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Innovations in Cancer Drug Discovery: A Review of the Latest Advances

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Abstract

Cancer happens when cells grow uncontrollably, forming tumors that can spread and affect other organs and body functions. It's one of the deadliest diseases today, claiming millions of lives each year. Treating cancer effectively is challenging due to differences in the disease's behavior, access to healthcare, and other social and economic factors. This review aims to highlight recent progress in cancer drug research, drawing from studies. Information was gathered from trusted sources like PubMed Central, Google Scholar, and ScienceDirect. The review covers a wide range of developments, including new drug targets, plant-based therapies, chemical compounds tested in labs or living systems, and drugs originally developed for other conditions that have shown potential against cancer.Overall, this article brings together key findings from recent studies to provide a clear overview of emerging strategies and treatments in the fight against cancer, focusing on effective drug targets, plant-derived compounds, drug repurposing, and innovative chemical agents

Key Words: oncology therapeutics; novel drug targets; drug repositioning; anticancer agents cytotoxic compounds

Introduction

Cancer happens when cells grow out of control, forming abnormal lumps called tumors. These can spread to other parts of the body, messing up how organs and systems work.[1] Cancer is caused by a mix of factors working together, like genetic changes, pollution, contaminated food, viruses, chemicals, and radiation, making it a complex disease with multiple triggers.[2] Several ancient, well-preserved mechanisms carefully control how cells divide, ensuring that two identical cells are created with the same genetic information.[3] Cancer is one of the most fatal diseases in recent times, taking countless lives every year. How it's managed varies widely around the world, depending on differences in the disease itself, the quality of healthcare systems, and social and economic conditions.[4] According to the 2023 global cancer report, an extra 20 million cancer cases and 10 million deaths are expected. Over the next 20 years, the number of cancer cases is projected to rise by about 60%, putting more pressure on individuals, communities, and healthcare systems.

A study conducted in Ethiopia from 2000 to 2016 showed that cancer caused around 50,913 deaths (95% confidence level) among people of all ages and both genders, with most of the patients being women. The crude death rate was 49.7 per 100,000 people, and the age-adjusted death rate was 93.5 per 100,000. One major reason for the rise in cancer cases is that people are living longer.

In response, the pharmaceutical industry has poured a lot of money into cancer treatment research. However, despite these investments, developing effective cancer drugs remains a major challenge, and the expected improvements in treatment results have yet to be achieved.[5] Since the early 20th century, drug companies have kept developing cancer medicines—even though they're expensive—because our growing understanding of how the disease works has made it possible to create more targeted and effective treatments.[6,7] Pharmaceutical companies have developed different types of cancer-fighting drugs, including those that kill cancer cells directly (like alkylating agents, antimetabolites, antibiotics, and plant-based compounds), as well as hormone-based treatments and drugs that help boost or control the immune system.[8,9]

However, traditional chemotherapy has several problems—it often harms healthy cells, isn't very specific to cancer cells, can lead to drug resistance, and may even encourage the growth of stem-like cancer cells. Finding new molecular targets has given hope for better treatments. Monoclonal antibodies and antibody-drug combinations have helped tackle two major challenges in cancer treatment: making drugs more selective and reducing side effects.[5,10]

Drug makers and researchers have produced a large amount of research focused on cancer drug development, especially considering the challenges like toxicity, lack of selectivity, and side effects. This review aims to gather and summarize studies that focus on new chemical compounds that can kill cancer cells in the lab, as well as highlight new biomarkers and target proteins that might be useful for future cancer treatments.

1.1. Search Strategy

Between March 20 and May 12, information from earlier studies on cancer drug discovery was collected from journals available on PubMed Central, Google Scholar, and Science Direct. To make referencing easier, the literature was carefully chosen based on how closely it related to the topic and how recent it was, and then directly cited from the original sources.

2. Materials and Methods

For this review, the researcher used online platforms like Google Scholar, PubMed Central, and Science Direct to search for information, using a personal computer and related devices.

2.1. Search Results

After searching and sorting through recently published articles using the methods mentioned above, I found many relevant studies on the latest developments in cancer drug discovery. These findings are categorized into three main areas: cancer drug targets and biomarkers, laboratory and animal studies on new cancer-killing drugs, and advances using plant-based treatments. The review also includes progress in drug repurposing, which involves using existing, discontinued, or unused drugs with potential anticancer effects. Additionally, research on electrochemotherapy, gene therapy, plant medicine (phytomedicine), and immunotherapy is also discussed.

3. General Overview of Anticancer Drug Discovery

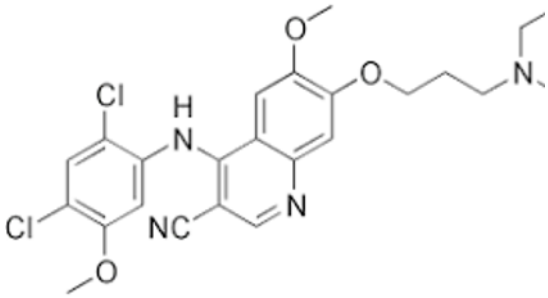
Designing and discovering cancer drugs is a complex, expensive, and time-consuming process, presenting major challenges for researchers and drug companies.[11] In addition to being complicated, traditional cancer treatments are highly toxic and often don't specifically target cancer cells.[12,13] Even though drug manufacturers are actively working on cancer treatments, it remains important to create new, targeted small-molecule drugs. This is especially true with the help of in silico tools, which have become more advanced in recent years.[14] Recently, artificial intelligence (AI) has become a powerful and promising technology for designing cancer drugs more quickly, cheaply, and efficiently than the older computer-aided drug design (CADD) methods.[11] Artificial intelligence can accelerate both the discovery of new drug molecules and the creation of more effective ones. The process of developing cancer drugs starts with identifying potential targets, followed by various screening methods such as structure-based, ligand-based, and fragment-based approaches to find successful compounds. AI also aids in designing new cancer drugs for larger compounds, repurposing existing drugs for cancer treatment, and predicting how cancer drugs will react in specific cases. [15,16] Cancer medications are developed either from natural products or through synthetic methods, considering both the toxicity and effectiveness of the drugs. Artificial intelligence-based technology, along with previous computer-aided drug design (CADD) tools, are used in the process of drug design and discovery. Recently, drug repurposing, which involves finding new uses for existing drugs based on promising targets, has also gained popularity.[17-19] However, cancer immunotherapy has some drawbacks, including resistance, the ability of cancer cells to escape the immune system, and challenges with how the therapy is delivered.[20] Recent advancements suggest that nanoparticles, using nanocarriers as delivery vehicles, could help address these issues.[21] Because of their unique properties, like being biocompatible, having lower toxicity, better permeability, enhanced stability, precise targeting, and a longer-lasting effect,[22] Nanoparticles can be used to treat cancer due to these beneficial properties.

4. Recent Advances in Anticancer Drug Targets and Biomarkers

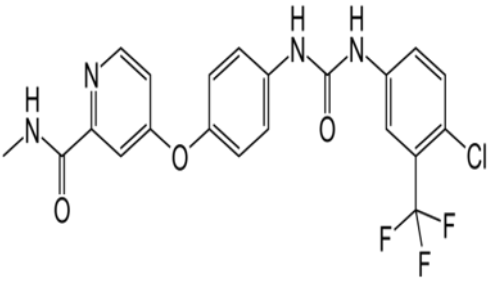
Targeted therapy is crucial for improving overall survival rates and reducing the harmful side effects of cancer treatments. Patients who received targeted therapies tailored to their condition showed a significant improvement in both overall survival and progression-free survival compared to those who did not receive such treatments.[23] Many drug targets for cancer treatment have been identified, but most molecularly targeted drugs have been ineffective due to issues with either their effectiveness or toxicity. Recent advances in molecular biology and a deeper understanding of cancer's molecular causes are encouraging researchers to focus on drug targets that could potentially lead to completely eliminating the disease.[24]

4.1. Kinases as Targets

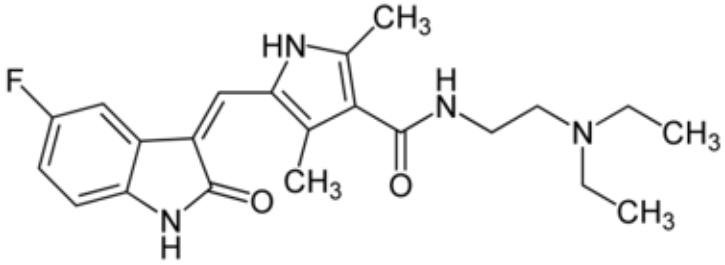
Kinase inhibitors are a type of anti-cancer drug that work by directly blocking the active site of the target enzyme to stop kinase activity. It is estimated that the human genome has around 2,000 kinases, which are either serine/threonine-specific or tyrosine-specific and are interconnected. Imatinib was the first kinase inhibitor introduced in clinical oncology, followed by bosutinib, sorafenib, and sunitinib. Although these drugs all work by inhibiting ATP at the tyrosine kinase binding site, they differ in the range of kinases they target, their pharmacokinetics, and the specific side effects they cause.[25]



bosutnib



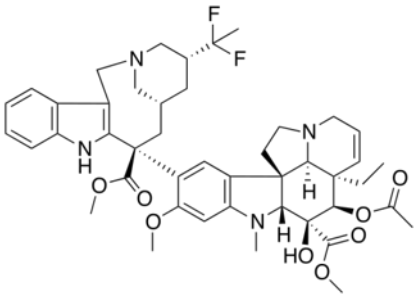
sorafenib



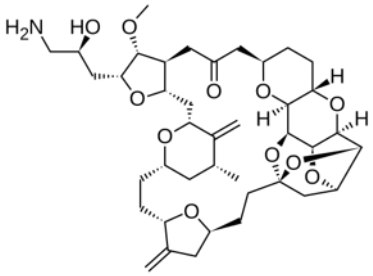
Sunitinib

4.2. Tubulin/Microtubule as Targets

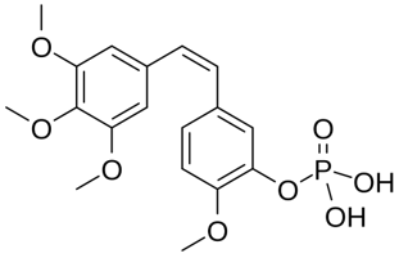
Microtubules, which are a key part of the eukaryotic cytoskeleton, are made by the polymerization of tubulin, a protein with a molecular weight of 52 KD. During the cell cycle, microtubules constantly grow and shrink. Cancer cells divide and grow much faster than normal cells, making microtubules an important target for cancer treatment. Since microtubules are crucial for cell division and growth, developing drugs that target them is a focus in cancer treatment, with tubulin now being one of the main targets for these drugs. To discover and create safer and more effective drug options, several tubulin-targeting agents have been developed, and research has been conducted to study the relationship between their structure and activity.[24-26]



Vinflunine



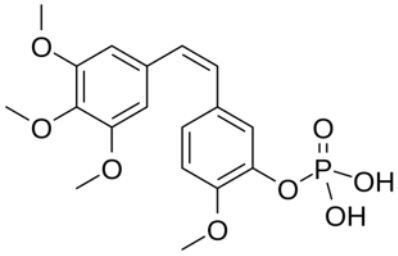
Eribulin



Bevacizumab

4.3. Vascular Targeting Agents

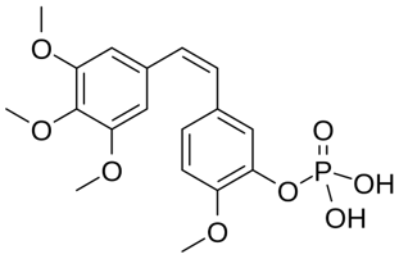
Vascular targeting agents (VTAs) are cancer treatments designed to specifically target the blood vessels that supply tumors, thereby preventing the growth and spread of cancer. Since blood-based medications are available, this approach has proven to be effective in cancer treatment. Tumor cells need a constant supply of oxygen and nutrients to grow quickly, which is why the growth of blood vessels is essential for tumor development, progression, and metastasis. Vascular disrupting agents (VDAs) can block blood flow to tumors, helping to stop their growth.[27,28]



Fosbretabulin

4.4.Angiogenesis Inhibitors

Angiogenesis inhibitors are a new type of medicine developed to stop the formation of blood vessels that supply tumors. In tumor growth, invasion, and spreading, VEGF-A is produced in large amounts. Currently, drugs that block VEGF-A and its receptor VEGFR2 are being used to target this process.[28] Angiogenesis inhibitors like bevacizumab and ramucirumab are used to treat non-small-cell lung cancer (NSCLC). These drugs work by blocking VEGF proteins that help tumors form new blood vessels.[29]



Bevacizumab

4.5. Monoclonal Antibodies

A new group of drugs called angiogenesis inhibitors is being developed to block the formation of blood vessels that feed tumors. In cases of tumor growth, invasion, and spreading, VEGF-A levels are unusually high. Right now, treatments that block VEGF-A and its receptor VEGFR2 are being used to target this problem.[28] Angiogenesis inhibitors (such as bevacizumab and ramucirumab) are drugs used to treat non-small cell lung cancer (NSCLC). They work by blocking VEGF proteins, which tumors need to grow new blood vessels. By cutting off this supply, the drugs help slow or stop cancer growth.[29]

5. Recent Advances in Drug Repurposing for the Discovery of New Anticancer Drugs

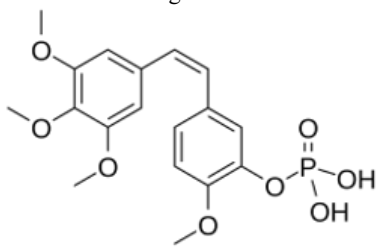
. Drug repositioning, also called drug repurposing, is when scientists explore whether a medicine that's already approved for one disease might also work to treat other conditions.[30-32

5.1. Antiplatelet Agents

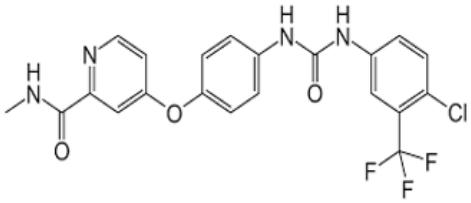
Aspirin is mainly known for helping prevent heart problems because it stops blood clots from forming. Even though researchers have found that taking aspirin regularly might lower the risk of breast cancer, its main job is still heart-related. However, a study by Henry and colleagues suggests that aspirin could also be used alongside PI3K inhibitors as part of a combo treatment for breast cancer.[33]

5.2. Anti-inflammatory drugs

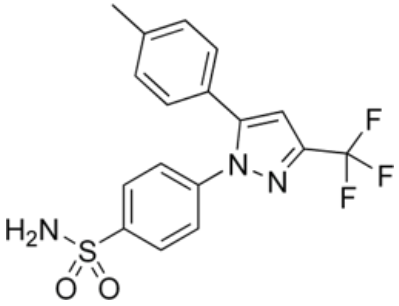
Recent studies in live mice showed that diclofenac can slow down the growth of pancreatic tumors. When scientists looked at the tumors after surgery, they found that diclofenac treatment caused more cancer cells to die (apoptosis) and reduced the tumor's ability to form new blood vessels (angiogenesis). They also tested a combination of diclofenac and sorafenib (a drug that blocks certain cancer signals) on melanoma cells, and the combination worked well against all the cancer cells they tested.[34] In live rat studies, the drug celecoxib, which specifically blocks COX-2, was able to slow down the growth of breast cancer cells and reduce the formation of tumors. Researchers found that how much COX-2 the cancer cells produced, along with how aggressive the tumor cells were, played an important role in how well celecoxib worked to stop their growth.[35] Mesalazine has also been reported to have anti-cancer effects in several types of cancer, such as colorectal, stomach, breast, and colon cancers.[36]



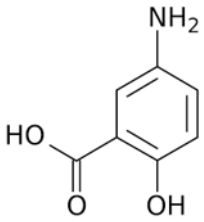
Diclofenac



Sorafenib



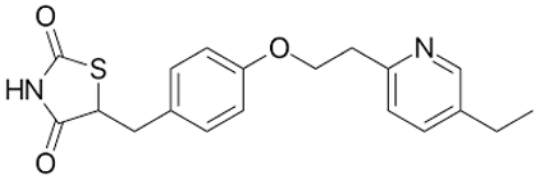
Celcoxib



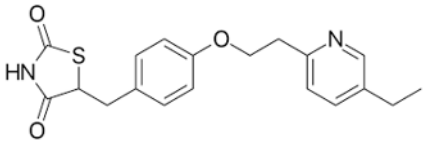
Mesalazine

5.3 Antidiabetic agents

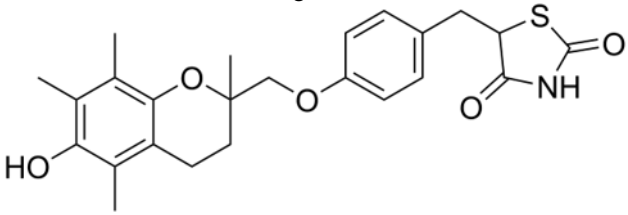
Metformin, a common oral drug used as the first treatment for type 2 diabetes, has also been found to have anti-cancer effects in several types of cancer, including pancreatic, endometrial, breast, lung, and prostate cancers.[37] Many early lab and clinical studies have shown that thiazolidinediones (TZDs), a type of drug, could be promising for treating breast and prostate cancer. The main drugs in this group are troglitazone, rosiglitazone, and pioglitazone.[38]



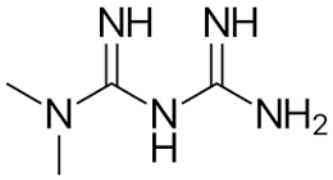
Pioglitazone



Rosiglitazone



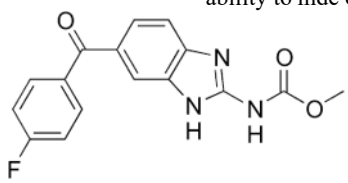
Tyoglitazone



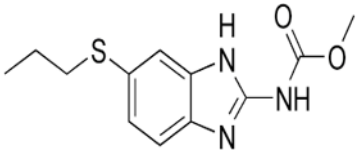
Mitformin Tiazolidinediones(TZDS)

5.4 Anthelmintic agents

Repurposing common deworming drugs like flubendazole and albendazole for cancer treatment has recently gained attention. These drugs are cheap, easy to get, and have been safely used in people for a long time. Research shows they can do a lot more than fight parasites—they can block cancer cell growth by messing with cell structures, stopping new blood vessels from forming, preventing cancer spread, and boosting the immune system. They also help kill cancer cells, fight drug resistance, and reduce the cancer cells' ability to hide or become more aggressive.[30]



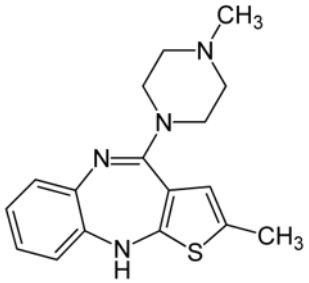
Flubendazole



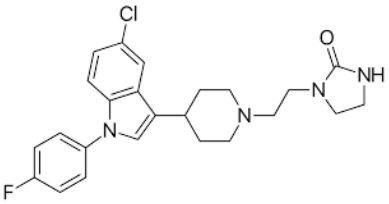
Albendazole

5.5. Antipsychotic Agents

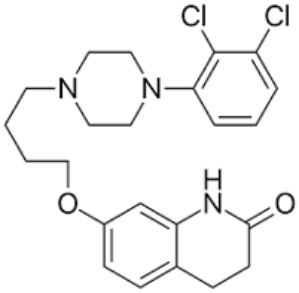
Some studies have found that people who take antipsychotic medications for mental health conditions like schizophrenia tend to have lower rates of certain cancers, including colon, rectal, and prostate cancer.[39] This suggests that antipsychotic drugs might help fight cancer. For example, aripiprazole—a medication often given to people with schizophrenia—has been shown to slow down how quickly cancer cells grow in colon, brain (glioma), and stomach cancers.[40,41] Sertindole looks like a promising drug that could potentially help treat stomach and breast cancers.[42] Valproic acid, a drug commonly used to treat epilepsy, bipolar disorder, and migraines, works in part by affecting the way genes are turned on or off. It helps slow down the growth of cancer cells, encourages them to mature, prevents the formation of new blood vessels that tumors need to grow, and ultimately causes the cancer cells to die.[43] Studies have shown that phenothiazines can stop DNA polymerase in the mitochondria, promote the maturity of cancer stem cells, and slow down the growth of tumor cells. Olanzapine, a drug used to treat bipolar disorder, schizophrenia, and Tourette syndrome, can kill cancer cells by disrupting the balance of cholesterol in the body.[44] There is evidence that selective serotonin reuptake inhibitors (SSRIs) can slow down the growth of cancer cells, eventually causing them to die.[45]



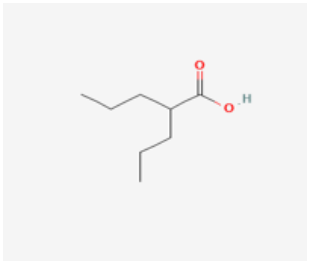
olanzapine



Sertindole



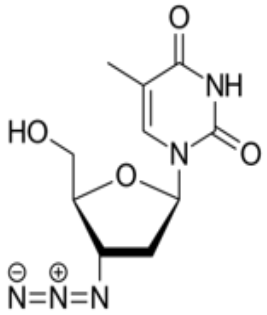
Aripiprazole



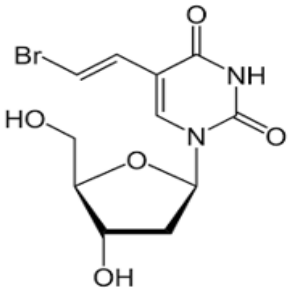
Valproic acid

5.6. Antiviral Drugs

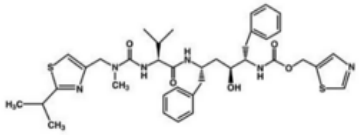
Zidovudine, originally the first drug approved to treat HIV, also has cancer-fighting effects against several types of cancer, including pancreatic cancer, leukemia, and Kaposi sarcoma. Similarly, Brivudine, which is used to treat herpes simplex virus, has shown potential in reducing resistance to chemotherapy and fighting cancer. Ritonavir, a drug used for HIV, has been found to slow the growth and division of cancer cells in ovarian, pancreatic, and breast cancers, while also speeding up the process that leads to cancer cell death.[46,47]



Zidovudine



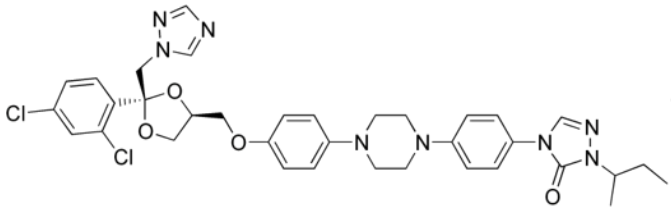
Brivudine



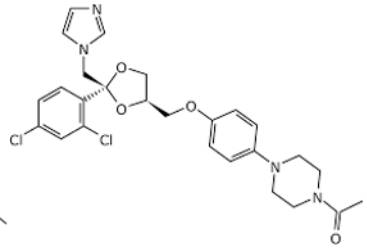
Ritonavir

5.7. Antifungal Agents

Itraconazole, an antifungal drug, has been shown to block a specific signaling pathway (AKT/mTOR) in various types of cells, including those from the blood vessels, endometrial cancer, melanoma, and brain tumors. It also affects the Hedgehog signaling pathway, helps overcome chemotherapy resistance caused by P-glycoprotein, and prevents the growth of new blood vessels and lymphatic vessels in cancer cells.[48] Additionally, ketoconazole has shown anti-cancer effects against liver cancer, prostate cancer, melanoma, and breast cancer. It works by blocking the formation of exosomes in prostate cancer cells and is generally better tolerated, with fewer side effects compared to other treatments.[49]



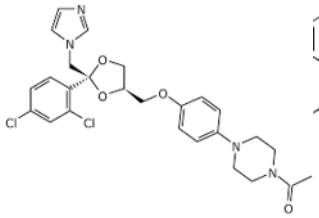
Itraconazole



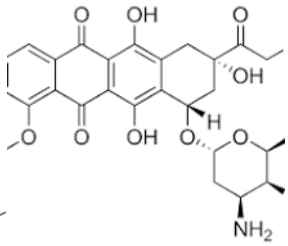
kitokonazole

5.8. Antibacterial Agents

Doxorubicin is known to be effective in treating breast cancer by interfering with DNA, which stops the cells from replicating. When used together with a COX-2 inhibitor, doxycycline helps prevent the growth of colon cancer cells by halting their progression at a specific stage of the cell cycle and blocking certain enzymes that help tumors spread. Doxycycline also disrupts the production of new mitochondria and affects the stem cell-like behavior of cancer cells in breast cancer.[50,51]



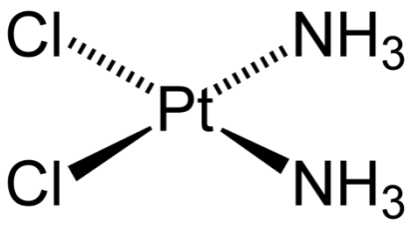
Dexycycline



Doxorubicin

5.9. Heterometallic Compounds

Platinum-based drugs are commonly used in medical treatments, but their effectiveness is limited because they can be toxic. This is due to interactions between platinum and biomolecules that contain sulfur, such as thiols and thioethers.[52] To address the toxicity of platinum-based drugs, new methods are being developed to create novel heterometallic complexes. These complexes use metal centers with different structures and properties, which improve how they interact with biologically important molecules, reducing the harmful effects of platinum.[53] Drugs made from heterometallic materials have a promising future because they may be more effective than platinum-based drugs and have the added benefit of lower toxicity.[54] Platinum, gold, and titanium are among the most common metals used in promising heterometallic compounds for cancer treatment.[55,56] A number of new heterocyclic compounds, including thiazolidin-4-ones, 1,3,4-thiadiazoles, and thiazoles with thymol, have been developed and tested under mild conditions. These compounds showed significant anticancer activity, with IC50 values ranging from 7 to 19 micromolar against various human cancer cell lines.[57] Pyrazole, a five-membered ring structure with two nitrogen atoms next to each other, is found in many natural substances. Because of this, it is considered a promising candidate in medicine, with the potential to target a wide range of biological activities for therapeutic purposes.[58] Recent laboratory tests have shown that bisheterocyclic compounds are making progress as effective cancer treatments. This goes beyond just focusing on the potential of heterocyclic compounds for treating cancer.[59]



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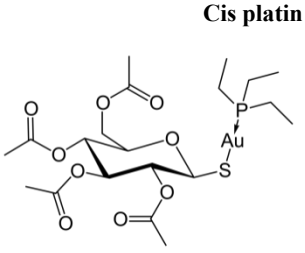
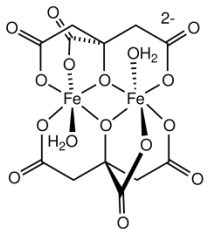


Auranofin



Iron(III)citrate

6.Conclusion

Cancer has an incredibly negative impact on the global population. From the discovery of the first nitrogen mustards, researchers and pharmaceutical companies have been working hard to find effective cures. However, despite a variety of treatment options, cancer's ability to spread and the challenges posed by a lack of selectivity, side effects, and effectiveness make treatment difficult.

Recent advancements in molecular biology and a better understanding of cancer's molecular causes have led researchers to focus on identifying drug targets that could help eliminate the disease completely. This review

highlights recent progress in discovering anticancer drugs. Thanks to these advancements, researchers are now able to pinpoint treatments with fewer side effects and better tolerability. Many drug targets have been identified for cancer treatment, with a focus on improving effectiveness and reducing toxicity. The most promising areas for cancer treatment include kinase inhibitors, microtubule targeting, vascular targeting, angiogenesis, and monoclonal antibodies.

In addition to developing new treatments, researchers are also exploring the repurposing of existing drugs for cancer treatment. This strategy helps reduce the cost, time, and effort needed for research. Repurposed drugs include antiplatelet, antidiabetic, anti-inflammatory, antimicrobial, and antipsychotic agents.

Phytochemicals are another exciting area for finding new anticancer agents, with substances like quercetin, ginseng, artemisinin, and curcumin showing potential. Natural products are also being recognized as powerful and effective chemotherapeutic agents. Moreover, new approaches are being developed to design novel heterometallic complexes, as well as heterocyclic and bis-heterocyclic compounds, like thiazolidin-4-ones, 1,3,4-thiadiazoles, and thiazoles, to overcome chemotherapy's toxicity and enhance its effectiveness.

7. Source of Funding

None.

8. Conflict of Interest

None.

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