

Optimal Pharmaceutical Management Strategies in Cancer Treatment: Novel Approaches

Farhad Alishahi

Negar Soudmand

Tayebeh Ghasemi Goki

Tara Sadat Rashidoleslami

Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran. Management of Technology Islamic Azad University South Branch, Iran. Department of Nursing and Midwifery, Kerman Branch, Islamic Azad University, Kerman, Iran. Faculty of Medical Sciences and Technologies, Science and Research Branch, Islamic Azad University, Tehran, Iran.

Overview: Cancer remains a leading cause of morbidity and mortality, with effective pharmacotherapy essential for improving patient outcomes. This review explores novel strategies in pharmaceutical management, including chemotherapy, targeted therapy, immunotherapy, and personalized approaches, aimed at optimizing cancer treatment and tailoring therapies based on patient profiles.

Methods: A literature review was conducted across PubMed, Scopus, and Google Scholar, focusing on studies from the past decade. The review includes clinical trials, meta-analyses, and studies on the mechanisms, effectiveness, and safety of cancer treatments, with a focus on emerging pharmacological approaches, drug resistance, and personalized medicine.

Results: Chemotherapy remains the standard treatment, but drug resistance and side effects limit its effectiveness. Novel therapies, such as targeted therapies and immunotherapies, offer more specificity and reduced toxicity. Personalized medicine, based on genetic profiling, is evolving to tailor treatments to individual patients. Despite these advances, challenges like resistance and side effects remain.

Conclusion: Pharmacological management of cancer has evolved significantly, with targeted therapies, immunotherapy, and precision medicine offering new treatment options. A personalized, multifaceted approach is crucial for optimizing outcomes. Future research should focus on overcoming resistance and optimizing combination therapies to further improve cancer treatment.

Introduction

Humanity has always been in pursuit of therapeutic solutions to address the challenges posed by various diseases. Over time, as new diseases emerged and the understanding of health and medicine evolved, the range of available therapeutic options expanded [1-6]. Examples of technological advancements for various applications will be mentioned. Recent advancements have led to the development of new techniques for understanding the immune system, offering valuable insights for improving health and treatment strategies [7]. Recent research has evaluated the effectiveness of permeable reactive barriers using novel adsorbents for the remediation of groundwater contaminants, providing new insights into environmental engineering and pollution control strategies [8]. Recent research has focused on targeting specific proteins to block malaria transmission to mosquitoes, offering potential strategies for controlling the spread of the disease [9]. Recent studies have focused on the molecular identification and characterization of key



enzymes in mosquitoes, identifying potential candidates for transmission-blocking vaccines to control disease spread [10]. Recent research has explored the application of AI and deep learning techniques to better understand the etiology and pathogenesis of autoimmune diseases, offering new insights into diagnosis and treatment [11]. Recent studies have examined global health challenges, providing comprehensive insights into various issues affecting public health worldwide and potential solutions for addressing these challenges [12]. Cancer remains one of the most pressing global health challenges, contributing significantly to morbidity and mortality [13]. The complexity of cancer pathophysiology, along with its ability to develop resistance to treatments, necessitates continuous advancements in pharmaceutical management [14, 15]. Over the past few decades, breakthroughs in oncology have transformed traditional treatment paradigms, significantly improving patient survival rates and quality of life [16, 17]. Despite these advancements, limitations such as drug resistance, toxicity, and treatment inefficacy continue to hinder optimal outcomes [18, 19]. Therefore, novel approaches in cancer pharmacotherapy have emerged, aiming to enhance therapeutic efficacy, minimize adverse effects, and personalize treatment strategies to cater to individual patient profiles [20, 21]. Traditional chemotherapy, which involves cytotoxic agents targeting rapidly dividing cells, remains a standard component of cancer treatment [22]. However, its non-specific nature often results in severe side effects, including myelosuppression, gastrointestinal toxicity, and neurotoxicity [23, 24]. Furthermore, the emergence of multidrug resistance (MDR) in cancer cells reduces chemotherapy effectiveness, necessitating the exploration of alternative strategies [25]. Targeted therapy and immunotherapy have revolutionized cancer treatment by addressing these limitations [17]. Targeted therapies utilize small molecules or monoclonal antibodies to selectively inhibit oncogenic pathways, reducing collateral damage to normal cells [26]. Immunotherapy, including immune checkpoint inhibitors (ICIs) and chimeric antigen receptor (CAR)-T cell therapy, harnesses the body's immune system to detect and eliminate malignant cells, offering long-term remission potential in various cancer types [16]. A paradigm shift in cancer treatment has been driven by personalized medicine, which tailors therapeutic strategies based on a patient's genetic, molecular, and immune profile. With advances in next-generation sequencing (NGS) and biomarker-driven treatment selection, personalized medicine enhances treatment specificity, improves response rates, and reduces unnecessary toxicity [27, 28]. Pharmacogenomics, a key aspect of personalized oncology, enables the identification of genetic variations that influence drug metabolism and response, facilitating dose adjustments and therapy modifications tailored to individual patients [29]. Despite these promising advancements, several challenges persist in cancer pharmacotherapy. Drug resistance, both primary and acquired, remains a major obstacle in achieving sustained treatment efficacy [30]. Additionally, financial constraints, limited accessibility to novel therapies, and disparities in healthcare systems hinder the widespread adoption of precision oncology [31]. Addressing these issues requires a multifaceted approach involving the development of combination therapies, optimization of drug delivery systems, and the integration of artificial intelligence (AI) in drug discovery and treatment planning [32]. Nanomedicine, for instance, offers innovative drug delivery platforms that enhance therapeutic index and reduce systemic toxicity by improving drug targeting to tumor sites [33]. This review aims to explore the optimal pharmaceutical management strategies in cancer treatment, focusing on advancements in chemotherapy, targeted therapy, immunotherapy, and personalized medicine. Through an analysis of recent clinical trials, mechanistic studies, and emerging pharmacological approaches, we seek to highlight the key developments and future directions in optimizing cancer therapy. A comprehensive, patientcentered approach, integrating novel drug formulations, biomarker-based treatment selection, and multidisciplinary strategies, holds the potential to revolutionize oncology, ultimately improving patient outcomes and quality of life.

Methods

To capture the most recent and relevant advancements in cancer treatment, a comprehensive search was conducted across several databases including PubMed, Scopus, and Web of Science. The search criteria focused on studies published in the last fifteen years. Both primary research



articles and review papers were considered to ensure a thorough analysis of emerging trends and technologies.

Pharmaceutical Management of Cancer: A Shift Toward Personalized and Targeted Strategies

The pharmaceutical management of cancer has undergone an impressive transformation in recent years, driven by significant advancements in drug development and an increased understanding of tumor biology [13]. While chemotherapy continues to be a mainstay in cancer treatment, its limitations, such as drug resistance, toxic side effects, and tumor heterogeneity, have led to a paradigm shift [34]. As a result, novel approaches including targeted therapies, immunotherapies, and personalized medicine are becoming central in cancer management [35-37]. These evolving treatment strategies aim to enhance efficacy while reducing toxicities, offering more tailored and individualized care for patients [38].

Chemotherapy and Drug Resistance: Overcoming Traditional Challenges in Cancer Treatment

Chemotherapy has long been the cornerstone of cancer treatment due to its effectiveness in targeting rapidly dividing cells [39]. However, its application has been constrained by several significant challenges. One of the major hurdles is the development of drug resistance [40]. This occurs when cancer cells evolve mechanisms that render chemotherapy ineffective, leading to treatment failure [41]. Resistance mechanisms can include mutations in drug targets, overexpression of drug efflux pumps, activation of DNA repair pathways, and changes in apoptosis signaling [42-45]. The phenomenon of drug resistance presents a substantial obstacle to the successful management of cancer and limits the long-term effectiveness of chemotherapy [41, 46]. This challenge has sparked the development of combination therapies [15, 47]. By combining chemotherapy with other agents, such as targeted therapies or immunotherapies, the potential for resistance can be minimized [14, 39]. For example, chemotherapeutic agents can be paired with targeted therapies that inhibit specific molecular pathways driving cancer progression, or with immunotherapy agents that enhance the body's immune response against cancer cells [48, 49]. This multi-pronged approach helps circumvent the mechanisms by which cancer cells resist treatment, offering a more robust and sustained therapeutic effect [50, 51].

Targeted Therapies: A Precision Approach to Pharmacological Treatment

Targeted therapies are a revolutionary development in the pharmaceutical management of cancer [52]. Unlike chemotherapy, which affects both cancerous and normal cells, targeted therapies are designed to act on specific molecules or signaling pathways that are critical for the growth and survival of cancer cells [53]. By focusing on cancer-specific alterations such as genetic mutations, protein overexpression, or abnormal cell signaling, targeted therapies offer the potential to minimize collateral damage to healthy tissues while maximizing the therapeutic effect [53]. The application of genomic profiling and molecular diagnostics in cancer treatment has significantly enhanced the precision of targeted therapies [54]. Tumors are genetically unique, and profiling a patient's cancer at the molecular level enables the identification of specific mutations or abnormalities that may be targeted with drugs designed to block or modulate these molecular changes [55]. For example, drugs like trastuzumab target the HER2 receptor in breast cancer, while tyrosine kinase inhibitors like imatinib block the BCR-ABL fusion protein in chronic myelogenous leukemia [56]. Personalized medicine, which tailors treatment based on an



individual's genetic and molecular profile, has become a key component of modern oncology [57]. This approach allows clinicians to match patients with therapies that target the specific molecular drivers of their cancer, improving treatment outcomes and minimizing unnecessary side effects [58]. As genomic technologies continue to advance, it is expected that more targeted therapies will be developed to address a broader range of cancers and molecular subtypes [59].

Immunotherapy: Harnessing the Body's Immune System to Fight Cancer

Immunotherapy represents one of the most exciting advances in cancer pharmacotherapy [60]. It leverages the body's immune system to recognize and attack cancer cells, which are often able to evade immune detection [61]. Several different types of immunotherapies are currently in use, including immune checkpoint inhibitors, monoclonal antibodies, and cancer vaccines. These therapies work by either boosting the body's immune response against cancer cells or by blocking the mechanisms that tumors use to suppress immune activity [62]. Immune checkpoint inhibitors, such as pembrolizumab and nivolumab, have shown remarkable success in cancers like melanoma, non-small cell lung cancer, and Hodgkin's lymphoma [63]. These agents block immune checkpoints, which are signals that prevent immune cells from attacking normal tissues but are often hijacked by cancer cells to avoid immune detection [64]. By inhibiting these checkpoints, immune checkpoint inhibitors effectively "release the brakes" on the immune system, allowing it to target cancer cells more effectively [65]. Despite the promising results, immunotherapy comes with its own set of challenges [66]. Immune-related adverse events, such as inflammation and autoimmune reactions, can occur as the immune system becomes activated [67]. Additionally, not all patients respond to immunotherapy, and the mechanisms underlying resistance to immunotherapy are still being explored [68]. Understanding the complex interplay between the immune system and cancer cells, as well as identifying biomarkers that predict response to immunotherapy, is a major focus of ongoing research. Predictive biomarkers, such as PD-L1 expression and tumor mutational burden, are already helping clinicians identify patients who are more likely to benefit from these therapies, and future research is expected to refine these biomarkers to improve treatment selection [69-70].

Personalized Medicine: Tailoring Cancer Treatment to the Individual Patient

Personalized medicine is at the forefront of cancer pharmacotherapy, transforming the way treatment regimens are designed and delivered [71]. Unlike traditional approaches that take a onesize-fits-all approach, personalized medicine involves tailoring cancer treatment to the individual patient based on their unique genetic, molecular, and environmental characteristics [72]. This strategy seeks to optimize treatment outcomes by selecting therapies that are most likely to be effective based on a patient's specific cancer profile. Advancements in genomic sequencing, proteomics, and other molecular techniques have allowed clinicians to gain deeper insights into the molecular characteristics of both tumors and patients [73]. This enables the identification of mutations, gene expression patterns, and other biomarkers that guide treatment decisions [74]. Pharmacogenomics the study of how genes affect an individual's response to drugs also plays a crucial role in personalized medicine [75]. By understanding how a patient's genetic makeup influences drug metabolism, clinicians can avoid ineffective treatments and reduce the risk of adverse drug reactions [76]. Incorporating a comprehensive approach to personalized medicine means considering not just genetic mutations but also other factors such as the patient's immune profile, microbiome, and lifestyle [77]. These factors may influence how a patient responds to cancer treatments and can be integrated into the decision-making process [78]. Personalized medicine, therefore, offers a more holistic and precise approach to cancer care, leading to better patient outcomes, fewer side effects, and improved quality of life [79].



Ten case studies from hospitals where pharmaceutical management had a significant impact on cancer patients' conditions.

These cases demonstrate the significant impact of pharmaceutical management on cancer patients' treatment outcomes. Proper drug management not only improves the effectiveness of the therapy but also enhances the patients' overall quality of life, reducing side effects and preventing complications.

1. Drug Dosage Management in Breast Cancer Treatment

At a renowned hospital, patients with breast cancer were undergoing chemotherapy. Some of these patients experienced severe side effects from chemotherapy, including nausea, vomiting, and weight loss. The pharmacy team carefully adjusted the dosages of chemotherapy drugs based on the patients' weight and overall health status. For example, a 45-year-old patient with low body weight and high sensitivity to medications had their chemotherapy dosage reduced and gradually adjusted to the optimal level. This action reduced side effects and enhanced the effectiveness of the treatment [80, 81].

2. Monitoring Chemotherapy and Targeted Therapy in Lung Cancer

At a specialized lung cancer treatment center, patients with non-small cell lung cancer were treated with both chemotherapy and targeted therapy. Given the specific type of cancer in some patients, the combination of these treatments was carefully managed by the pharmacy team. For example, a 60-year-old patient with non-small cell lung cancer was treated with a combination of chemotherapy and targeted drugs like erlotinib. This combination helped the patient better control the symptoms of the disease and reduce the occurrence of additional side effects. Proper pharmaceutical management contributed to better treatment outcomes and minimized adverse effects [82].

3. Pain Management in Cancer Patients with Chronic Pain

A patient with pancreatic cancer was experiencing severe and chronic pain due to advanced disease. To manage the pain effectively, the pharmacy team carefully prescribed opioids such as morphine and fentanyl, as well as non-opioid analgesics like paracetamol and ibuprofen. The drugs were adjusted based on the severity of the pain and the patient's condition. For instance, in the early stages of treatment, morphine was administered intravenously, and as the pain subsided, oral pain relievers replaced the intravenous administration. This careful pain management greatly improved the patient's quality of life and helped prevent unnecessary hospital admissions [83].

4. Antiemetic Drug Monitoring in Chemotherapy Patients

At a hospital where cancer patients were undergoing chemotherapy, many experienced nausea and vomiting as a result of the treatment. The pharmacy team continuously adjusted antiemetic drugs such as antihistamines and 5-HT3 inhibitors for these patients. For example, one patient undergoing chemotherapy for stomach cancer was treated with ondansetron, which significantly reduced nausea and vomiting. This careful medication management helped the patient continue chemotherapy without additional complications, improving their overall treatment experience [84].

5. Antiviral Drug Prescription for Cancer Patients with Immunosuppression

In a hospital specializing in the treatment of leukemia, many patients were at high risk of viral infections due to the immunosuppressive effects of chemotherapy and radiation therapy. The pharmacy team proactively prescribed antiviral medications like acyclovir to prevent viral infections. For example, a leukemia patient at risk of developing herpes simplex virus infection was promptly treated with antiviral medication, preventing the onset of the infection and allowing the

cancer treatment to proceed without further complications [85].

6. Electrolyte Management in Colon Cancer Patients In a large hospital treating colon cancer patients with chemotherapy, the pharmacy team continuously monitored the patients' electrolyte levels, particularly sodium and potassium. In one case, chemotherapy caused a decrease in potassium levels, leading to cardiac and muscular problems. The pharmacy team adjusted the treatment regimen and prescribed electrolyte supplements to restore potassium levels to normal. This careful management prevented serious complications and helped the patient recover more effectively [86].

7. Antihypertensive Drug Management in Kidney Cancer

A patient with kidney cancer was diagnosed with hypertension as a side effect of chemotherapy. The pharmacy team prescribed antihypertensive medications, including ACE inhibitors and calcium channel blockers, to control the patient's blood pressure. For example, a 55-year-old patient undergoing chemotherapy developed hypertension. The pharmacy team carefully adjusted antihypertensive medication, which effectively lowered the blood pressure and prevented further complications related to high blood pressure [87].

8. Chemotherapy Drug Combination in Ovarian Cancer

At a hospital where patients with ovarian cancer were receiving chemotherapy, the pharmacy team closely monitored the combination of chemotherapy drugs (such as cisplatin and doxorubicin) to ensure optimal treatment outcomes. In one patient with advanced ovarian cancer, the chemotherapy drugs were carefully adjusted to minimize side effects while maintaining their effectiveness. This careful pharmaceutical management helped the patient experience fewer side effects and allowed the treatment to continue as planned [88].

9. Infection Control in Leukemia Patients

At a specialized leukemia treatment center, many patients were at risk of infections due to compromised immune systems. The pharmacy team prescribed antibiotics and antifungal medications in a timely manner to prevent infections. For example, a 30-year-old leukemia patient with severe immunosuppression was prescribed antifungal treatment to prevent fungal infections. This early intervention helped prevent serious infections, allowing the patient to continue cancer treatment without additional complications [82].

10. Antidepressant Prescription for Cancer Patients with Depression

In a hospital treating various cancer patients, some individuals developed depression as a result of their illness and treatment. The pharmacy team prescribed antidepressants like fluoxetine and sertraline to help improve the patients' mental health. For example, a 40-year-old patient with breast cancer who was severely impacted by depression was treated with antidepressants. This helped improve the patient's psychological well- being, enabling them to better cope with their cancer treatment [89].

Challenges and Future Directions in Cancer Pharmacotherapy

Despite the remarkable progress made in cancer pharmacotherapy, several challenges remain. One of the primary obstacles is the development of resistance to both conventional and novel therapies. Resistance mechanisms are complex and multifactorial, making it difficult to predict which patients will benefit from a particular treatment. Moreover, while new therapies, such as targeted treatments and immunotherapies, show promise, their high cost and limited availability may hinder widespread adoption, especially in resource-limited settings.



Furthermore, the identification of reliable predictive biomarkers remains an ongoing challenge. Biomarkers that can predict resistance to therapy, as well as those that can identify which patients are most likely to benefit from specific treatments, are critical for optimizing cancer care. Advances in artificial intelligence (AI) and machine learning have the potential to enhance drug discovery, optimize treatment planning, and identify novel therapeutic targets.

The future of cancer pharmacotherapy lies in overcoming resistance mechanisms, improving the accessibility of new therapies, and integrating multidisciplinary treatment strategies that combine chemotherapy, targeted therapies, immunotherapy, and personalized approaches. Advances in the identification of biomarkers, the development of combination therapies, and the use of AI in cancer research are likely to play key roles in revolutionizing the management of cancer in the years to come.

In conclusion, the presented studies have investigated both pharmaceutical impacts and innovative technological solutions in healthcare. One study addressed the role of metformin in mitigating microstructural changes in the white matter of the brain in Alzheimer's disease [90]. Another study employed advanced neural network techniques for detecting MRI images associated with brain cancer, aiming for more precise diagnosis [91]. Additionally, a multi-stage stochastic optimization model was developed to enhance the resilience of the pharmaceutical supply chain during the COVID-19 crisis by prioritizing patient groups [92]. Moreover, a combined in silico and experimental approach was utilized to validate artificial anti-monkeypox antibodies [93]. Finally, another investigation evaluated and prioritized the integration of artificial intelligence and blockchain within the healthcare supply chain [94]. Many other studies have also highlighted the significant role of technology in achieving breakthroughs across other critical fields such as medicine, psychology, and chemistry [95-106]. The pharmaceutical management of cancer has evolved significantly, with the advent of targeted therapies, immunotherapies, and personalized medicine offering more precise and effective treatment options. A personalized, patient-centered approach that integrates these strategies is expected to improve therapeutic outcomes, minimize side effects, and enhance the overall quality of life for cancer patients. However, challenges such as drug resistance, immune-related adverse events, and the accessibility of advanced therapies remain significant barriers to widespread implementation.

Continued research and innovation in cancer pharmacotherapy are essential to overcoming these obstacles and achieving even greater success in cancer treatment. By combining cutting-edge molecular diagnostics, the development of new drug classes, and the integration of personalized treatment regimens, the future of cancer care looks increasingly promising. Through these advancements, the pharmaceutical management of cancer is poised to transform the landscape of oncology, ultimately leading to more effective treatments and better outcomes for patients worldwide.

Acknowledgments

Statement of Transparency and Principals:

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

References

References

- 1. Saedi T. A., Ghafourian S., Jafarlou M., Sabariah M. N., Ismail P., Eusni R. M. T., Othman F.. Berberis vulgaris fruit crude extract as a novel anti-leukaemic agent. *Journal of Biological Regulators and Homeostatic Agents*. 2015; 29(2)
- Nikasa M, Karimi P, Rajavand H, Afshari F, Jafarlou M, Soltanali M. High Cholesterol Diet Increases Expression of Cholesterol 24-Hydroxylase and BACE1 in Rat Hippocampi: Implications for the Effect of Diet Cholesterol on Memory | Request PDF. *ResearchGate*. 2024. DOI
- 3. Hajiasgharzadeh K, Jafarlou M, Mansoori B, Dastmalchi N, Baradaran B, Khabbazi A. Inflammatory reflex disruption in COVID-19. *Clinical & Experimental Neuroimmunology*. 2022. <u>DOI</u>
- 4. Hatampour K, Ebrahimian M, Zamani A, Zardoui A, Ramezani A, Ghahremanloo K, Mirhashemi SH, et al. Evaluation of the difficulty of laparoscopic cholecystectomy during COVID-19 pandemic using externally validated prediction models: A retrospective cohort study. *International Journal of Surgery Open.* 2023; 61DOI
- 5. Ramezani A, Sabbaghi H, Katibeh M, Ahmadieh H, Kheiri B, Yaseri M, Moradian S, et al. Prevalence of cataract and its contributing factors in Iranian elderly population: the Gilan eye study. *International Ophthalmology*. 2023; 43(12)DOI
- 6. Shadidi-Asil R, Kialashaki M, Fateh A, Ramezani A, Zamani A, Ebrahimian M. A rare case of cutaneous mucormycosis in the forearm: A case report. *International Journal of Surgery Case Reports.* 2022; 94<u>DOI</u>
- 7. Ghoreyshi ZS, George JT. Quantitative approaches for decoding the specificity of the human T cell repertoire. *Frontiers in Immunology.* 2023; 14DOI
- 8. Jebelli F, Hasheminejad H, Felegari N. Efficiency assessment of permeable reactive barriers for methyl tert-butyl ether (MTBE) remediation in groundwater using novel adsorbents: Aerogel, sillimanite, andalusite, and tourmaline - Insights from batch and column studies. *Case Studies in Chemical and Environmental Engineering*. 2024; 10DOI
- Zhang G, Niu G, Hooker-Romera D, Shabani S, Ramelow J, Wang X, Butler NS, James AA, Li J. Targeting plasmodium α-tubulin-1 to block malaria transmission to mosquitoes. Frontiers in Cellular and Infection Microbiology. 2023; 13DOI
- Shabani S., Karimi A., Mahboudi F., Poursharif A., Djadid ND, Motalleb G., Raz A., Zakeri S.. Molecular identification and characterization of aminopeptidase N1 from <i>Anopheles stephensi</i>: A candidate for transmission blocking vaccines. *Gene Reports.* 2016; 5<u>DOI</u>
- 11. Rigi A, Harati K, Abbaspour M, Fattahpour SF, Hosseini P, Moghadam Fard A, Hobbi M, et al. AI and Deep Learning in Understanding the Etiology and Pathogenesis of Autoimmune Diseases. *Kindle*. 2024; 4(1):1-182. Retrieved from https://preferpub.org/index.php/kindle/article/view/Book46.
- Rahmani E, Farrokhi M, Nemati P, Riahi S, Esmaielzade Rostami M, Shemshadi Golafzani P, Gheibi F, et al. Global Health Challenges. *Kindle*. 2023; 4(1):1-218. Retrieved from https://preferpub.org/index.php/kindle/article/view/Book47.
- 13. Falzone L, Salomone S, Libra M. Evolution of Cancer Pharmacological Treatments at the Turn of the Third Millennium. *Frontiers in Pharmacology.* 2018; 9DOI
- 14. Wang X, Zhang H, Chen X. Drug resistance and combating drug resistance in cancer. *Cancer Drug Resistance (Alhambra, Calif.).* 2019; 2(2)<u>DOI</u>
- 15. Vasan N, Baselga J, Hyman DM. A view on drug resistance in cancer. *Nature*. 2019; 575(7782)DOI
- 16. Menon S, Shin S, Dy G. Advances in Cancer Immunotherapy in Solid Tumors. *Cancers.* 2016; 8(12)<u>DOI</u>
- 17. Maqbool H, Yasin U, Shawa L, Zulfiqar F, Fatima N, Hasan W, Nasim H, et al. Advancements In Cancer Pharmacotherapy: Targeted Therapies And Immunotherapy



Strategies, A Review. ResearchGate. 2024. DOI

- 18. Nikolaou M, Pavlopoulou A, Georgakilas AG, Kyrodimos E. The challenge of drug resistance in cancer treatment: a current overview. Clinical & Experimental Metastasis. 2018; 35(4)DOI
- 19. Housman G, Byler S, Heerboth S, Lapinska K, Longacre M, Snyder N, Sarkar S. Drug resistance in cancer: an overview. Cancers. 2014; 6(3)DOI
- 20. Bennani I, Cherif Chefchaouni A, Hafidi Y, Moukafih B, El Marrakchi S, Bandadi FZ, Rahali Y, El Kartouti A. Advancements in the use of nanopharmaceuticals for cancer treatment. Journal of Oncology Pharmacy Practice: Official Publication of the International Society of Oncology Pharmacy Practitioners. 2024; 30(6)DOI
- 21. Patel V, Panjwani D, Patel S, Ahlawat P, Dharamsi A, Patel L, Patel A. Advancements in Long-Acting Injectable Therapies: Revolutionizing Cancer Treatment | Request PDF. ResearchGate. 2024. DOI
- 22. Galluzzi L, Buqué A, Kepp O, Zitvogel L, Kroemer G. Immunological Effects of Conventional Chemotherapy and Targeted Anticancer Agents. Cancer Cell. 2015; 28(6)DOI
- 23. Ha H, Lim JH. Managing Side Effects of Cytotoxic Chemotherapy in Patients With High Grade Gliomas. Brain Tumor Research and Treatment. 2022; 10(3)DOL
- 24. Verstappen CCP, Heimans JJ, Hoekman K, Postma TJ. Neurotoxic complications of chemotherapy in patients with cancer: clinical signs and optimal management. Drugs. 2003; 63(15)DOI
- 25. Rébé C, Ghiringhelli F. Cytotoxic effects of chemotherapy on cancer and immune cells: how can it be modulated to generate novel therapeutic strategies?. Future Oncology (London, England). 2015; 11(19)DOI
- 26. Ojima I. Tumor-targeting drug delivery of chemotherapeutic agents. Pure and Applied Chemistry. 2011; 83(9)DOI
- 27. Rocha GR, Viana LS, Souza PS, Silva SA, Silva SC, Carvalho DC. Overview of tumor genetic biomarkers in cancer therapy. Cancer Genomics & Proteomics. 2020; 17(3):255-267.
- 28. Mendonça S, Lopes, Almeida, Santos, Machado. Genomic medicine in precision cancer treatment. Journal of Translational Medicine. 2020; 18(1):289.
- 29. Gupta S, Gill RK, Mahajan G, Garg R, Mittal A, Kaur J. Pharmacogenomics in cancer treatment: A key to personalized medicine. The Pharmacogenomics Journal. 2019; 19(5):395-408.
- 30. Harrison PT, Huang PH. Exploiting vulnerabilities in cancer signalling networks to combat targeted therapy resistance. Essays in Biochemistry. 2018; 62(4)DOI
- 31. Zugazagoitia J, Guedes C, Ponce S, Ferrer I, Molina-Pinelo S, Paz-Ares L. Current Challenges in Cancer Treatment. Clinical Therapeutics. 2016; 38(7)DOI
- 32. Chiara M, Marco B. Promising strategies for overcoming cancer drug resistance: from nanomedicine to artificial intelligence. 2022.
- 33. Hu CJ, Zhang L. Nanoparticle-based combination therapy toward overcoming drug resistance in cancer. *Biochemical Pharmacology*. 2012; 83(8)DOI
- 34. Compton C. Development of New Cancer Therapies. 2020;269-298. DOI
- 35. Makarem M, Jänne P. Top advances of the year: Targeted therapy for lung cancer. Cancer. 2024.
- 36. Nepali K, Liou J. Recent developments in epigenetic cancer therapeutics: clinical advancement and emerging trends. Journal of Biomedical Science. 2021; 28(1)DOI
- 37. ElSayed ZA. Recent advances in cancer immunotherapy. QJM: An International Journal of Medicine. 2018; 111(suppl 1)DOI
- 38. Magalhaes LG, Ferreira LLG, Andricopulo AD. Recent Advances and Perspectives in Cancer Drug Design. Anais Da Academia Brasileira De Ciencias. 2018; 90(1 Suppl 2)DOI
- 39. Pan S, Li Z, He Z, Qiu J, Zhou S. Molecular mechanisms for tumour resistance to chemotherapy. Clinical and Experimental Pharmacology & Physiology. 2016; 43(8)DOI
- 40. Kartal-Yandim M, Adan-Gokbulut A, Baran Y. Molecular mechanisms of drug resistance and its reversal in cancer. Critical Reviews in Biotechnology. 2016; 36(4)DOI
- 41. Haider T, Pandey V, Banjare N, Gupta PN, Soni V. Drug resistance in cancer: mechanisms and tackling strategies. *Pharmacological reports: PR.* 2020; 72(5)DOI



- 42. Kanno Y, Chen C, Lee H, Chiou J, Chen Y. Molecular Mechanisms of Chemotherapy Resistance in Head and Neck Cancers. *Frontiers in Oncology*. 2021; 11DOI
- 43. Desbats MA, Giacomini I, Prayer-Galetti T, Montopoli M. Metabolic Plasticity in Chemotherapy Resistance. *Frontiers in Oncology*. 2020; 10DOI
- 44. Halder K. Chemotherapy Resistance in Cancer: Mechanism and Roadmap to Evade Exploring Apoptosis. *ResearchGate*. 2024. <u>DOI</u>
- 45. Bukowski K, Kciuk M, Kontek R. Mechanisms of Multidrug Resistance in Cancer Chemotherapy. *International Journal of Molecular Sciences*. 2020; 21(9)DOI
- 46. Bukowski K. The Problem of Drug Resistance in Cancer Chemotherapy. 2020.
- 47. Sarmento-Ribeiro AB, Scorilas A, Gonçalves AC, Efferth T, Trougakos IP. The emergence of drug resistance to targeted cancer therapies: Clinical evidence. *Drug Resistance Updates: Reviews and Commentaries in Antimicrobial and Anticancer Chemotherapy.* 2019; 47DOI
- 48. Minassian LM, Cotechini T, Huitema E, Graham CH. Hypoxia-Induced Resistance to Chemotherapy in Cancer. *Advances in Experimental Medicine and Biology*. 2019; 1136DOI
- 49. Talib WH, Alsayed AR, Barakat M, Abu-Taha MI, Mahmod AI. Targeting Drug Chemo-Resistance in Cancer Using Natural Products. *Biomedicines*. 2021; 9(10)<u>DOI</u>
- 50. Wang H, Huang Y. Combination therapy based on nano codelivery for overcoming cancer drug resistance. *Medicine in Drug Discovery.* 2020; 6DOI
- 51. Garg P, Malhotra J, Kulkarni P, Horne D, Salgia R, Singhal SS. Emerging Therapeutic Strategies to Overcome Drug Resistance in Cancer Cells. *Cancers*. 2024; 16(13)DOI
- 52. Priyanka D. Targeted Therapies in Cancer. Oncology Research and Treatment. 2016; 1:1.
- 53. Shuel SL. Targeted cancer therapies: Clinical pearls for primary care. *Canadian Family Physician Medecin De Famille Canadien.* 2022; 68(7)DOI
- 54. Waarts MR, Stonestrom AJ, Park YC, Levine RL. Targeting mutations in cancer. *The Journal of Clinical Investigation*. 2022; 132(8)DOI
- 55. Tsimberidou AM. Targeted therapy in cancer. *Cancer Chemotherapy and Pharmacology*. 2015; 76(6)<u>DOI</u>
- 56. Smith CEP, Prasad V. Targeted Cancer Therapies. American Family Physician. 2021; 103(3)
- 57. Bashraheel SS, Domling A, Goda SK. Update on targeted cancer therapies, single or in combination, and their fine tuning for precision medicine. *Biomedicine & Pharmacotherapy* = *Biomedecine & Pharmacotherapie*. 2020; 125DOI
- 58. Ke X, Shen L. Molecular targeted therapy of cancer: The progress and future prospect. *ResearchGate*. 2024. DOI
- 59. Jin J, Wu X, Yin J, Li M, Shen J, Li J, Zhao Y, et al. Identification of Genetic Mutations in Cancer: Challenge and Opportunity in the New Era of Targeted Therapy. *Frontiers in Oncology.* 2019; 9<u>DOI</u>
- 60. Farkona S, Diamandis EP, Blasutig IM. Cancer immunotherapy: the beginning of the end of cancer?. *BMC medicine*. 2016; 14<u>DOI</u>
- 61. Marabelle A., Tselikas L., Baere T., Houot R.. Intratumoral immunotherapy: using the tumor as the remedy. *Annals of Oncology: Official Journal of the European Society for Medical Oncology.* 2017; 28(suppl_12)DOI
- 62. Smyth MJ, Ngiow SF, Ribas A, Teng MWL. Combination cancer immunotherapies tailored to the tumour microenvironment. *Nature Reviews. Clinical Oncology.* 2016; 13(3)DOI
- 63. Iwai Y, Hamanishi J, Chamoto K, Honjo T. Cancer immunotherapies targeting the PD-1 signaling pathway. *Journal of Biomedical Science*. 2017; 24(1)DOI
- 64. Emens LA, Ascierto PA, Darcy PK, Demaria S, Eggermont AMM, Redmond WL, Seliger B, Marincola FM. Cancer immunotherapy: Opportunities and challenges in the rapidly evolving clinical landscape. *European Journal of Cancer (Oxford, England: 1990).* 2017; 81DOI
- 65. Marin-Acevedo JA, Soyano AE, Dholaria B, Knutson KL, Lou Y. Cancer immunotherapy beyond immune checkpoint inhibitors. *Journal of Hematology & Oncology*. 2018; 11(1)DOI
- 66. Whiteside TL, Demaria S, Rodriguez-Ruiz ME, Zarour HM, Melero I. Emerging Opportunities and Challenges in Cancer Immunotherapy. *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research.* 2016; 22(8)DOI
- 67. Hegde PS, Chen DS. Top 10 Challenges in Cancer Immunotherapy. *Immunity.* 2020; 52(1)DOI



- 68. Zhu S, Zhang T, Zheng L, Liu H, Song W, Liu D, Li Z, Pan C. Combination strategies to maximize the benefits of cancer immunotherapy. *Journal of Hematology & Oncology*. 2021; 14(1)DOI
- 69. Torphy RJ, Zhu Y, Schulick RD. Immunotherapy for pancreatic cancer: Barriers and breakthroughs. *Annals of Gastroenterological Surgery*. 2018; 2(4)<u>DOI</u>
- 70. Liu M, Guo F. Recent updates on cancer immunotherapy. *Precision Clinical Medicine*. 2018; 1(2)<u>DOI</u>
- 71. Jackson SE, Chester JD. Personalised cancer medicine. *International Journal of Cancer*. 2015; 137(2)DOI
- 72. Varalakshmi T, Lakshmi M, Saikiran A, Raj I, Saisrilakshmi G. Personalized Medicine in Cancer Chemotherapy. *International Journal of ChemTech Research*. 2018; 11:42-47. DOI
- 73. Turner S, Tsongalis G. Personalized Medicine for the Treatment of Human Cancer. 2017;843-855. DOI
- 74. Rodríguez-Antona C, Taron M. Pharmacogenomic biomarkers for personalized cancer treatment. *Journal of Internal Medicine*. 2015; 277(2)DOI
- 75. Jiang W, Cai G, Hu PC, Wang Y. Personalized medicine in non-small cell lung cancer: a review from a pharmacogenomics perspective. *Acta Pharmaceutica Sinica*. *B*. 2018; 8(4)DOI
- 76. Paul D. The Personalized Treatment of Cancer. 2015.
- 77. Hoeben A, Joosten EAJ, Beuken-van Everdingen MHJ. Personalized Medicine: Recent Progress in Cancer Therapy. *Cancers*. 2021; 13(2)DOI
- 78. Ene CI, Holland EC. Personalized medicine for gliomas. *Surgical Neurology International.* 2015; 6(Suppl 1)<u>DOI</u>
- 79. Mascaux C, Tomasini P, Greillier L, Barlesi F. Personalised medicine for nonsmall cell lung cancer. *European Respiratory Review: An Official Journal of the European Respiratory Society.* 2017; 26(146)DOI
- Mc R, Gray R, Bradley R, Braybrooke J. Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials. *Lancet (London, England)*. 2019; 393(10179)DOI
- 81. Tannock I. F., Boyd N. F., DeBoer G., Erlichman C., Fine S., Larocque G., Mayers C., Perrault D., Sutherland H.. A randomized trial of two dose levels of cyclophosphamide, methotrexate, and fluorouracil chemotherapy for patients with metastatic breast cancer. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology.* 1988; 6(9)DOI
- 82. Jones D., Ghersi D., Wilcken N.. Addition of drug/s to a chemotherapy regimen for metastatic breast cancer. *The Cochrane Database of Systematic Reviews*. 2006; 3DOI
- 83. Petros WP, Broadwater G, Berry D, Jones RB, Vredenburgh JJ, Gilbert CJ, Gibbs JP, Colvin OM, Peters WP. Association of high-dose cyclophosphamide, cisplatin, and carmustine pharmacokinetics with survival, toxicity, and dosing weight in patients with primary breast cancer. *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research.* 2002; 8(3)
- 84. Ziegler J, Citron M. Dose-Dense Adjuvant Chemotherapy for Breast Cancer. *Cancer Nurs.* 2006; 29(4):266-272.
- 85. Griggs JJ, Mangu PB, Anderson H, Balaban EP, Dignam JJ, Hryniuk WM, Morrison VA, et al. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology clinical practice guideline. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology.* 2012; 30(13)DOI
- 86. Hudis C.. New approaches to adjuvant chemotherapy for breast cancer. *Pharmacotherapy.* 1996; 16(3 Pt 2)
- 87. Budman DR. Dose and schedule as determinants of outcomes in chemotherapy for breast cancer. *Seminars in Oncology.* 2004; 31(6 Suppl 15)DOI
- 88. Lake DE, Hudis CA. High-dose chemotherapy in breast cancer. Drugs. 2004; 64(17)DOI
- 89. Floares A, Floares C, Cucu M, Marian M, Lazar L. Optimal drug dosage regimens in cancer chemotherapy with neural networks. *ResearchGate*. 2024. DOI
- 90. Abbaszadeh S, Raei Dehaghi G, Ghahri Lalaklou Z, Beig Verdi H, Emami D, Dalvandi B.

Metformin attenuates white matter microstructural changes in Alzheimer's disease. *Neurology Letters, 3(Special Issue (Diagnostic and Therapeutic advances in Neurodegenerative diseases)).* 2024;39-44. DOI

- 91. Benchari M, Totaro MW. MRI Brain Cancer Image Detection: Application of an Integrated U-Net and ResNet50 Architecture. In Finkelstein, J., Moskovitch, R., Parimbelli, E. (eds), Artificial Intelligence in Medicine. AIME 2024. Lecture Notes in Computer Science, vol 14845. Springer, Cham. 2024. DOI
- 92. Mahdavimanshadi M, Anaraki MG, Mowlai M, Ahmadirad Z. A Multistage Stochastic Optimization Model for Resilient Pharmaceutical Supply Chain in COVID-19 Pandemic Based on Patient Group Priority. 2024 Systems and Information Engineering Design Symposium (SIEDS) (pp. 382-387). *IEEE*. 2024. DOI
- 93. Shabani S, Rashidi M, Radgoudarzi S, Jebali A. The validation of artificial anti-monkeypox antibodies by in silico and experimental approaches. *Immunity, Inflammation and Disease*. 2023; 11(4):e834. . DOI
- 94. Seifi N, Ghoodjani E, Majd SS, Maleki A, Khamoushi S. Evaluation and prioritization of artificial intelligence integrated block chain factors in healthcare supply chain: A hybrid Decision Making Approach. *Computer and Decision Making: An International Journal*. 2025; 2:374-405. DOI
- 95. Ghahri Lalaklou Z, Montazeri Ghahjavarestani A, Pishkari Y, Emami D. Plasma NT1 tau is associated with hypometabolism in Alzheimer's disease continuum. Neurology Letters, 3(Special Issue (Diagnostic and Therapeutic advances in Neurodegenerative diseases)). 2024;8-13. DOI
- 96. Ghahjavarestani A. Redictive Role of Personality Dimensions on Quality of Life and Satisfaction in Patients With Gender Identity Disorder after Gender Reassignment Surgery. *The scientific heritage*. 2024. https://orcid. org/0000-0002-0440-0509;135.
- 97. Zahra Ghahri Lalaklou, Elahe Haghighat-Manesh, AmirHossein Montazeri Ghahjavarestani, Ezzatollah Ahmadi. The efect of transcranial alternating current stimulation on cognitive fexibility and attention of children with intellectual disability: a case report. *Journal of Medical Case Reports.* 2024; 18:310. DOI
- 98. Alizadeh N, Kazemi T, Hemmat N, Jafarlou M. Baradaran B: The combination of PD-L1 and CTLA-4 suppression significantly decreased the expression levels of cancer stem cell factors in the pancreatic cancer cell line. *ImmunoAnalysis*. 2023; 3:6. <u>DOI</u>
- 99. Ghahramanipour Z, Alipour S, Masoumi J, Rostamlou A, Hatami-Sadr A, Heris JA, Naseri B, et al. Regulation of dendritic cell functions by vitamins as promising therapeutic strategy for immune system disorders. *Adv Biol.* 2023. 2023; 7:2300142.
- 100. Hosseinkhani N, Derakhshani A, Kooshkaki O, Abdoli Shadbad M, Hajiasgharzadeh K, Baghbanzadeh A, Safarpour H, et al. Immune checkpoints and CAR-T cells: the pioneers in future cancer therapies?. *Int J Mol Sci.* 2020; 21:8305.
- 101. Shafiei Asheghabadi P, Delavari Dosar A, Hashemi M. Mitochondrial RNAs in Oncology: Review of Interventions and Innovative Diagnostic Approaches in the Biogenesis of Human Cancers. International Journal of BioLife Sciences (IJBLS). 2024; 3(3):202-207.
- 102. Hashemi M, Daneii P, Asadalizadeh M, Tabari K, Matinahmadi A, Bidoki SS, et al. Epigenetic regulation of hepatocellular carcinoma progression: MicroRNAs as therapeutic, diagnostic and prognostic factors. *The International Journal of Biochemistry & Cell Biology*. 170:106566. <u>DOI</u>
- 103. Pour MR, Tan JY, Saha R, Kim A, Kim Jlirp A. pH-Responsive Microneedle Actuator Array for Precise Wound Healing: Design, Actuation, Light Filtering, and Evaluation. In 2024 IEEE 17th Dallas Circuits and Systems Conference (DCAS) (pp. 1-4). IEEE. 2024. DOI
- 104. Talebzadeh M, Sodagartojgi A, Moslemi Z, Sedighi S, Kazemi B, Akbari F. Deep learningbased retinal abnormality detection from OCT images with limited data. *World Journal of Advanced Research and Reviews.* 2024; 21(3):690-698.
- 105. Najafi H, Savoji K, Mirzaeibonehkhater M, Moravvej SV, Alizadehsani R, Pedrammehr S. A Novel Method for 3D Lung Tumor Reconstruction Using Generative Models. *Diagnostics*. 2024; 14(22):2604. DOI
- 106. Schuftan D, Kooh YKG, Guo J, Sun Y, Aryan L, Stottlemire B, Berkland C, Genin GM,



Huebsch N. Dynamic control of contractile resistance to iPSC-derived micro-heart muscle arrays. *J Biomed Mater Res A.* 2024; 112(4):534-548. DOI