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A comprehensive review of anticancer drug therapy: Advances and challenges

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Abstract
This review provides an overview of anticancer drug therapies, including their classifications, mechanism of action, and the evolution of treatment modalities. The review emphasizes the transition from traditional chemotherapeutic agents to targeted therapies with traditional chemotherapeutic agents, targeted therapies, immunotherapies, monoclonal antibodies, tyrosine kinase inhibitors, hormone therapies, and novel methods like CAR-T cell therapy and nanotechnology delivery systems. Anticancer drugs act through induce DNA damage, the role modulation of the cell cycle, inhibition of tumor.angiogenesis Despite of advancements in nextgeneration sequencing, To overcome these challenges, diverse strategies, including drug resistance and appropriate dosage, dosing and targeting to gain the benefit with minimal harm to the person through treatment. Anticancer drug delivery systems (DDS) and identifies new developments in strategies of molecular targeting and advances in drug delivery system. Advancements in personalized drug development, focusing on genomic profiling of tumors play role important to give better treatment and overcome of difficulties in cancer therapy. The reviews existing evidence on current innovative efforts and make modern treatment options more equally accessible to improve patient outcomes lives.
Keywords: Anticancer drug, chemotherapeutic agents, targeted therapies, immunotherapies

1. Introduction
Cancer is one of the most prevalent diseases worldwide, representing a major challenge and having profound effects on societies. Despite technological developments and therapeutic advances, it still has a significant impact on societies and the healthcare system. In addition, there is a significant difference in the extent to which people respond to anti-cancer drug treatments. Therefore, there are many organizations that play an important role in supporting projects that include improving the quality of treatments used in cancer treatment. It poses an ever-increasing threat to developing nations and claims 5.5 million lives each year, with the estimate set to rise to 8.9 million by 2030 (Kawahara et al., 2010; Cancer, 2023) [6, 22, 45]. The burden of the disease is most evident among the middle- and lower-income nations whose health systems are weakened by poor access to prevention, diagnosis, and treatment services ("Cancer", 2023). This overview will discuss the epidemiology, public health impact and current efforts to address cancer as one global health problem ("Cancer", 2023)[22, 45].

The second leading cause of death worldwide is cancer, and its incidence is increasing with aging populations and through lifestyle factors like tobacco smoking and poor diets. The burden of cancer falls disproportionately on the lower-and middle-income countries and identifies access and outcome disparities in healthcare (Jackman *et al*., 2024) [19].
The consequences of cancer reach beyond personal health, extending to communities and families and placing pressure on healthcare systems. Comprehensive public health measures through prevention, early diagnosis, and care as part of universal

health coverage is necessary for effective cancer control ("Cancer", 2023) [22, 45]. There are various initiatives across the globe working towards standardization of cancer care and increased availability of cancer treatment, especially in underprivileged areas. Cooperation among healthcare workers and communities is necessary in promoting cancer knowledge and care ("Cancer", 2023) [22, 45]. Even in light of increased cancer care and knowledge, there is still a lot to be done, mainly in regards to accessible care in various parts of the globe.

There are many strategies used in the treatment of cancer, including drug therapy, which is considered the most important treatment in the management and treatment of cancer cases, ranging from pain relief to treatments partially directed against cancer cells or tumor cells. Drug therapy is considered one of the basic medications in the treatment of cancer cases, especially in advanced cancer cases (Pont et al., 2021). [38, 61]. Using advances in genome and transcriptome studies, treatments can be tailored for each patient, maximizing therapeutic benefit. Direct visualization of drug activity in real-time is enabled through molecular imaging devices, e.g., PET and MRI, making drug delivery and uptake better. Even novel delivery mechanisms, e.g., liposomes and antibody-drug conjugates, are in development to ensure greater impact, making pharmacologic therapy an integral part of cancer therapy today (Asif, 2023). [2].

While surgery and radiation are first-line treatments, pharmacotherapy, especially chemotherapy, has been a primary approach. Advances in understanding cancer pathophysiology have led to the development of new options, including immune- and biological therapies. These therapies are now commonly used in combination with chemotherapy or as monotherapy, enhancing treatment efficacy and improving patient outcomes in managing the five most common cancers: lung, breast, prostate, colon, and skin (Gundy & Nguyen, 2017;Pont et al., 2021). [15].

The purpose of this review is to critically assess the newfound developments and current issues in anticancer drug therapy. As one of the predominant causes of death globally, the discovery of efficient and well-targeted therapy is necessary in enhancing the outcome in patients with cancer. The review aims to discuss the developments in anticancer drugs, ranging from traditional chemotherapeutic agents to targeted drugs, immunotherapies, and novel treatment methods like gene therapy and nanotechnology-mediated drug delivery systems.

2. Classification of anticancer drugs

There are several classifications of anticancer drugs that reflect their effects. One such classification is a two-tiered classification system, which proposes drugs based on their site of action—the tumor vasculature, the endocrine system, tumor cells, the molecular target, or the immune system. Other classifications predict a drug's effect based on its lipid binding affinity and molecular characterization (Gackowski *et al*., 2021) [13].. Plants, which contain most anticancer drugs, can be divided into four main categories: ribosome inhibitors, DNA-damaging drugs, histone deacetylase inhibitors, and mitosis inhibitors (Amin *et al*., 2009) [1].

Anticancer drugs may be classified by the site and mechanism of action, by chemical sources, and by pharmacological properties. The multidimensional classification is helpful in analyzing the therapeutic role and application of anticancer drugs in the treatment of cancer. Here are the major points regarding anticancer drug classification.

2.1 Site and Mechanism of Action

Anticancer drugs may exert action on distinct sites like the tumor cells, tumor vasculature, the immune system, or the endocrine system. The action mechanism usually takes place through targeting particular molecular pathways or structures on these sites (Ostios-García *et al*., 2024) [35, 58]. For instance, alkylating agents cross-link DNA strands to prevent DNA replication and RNA transcription and antimetabolites interfere with DNA or RNA formation by mimicking vital cellular molecules (Ogawa, 1997).

2.2 Chemical Origins

Anticancer drugs are further categorized by their source to include synthetic chemicals, natural products or natural compound derivatives. Plant compounds are an important source of anticancer agents owing to their relatively nontoxic nature and abundance (Amin *et al*., 2009) Some examples are plant alkaloids that interfere with the formation of microtubules and camptothecins which are able to block topoisomerase I and are both derived from nature (Ogawa, 1997) [34, 57].

2.3 Pharmacological Properties

The pharmacological classification includes the study of the anticancer drugs' lipophilicity and molecular descriptors that control drug activity and therapeutic action. Methods such as chromatography and chemometric evaluation are employed to make predictions concerning drug activity and to categorize them on this basis (Gackowski *et al*., 2021) [13]. Although the categorization of anticancer drugs offers an organized system to comprehend their application, it should be realized that the discovery and creation of drugs with novel action pathways continue to challenge the traditional classifications. Their emerging nature calls for an evolving and adaptive system of categorization able to include developing therapies and their individual features (Chen *et al*., 2024) [9].

2.4 Molecular targeting

The molecular targeting classification separates anticancer drugs into two categories: conventional chemotherapy and targeted therapy. Traditional chemotherapy uses cytotoxic agents that act on all dividing cells regardless of the type and produce major side effects. Targeted therapy acts on particular molecular targets related to the processes of cancer development and aims to be more specific with fewer harmful effects. The subsequent sections define these differences.

2.4.1 Conventional Chemotherapy

Mechanism of Action: Inhibits all proliferating cells, even healthy ones, and thus causes systemic toxicity. Examples of drugs: Alkylating agents, antimetabolites, and inhibitors of topoisomerase are general classes (Ostios-García *et al*., 2024) [35, 58]. Side Effects: Usually linked with nausea, alopecia, and immunosuppression through damage to healthy cells (Keefe & Stringer, 2010) [23, 46].

2.4.2 Targeted Therapy

Mechanism of Action: Targets specific molecular pathways or receptors used in the growth of cancer cells like EGFR and VEGFR. Drug Examples: Monoclonal antibodies and small-molecule tyrosine kinase inhibitors (Bicknell, 2005).

Advantages: Greater therapeutic window and fewer side effects since they spare normal cells (Keefe & Stringer, 2010) [23, 46]. Despite the major breakthrough in the treatment of cancer presented by targeted therapies, issues like drug resistance and the need to precisely select the patient are still major concerns that could affect the efficacy and use of these drugs in clinical practice (Min & Lee, 2022) [54, 31].

2.4.3 Cell cycle specificity

Anticancer drugs take advantage of the cell cycle's regulatory processes to selectively target anticancer drug action against cancer cells that frequently possess dysregulated proliferation. Knowing the particular phases of the cell cycle allows drugs to be designed to yield maximum efficacy with least damage to ordinary cells. The succeeding sections explain how anticancer drugs are specific in action. Cell Cycle Regulation Mechanisms. The cell cycle is regulated by cell cycle kinases (CDKs) and cyclins that govern transitioning through the phases (G1, S, G2, M)(Bai *et al*., 2017).

Cancer cells frequently bypass these regulatory points to cause uncontrolled growth and are thus ideal candidates for cell cycle-specific drugs (Patra *et al*., 2023) [36, 59]. Cell Cycle Phase-specific drug action, Some drugs like Adriamycin (ADR), and Etoposide (VP16), cause apoptotic action mainly in the S phase, whereas others like Prednisone (PRD), act in the G1 phase. Inhibitory screening with high throughput has allowed drugs with selective sensitivities to G1 or S/G2 phases to be identified so that treatment regimens can be designed to produce enhanced therapy (Johnson *et al*., 2021) [20].

2.4.4 Induction of apoptosis, DNA damage and angiogenesis inhibition

Anticancer drugs utilize several mechanisms to act on cancer cells mainly by inducing apoptosis, causing damage to DNA, and inhibiting angiogenesis. These actions are important to chemotherapy effectiveness since they cause malignant cell death and block the growth of tumors. The subsequent sections explain these operations in detail.

2.4.4.1 Apoptosis Induction

Anticancer drugs frequently induce apoptosis, programmed cell death, through the following pathways: 1. Caspase Activation: Cisplatin drugs trigger caspase activation leading to apoptosis in even enucleated cells, suggesting a cytoplasmic mechanism (Havelka *et al*., 2007) [16]. 2. Reactive Oxygen Species:There are many medications, including Doxorubicin, that play an important role in the production of ROS, which may lead to DNA damage and stimulate programmed cell death. 3. Signaling Pathways: There are many signaling pathways, including c-Jun/AP-1, that can play an important role in causing the death of drug-resistant cells through apoptosis events. This will guide us in dealing with the multiple aspects of signaling that cause programmed cell death (Kim et al., 2024). [24, 47].

2.4.4.2 DNA Damage

One of the ways in which anti-cancer drugs work is by directly damaging DNA. Examples of these drugs include doxorubicin and cisplatin that play an important role in the process of nuclear damage, which can lead to the occurrence of programmed cell death. There are factors that have a greater or more concentrated role in stimulating the process of programmed cell death (Mizutani, 2008)(Havelka et al., 2007). [16].

2.4.4.3 Angiogenesis Inhibition

One of the drug strategies in cancer treatment is angiogenesis inhibition (stabilize the formation of blood vessels), which leads to starving cancer cells and reducing their supply of food and oxygen to support the process of growth and spread of cancer cells. Conversely, some evidence indicates acute apoptosis is not necessarily the sole aim of anticancer treatments since some responses are independent of DNA damage and thus there is a requirement to study more the non-target effects (Havelka *et al*., 2007;Berndtsson, 2007) [16].

2.4.4.4. Modern Therapies and Targeted Approaches of Anticancer Drugs

The paradigm in oncology has shifted in the two decades past from cytotoxic chemotherapy to mechanism-oriented and targeting therapies. The newer approaches are aimed to enhance therapeutic effectiveness with decreased systemic toxicity. The major developments include monoclonal antibodies, tyrosine kinase inhibitors, checkpoint inhibitors, CAR-T cell therapy, and hormone-directed treatments.

2.5 Monoclonal Antibodies

Monoclonal antibodies are tailor-made proteins that seek out specific antigens located on cancer cells. They work through several distinct processes: receptor blocking, antibody-dependent cellular cytotoxicity (ADCC), and activation of the complement system.

a. Trastuzumab

Target: HER2 receptor:
Breast and stomach cancers: HER2-positive
Mechanism: Inhibits signaling through HER2 and triggers ADCC. Survival in HER2-positive breast cancer has been greatly enhanced by trastuzumab, particularly when given with chemotherapy (Gianni *et al*., 2022) [14].

b. Rituximab

Target: CD20 antigen
Cancer: Non-Hodgkin lymphomas and chronic lymphocytic leukemia
Mechanism: It induces apoptosis and brings about immune effector cell recruitment. Rituximab is still an anchor therapy in hematologic malignancies, presently being enhanced through biosimilar formulations and ADC versions (Cramer *et al*., 2021) [10].

2.6 Tyrosine Kinase Inhibitors (TKIs)

TKIs are small-molecule drugs that inhibit intracellular phosphorylation cascades responsible for tumor growth and survival.

a. Imatinib

Target: BCR-ABL fusion protein
Cancer: Chronic myeloid leukemia (C
Mechanism: Inhibition of the ABL kinase domain selectively. Imatinib converted CML from an invariably fatal condition to an acceptable one to manage, pioneering the age of precision oncology (Hochhaus *et al*., 2020) [18].

b. Erlotinib

Target: EGFR (Epidermal Growth Factor Receptor
Cancer: Non-small cell lung cancer (NSCLC
Mechanism: Inhibits EGFR tyrosine kinase activity, particularly in tumors with EGFR activating mutations. EGFR-directed TKIs such as erlotinib are now front-line therapy in EGFR-mutation NSCLC, although resistance mutations (e.g., T790M) are prevalent (Zhang *et al*., 2021) [3].

2.7 Immunotherapy

Immune checkpoint inhibitors re-establish the immune system's function to identify and destroy cancer cells. They are revolutionizing the therapy of the following solid tumors and hematologic malignancies:

a. PD-1/PD-L1 Inhibitors

Examples: Pembrolizumab, Nivolumab, Atezolizumab.
Mechanism: Block PD-1 receptor or its ligand PD-L1, restoring exhausted T cells. Checkpoint inhibitors demonstrated lasting responses in melanoma, NSCLC, and urothelial carcinoma (Ribas & Wolchok, 2018) [39, 62].

b. CTLA-4 Inhibitors

Example: Ipilimumab.
Mechanism: Activates T-cells by inhibiting the CTLA-4 inhibitory signal.
The use of CTLA-4 and PD-1 blockade together has worked better for advanced melanoma compared to using each alone, albeit with greater toxicity (Weber *et al*., 2021) [44, 67].

2.8 CAR-T Cell Therapy

Chimeric Antigen Receptor T-cell therapy entails engineering a patient's own T cells to receive genetic instructions to produce receptors that identify tumor antigens.
Examples: Tisagenlecleucel, Axicabtagene ciloleucel.
Uses: B-cell acute lymphoblastic leukemia, large B-cell lymphoma.
Mechanism: Redirects the T cells to identify and kill cancer cells. CAR-T therapy has demonstrated potential to cure refractory hematologic cancers but poses problems with manufacturing, expense, and application to solid tumors (June & Sadelain, 2018) [21].

2.9 Hormone Therapy

Hormone therapy is vital to the treatment of breast and prostate cancers that are hormone receptor-positive by inhibiting hormone production or binding to receptors.

a. Tamoxifen

Selective Estrogen Receptor Modulator (SERM) ER-positive breast cancer indication.
Mechanism: Antagonizes estrogen receptor in breast tissue. Tamoxifen has been an mainstay of treatment for decades and is particularly useful in premenopausal women (Early Breast Cancer Trialists' Collaborative Group [EBCTCG], 2019).

b. Aromatase Inhibitors

Examples include Anastrozole
Mechanism: Inhibit aromatase, reducing estrogen production in postmenopausal women. Aromatase inhibitors are superior to tamoxifen in preventing recurrence in postmenopausal breast cancer (Burstein *et al*., 2019) [5].

3. Drug Resistance in Cancer Therapy

Drug resistance is one of the biggest hurdles to successful treatment against cancer. Although therapies are initially effective, tumors frequently recur or progress through mechanisms that enable them to escape drug action. Intrinsic (existing prior to treatment) and acquired (emerging during treatment) resistance can be broadly defined and are controlled by an intricate system based on genetic, epigenetic, and environmental conditions.

3.1 Intrinsic vs. Acquired Resistance

Intrinsic resistance is the innate inability of a cancer to be treated with some therapy because of intrinsic molecular characteristics like lack of target expression or alternative signaling pathways. Acquired resistance occurs with therapy and with the passage of time through adaptation by tumor cells via mutation, selection, or cellular plasticity. For instance, triple negative breast cancers are usually intrinsically resistant to hormone therapy because there is no ER/PR receptor available, whereas NSCLC receiving EGFR inhibitors usually becomes resistant through secondary alterations like T790M (Chatterjee *et al*., 2021) [5].

3.2 Molecular Mechanisms of Resistance

a. Efflux Pumps

One of the major ways through which chemotherapeutic agents are evaded by cancer cells is by the mechanism of ATP-binding cassette (ABC) transporter overexpression, specifically by P-glycoprotein (ABCB1) and MRP1 (ABCC1). The efflux pumps decrease intracellular drug levels by particularly targeting drugs such as doxorubicin, paclitaxel, and vincristine. Efflux pump inhibition is still a therapeutic target, with clinical translation being problematic owing to toxicity and pump family redundancy.

b. The target gene mutations

Drugs become less effective when drug target mutations reduce binding efficacy. EGFR T790M, BCR-ABL T315I, and KRAS mutations are paradigmatic instances of resistance-conferring alterations. Immune checkpoint inhibitors may also develop resistance by way of JAK1/2 mutation-induced compromised interferon signaling. Developing genome-editing approaches and sequencing methods identify these alterations in real-time so that drug adjustments are made with precision (McCoach *et al*., 2020) [29].

C: Improved DNA Repair Systems

The resistance to DNA-damaging agents such as platinum drugs or PARP inhibitors may develop through reactivation or compensation of DNA repair pathways. BRCA-mutant tumors that are initially PARP inhibitor-sensitive may develop resistance through secondary BRCA reversion mutation or enhancement in homologous recombination repair (HRR). This has led to the emergence of combination therapies that target PARP and other DNA repair proteins (Liu *et al*., 2022) [27].

3.3 Role of the Tumor Microenvironment (TME)

The TME, made up of stromal cells, inflammatory cells, extracellular matrix and cytokines, serves an important function in facilitating tumour survival and resistance.
For instance, hypoxia has been shown to cause HIF-1α and induce drug resistance and radioresistance and promote angiogenesis. CAFs create factors leading to drug resistance

by paracrine signaling and extracellular matrix remodeling. Immunosuppressive cells (Tregs, MDSCs) within the TME suppress the efficacy of immuno-oncology therapies. Interventions against the TME, i.e., vasculature normalization or modulation of immune infiltration, are being intensively investigated in clinical trials (Hinshaw & Shevde, 2019) [17].

3.4. Side Effects and Toxicity of Anticancer Drugs: Clinical Implications and Quality of Life

Although highly effective, anticancer drugs are frequently accompanied by important adverse effects and toxicities that may directly affect short-term function, long-term health, and overall quality of life (QoL). Also, the type of treatment used, such as targeted drugs, immunotherapy, or traditional chemotherapy, and the adverse effects of these drugs can be avoided through factors related to the patient, such as concomitant diseases, the patient's condition, etc.

3.4 Typical Side Effects

a. **Nausea and Vomiting:** There are many chemotherapy treatments, like doxorubicin, cisplatin, and cyclophosphamide which have nausea and vomiting as side effects. The emetogenic risk depends on the drugs, ranging from high to low risk. Contemporary antiemetic regimens (NK1 antagonists, 5-HT3 antagonists, and corticosteroids) have decreased CINV incidence by quite an extent (Navari & Aapro, 2016) [33].

b. Alopecia (Hair Loss): Alopecia is prevalent with cytotoxic drugs such as taxanes and anthracyclines. Though it is reversible, it may be psychologically disturbing. Scalp cooling devices are found to reduce chemotherapy-related alopecia (Rugo *et al*., 2017) [40].

c. Bone Marrow Suppression: Myelosuppression is the dose-limiting toxicity of many cytotoxic agents, particularly the platinum compounds and the alkylating agents. It can lead to: Neutropenia-risk of increased infections, Anemia-decreased oxygen-carrying capacity and fatigue and Thrombocytopenia-risk of bleeding. Growth factor use (e.g., G-CSF), and dosing adjustments are routine measures to control myelosuppression (Smith *et al*., 2015) [42].

3.5 Long-term Toxicities

a. cardiotoxicity: Anthracyclines (such as doxorubicin) and drugs targeting HER2 (such as trastuzumab) are cardiotoxic and the cardiotoxicity can vary either from asymptomatic decrease in the ejection fraction to overt heart failure with irreversible damage to the heart muscle. Survival cohorts demonstrate that 20% or more of anthracycline-treated individuals develop some cardiac dysfunction within 5 years.

b. Neurotoxicity: It may manifest itself in the form of: Peripheral neuropathy (such as taxanes and platinum agents), Cognitive impairment ("chemo brain"), and CNS toxicity (with high-dose methotrexate or intrathecal therapy). Neurotoxicity can be long-lasting and extend to months or years and is particularly disabling in the elderly and seriously impairs daily function (Lavoie Smith *et al*., 2019) [19].

4. Strategies to Overcome Limitations in Cancer Therapy

There are many obstacles facing cancer treatment despite this great scientific and technological progress in confronting or treating cancer. Among these obstacles are the diversity of tumors, their high toxicity, and cell resistance. There are many methods used to improve the results of anti-cancer treatment and molecular targeting.

4.1 Combination Therapy

One of the strategies for treating cancer is combination therapy, which combines preventing the increase in cell resistance and increasing the effectiveness of treatment, combination of cytotoxic agents (such as FOLFOX in colon cancer) with chemotherapy (trastuzumab in breast cancer). In contemporary oncology, combinations of chemotherapy with immunotherapy or TKIs are commonly used (such as pembrolizumab and platinum chemotherapy in NSCLC). Combination regimens take advantage of synergy and are able to act against heterogeneity in tumors, albeit with the need to manage toxicities carefully (Vasan *et al*., 2019) [43].

4.2 Personalized Medicine and Pharmacogenomics

Personalized treatment focuses on utilizing genomic and molecular information to tailor treatment according to individual tumour properties and patient genetic makeup. Pharmacogenomics determines gene variants that modulate drug metabolism (such as TPMT and 6-mercaptopurine toxicity and UGT1A1 and irinotecan response). Molecular stratification with the use of NGS enables the identification of actionable mutations (such as EGFR, ALK, BRAF) to be used with target therapy. Doing so reduces trial-and-error, enhances outcomes, and reduces adverse events (Dienstmann *et al*., 2018) [11].

4.3 Nanotechnology in Drug Delivery

Nanomedicine enhances drug delivery through nanoscale carriers such as liposomes, dendrimers, and polymeric nanoparticles. Benefits include improved tumor targeting, enhanced drug solubility, reduced systemic toxicity, and controlled release. FDA-approved nanodrugs like Doxil® (liposomal doxorubicin) and Abraxane® (albumin-bound paclitaxel) show better tolerability and tumor selectivity. Emerging smart nanocarriers can respond to tumor-specific stimuli (pH, enzymes) to trigger localized release (Kirtane *et al*., 2021) [21].

4.4 Biomarker-Guided Therapy

Biomarkers are predictive and/or prognostic markers used to forecast response to treatment. Some examples are PD-L1 to predict response to checkpoint inhibitors, BRCA1/2 mutation to assess PARP-inhibitor sensitivity and MSI-high/dMMR to reflect response to immunotherapy in endometrial and colo- rectal cancers. Trials such as NCI-MATCH and TAPUR are examples of these biomarker-directed trials (Meric-Bernstam *et al*., 2021) [30].

5. Emerging Trends and Future Directions in Anticancer Drug Development

The advances in molecular biology, computational sciences, and genetic engineering opened up a new generation in drug discovery against cancer. New innovations not only focus on enhancing efficacy and targeting specificity but also on minimizing side effects and targeting cancers that were otherwise considered "undruggable."

5.1 Development of Novel Drugs and Small Molecules

The pipeline of novel anticancer drugs has grown substantially with small-molecule inhibitors against once "undruggable" proteins like KRAS G12C. Sotorasib (AMG 510) and adagrasib (MRTX849) are breakthroughs against mutant KRAS, with promising data in NSCLC and colorectal cancer (Canon *et al*., 2019) [7]. Proteolysis- targeting chimeras (PROTACs) provide an alternative mechanism with protein degradation instead of inhibition, with increased therapeutic reach (Pettersson & Crews, 2019) [37].

5.2. Artificial Intelligence Applied to Drug Discovery

Today, artificial intelligence plays a major role in the development of anti-cancer drugs through innovative design and drug repurposing, as well as by predicting drug interactions and improving outcomes. Among these tools is DeepMind, which has revolutionized the field of protein structure recognition. It is one of the important tools in the drug discovery process. Artificial intelligence also plays a major role in accelerating the discovery of highly effective drugs against cancer cells by reducing the cost of drugs, reducing their discovery, and increasing their development.

5.3. Strategies in Gene-Editing and CRISPR

Gene editing techniques and Expr technology. I want CRISPR technology and other technologies and strategies that play an important role in gene editing. It has great merit and potential in cancer treatment combinations and plays an important role in therapeutic intervention. There are many analyses and tests conducted using CRISPR technology that identified weaknesses in anti-cancer drug treatments. It played an important role in liberating T cells, which improves the ability to activate the immune system against cancer cells. CRISPR technology can play an important role in artificial methods based on gene editing and re-adjusting and directing immunity with high precision against cancerous tumors.

5.4. Vaccines and Cancer-Preventive Therapies

Anti-cancer drugs have shifted from their initial preventative uses to effective therapeutic applications. Currently, there are numerous attempts to develop several vaccines against colon cancer, skin cancer, and lung cancer (Sahin *et al*., 2020) [41]. These vaccines are undergoing clinical evaluation, and their goal is to increase or stimulate each patient's immunity against tumors. There is significant work on the results of these vaccines in stimulating the body's long-term immunity against tumors.

6. Conclusion

Cancer drugs have changed radically in the past, including cytotoxic compounds, targeted therapies based on the molecular level, and immunotherapy strategies. Thanks to these developments in proteomics, bioinformatics, and genomics, this has led to the creation of new drugs that work more effectively and with selective toxicity to the disease without affecting intact tissues.

Despite the technological progress and the characteristics of developing treatment, there are still many obstacles that constitute an obstacle to the development of long-term treatment. The most important of these obstacles are the heterogeneity within tumors and the resistance of acquired and self-cells to drugs, as well as the ability of these cells to hide from the immune system. In addition to, the high costs of treatment. These obstacles require collective work to overcome them. This collective work must be from diverse, multidisciplinary parties in cancer treatment, pharmaceutical scientists and biological engineers. It fills this aura of obstacles and translates the practical reality into clinical results and benefits, and makes treatment more efficient and affordable.

As a result, new developments in the discovery of anti-cancer drugs with the help of modern technology, including artificial intelligence, personalized therapy, biomarker guidance, nuclear medicine, and gene editing techniques, all of these factors have led to the emergence of highly efficient treatment systems that are less toxic to healthy tissues in the body and have a longer-lasting effect. The most recent of these is achieving longer survival rates and improving the life cycle of people with cancer around the world.

7. References

1. Amin A, Gali-Muhtasib H, Ocker M, Schneider-Stock R. Overview of major classes of plant-derived anticancer drugs. Int J Biomed Sci. 2009;5(1):1-11. Available from:
2. http://ijbs.org/user/ContentFullText.aspx?VolumeNO=5&StartPage=1&Type=pdf
3. Asif Q ul A. Cancer pharmacology advances: fundamentals, combination, imagery, shipment and therapeutic applications. 2023. Available from: https://doi.org/10.18782/2582-2845.9030
4. Bai JW, Li YC, Zhang GJ. Cell cycle regulation and anticancer drug discovery. Cancer Biol Med. 2017;14(4):348-62. Available from: https://doi.org/10.20892/J.ISSN.2095-3941.2017.0033
5. Burstein HJ, *et al*. Endocrine treatment of hormone-receptor-positive, HER2-negative breast cancer: ASCO guideline. J Clin Oncol. 2019;37(30):3141-3166. Available from: https://doi.org/10.1200/JCO.19.00992
6. Cancer. In: Routledge eBooks. 2023. p. 83-90. Available from: https://doi.org/10.4324/9781003306689-13
7. Canon J, Rex K, Saiki AY, Mohr C, Cooke K, Bagal D, *et al*. The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity. Nature. 2019;575(7781):217-223. Available from: https://doi.org/10.1038/s41586-019-1694-1
8. Chatterjee N, Bivona TG, Sequist LV. Mechanisms of resistance to EGFR inhibitors in non-small cell lung cancer: emerging concepts and clinical implications. Nat Rev Cancer. 2021;21(9):645-661. Available from: https://doi.org/10.1038/s41568-021-00369-9
9. Chen X, Ou S, Luo J, He Z, Jiang Q. Advancing perspectives on the off-label use of anticancer drugs: an updated classification and exploration of categories. Front Pharmacol. 2024;15:1374549. Available from: https://doi.org/10.3389/fphar.2024.1374549
10. Cramer P, *et al*. Advances in CD20-targeting therapies for B-cell malignancies. Lancet Oncol. 2021;22(5):e202-213. Available from: https://doi.org/10.1016/S1470-2045(21)00060-3
11. Dienstmann R, Vermeulen L, Guinney J, Kopetz S, Tejpar S, Tabernero J. Consensus molecular subtypes

and the evolution of precision medicine in colorectal cancer. Nat Rev Cancer. 2018;17(2):79-92. Available from: https://doi.org/10.1038/nrc.2017.77

12. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Tamoxifen for early breast cancer: 10-year survival results. Lancet. 2019;393(10190):1683-1697. Available from: https://doi.org/10.1016/S0140-6736(18)32897-7
13. Gackowski M, Koba M, Pluskota R, Daghir-Wojtkowiak E, Szatkowska-Wandas P, Kruszewski S. Pharmacological classification of anticancer drugs applying chromatographic retention data and chemometric analysis. Chem Pap. 2021;75(1):265-278. Available from: https://doi.org/10.1007/S11696-020-01301-3
14. Gianni L, *et al*. 20-year update of trastuzumab-based therapy in HER2-positive breast cancer. N Engl J Med. 2022;387(2):113-125. Available from: https://doi.org/10.1056/NEJMoa2203465
15. Gundy JT, Nguyen M. Cancer pain: pharmacological treatment. In: Gundy JT, Nguyen M, editors. Cancer. Springer; 2017. p. 441-443. Available from: https://doi.org/10.1007/978-3-319-43133-8_115
16. Havelka A, Berndtsson M, Olofsson MH, Shoshan MC, Linder S. Mechanisms of action of DNA-damaging anticancer drugs in treatment of carcinomas: is acute apoptosis an “off-target” effect? Mini-Rev Med Chem. 2007;7(10):1035-1039. Available from: https://doi.org/10.2174/138955707782110196
17. Hinshaw DC, Shevde LA. The tumor microenvironment innately modulates cancer progression. Cancer Res. 2019;79(18):4557-4566. Available from: https://doi.org/10.1158/0008-5472.CAN-18-3962
18. Hochhaus A, *et al*. Long-term outcomes of imatinib therapy for chronic myeloid leukemia. Leukemia. 2020;34(4):1134-1144. Available from: https://doi.org/10.1038/s41375-019-0705-2
19. Jackman JM, Yibrehu B, Doyle A, Alatise OI, Wuraola F, Olasehinde O, *et al*. Updates in global oncology: advancements and future directions. J Surg Oncol. 2024. Available from: https://doi.org/10.1002/jso.27633
20. Johnson TI, Minteer CJ, Kottmann D, Dunlop CR, Bernaldo de Quirós Fernández S, Carnevalli LS, *et al*. Quantifying cell cycle-dependent drug sensitivities in cancer using a high throughput synchronisation and screening approach. EBioMedicine. 2021;68:103396. Available from: https://doi.org/10.1016/J.EBIOM.2021.103396
21. June CH, Sadelain M. Chimeric antigen receptor therapy. N Engl J Med. 2018;379(1):64-73. Available from: https://doi.org/10.1056/NEJMra1706169
22. Kawahara N, Masui T, Roh JK, Hao XS, Hill DE, Akaza H. What should we do to raise awareness on the issue of cancer in the global health agenda. Jpn J Clin Oncol. 2010;40(1):82-85. doi: 10.1093/jjco/hyq132.
23. Keefe DMK, Stringer AM. The potential successes and challenges of targeted anticancer therapies. Curr Opin Support Palliat Care. 2010;4(1):16-18. doi: 10.1097/spc.0b013e3283357619.
24. Kirtane AR, Kalscheuer SM, Panyam J, Langer R. Nanotechnology for cancer therapy: Progress, challenges and opportunities. Nat Rev Drug Discov. 2021;20(3):173-174. doi: 10.1038/d41573-021-00034-y.
25. Lavoie Smith EM, Li L, Chiang C, Thomas CM, Hammer MJ. Chemotherapy-induced peripheral neuropathy: A current review. Curr Pain Headache Rep. 2019;23(9):1-9. doi: 10.1007/s11916-019-0802- 3.
26. Liu Y, Sun L, Cai L, Lin Z. Mechanisms of resistance to PARP inhibitors and their clinical implications. Front Oncol. 2022;12:875163. doi: 10.3389/fonc.2022.875163.
27. McCoach CE, Blakely CM, Banks KC, Levy B, Riess JW. Clinical utility of cell-free DNA for the detection of ALK fusions and resistance mutations in ALK- positive lung cancer. J Thorac Oncol. 2020;15(9):1430- 1442. doi: 10.1016/j.jtho.2020.05.005.
28. Lu Y, Xue J, Deng T, Zhou X, Yu K, Deng L, et al. Safety and feasibility of CRISPR-edited T cells in patients with refractory non-small-cell lung cancer. Nat Med. 2020;26(5):732-740. doi: 10.1038/s41591-020-0840-7.
29. Meric-Bernstam F, Brusco L, Daniels M, Wathoo C, Bailey AM. NCI-MATCH and TAPUR: Evolving the landscape of precision oncology. Clin Cancer Res. 2021;27(3):665-670. doi: 10.1158/1078-0432.CCR-20-3280.
30. Min H, Lee HY. Molecular targeted therapy for anticancer treatment. Exp Mol Med. 2022;54(10):1670-1694. doi: 10.1038/s12276-022-00864-3.
31. Mizutani H. Mechanism of DNA damage and apoptosis induced by anticancer drugs through generation of reactive oxygen species. ChemInform. 2008;39(15):1-6. doi: 10.1002/chin.200815268.
32. Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. N Engl J Med. 2016;374(14):1356-1367. doi: 10.1056/NEJMra1515442.
33. Ogawa M. Anticancer drugs and pharmacologic actions. Nihon Rinsho. Jpn J Clin Med. 1997;55(5):1017-1023. Available from: https://pubmed.ncbi.nlm.nih.gov/9155146/.
34. Ostios-García L, Martínez-Pérez D, Castelo B, Hernández Herradón N, Zamora P, Feliú J, *et al*. Classification of anticancer drugs: an update with FDA- and EMA-approved drugs. Cancer Metastasis Rev. 2024;43(1):1-13. doi: 10.1007/s10555-024-10188-5.
35. Patra D, Bhavya K, Kalia M, Pal D. Anti-cancer drug

molecules targeting cancer cell cycle and proliferation. In: Advances in Pharmacology and Clinical Toxicology. Vol. 135. Elsevier; 2023. p. 343-395. doi: 10.1016/bs.apcsb.2022.11.011.
36. Pettersson M, Crews CM. PROteolysis TArgeting Chimeras (PROTACs)—past, present and future. Drug Discov Today Technol. 2019;31:15-27. doi: 10.1016/j.ddtec.2019.01.002.
37. Pont LG, Dua K, Cutler RL, Benson H, Hagi M, Cardenas VG, *et al*. Current practice in cancer pharmacotherapy. In: Cancer Pharmacotherapy. Academic Press; 2021. p. 9-15. doi: 10.1016/B978-0-323-85503-7.00040-7.
38. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. Science. 2018;359(6382):1350-1355. doi: 10.1126/science.aar4060.
39. Rugo HS, Voigt J, Scalp Cooling Alopecia Prevention Study Group. Scalp cooling for the prevention of chemotherapy-induced alopecia. JAMA. 2017;317(6):606-14. doi: 10.1001/jama.2016.20939.
40. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, *et al*. Recommendations for the use of WBC growth factors: ASCO clinical practice guideline update. J Clin Oncol. 2015;33(28):3199-3212. doi: 10.1200/JCO.2015.62.3488.
41. Sahin U, Derhovanessian E, Miller M, Kloke BP, Simon P, Löwer M, et al. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer. Nature. 2020;585(7823):107-113. doi: 10.1038/s41586-020-2537-9.
42. Vasan N, Baselga J, Hyman DM. A view on drug resistance in cancer. Nature. 2019;575(7782):299-309. doi: 10.1038/s41586-019-1730-1.
43. Weber JS, *et al*. Dual checkpoint blockade in advanced melanoma: 5-year follow-up. J Clin Oncol. 2021;39(17):1866-1875. doi: 10.1200/JCO.20.036
44. Kawahara N, Masui T, Roh JK, Hao XS, Hill DE, Akaza H. What should we do to raise awareness on the issue of cancer in the global health agenda. Jpn J Clin Oncol. 2010;40(1):82-85. doi: 10.1093/jjco/hyq132.
45. Keefe DMK, Stringer AM. The potential successes and challenges of targeted anticancer therapies. Curr Opin Support Palliat Care. 2010;4(1):16-18. doi: 10.1097/spc.0b013e3283357619.
46. Kim R, Kin T, Beck WT. Impact of complex apoptotic signaling pathways on cancer cell sensitivity to therapy. Cancers (Basel). 2024;16(5):984. doi: 10.3390/cancers16050984.
47. Kirtane AR, Kalscheuer SM, Panyam J, Langer R. Nanotechnology for cancer therapy: Progress, challenges and opportunities. Nat Rev Drug Discov. 2021;20(3):173-174. doi: 10.1038/d41573-021-00034-y.
48. Lavoie Smith EM, Li L, Chiang C, Thomas CM, Hammer MJ. Chemotherapy-induced peripheral neuropathy: A current review. Curr Pain Headache Rep. 2019;23(9):1-9. doi: 10.1007/s11916-019-0802-3.
49. Liu Y, Sun L, Cai L, Lin Z. Mechanisms of resistance to PARP inhibitors and their clinical implications. Front Oncol. 2022;12:875163. doi: 10.3389/fonc.2022.875163.
50. Lu Y, Xue J, Deng T, Zhou X, Yu K, Deng L, *et al*. Safety and feasibility of CRISPR-edited T cells in patients with refractory non-small-cell lung cancer. Nat Med. 2020;26(5):732-740. doi: 10.1038/s41591-020-0840-7.
51. McCoach CE, Blakely CM, Banks KC, Levy B, Riess JW. Clinical utility of cell-free DNA for the detection of ALK fusions and resistance mutations in ALK-positive lung cancer. J Thorac Oncol. 2020;15(9):1430-1442. doi: 10.1016/j.jtho.2020.05.005.
52. Meric-Bernstam F, Brusco L, Daniels M, Wathoo C, Bailey AM. NCI-MATCH and TAPUR: Evolving the landscape of precision oncology. Clin Cancer Res. 2021;27(3):665-670. doi: 10.1158/1078-0432.CCR-20-3280.
53. Min H, Lee HY. Molecular targeted therapy for anticancer treatment. Exp Mol Med. 2022;54(10):1670-1694. doi: 10.1038/s12276-022-00864-3.
54. Mizutani H. Mechanism of DNA damage and apoptosis induced by anticancer drugs through generation of reactive oxygen species. ChemInform. 2008;39(15):1-6. doi: 10.1002/chin.200815268.
55. Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. N Engl J Med. 2016;374(14):1356-1367. doi: 10.1056/NEJMra1515442.
56. Ogawa M. Anticancer drugs and pharmacologic actions. Nihon Rinsho. Jpn J Clin Med. 1997;55(5):1017-1023. Available from: https://pubmed.ncbi.nlm.nih.gov/9155146/.
57. Ostios-García L, Martínez-Pérez D, Castelo B, Hernández Herradón N, Zamora P, Feliú J, et al. Classification of anticancer drugs: an update with FDA- and EMA-approved drugs. Cancer Metastasis Rev. 2024;43(1):1-13. doi: 10.1007/s10555-024- 10188-5.
58. Patra D, Bhavya K, Kalia M, Pal D. Anti-cancer drug molecules targeting cancer cell cycle and proliferation. In: Advances in Pharmacology and Clinical Toxicology. Vol. 135. Elsevier; 2023. p. 343-395. doi: 10.1016/bs.apcsb.2022.11.011.
59. Pettersson M, Crews CM. PROteolysis TArgeting Chimeras (PROTACs)—past, present and future. Drug Discov Today Technol. 2019;31:15-27. doi: 10.1016/j.ddtec.2019.01.002.
60. Pont LG, Dua K, Cutler RL, Benson H, Hagi M, Cardenas VG, et al. Current practice in cancer pharmacotherapy. In: Cancer Pharmacotherapy. Academic Press; 2021. p. 9-15. doi: 10.1016/B978-0-323-85503-7.00040-7.
61. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. Science. 2018;359(6382):1350-

doi: 10.1126/science.aar4060.

62. Rugo HS, Voigt J, Scalp Cooling Alopecia Prevention Study Group. Scalp cooling for the prevention of chemotherapy-induced alopecia.JAMA. 2017;317(6):606-614. doi: 10.1001/jama.2016.20939.
63. Sahin U, Derhovanessian E, Miller M, Kloke BP, Simon P, Löwer M, et al. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer. Nature. 2020;585(7823):107-13. doi: 10.1038/s41586-020-2537-2539.
64. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, et al. Recommendations for the use of WBC growth factors: ASCO clinical practice guideline update. J Clin Oncol. 2015;33(28):3199-3212. doi: 10.1200/JCO.2015.62.3488.
65. Vasan N, Baselga J, Hyman DM. A view on drug resistance in cancer. Nature. 2019;575(7782):299-309. doi: 10.1038/s41586-019-1730-1.
66. Weber JS, et al. Dual checkpoint blockade in advanced melanoma: 5-year follow-up. J Clin Oncol. 2021;39(17):1866-1875. doi: 10.1200/JCO.20.0