation, and pharmacological antiaging properties of Robusta coffee beans. Robusta Coffee beans have been reported its pharmacological activities, including antidiabetic, androgenic, antiaging, and antioxidant. Coffee bean can be extracted using several methods, including maceration and soxhletation, using an organic solvent such as n-hexane, ethyl acetate, and ethanol. The coffee beans extract contains polyphenols, chlorogenic acid, and caffeine, which have antioxidant activity by inhibits the formation of free radicals, which has potential to protect cells from aging. Caffeine and chlorogenic acid showed an anti-senescence and tissue damage-protection activity in vitro and in vivo. Robusta coffee beans have an opportunity to be developed as a biomaterial in cosmeceutical and nutraceutical products for preventing cells aging.

Keywords: Robusta coffee beans, antiaging, antioxidants, cosmeceutical, nutraceutical.

DOI:10.31557/APJCB.2020.5.S1.1-159

Code: 122-A-P

Probing Clove (*Syzygium Aromaticum* L.) Prospect as an Active Compound of Organic Anti-Aging and Anti-Wrinkle Skincare: A Poster Review

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Abstract

UV rays and daily activity induct wrinkles and leads to the aging of skin. Many skincares are efficacious to prevent wrinkles, but somehow, it is not suitable for human skin and induces irritation of skin. Recently, organic skincares are popular and have minimum side effects. Clove (*Syzygium aromaticum* L.) is well-known for rich eugenol which has potent antioxidant activity. This study conducted to examine the potency of clove extract as an active compound in organic skincare to prevent aging and wrinkles. This review uses Boolean search technique to retrieve the literature from PubMed and ScienceDirect journal databases. Based on literature study, informed that clove extract contains eugenol as a main compound and plays a key role as clove's anti-aging profile. Clove's anti-aging and anti-wrinkes profile was shown by previous study through various molecular pathways, including inhibition of skin fibroblast's elastase, inhibition of MMP-1 activity, inhibition of melanin formation, as well as increasing skin hydration. It can be concluded that clove extract has great potency to be developed as a compound in organic anti-wrinkles and anti-aging skincare to be a solution of basic skincare side effects.

Keywords: Anti-aging, anti-wrinkle, clove (*Syzgium aromaticum* L.), organic skincare, eugenol.

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Code: 125-A-P

A Review of Synbiotic Product of Iron-Fortified Kluthuk Banana and Lactobacillus for Gut Microbiome Modulation: New Strategy for Iron-Deficiency Anemia Prevention

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Abstract

Anemia is a global health problem that affects 27% of the world's population and affects 1 out of 5 Indonesians over one year old. The standard treatment for anemia is to provide iron (Fe) supplementation, though this triggers gastrointestinal disorders and an imbalance of the intestinal microbiota. This paper reviews the use of synbiotic Kluthuk banana flour fortified with iron and Lactobacillus sp. as a functional food alternative to treat iron deficiency anemia. Lactobacillus sp. acts as a probiotic while Kluthuk banana as a prebiotic. Articles were collected from Scopus, ScienceDirect, PubMed, and Google Scholar. Keywords were used to find related articles with Boolean operator. Articles used were open access with year publication of 2010-2020. Data were extracted and compiled then written into narrative review. Studies have shown that both of them play an essential role in increasing iron absorption. Lactobacillus sp. regulates the composition of the intestinal microbiota and increase the absorption of iron through bacterial metabolite products, increased mucin secretion, and an anti-inflammatory response while the Kluthuk banana flour is a prebiotic source in the form of inulin and fructooligosaccharide (FOS) which play a significant role in lowering pH in the intestine and increasing the number of Lactobacillus sp., resulting in increased solubility and absorption of iron by Divalent Metal Transporter-1 (DMT-1) in the colon. This review proved that the synbiotic kluthuk banana flour fortified with iron and Lactobacillus sp. can be developed into functional foods to prevent anemia.

Keywords: lactobacillus, kluthuk banana, iron, anemia, microbiota.

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Code: 129-A-P

Ph-Trigerred and Bio-Imaging Features of Carbon Quantum Dots Embedded Amines-Functionaized Porous Cellulose for Controlled Release of Quercetin

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Abstract

Non-targeted delivery of drugs becomes a major issue in cancer therapy which arised a negative effect suffered by cancer patients. Moreover, tracking of cancer cells requires lot of times and complex procedure, as well as expensive. Therefore, development of drug carrier having targeted delivery and bio-imaging features is addressed in this study. Oil palm empty fruit bunches (OPEFBs) are enriched with cellulose can be potentially utilized as drug carrier. The porous cellulose (PC) derived from OPEFBs was synthesized *via* dissolution-precipitation method. The surface of PC was engineered through silylation technique to introduce an amines group acted as active site to tighly bind quercetin drug molecules. The carbon quatum dots (CDs), prepared from OPEFBs by hydrothermal method, were embedded to the surface of PC after the quercetin loaded onto the amines-functionalized PC (PC-NH_2). The PC-NH_2/CDs and Quercetin loaded PC-NH_2/CDs (Q@PC-NH_2/CDs) were fully characterized by FTIR, BET, BJH, DSC, TGA, and UV-Vis to confirm the surface functionality and quercetin loading amount. As a result, the targeted material (PC-NH_2/CDs) were succefully obatined having porous structure with pore size of 2.25 nm, high BET surface area of 357.1 m^2 g^{-1}, high thermal stability, and high quercetin loading capacity up to 614.68 mg g^{-1}. The UV 365 nm radiation revealed a green fluorescent inducing a bio-imaging feature. Less than 10% of quercetin was released under physiological condition (pH = 7.4), but it was stormly released at cancer microenviroment (pH = 5.4). Therefore, the PC-NH_2/CDs is potentially used as targeted chemo treatment for cancer therapy.

Keywords: Bioiamging, drug delivery system, porous cellulose, quercetin, targeted-delivery.

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Code: 130-A-P

1,25-Dihydroxyvitamin D3 as a Potential Curative agent for Chronic Obstructive Pulmonary Disease

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a disease characterized by progressive airflow limitation that is not fully reversible. COPD is clinically manifested by emphysema and bronchitis which lead to the destruction of lung cells, decreasing of the elastic recoil and weakening of the respiratory function in patients. Nowadays, curative treatment of COPD only focused to relieve symptoms. No one curative agent can induces lung cells regeneration. 1,25-dihydroxyvitamin D3 (VD3) currently used to treat osteoporosis by increasing bone mass. However, there are potential effects of VD3 to induce regeneration in normal cells. To reveal the potential effect of VD3 to initiate lung cells regeneration, stimulating bone mass density, lung elasticity and respiratory function. We conducted a narrative review of articles from scientific database such as Pubmed and Scopus using following terms: 'vitamin D', 'lung repair', and 'COPD'. Pulmonary administration of VD3 used dosage 0.1 µg/kg after 2 weeks showing VD3-treated group had significant improvement in lung elasticity and respiratory function compared with the control group. Furthermore, after 30 weeks, VD3 had a significant effect as alveolar repair agent and affected bone mass density using dosage 0.1 µg/kg. VD3 showing alveolar-repairing effect and have potential to be developed as therapeutic candidate for COPD. Nonetheless, these studies were pre-clinical trials using mice as research subjects. Clinical trials are required in the future to provide better understanding of dosage, efficacy and safety aspect of VD3 as a curative agent of COPD in human.

Keywords: 1,25-dihydroxyvitamin D3, COPD, lung repair.

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Code: 132-A-P

Lignan Phytoestrogen Potency of Pumpkin Seeds (*Cucurbita Moschata*) to Overcome Estrogen Deficiency

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Abstract

An estrogen deficiency hormone could happen in menopausal women. It causes many negative effects such as osteoporosis, hyperlipidemia, cardiovascular diseases, dyslipidemia, and joint pain. In replacing the estrogen deficiency, a lot of people took supplementary from the outside. We could find estrogenic agents in pumpkin seeds (*Cucurbita moschata*). Pumpkin belongs to the family of Cucurbitaceae. The seed of Cucurbita moschata contains lignan phytoestrogens such as Dehydrodiconiferyl alcohol (DHCA), secoisolariciresinol, and lariciresinol which can bind with estrogen receptors signaling pathway. Dehydrodiconiferyl alcohol can exert anti-osteoclastogenic effects by acting as an agonist in estrogen receptors. DHCA also controls osteoblast differentiation by PPARγ-related actions as well as estrogen receptors. DHCA promotes osteoblast differentiation by interacting with either Estrogen Receptor α or Estrogen Receptor β as an agonist for both receptors. Using MOE software, both secoisolariciresinol and lariciresinol can visualize that they shared similar profiles with the native ligand by interacting with the amino acid residue as well as indicating the possibility to interact on the binding site of 17β-estradiol. Lariciresinol also works by binding to the receptor as an agonist. Lariciresinol has a better affinity to Estrogen Receptor β and can compete with 17β-estradiol on Estrogen Receptor α. This review is retrieved from Pubmed, ScienceDirect, and Google Scholar. According to the explanation above, pumpkin seeds have lignan phytoestrogen potency to overcome estrogen deficiency. However, further research is needed to reveal the estrogenic potency of pumpkin seeds.

Keywords: Menopause, estrogen, supplement, *Cucurbita moschata* seeds, lignan phytoestrogens.

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Code: 133-A-P

Revealing the Potency of *Curcuma Zedoaria* Essential Oil as Chemotherapeutic agents through Inhibit Metastasis Processes

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Abstract

Cancer is the second deadliest disease globally because cancer cells divide relentlessly, forming solid tumors or flooding the blood with abnormal cells with the potential to be spread to other parts of the body (metastatic cancer). The most common cancer treatment is chemotherapy, but it is costly and often causes side effects such as cardiotoxic and immune suppression. Therefore, it is needed to explore other alternative agents to inhibit metastasis and angiogenesis processes by utilizing natural sources such as *Curcuma zedoaria* to promote minimal side effects and more cost-effectiveness. This review aims to reveal the prospect of *Curcuma zedoaria* as a chemotherapeutic agent by inhibiting angiogenesis and metastasis processes. Various literature studies collected from PubMed, Science Direct, Springer, EBSCO machine search engine, selected only for related themes, and statistical data from Global Cancer Observatory (GCO). Based on the literature, *Curcuma zedoaria* Essential Oil (CZ-EO) contain sesquiterpenes compound such as curcumenol, zedoforan, 4,8-dioxo-6β-methoxy-7α,11-epoxycarabrane; which have anticancer activities by inhibiting angiogenesis through suppression on sprouting vessels of aortic ring and formation of microvessels as well as reducing the expression of the Matrix Metallopeptidase (MMP)-2 and MMP-9 enzymes that play a role in metastasis process. Moreover, CZ-EO exhibits increased the level of Reactive Oxygen Species (ROS) by increased the levels of p53 and inhibited AKT/NF-κB also decreases the levels of Bcl-2 and Bcl-xL and increase the Bax/Bcl-2 ratio. The findings of these studies proved that CZ-EO potentially to be developed as chemotherapeutic agents.

Keywords: *Curcuma zedoaria* essential oil, anti-cancer, anti-metastasis, chemotherapeutic agents.

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Code: 152-A-P

The Role of Pharmacist in the Control of Antibiotic Resistance

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Abstract

The role of a pharmacist is not just to mix and administer drugs to patients. Social pharmacy and clinical pharmacy have a close relationship with the performance and oath of a pharmacist. This is closely related to pharmaceutical care, which is oriented towards patient service. Clinical pharmacy activities regarding standard pharmacy services in hospitals include assessment and prescription services, tracking the history of drug use, drug reconciliation, drug information services, counseling, visits, monitoring drug therapy, monitoring drug side effects, evaluating drug use, dispensing sterile preparations, and monitoring drug levels in the blood, and pharmacy services at home (Pharmacy Home Care). All services performed by pharmacy are carried out to achieve a goal, one of which is the control of antibiotic resistance that often occurs in patients. Antibiotic resistance according to WHO (2015), resistant bacteria is a condition in which bacteria become resistant to antibiotics which are initially effective for the treatment of infections caused by these bacteria. The death rate due to antibiotical resistance until 2014 is around 700,000 people per year.

Keywords: Pharmaceutical Care, Clinical Pharmacy, Antibiotic Resistance, Antibiotic Abuse.

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Abstract
Cancer Biology and Cancer (chemo)prevention (Poster Competition)

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Code: 59-A-P

The Effect of Chemotherapy on Breast Cancer

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Abstract

Cancer is a disease caused by abnormal growth of body tissue cells. A common type of cancer in Indonesia is breast cancer. Breast cancer is a malignancy that occurs in breast tissue derived from the duct epithelial and lobelus. There are several types of treatment that can be done in breast cancer patients, one of which is by using chemotherapy. Chemotherapy is the use of special drugs to turn off cancer cells that can be used with the insertion through venous infuse, injections, in the form of pills or fluids. Chemotherapy commonly used in breast cancer patients are: ajuvant chemotherapy, neoajuvant chemotherapy, and palliative chemotherapy. Breast cancer prevention consists of primary prevention and secondary prevention. Primary prevention is to reduce or eliminate risk factors that are thought to be very closely related to the increased incidence of breast cancer. Meanwhile, secondary prevention can be done by screening breast cancer. Breast cancer screening can be self-examination, clinical examination, clinical examination by trained officers, mammography screening. The background to this research is that given the growing cases of breast cancer in Indonesia, the authors are interested in making the case a research material. The purpose of this study is to find out the prevention and effect of chemotherapy on breast cancer patients or can be used as education. The research method used is a descriptive method, which is done by collecting information from various sources obtained. The conclusion of the study on breast cancer is that it can be identified breast cancer treatment using a method of chemotherapy that is divided into three kinds, namely ajuvant, neoajuvant, and palliative.

Keyword: type of chemotherapy, breast cancer, prevention, skrinning, method.

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Code: 62-A-P

Quercetin in Red Onion's Extract (*Allium Cepa* L.) as an Adjuvant Therapy in Lung Cancer with KRAS Gene Mutation

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Abstract

Lung cancer is the most common cancer to be diagnosed. Having targeted therapy as the best approach today, lung cancer with KRAS gene mutation shows a bad prognosis due to resistance. Unfortunately, the soon to be specific inhibitor of KRAS mutation agent, is predicted to acquire resistance to MEK/ERK pathway. Several studies have determined that quercetin has the ability to suppress MEK/ERK pathway resistance if used as a combinatorial therapy. *Allium cepa* L. (red onion) is known to have abundance quercetin. This review aims to explain the potency of red onion's quercetin as an adjuvant therapy in lung cancer with KRAS mutation. Quercetin content in red onion's methanolic extract is 19.85±0,03/100 gram dry weight. The growth of transplanted lung tumors induced by A549 cells in BALB/cA nude mice was inhibited by quercetin (8.4 mg/kg). Quercetin could inhibit CK2 and STAT3 gene expressions, two genes that caused resistance in KRAS therapy. Red onion dry weight's dose of 42,317 g/kgBB (equals to 8.4 mg/kg quercetin) has an anticancer potency in mice with KRAS-mutated lung cancer. Quercetin content in red onion may potentially be used as an adjuvant therapy by down-regulating CK2 and STAT3 genes expression.

Keywords: lung cancer, KRAS mutation, *Allium cepa* L., quercetin, adjuvant therapy.

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Code: 86-A-P

The Effect of Hypoxic Mesenchymal Stem Cells-Conditioned Medium in Resolving Renal Failure on acute Renal Failure Animal Model

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Abstract

Acute renal failure (ARF) is a loss of renal function in which is occurred immediately following nephrotoxic drug induction or ischemic insult. The current treatment of ARF such as hemodialysis has not yet improved renal function. The conditioned medium of hypoxic mesenchymal stem cell (hMSC-CM) contains various growth factors that potentially contribute to renal regeneration leading to ARF improvement. This study aimed to analyze the effect of hMSC-CM administration in decreasing blood urea nitrogen (BUN) level which reflects renal function improvement. Fifteen male Wistar rats were injected with gentamicin to induce ARF model, then were randomly divided into three groups consists of: a control group (NaCl administration) and two treatment groups (treated by hMSC-CM at a high dose (T1) and at a low dose (T2)). The BUN levels were measured using the colorimetric method on day 8 after treatment. The result showed that there was a significant decrease in the BUN level ($p<0.05$) at a high dose of hMSC-CM groups. Based on this study, we conclude that hMSC-CM may improve renal function characterized by the decrease of the BUN level in an animal model of gentamicin-induced ARF.

Keywords: ARF, MSC, hMSC-CM, BUN, regenerative therapy.

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Code: 87-A-P

A Comparison of HP-Mscs and Mscs with Curcumin in Reducing Ureum Levels on acute Renal Failure Animal Models

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Abstract

Acute Renal Failure (ARF) is a sudden deterioration of the structure and function of the kidneys. Kidney transplantation may cause high infection and rejection of donor recipients. MSCs have paracrine ability to stimulate tissue formation in repairing and regenerating ARF. Curcumin can activate the antioxidant pathway to improve renal function. Hypoxic-precondition mesenchyme stem cells (HP-MSCs) were able to strengthen the MSCs' capability. However, its efficacy in improving ARF is still unclear. We aimed to compare the effect of HP-MSCs and MSCs with curcumin in improving renal function, characterized by blood urea nitrogen (BUN) level. Eighteen male Wistar rats were injected with gentamicin to induce ARF then randomly distributed into three groups: the control group receiving PBS injection, treatment group receiving intravenous injection of $1x10^6$ Hypoxia preconditioned-MSCs (HP-MSCs), and $1x10^6$ MSCs with curcumin 200 mg/kg BW. The BUN levels were evaluated using the spectrophotometer method on day 8. The result showed there is a significant decrease ($p<0.05$) of BUN levels in HP-MSCs and MSCs with curcumin groups. We conclude that HP-MSCs have a more potential effect than MSCs with curcumin in improving renal function of the gentamicin-induced ARF animal model.

Keywords: MSCs, HP-MSCs, Curcumin, ARF, BUN.

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Code: 88-A-P

Gene Expression of Selected Apoptotic Markers in Human Oral Squamous Carcinoma HSC-3 Cell Line Treated with Myrmecodia Pendans Plant Extract

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Abstract

Myrmecodia pendans (M. pendans), or Sarang Semut, is an epiphyte with anticancer potential. It was recently reported that it induces apoptotic activity in the human oral squamous carcinoma (HSC-3) cell line. This study aimed to investigate the effect of *M. pendans* treated samples on the expression of apoptotic markers, Bax and Bcl-2. *M. pendans* was purchased from West Papua, Indonesia. The hypocotyl was dried thoroughly and then extracted aqueously. The apoptotic activity was detected via flow cytometry. Bax and Bcl-2 expression was analyzed by quantitative real-time polymerase chain reaction. Results of our cell cycle analysis reveal that aqueous extract of *M. pendans* induced apoptosis in 2.5 and 5 mg/mL but no change between these two concentrations. Apoptosis was observed at 24 h but not at 48 h. Bax and Bcl-2 expression in HSC-3 cells was affected by *M. pendans*. At 24 h, upregulation of Bax was observed at 2.5 mg/mL. However, after 48 h, Bax expression showed no changes at any concentration. Bcl-2 was significantly downregulated after 48 h of treatment. *M. pendans* extract induced apoptosis in HSC-3 cells, which might occur via the proapoptotic (Bax) and antiapoptotic (Bcl-2) pathways.

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Code: 89-A-P

Chemopreventive Activity of Clinacanthus Nutans L. Ethyl Acetate Fraction on T47D Breast Cancer and Vero Normal Cell Line Based in Vitro and in Silico Study

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Abstract

In Indonesia, breast cancer is the highest type of cancer suffered by women with 22,692 deaths. Problems at arise from cancer treatment with chemotherapy is severe side effects. So, we develop a chemopreventive agent from natural plat. This study aims to determine the chemopreventive activity of *Clinacanthus nutans* L. Ethyl Acetate fraction by *in vitro* and *in silico* study. Etyl Acetate Frraction of Clinacanthus nutans L. was prepared by maceration using 70% ethanol and fractionated using Etyl Acetate. *In silico* test used molecular docking. The antioxidant test by DPPH method, that quercetin as standard. Cytotoxic study on T47D was evaluated by MTT test, results were expressed as an IC_{50}. The results showed that EtAc fraction contained flavonoid. The EtAc has a weak antioxidant activity with IC_{50} 576.904 µg/mL. Vitexin stronger binding affinity with HER2 protein than EGFR with a docking score -9.3 kcal/mol. Single cytotoxic assay on Vero and T47D cell line showed the IC50 1452.835 µg/mL and 340.122 µg/mL, respectively, with selectivity index 4.271. *Clinacanthus nutans* L. Ethyl Acetate fraction is quite toxic and selective on T47D breast cancer cell line.

Keyword: Clinacanthus nutans L., Breast Cancer, HER2 protein, cytotoxic, selectivity.

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Code: 91-A-P

The Role Anticancer Activity of Secondary Metabolite *Bambusa Sp.* Mediated *Reactive Oxygen Species* (ROS)

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Abstract

Cancer still the leading cause of death in many countries. In the other side, bamboo leaf (*Bambusa sp.*) contains many secondary metabolites. Secondary metabolites content of leaf extract *Bambusa sp.* such as isovitexin, vitexin, isoorientin, tricin, catechin, afzelin, swertiajaponin, and orientin are compounds that are proven to have anticancer activity that was mediated by *reactive oxygen species* (ROS). The aim of *review* is to provide a perspective on the role of *Bambusa sp.* leaves extract and its secondary metabolites as anticancer agents through the mediation of regulation ROS. Bioinformatics approach and its secondary metabolites *Bambusa sp.* were carried out by conducting phytochemical screening and searching for secondary data. Collection of secondary metabolite compounds using literature articles on PubMed, NCBI, Sciencedirect, and Google scholar. The bioinfomatics database used PubChem, PASS Online, Similarity Ensemble Approach, SWISSTargetPrediction, STRING-DB, and Cytoscape-Cytohubba. This study showed that extract of *Bambusa sp.* leaves effective in suppressing proliferation, inducing apoptosis, preventing migration and metastasis mediated by ROS through *down*-regulation of Bcl-2, VEGF, MMP-2, and MMP-9 as well as *up*-regulation of Bax, Caspase-9, Caspase-3, Caspase-8, p53, and p21. *Bambusa sp.* can possibly be used as a natural anticancer therapy with less side effect.

Keywords: leaves *Bambusa sp.*, ROS, anticancer, bioinformatics, molecular mechanisms.

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Code: 93-A-P

PDL-1 Genome Editing in Lung Cancer Cells

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Abstract

Lung cancer often occurs in military health service due to a higher incidence and a lower survival in deployment-military officer compared to civilian. Military personnel have a tremendous risk of being exposed to carcinogens mustard gas, orange agents, asbestos, and depleted uranium. One of treatments for lung cancer is immunotherapy by antagonised targeted proteins such as PDL-1, CD 24, and CD 47. Nevertheless, cancer cells can evade the immune system by sending camouflage signal to them. Accordingly, we are proposing a new treatment using CRISPR-Cas-9 systems. This study is expected to provide a new prospective idea in lung cancer treatment by editing PDL-1 gene. We determined our domain of interest, followed by designing a single guide RNA (sgRNA). Our sgRNA, in conformity with Cas-9 navigate its enzyme to cut our interest gene. Subsequently, non-homologous end join (NHEJ) is being a repair pathway to facilitated knock out of PDL-1 from lung cancer. We proposed to knock out the PDL-1 in lung cancer cells. Consequently, it is expected to provide a new effective treatment for lung cancer. This study provides new ideas for lung cancer treatment by editing PDL-1 through CRISPR-Cas-9 systems.

Keywords: CRISPR-Cas-9, Lung Cancer, PDL-1, CD 274 Gene, Carcinogens.

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Immunopotential Therapy from Black Cumin *(Nigella Sativa L)* Extract as Cancer Immunotherapy

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Abstract

Cancer diseases caused by the abnormal growth of cells. During their development, these cancer cells can spread to other tissues or organs. Normally, the abnormal cells can be eliminated by the body immune system. However, cancer cells have the ability to avoid it, a proses called cancer immunosurveillance. Immunopotentiation therapy is a treatment to improve immune system function by stimulating the immune system which can help in the chemotherapy process. One of natural products that has immunomodulatory activites is black cumin (*Nigella sativa* L.). It has various pharmacological activities, such as antibacterial, antioxidant, anti-inflammatory, anticancer, antihistamine, bronchodilator, immunomodulatory, and anticonvulsants. Black cumin is a phytogenic immunostimulant that help build and strengthen the immune system. The part that is commonly used is the seeds that are processed into extracts and essential oils. Based on various research, its major compound is thymoquinone, which has immunomodulatory activities by elevating interleukin (IL)-3, IL-2, and IL-4 secretions; and suppressing the proliferation of B lymphocytes. This study aims to examine the activity of black cumin and its active compound in the inflammation and immunomodulation, and its potency as a cancer immunotherapy. This study employs literature study methods by citing primary and secondary data from several databases such as PubMed, ScienceDirect, and Google Scholar. Black cumin extract contains protein that has unstable physicochemical properties when taken orally. Thus, the development strategy is to find pharmaceutical preparations that can deliver the compounds by a specific carrier system or adding a protease inhibitor and an enhancer.

Keywords: Immunomodulator, Black cumin (*Nigella sativa* L.), Cancer, Immunotherapy.

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The Co-Chemotherapy Activity of Binahong N-Hexane Fraction (*Anredera Cordifolia*) with 5-Fluorouracil against Widr Colon Cancer Cells Line

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Abstract

Cancer is a non-communicable disease that cause the second-largest death in the world. Colon cancer incidence ranks third in most cases in Indonesia. On the other hand, cancer treatments with chemotherapeutic agents often have serious adverse side effects. Further, it needs to develop co-chemotherapy agents from nature to decrease the side effect. This study aims to determine the co-chemotherapy activity of *Anredera cordifolia* leaf n-hexane fraction (ALHF) on WiDr colon cancer cells line by in vitro and in silico assay. *Anredera cordifolia* leaf powder was macerated using 70% ethanol and fractionated with n-hexane to obtain ALHF. The identification of flavonoid compounds using the TLC method. In silico molecular docking test with Autodock Vina. The DPPH method was used for antioxidant test with quercetin as reference. The cytotoxic assay was done by MTT Assay method on colon cancer cells WiDr and its combination with chemotherapy agent of 5-Fluorouracil. The results of TLC showed that ALHF contained flavonoids compound. The ALHF has stronger binding affinity with IKK (-9.0 kcal/mol) than the other compound based on molecular docking. The ALHF has weak antioxidant activity with IC_{50} value of 2851 µg/mL. The cytotoxic result showed the quite strong activity on WiDr colon cancer cells with IC_{50} value of 191 µg/mL and had a synergistic combined activity with 5-Fluorouracil with the CI value of 0,80-28,92. We can conclude that the ALHF has the potency to inhibit the development of WiDr colon cancer cells by in vitro and in silico assay.

Keywords: *Anredera cordifolia*, colon cancer, WiDr, IKK, 5-Fluorouracil.

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Cytotoxic Activity the Ethanol Fraction of Binahong Leaves (*Anredera Cordifolia* (Ten.) Stennis) on MCF-7 Breast Cancer Cells and Vero Normal Cells

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Abstract

Breast cancer occurs because of an imbalance between proliferation, differentiation, and apoptosis of breast glands. Chemotherapy is one of therapeutic choice for breast cancer sufferers but can causes several side effects. Therefore, it is necessary to develop cytotoxic agents from the natural ingredients with minimum side effect. This study aims to determine the cytotoxic activity the Ethanol Fraction of *Anredera cordifolia* Leaf (EFAL) on MCF-7 breast cancer cells and Vero normal cells by in vitro and in silico assay. The study started by the extraction and fractionation to obtain the EFAL. The identification of flavonoid compounds using TLC method. Molecular docking was carried out by Autodock Vina method. The antioxidant test was performed by the DPPH method, with quercetin as reference. A cytotoxic study was done by MTT Assay on MCF-7 breast cancer cells and Vero normal cells. The TLC result showed that EFAL contained flavonoids compound. The EFAL has stronger binding affinity with Bcl-2 (docking score of -7.5 kcal/mol) based on molecular docking compare with the other compound. The EFAL showed weak antioxidant activity with IC_{50} value of 4940 μg/mL. The cytotoxic test on Vero cells and MCF-7 cells showed IC_{50} values of 1064 μg/mL and 495 μg/mL, respectively, with the selectivity index of 2.149. The EFAL showed selective activity against MCF-7 breast cancer cells and Vero normal cells, so it has potential to develop as chemopreventive agent on breast cancer cells.

Keywords: *Anredera cordifolia,* breast cancer, MCF-7, Bcl-2, Normal Vero cells.

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Circumventing Chemoresistance with *Boesenbergia Pandurata* Apoptosis Induction Activity: An Overview

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Abstract

First-line chemotherapeutic agent used for many cancer types, often shows chemoresistance. Thus, co-chemotherapeutic agents that return chemotherapy agent pro-apoptosis factors' functions are needed to tackle chemoresistance. *Boesenbergia pandurata* (fingerroot), a widely used-herbal in Indonesia, contains prenylated flavonoids such as Panduratin A and Boesenbergin A which acted as pro-apoptosis activator to decrease chemoresistance. Various literature gained from 2003-2018 through NCBI, Pubmed, and ScienceDirect. Keywords such as chemotherapeutic agent, apoptosis, *Boesenbergia pandurata*, fingerroot, Panduratin A, and Boesenbergin A, were categorized and discussed. This review brings an insight into fingerroot's potency as a co-chemotherapy agent to help prevent chemoresistance. Cisplatin chemoresistance occurs due to the dysfunction of pro-apoptotic proteins and signalling pathways in cisplatin-resistant cancer cells that lead to disruption of apoptotic. Based on the literature study, the apoptosis induction activity on Boesenbergin A occurs via mitochondrial dysregulation, caspase-3,7,8, and 9 expression, downregulation of Hsp70 protein, and inhibition of the expression of anti-apoptotic protein Bcl-2. Panduratin A has the ability to inhibit NF-κB translocation that leads to apoptotic activity. Hence, fingerroot is a potential co-chemotherapy agent that can restore the dysfunction pro-apoptotic protein and pathways in cisplatin-resistant cancer cells, lowering cisplatin resistance in cancer cells.

Keywords: Fingerroot (*Boesenbergia pandurata*), panduratin A, boesenbergin A, apoptosis, chemotherapy.

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Efficacy Prospect Ethanolic Extract of Flat-Top Mille Graines (*Hedyotis Corymbosa*) as a Co-Chemotherapeutic agent

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Abstract

Cancer remains as a heterogenous diseases that it becomes urged for the development the novel candidate of drug which efficacious on eliminating cancer cells with minimum side effect against normal cells. The extensive exploration of natural resources as anticancer agent become alternative cancer treatment options in encounter chemotherapeutic agents' side effect problems. Ethanolic extract of flat-top mille graines (*Hedyotis corymbosa L.*) contains flavonoids, ursolic acid, oleanolic acid, and gamma sitosterol which attribute for their co-chemotherapeutic activities. Therefore, it is necessary to do further studies and explorations on *H. corymbosa* as co-chemotherapy agent. This study aimed to determine the potency of *H. corymbosa* and its molecular mechanism in eliminating cancer cells according to several published research articles. We used several reputable journal databases such as PubMed, ScienceDirect, and Scopus to collect all the studies related to *H. corymbosa* and its constituents against cancer. The ethanolic extract of *H. corymbosa* contains ursolic acid that performs antiproliferative activity, while its flavonoids content inhibit the carcinogenesis process both in vitro and in vivo. Moreover, the extract also exhibits a cytotoxicity effect in 4T1 metastatic cancer cell through inhibition of NF-κB activation. These findings also may correlate with the effect from *H.corymbosa* extract that suppress MMP-9 activity, which plays important role in metastasis and the expression of MMP-9 also regulated through NF-κB activation. Thus, *H. corymbosa* promotes great potential to be develop in the further as co-chemotherapeutic agent.

Keywords: *Hedyotis corymbosa* L., ursolic acid, cytotoxic, metastatis, antiproliferative, co-chemotherapeutic agent.

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Soursop's (*Annona Muricata* L.) Potency as a Cochemotherapeutic agent by Its Selective Antiproliferation Activity: An Overview

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Abstract

Cancer is a disease with high prevalence in Indonesia. Chemotherapy is one of other solutions to reduces cancer growth, but many of them have been shown to have non-selective cytotoxicity on cancer cells. Soursop (*Annona muricata* L.) is a plant that is commonly found in Indonesia. The leaf of soursop contains compound that known to have antiproliferation activity, such as acetogenin group. The discussion of the potential of soursop was carried out by quoting secondary data from NCBI, PubMed, and ScienceDirect. Ethanolic extract of soursop leaf selectively induces apoptosis of cancer cells by inhibiting NADH oxydoreductase in mitochondria, inhibiting P-type ATPase in NKA and SERCA pump, also stopping cell cycle at G1 phase. Based on a research, soursop leaf extract is selectively toxic toward Hep-2, Sum-159, and MCF10A cancer cells, but non-toxic toward its normal cells. This special effect might be related to its sensitivity toward cells with high amount of ATP. A study showed that soursop leaf extract can be developed as a cochemotherapeutic agent because of its selective antiproliferation activity. However, we suggest to conduct further research to formulate soursop leaf extract as cochemotherapeutic agent.

Keywords: cancer, soursop (*Annona muricata* L.), cochemotherapy, antiproliferation, selective.

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The Secret of *Pangium Edule* as a Antisenescence and Natural Antioxidant

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Abstract

Unbalance between endogenous antioxidants and Reactive Oxygen Species (ROS) can lead senescence that triggers premature aging. Kluwak seeds (Pangium edule Reinw) contain various compounds which are potent antioxidants such as: vitamin E, vitamin C, flavonoids, and β-carotene. This article aims to reveal the potential of kluwak as an antisenescence agent and natural antioxidant. Several keywords use in this literature study were combined with the Boolean search technique using AND, OR, and NOT notation to search the literature. Based on literature studies, kluwak extract and compounds have antioxidant activity through DPPH radical scavenging activity which works synergistically to prevent premature aging which is made in topical preparation because it can act directly on skin and it has a fairly fast onset when compared to oral preparations. Kluwak has a big potential to be developed as an antisenescence agent and natural antioxidant. It can be served in topical preparation such as hydrogels which have advantages in giving cooling effect on the skin, keeping skin moisturized longer, and is not causing irritation. Further research was carried out by looking at the antioxidant activity and antisenescence effect in vitro and formulate the topical hydrogel of kluwak's seed extract.

Keyword: kluwak, antioxidant, senescence, polyfenol, hydrogel.

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Noni Fruit 'S (*Morinda Citrifolia*) Potency as Immunomodulator in Cancer Chemoterapy Patients

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Abstract

Immunomodulator is very important for cancer chemotherapy patient. Chemotherapy can cause immunosuppression because of neutropenia. Neutropenia is when the number of neutrophils in our blood stream is lower than normal. *Morinda citrifolia* known as *Mengkudu* is a tropical fruit that commonly used as traditional medicine such as for hypertension medication. It contains many active compounds, such as polysaccharide, scopoletin, xeronine, proxeronine, and ascorbic acid. Those compounds were reported had immunomodulatory activities. This study was conducted by review literature collected from Google Scholar and Science Direct. Based on previous study, Polysaccharide can increase the production of immunoglobulin M, immunoglobulin G and stimulates phagocytosis. Polysaccharide activate immune cells such as macrophage, monocyte, neutrophil, and T cell and Scopoletin can induce cell proliferation on normal T lymphocytes. So, these results indicate that *Morinda citrifolia* is potential to be an immunomodulator in cancer chemotherapy patients.

Keywords: *Morinda citrifolia*, polysaccharide, immunomodulator, cancer chemotherapy patients.

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Potential of Melinjo (*Gnetum Gnemon*) as the Chemoprevention Agent - A Review

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Abstract

Melinjo (*Gnetum gnemon*) is one of the *Gnetaceae* that commonly used as food ingredients in Indonesia. Melinjo contains such as alkaloids, flavonoids, steroids, tannins, and stilbenoids that found in leaves, fruits, and seeds. This review discusses potential *Gnetum gnemon* as a chemoprevention agent. The literature used in this review were retrieved from Google Scholar, NCBI, Pubmed, Science Direct, and ACS Publications from 2005-2020. Several studies have reported, that one of the active compound in melinjo that has potential as a chemoprevention agent is resveratrol. Resveratrol is a group of stilbenoid that abundant in extracts of melinjo seeds. Resveratrol induces the intrinsic apoptotic through reducing the mitochondrial transmembrane potential ($\Delta\Psi m$), increasing the release of cytochrome-c, and increasing the activity of caspase 3 and caspase 9. Based on these studies, *Gnetum gnemon* has prospect of being studied further as a chemoprevention agent combined with chemotherapy agents to increase the effectiveness and reduce the side effects of chemotherapy. For its application, several studies have shown *Gnetum gnemon* potentially formulated as a nutraceutical product in the form of effervescent tablets and tablets.

Keywords: *Gnetum gnemon*, Melinjo, Chemoprevention, Chemotherapy, Resveratol.

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Code: 131-A-P

Revealing the Potential of Cangkring Stem Bark (*Erythrina Fusca* Lour) against Immune System Cancer Co-Chemotherapy

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Abstract

Chemotherapy is one of the most effective treatment in cancer therapy. Though in clinical practice, chemotherapy promotes side effect that harmful to the immune system, by causing immunosuppression such as doxorubicin. The function of cancer chemotherapy is destroying cancer cell whether has side effect such as immunosuppression. So, adjuvant chemotherapy is one alternative to reduce the side effects of immunosuppression against chemotherapy. Cangkring is a natural product that has activity as antioxidant and toxicity in several cancer cells but selective for normal cells. So, cangkring has prospect as co-chemotherapy to alleviate side effect of chemotherapy.This article aims to reveal the potential of cangkring bark (*Erythrina fusca* Lour) to modulate the immune system. This article is prepared by searching for literature from accredited international journals. Based on previous study, cangkring stem bark contains pterocarpan, isoflavonoids that have inhibitory effect on nitric oxide and cytokine production on immune cells, as well as antioxidant activity. These results indicate that cangkring bark has the potential as an immunomodulatory adjuvant in cancer chemotherapy patients.

Keywords: cancer, co-chemotherapy, adjuvant immunomodulators, *Erythrina fusca*, immune system.

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S-Coca (Self Nanoemulsifying Drug Delivery System *Cosmos Caudatus* Kunth) as Targeted Treatment of Breast Cancer

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Abstract

Over 40.5 million or 71% of the 56.9 millions global deaths in 2016, were caused by non-communicable diseases. According to WHO (2020), cancer is the cause of death by 22% of all non-communicable disease deaths, after cardiovascular disease. Breast cancer is the most common cancer of various types of cancer, which is 46.3%. The first-line chemotherapy agent for breast cancer is doxorubicin. The use of doxorubicin can cause cardiotoxicity, cardiomyopathy, and congestive heart failure. However, natural ingredient for breast cancer therapy such as kenikir can be developed. Kenikir (*Cosmos caudatus* Kunth) contains quercetin which can inhibit DNA Topoisomeras enzym and cause an apoptosis in MCF-7 cells. Based on the results of in vitro studies, SNEDDS (Self Nanoemulsifying Drug Delivery System) will increase the absorption of quercetin by improving the transportation quercetin through Caco-2 monolayer cell and increase the solubility of the quercetin up to 5 mg/mL. Meanwhile, the results of in vivo studies shows SNEDDS can improve its solubility, gastrointestinal absorption, pharmacodynamic properties, and bioavailability of quercetin up to 33.51 times compared to quercetin dispertion. Therefore, *Cosmos caudatus* Kunth with the SNEDDS has the potential as an chemoprevention therapy of breast cancer.

Keywords: breast cancer, SNEDDS, *Cosmos caudatus*, quercetin, apoptosis.

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