



Possible herbal medications and human cancer targets

Md Tanwir Athar ¹

- ¹ Department of Pharmacognosy and Pharmaceutical Chemistry, College of Dentistry and Pharmacy, Buraydah Colleges, Buraydah-51418, Al-Qassim, Saudi Arabia.
- * Correspondence: tantab001@gmail.com (M.T.A.)

Citation: Athar M.T. Possible herbal medications and human cancer targets. *Jour. Bas. Sci.* 2025, 1(2). 1-12.

Received: November 01, 2024 Revised: November 14, 2024 Accepted: December 22, 2024 Published: January 02, 2025 **Abstract:** Numerous phytochemical substances found in food and their artificial derivatives have recently been suggested as cancer treatments. Unfortunately, there is a dearth of information regarding compounds produced from non-edible plants, while the data accessible in relevant literature focuses on the anti-cancer activities of compounds derived from edible plants. Therefore, it is still unclear what mechanisms underlie their anti-cancer actions. The existing information on the anti-cancer properties of six phytochemical-derived compounds—rottlerin, berbamine, sparstolonin B, sulforaphane, plumbagin, and 6-shogaol—derived from both edible and non-edible plants is compiled in this review. These substances serve as bioactive indicators of tumor cytotoxicity. Therefore, knowing how they work will give the justification for using these substances in combination with other medications to fight cancer. Thus, we have summarized the works as a review to present the therapeutic application of herbal drugs for cancer therapeutics.

Keywords: Phytomedicines; Herbal drugs; human cancer; cancer therapeutics; potential targets

1. Introduction

It has been estimated that 25%-48% of current approved therapies by the Food and Drug Administration (FDA) are derived from plants. Phytochemicals in fact are non-nutritive compounds derived from plants. These compounds have unique properties which enable them to act as potent anti-inflammatory and anti-cancer agents. Fruits, vegetables and herbs are the main source for these phytochemical-derived compounds. Surprisingly, more than 10,000 phytochemicals have been identified and used in cancer treatment due to their anti-cancer properties. Additionally, phytochemicals could synergistically increase the efficiency of anti-cancer drugs and reduce their toxic effects[1-10].

The potential of medicinal herbs and the phytocompounds derived from them as effective supplemental cancer treatments is becoming more widely acknowledged. The positive effects of herbal remedies on cancer patients' quality of life (QOL), immunological regulation, and survival when combined with traditional therapies have been documented in several clinical studies. It is also of potential interest to go over a few clinical study examples that looked into the use of herbal remedies for different types of cancer and the creation of randomized controlled trials (RCTs) in this new field of study[4, 6, 9, 11-18]. Spices have influenced numerous global events throughout history. Many explorers have searched the oceans for valuable spices. In many different cultures, these precious commodities are used as colorants, preservatives, and flavoring agents. Spices are valued more and more these days for their possible health advantages as well as their culinary qualities. Spices' antioxidant qualities may contribute to their health benefits, but their capacity to alter several cellular functions, such as drug metabolism, cell division, apoptosis, differentiation, and immunocompetence, may be the source of their biological effects (Figure 1) [19-22].

The criteria used to determine what qualifies as a culinary spice and how it differs from culinary herbs are the first indication of how difficult it is to comprehend the biological reaction to spices. In the scientific and popular literature, both terms are frequently used interchangeably. A spice is defined by the U.S. Food and Drug Administration (FDA) as a "aromatic vegetable substance, in the whole, broken, or ground form," from which "no portion of any volatile oil or other flavoring principle has been removed," and whose main use in food is "seasoning rather than nutrition." Although this description is sound, it ignores how these products differ from herbs and the biological effects of taking them. Spices can be defined as "flavorings (often of tropical origin) that are dried and culinary herbs that are fresh or dried leaves from plants which can be used for flavoring purposes in food preparation," according to the U.S. National Arboretum (United States National Arboretum 2002). We must keep in mind that the importance of an object is not determined by how much of it is consumed. Therefore, it would seem incorrect to omit the health significance from any definition. The primary source of medication prior to the advent of contemporary drugs was plants. The Dietary Supplement Health and Education Act (DSHEA) now classifies herbal items as "dietary supplements," and many Americans utilize them as a

component of a complementary health strategy. Cancer patients seem to utilize these supplements more frequently than people in the general community. To reduce symptoms and stop recurrence, most use them in addition to chemotherapy or other cancer therapies. Furthermore, a third of cancer survivors have reported using herbs, indicating increased use. This use is motivated by particular health beliefs and follows advice from medical professionals and families. In contrast to intrusive therapies, herbal medications are usually seen as "natural" and "safe". The US Food and Drug Administration (FDA) does not regulate these goods as medications, nevertheless. Serious herb-drug interactions, inconsistent levels of active components, poor manufacturing techniques, and product contamination have all been documented. The "herbs" that cancer patients and survivors utilize are the main topic of this article. These goods come from plants and are utilized as food, spices, nutritional supplements, and traditional medicine[6, 23-33].

Uncontrolled cellular proliferation, evasion of cell death mechanisms, and the acquisition of replicative immortality are only a few of the diverse characteristics that define the complex group of disorders known as cancer. It can be roughly divided into two groups: solid tumors, which develop from aberrant cell proliferation and create localized lumps called tumors, and hematologic malignancies, which involve cancers of the blood cells[34-38]. Solid tumors can spread to distant locations through the circulation, bone marrow, or lymphatic system after locally invading nearby tissues. Surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapies are only a few of the many modalities that make up the comprehensive approach to cancer management. Several medication types, such as antimetabolites, alkylating agents, anthracyclines, antitumor antibiotics, mitotic inhibitors, and topoisomerase inhibitors, are administered as part of chemotherapy. Corticosteroids may be used in hormonal therapy, whilst trastuzumab and other medicines may be used in targeted therapies. The information that is currently available shows that cancer patients utilize these products more frequently than the general population, coupled with traditional treatments. Such use is justified by the claims that it improves health, lowers



Figure 1. Herbal drugs and its association with KEGG pathways.

the chance of recurrence, and lessens the negative effects of cancer treatments. Biologically active chemicals found in herbs, however, may interact with prescription pharmaceuticals, such as chemotherapy drugs[39-50].

Enhancing cure rates, improving survival outcomes, and preventing local progression or distant metastases are the main objectives of cancer management. A considerable percentage of cancer patients are treated with chemotherapy and chemoradiotherapy, which have shown beneficial in terms of anticancer activity. These treatment techniques do have certain limits, though, which can reduce their effectiveness and result in treatment failure despite their therapeutic potential. The effect of these drugs on healthy cells and tissues is a significant worry since they can cause a variety of negative side effects. For instance, the widely used chemotherapeutic medication doxorubicin might result in cardiac issues, myelosuppression, and kidney damage. Similarly, another often used chemotherapy, 5-fluorouracil, can cause myelotoxicity, cardiotoxicity, and in rare instances, vasospasm. Ototoxicity, renal toxicity, and low blood counts are side effects of cisplatin, an authorized chemotherapy drug used to treat a variety of malignancies, including breast, ovarian, cervical, lung, and head-neck cancers[19, 26, 51-59].

Chemotherapeutic drugs have also been linked to a number of inherent side effects, such as nausea, vomiting, diarrhea, anorexia, and oral mucositis. The quality of life for cancer patients receiving chemotherapy or chemoradiotherapy can be greatly impacted by these adverse effects. In order to reduce the negative effects of anticancer drugs and enhance the general health of cancer patients, more research and creative solutions are required. Chemotherapy or chemoradiotherapy side effects frequently have a major negative influence on patients' quality of life and can even make it difficult for them to stick with their treatment. Even with the implementation of numerous strategies to control or avoid these negative consequences, they are still insufficient. The development of chemoresistance, in which cancer cells grow resistant to the actions of chemotherapy medications, is another important drawback of anticancer therapies. This leads to a reduction in treatment efficacy and, eventually, treatment failure. Furthermore, many patients—especially those who live in underdeveloped nations—face a significant financial burden due to the high cost of anticancer drugs. Given the current drawbacks of traditional anticancer treatments, investigating alternate strategies such using herbal medicine either by itself or in conjunction with conventional anticancer treatments may be a viable and affordable alternative[7, 60-70].

Recent research on the cellular and biochemical mechanisms of herbal remedies in particular tumor microenvironments and the possible use of particular phytochemicals in cell-based cancer vaccination systems has been reported. Additionally, there are studies that offer helpful technological assistance for the evidence-based use of herbal remedies in cancer treatment.

2. Herbal drugs with cancer therapeutics potential

The terms herbs, herbal substances, herbal preparations, and finished herbal products that contain active components originating from plants or other materials are referred to as herbal medicine, botanical medicine, phytomedicine, or phytotherapy. Herbal remedies use seeds, leaves, roots, berries, fruits, flowers, bark, and even whole plants. Plantbased anticancer medications have been produced over time and are currently used in clinical settings to treat a variety of cancer types. Herbal medicine has been used for 8,000 years in China and 60,000 years in Iraq, according to archeological research. The earliest known written accounts of medicinal plants stretch back at least 5,000 years to the Sumerians, who recorded the long-standing therapeutic applications of plants like laurel, caraway, and thyme. This demonstrates unequivocally that people have utilized plant-based medicines and treatments to address a range of medical issues (Figure 2). Herbal remedies are still a good way to find potential pharmaceutical compounds. Traditional Chinese medicine (TCM) is a popular herbal remedy that has been demonstrated in numerous trials to increase the effectiveness of chemotherapy, lessen its side effects, and cause malignant cells to undergo apoptosis. Similar to traditional medical methods that were created over ages in many different countries, TCM is a type of tailored or customized medicine that is used to treat a variety of illnesses, including cancer[12, 18, 45, 59, 71-74].

Ayurvedic expertise in our nation has led to the hopeful use of natural goods, particularly plants, for the treatment of a variety of ailments over the years. Herbal medicine is the source of new drug discoveries in underdeveloped nations, which can result in a variety of healthcare problems and the creation of novel formulations. In contrast to other drug discovery sources, traditional medicine has produced a large number of innovative therapeutic molecules for both preventive and curative medicine. Numerous studies have documented the antimutagenic and anticancer activities of secondary metabolites, such as polyphenols, terpenes, and alkaloids. Since medicinal plants are antioxidant stores and have no toxicity compared to modern drugs, the idea of combining Ayurveda with advanced drug discovery may lead to some lead compounds that address a variety of human sufferings. This is why numerous studies on cancer drugs and the discovery of new lead molecules towards anticancer activity by using medicinal plants were proposed.

When a combination of components is more effective than a single one, this is known as a synergistic impact. Novel techniques, such as the use of natural chemicals in combination therapies, have been characterized as a result of data focused on the harmful events of chemotherapy. The inclusion of natural chemicals in cancer chemotherapies aims to reduce the incidence of chemotherapy resistance and increase the therapeutic window of the chemotherapeutic medicines. The following section will provide a summary of natural substances and herbal or folk medicines that are used in clinical settings as chemotherapeutic

protectors, chemoresistance reducers. or chemosensitizers. When combination а of components is more effective than a single one, this is known as a synergistic impact. Novel techniques, such as the use of natural chemicals in combination therapies, have been characterized as a result of data focusing on the harmful events of chemotherapy. Incorporating natural chemicals into cancer chemotherapies aims to (a) increase the therapeutic window of the medications used in the treatment and (b) reduce the incidence of chemotherapy resistance. The following section will provide a summary of natural substances and herbal or folk medicines that are used in clinical



Figure 2. Herbal drug(s) and the putative target(s).

settings as chemotherapeutic protectors, chemoresistance reducers, or chemosensitizers.

Cancer, which is defined by abnormal cell proliferation, is one of the most deadly diseases and poses several health risks in both developed and developing nations. Every biological alteration is seen when a healthy cell develops into a malignant one. Despite the fact that there are numerous cancer treatment options, cancer remains the second most common cause of death worldwide. More adverse effects were documented by patients receiving chemotherapy and contemporary cancer medications. Each year, millions of people receive a cancer diagnosis, which ultimately results in mortality. Every year, cancer claims the lives of approximately 3500 million people globally, accounting for more than 2-3% of all recorded deaths. Chemopreventive drugs are used to treat cancer with some degree of success, but their toxicity puts users at danger. High rates of cancer disease are caused by smoking, hormones, nutritional abnormalities, and persistent infections that cause chronic inflammation. There should be an immediate search for safer and alternative

treatment options for cancer due to the severe side effects of chemotherapy and radiation therapy. As the saying goes, "prevention is always better than cure." Cancer can be avoided by adopting healthy eating habits, abstaining from tobacco use, properly treating inflammatory disorders, and taking immune-boosting nutritional supplements. Chemotherapy is currently the only effective treatment option for controlling advanced cancer stages, although it is extremely damaging to healthy tissues. With the discovery of Podophyllotoxin in the late 1960s, the hunt for natural cancer medications began. This led to the discovery of vincristine, vinblastine, campthothecin, and taxol. There are around 1000 different plant species in nature that have strong anti-cancer effects. Etoposide, a synthetic derivative of Podophyllotoxin, is known to be effective for small cell malignancies of the lungs and testes. Taxol, one of the most remarkable drugs, has been proven to be helpful in treating refractory ovarian, breast, and other cancers. Finding medicinally significant plants and understanding how they work might offer a different and more efficient way to avoid cancer. Numerous medications have been created over the years using strong chemicals that have been extracted from medicinal plants. Three primary research methodologies are used in the drug discovery and development process: (1) Rational drug design entails the synthesis and modification of analogs; (2) Bioactivity is based on the mechanism of specific action-directed isolation and characterisation of active compounds; and (3) Mechanism of Action.

2.1. Natural substances that sensitize patients to chemotherapy drugs: Chemosensitization is the process by which various low molecular weight (MW) substances enhance the tumoricidal effect of chemotherapy medications, such as increasing the susceptibility of cancer cells to chemotherapeutic drugs. Both manufactured and natural substances can be used as chemosensitizers. The naturally occurring chemosensitizers that alert cancer cells to reacting medicinal drugs will be covered in this section. A natural alkaloid called vincristine, which was extracted from Catharanthus roseus, is being used to treat neuroblastoma and acute lymphocytic lymphoma. However, its limited therapeutic window and severe cytotoxicity limit its further usage, particularly in pediatric cancer. Another plant extract from Centaurea albonitens has also been discovered to have the potential to greatly increase vincristine's cytotoxicity against leukemia cell lines while lowering its toxicity to healthy cells. Many plant extracts have been tried in conjunction with doxorubicin to screen for synergistic effects and lessen the cardiotoxicity and resistance caused by the drug. Thus far, it has been demonstrated that an aqueous extract of Solanum nigrum Linn. can enhance the effects of doxorubicin against ovarian and colorectal cancer by inducing autophagy[45, 75-77].

2.2. Compounds from herbs lessen resistance to cancer treatment: Herbal remedies have been shown in clinical settings to lessen cancer treatment resistance, which is a serious worry. The most difficult part of treating cancer, particularly NSCLC and prostate cancer, is still medication resistance in cancer cells. Such resistance in malignancies indicates that the cells have changed from being receptive to drugs to being resistant to them, which increases toxicity and treatment costs. Cancer resistance is closely linked to 80-90% of cancer deaths and 90% of treatment failures in recurrent cancer therapy. The prevalent mechanisms of chemoresistance are divided into seven phases: drug flux, DNA damage repair, cell death inhibition, epithelial-mesenchymal transition (EMT), drug target alteration, drug inactivation, and epigenetics. Of these, drug flux is the most concerning issue. The ABCC family of transporters, also known as the multidrug resistance (MDR) proteins, and the Hedgehog receptor Patched 1 (protein patched homolog 1, PTCH1) are used by cancer cells to pump chemotherapeutic agents out of the cells. This reduces drug accumulation within cancer cells and, consequently, lowers the efficacy of drugs. MRPs, especially MRP1, are over-expressed in recurrent cancer cells, and their over-expression is linked to bad prognosis. PTCH1 is a recently identified drug efflux transporter that is also overexpressed in many metastatic cancers. PTCH1 also functions as a receptor in the Hedgehog/Gli signaling pathway, which activates Smoothened (Smo)/Gli transduction and results in growth factor expression. Certain chemotherapeutic agents, such as gefitinib, trastuzumab, and bevacizumab, specifically target growth factor signaling; however, cancer cells activate EMT, which causes anoikis resistance and ongoing activation of growth factor signaling during cancer invasion. EMT-induced chemoresistance has been found in a number of cancer types, including breast, prostate, and lung cancer[45].

According to recent research on natural substances' impact on chemoresistance, they either further decrease MDR protein expressions or block MDR protein activity. It demonstrates that MDR inhibition accounts for the highest incidence, even if there are MDR inhibitors and drugs that work through other routes. Interestingly, by suppressing the expression of glucose transporter 1 (GLUT1), silybin, a naturally occurring lignan that was separated from Silybum marianum, enables doxorubicin to overcome drug resistance in colorectal cancer. The Wnt/ β -catenin signaling system, which has been found to be a cisplatin resistance promoter through the ATM-mediated signaling pathway in laryngeal squamous cell carcinoma cells, may influence the expression of GLUT1[78-83].

By inhibiting ABC transporters, eleven distinct polyoxypregnanes that were isolated from Marsdenia tenacissima can fight doxorubicin resistance in multidrug-resistant cancer cell lines. A group of bisbenzylisoquinoline alkaloids block the transporter P-gp, which causes MCF-7/ADR breast cancer cells to accumulate a lot of doxorubicin and become considerably more cytotoxic. Six ergot alkaloids from Claviceps purpurea were investigated for their anticancer activity. The results indicated that these alkaloids may circumvent chemoresistance mechanisms in a variety of malignancies by means of unidentified signaling pathways. Furthermore, resveratrol and ellagic acid stopped ovarian cancer from

developing cisplatin resistance. Another stilbenoid, resveratrol, enhanced cisplatin absorption and efficacy, while (Z)-3,4,3',5'-tetramethoxystilbene, a stilbenoid, enhanced the anticancer activity of cisplatin in cisplatin-resistant osteosarcoma cells both in vitro and in vivo. In resistant uterine sarcoma cells, β -phenylethyl isothiocyanate and 6gingerol simultaneously reversed resistance to doxorubicin and cisplatin and down-regulated intracellular GSH levels. All things considered, the evidence points to the potential benefits of using herbal remedies in conjunction with existing treatments to treat recurring malignancies[7].

2.3. Bioactive Substances in Medicinal Plants: Bioactive substances with a range of pharmacological actions, including anti-cancer qualities, are abundant in medicinal plants. These substances fall into a number of major classes, including polyphenols, terpenoids, alkaloids, and flavonoids. Almost all fruits and vegetables include flavonoids, a diverse group of phytonutrients. They are well-known for having antioxidant qualities that aid in shielding cells from harm brought on by free radicals. Certain flavonoids are intriguing options for cancer prevention and treatment since they have been demonstrated to lower inflammation and stop the formation of cancer cells. Another important class of bioactive substances present in therapeutic plants are alkaloids. They have a variety of pharmacological properties, including as analgesic, anti-malarial, and anti-cancer actions, and are distinguished by their nitrogen-containing structures. Because of their strong anti-cancer effects, some well-known alkaloids, such vincristine and vinblastine, which are extracted from the Madagascar periwinkle, are already utilized in clinical settings. The largest and most varied class of secondary metabolites found in plants are terpenoids, sometimes referred to as isoprenoids. They have a variety of therapeutic uses and are essential to the growth and development of plants. Because terpenoids like taxol, which are taken from the bark of the Pacific yew tree, can stop cancer cells from dividing, they are frequently employed in cancer chemotherapy. A class of chemicals known as polyphenols is distinguished by the presence of many phenol groups. Their anti-inflammatory and antioxidant qualities are well-known. By altering several signaling pathways involved in cell development and death, polyphenols like resveratrol, which are present in grapes and red wine, have been investigated for their potential to prevent and treat cancer. In conclusion, a variety of pharmacological effects are provided by the bioactive substances found in medicinal plants, such as flavonoids, alkaloids, terpenoids, and polyphenols, which can be used to cure and prevent cancer. The entire potential of these molecules is still being discovered via ongoing research, opening the door for the creation of novel and potent medicinal medicines[84-86].

2.3.1. Flavonoids: One kind of polyphenolic molecule that is frequently present in plants is flavonoids. Two aromatic rings joined by a three-carbon bridge make up their fundamental structure. Subgroups of flavonoids, including flavonols, flavones, flavones, isoflavones, and anthocyanidins, can be further separated. Numerous fruits, vegetables, cereals, nuts, and drinks including tea and wine contain flavonoids. Citrus fruits, berries, onions, soybeans, and green tea are notable sources. Through a variety of methods, such as apoptosis induction, cell proliferation inhibition, angiogenesis suppression, and signaling pathway modulation linked to cancer progression, flavonoids have demonstrated anti-cancer benefits. For example, it has been shown that quercetin inhibits cell proliferation and causes apoptosis in a range of cancer cell lines[87-90].

2.3.2. Alkaloids: Alkaloids are a broad class of chemicals that include nitrogen and are distinguished by their heterocyclic ring structure. They are commonly utilized as medicinal agents and are well-known for their strong biological activity. Many plant groups, including the Solanaceae, Papaveraceae, and Ranunculaceae, contain alkaloids. By blocking topoisomerase enzymes, triggering apoptosis, and altering microtubule dynamics, a variety of alkaloids have demonstrated encouraging anticancer effects. For instance, strong topoisomerase I inhibitors used in cancer treatment include camptothecin, which is derived from the Chinese tree Camptotheca acuminata, and its variants. By preventing DNA repair, this activity stops cancer cells from proliferating. Similar to this, vinca alkaloids and taxanes cause apoptosis, or programmed cell death, in cancer cells by interfering with microtubule dynamics, which are necessary for cell division. Alkaloids like morphine are effective analgesics outside of oncology, while quinine has been essential in antimalarial therapies. However, because alkaloids can be toxic, their therapeutic use needs to be carefully controlled; exact dosage management is necessary because the difference between a therapeutic and toxic dose can be very thin. Because of their intricate structures, semi-synthetic derivatives are frequently created to maximize their pharmacological advantages and minimize their negative effects. Alkaloids' effectiveness in treating diseases, especially cancer, where new mechanisms of action are essential for overcoming resistance and improving patient outcomes, is increased by ongoing research into these substances, which also refines current ones[91].

2.3.3. Terpenoids: Terpenoids, sometimes referred to as isoprenoids, are a broad and varied class of naturally occurring substances made composed of five-carbon isoprene units. They can be divided into monoterpenes, sesquiterpenes, and triterpenes based on the quantity of isoprene units they contain. Terpenoids are present in a variety of plant materials, such as latex, resins, and essential oils. Citrus fruit limonene, Artemisinin from Artemisia annua, and Pacific yew paclitaxel are a few examples. By triggering apoptosis, preventing cell division, reducing angiogenesis, and altering signaling pathways, terpenoids have demonstrated anticancer effects. For instance, the chemotherapy drug paclitaxel, a diterpenoid, causes cell cycle arrest and apoptosis by interfering with microtubule dynamics. Because of its ability to stabilize microtubules, paclitaxel is a prime illustration of the therapeutic potential of terpenoids in the treatment of cancer.

6 of 12

It is used extensively in chemotherapy for a variety of tumors. Terpenoids' therapeutic application, however, presents difficulties like guaranteeing sufficient bioavailability, controlling possible toxicity, and resolving the difficulties posed by their natural production or extraction. These compounds are still being investigated for the creation of novel drugs, with an emphasis on structural changes to increase efficacy, lower toxicity, and improve delivery systems, thus expanding their use in oncology and other therapeutic fields[91].

2.3.4. Polyphenols: The presence of many phenolic rings distinguishes the broad class of chemicals known as polyphenols. They can be divided into subcategories such lignans, stilbenes, and phenolic acids. Plants are rich in polyphenols, especially in fruits, vegetables, cereals, and drinks like wine and tea. Green tea, almonds, berries, and grapes are important sources. Through a variety of mechanisms, including antioxidant activity, signaling system modification, apoptosis induction, and angiogenesis suppression, these substances have shown anticancer effects. For instance, it has been demonstrated that resveratrol, a stilbene present in grapes, inhibits cell proliferation and triggers apoptosis in a number of cancer cell lines. The bioactive substances obtained from therapeutic plants are attractive candidates for the creation of new anticancer drugs since they display a variety of chemical structures and modes of action. Nevertheless, more investigation is required to completely grasp their potential and maximize their therapeutic uses[92].

3. Therapeutic applications of herbal mdeicines for cancer therapy: The potential of medicinal herbs and the phytocompounds derived from them as effective supplemental cancer treatments is becoming more widely acknowledged. When used in conjunction with conventional therapies, herbal medicines have been shown in numerous clinical studies to improve cancer patients' quality of life, immune system function, and survival rate. Here, I quickly go over a few instances of clinical research that looked into the application of herbal remedies for different types of cancer as well as the creation of randomized controlled trials in this new field of study. Furthermore, I also provide new research on the cellular and biochemical mechanisms of herbal remedies in particular tumor microenvironments as well as the possible use of particular phytochemicals in cell-based cancer vaccine systems[9, 41, 50, 87, 88, 93-101].

Many anti-breast cancer drugs have been discovered through research into traditional Chinese medicines (TCM), however the majority of their modes of action are still unclear. These six types of TCM herbs-alkaloids, coumarins, flavonoids and polyphenols, terpenoids, quinone, and artesunate-have antibreast cancer properties. Curcumin and artemisinin are two examples of these phytochemicals with well-known chemical structures. For many years, substances in these categories have been consumed as dietary supplements or health foods. For normal general use or certain therapeutic uses, evidence-based in vivo research and clinical trials are still advised. It has been demonstrated that the oriental medicinal herb Wedelia chinensis (Asteraceae), which contains luteolin, apigenin, wedelolactone, and indole-3-carboxylaldehyde, can inhibit androgen action. Furthermore, W. chinensis extract inhibited the growth of prostate cancer when taken orally. Three active chemicals that can block the androgen receptor (AR) signaling pathway were later shown to be responsible for the anticancer effect of W. chinensis extract. According to recent findings, herbal medications and their phytochemicals, which appear to have little or no toxicity, may offer a promising treatment option for lung cancer. Historically, lung cancer has been treated with herbal plants like Platycodon grandiflorum (Campanulaceae), Morus alba (Moraceae), Prunus armeniaca (Rosaceae), Rhus verniciflua (Anacardiaceae), Perilla frutescens (Labiatae), Stemona japonica (Stemonaceae), Tussilago farfara (Compositae), and Draba nemorosa (Brassicaceae). Clinically, up to 77% of patients with lung cancer use herbal remedies as adjuvants in addition to traditional (such as chemotherapy) treatment. Herbs are mostly used to treat lung cancer in order to lessen the toxicity and symptoms of the disease that come with medication, and occasionally to directly boost anticancer benefits. The main arguments in favor of using traditional herbal medicines, however, continue to be case studies, empirical data, and potential physiological consequences. It is crucial to remember that some CAM techniques or therapies may have negative side effects or lessen the effectiveness of conventional treatment. Compound 861 is a combination of 10 herbs, including the pharmacologically active "king herbs" (Sage, Astragalus membranaceus, and Spatholobus suberectus) and seven other toxicity modifiers (modifiers of toxicity that work in concert with the king herbs to enhance immune function) that have been tested for antifibrotic properties in a number of experimental studies. Compound 861 was found to have positive effects on liver fibrosis in two uncontrolled open trials involving 60 and 22 individuals with chronic hepatitis B. Most treated patients showed both clinical and histological improvement[1-6, 9, 14].

Conclusions and future perspectives: Rich in herbal qualities, medicinal plants aid in the development of novel medications to treat a range of illnesses, including cancer, without having any harmful side effects on the patients they treat. Cancer research is reaching a significant milestone with the use of natural goods and traditional therapy based on Ayurvedic principles. The author of this review briefly discussed the value of traditional medicine, the use of medicinal plants to cure cancer, and the anti-cancer qualities of natural goods. Medicinal herbs are anticancer drugs because of their strong immunomodulatory and antioxidant qualities. Of the approximately 1000 species of plants, only a small number have been studied for their biological activity; therefore, more research into the anticancer potential of the plants exhibiting promising activity needs to be done. Vinblastine and Vincristine, two alkaloids of Vinca rosea, are among the strongest anticancer medications available. Taxol, which was extracted from Taxus brevifolia, has a significant role in

cancer treatment. According to this analysis, the primary cause of death in emerging nations like India is cancer. Rural and impoverished people may find that the less costly herbal medication treatment is a great option for efficiently treating malignancies of all kinds.

Most human societies have utilized a variety of plants-many of which are categorized in traditional Chinese medicineas medicines and medical treatments for centuries. As this review illustrates, during the past 20 years, a great deal of information has been produced, including clinical studies and trials on the pharmacological effects, use, and development into future medicines of herbs and derivative medicinal phytochemicals as anti-tumor and chemoprevention agents, as a result of renewed public interest and research efforts from scientific and medical communities worldwide. Even though a lot of work has gone into upgrading and verifying many traditional treatments or formulations that use numerous herbs, systematic, standardized research, FDA regulatory processes, and defined clinical studies are still relatively restricted and require deliberate pursuit. In order to speed up the discovery and development of new phytomedicines and botanical drugs, scientists, clinicians, and regulatory agencies must actively consider how to develop new, improved, or modified clinical surveys, studies, and trial mechanisms that use the strict trial standards of the twenty-first century while also incorporating, at the international level, the wealth of old empirical but incomplete data from various records and documents accumulated by traditional medicine practices worldwide. In the last few years, there have been some noteworthy "breakthroughs" in the field of medical plant research and botanical medications, although ongoing and methodical effort is still required. Veregen, a largely purified fraction of the aqueous extract of green tea leaves from Camellia sinensis, was previously licensed by the FDA as the first botanical medication for the topical treatment of external genital and perianal warts.

Author Contributions: Conceptualization, M.T.A.; methodology, M.T.A.; software, M.T.A.; validation, M.T.A.; formal analysis, M.T.A.; investigation, M.T.A.; resources, M.T.A.; data curation, M.T.A.; writing—original draft preparation, M.T.A.; writing—review and editing, M.T.A.; visualization, M.T.A.; supervision, M.T.A.; project administration, M.T.A.; funding acquisition, M.T.A. The author has read and agreed to the published version of the manuscript.

Funding: Not applicable.

Acknowledgments: We are grateful to the Department of Pharmacognosy and Pharmaceutical Chemistry, College of Dentistry and Pharmacy, Buraydah Colleges, Buraydah-51418, Al-Qassim, Saudi Arabia for providing us all the facilities to carry out the entire work.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

- Balkrishna, A., et al., Exploring the Safety, Efficacy, and Bioactivity of Herbal Medicines: Bridging Traditional Wisdom and Modern Science in Healthcare. Future Integrative Medicine, 2024. 3(1): p. 35-49.
- 2. Cheng, Y.Y., C.H. Hsieh, and T.H. Tsai, *Concurrent administration of anticancer chemotherapy drug and herbal medicine on the perspective of pharmacokinetics*. J Food Drug Anal, 2018. **26**(2S): p. S88-S95.
- Colalto, C., Herbal interactions on absorption of drugs: Mechanisms of action and clinical risk assessment. Pharmacol Res, 2010.
 62(3): p. 207-27.
- 4. Damery, S., et al., *The use of herbal medicines by people with cancer: a cross-sectional survey*. Br J Cancer, 2011. **104**(6): p. 927-33.
- Kuete, V. and T. Efferth, *Pharmacogenomics of Cameroonian traditional herbal medicine for cancer therapy*. J Ethnopharmacol, 2011.
 137(1): p. 752-66.
- 6. Kuruppu, A.I., P. Paranagama, and C.L. Goonasekara, *Medicinal plants commonly used against cancer in traditional medicine formulae in Sri Lanka*. Saudi Pharm J, 2019. **27**(4): p. 565-573.
- Lin, S.R., et al., Natural compounds as potential adjuvants to cancer therapy: Preclinical evidence. Br J Pharmacol, 2020. 177(6): p. 1409-1423.
- 8. Tavakoli, J., et al., *Evaluation of effectiveness of herbal medication in cancer care: a review study*. Iran J Cancer Prev, 2012. 5(3): p. 144-56.
- Yin, S.Y., et al., *Therapeutic applications of herbal medicines for cancer patients*. Evid Based Complement Alternat Med, 2013.
 2013: p. 302426.
- 10. Zhou, W., et al., *Systems pharmacology uncovers the mechanisms of anti-asthma herbal medicine intervention (ASHMI) for the prevention of asthma*. Journal of Functional Foods, 2019. **52**: p. 611-619.

- 11. Gavanji, S., et al., *Cytotoxic Activity of Herbal Medicines as Assessed in Vitro: A Review.* Chem Biodivers, 2023. **20**(2): p. e202201098.
- 12. Hogle, B.C., et al., *PXR as a mediator of herb-drug interaction*. J Food Drug Anal, 2018. **26**(2S): p. S26-S31.
- Liu, L., et al., Berbamine dihydrochloride suppresses the progression of colorectal cancer via RTKs/Akt axis. J Ethnopharmacol, 2023.
 303: p. 116025.
- 14. Majumdar, A., S. Saraf, and S.P. Rao, *Current Trends in Herbal Medicines Targeting to Renal Cell Metabolic Pathways in the Treatment of Cancer*. Pharmacological Research Natural Products, 2024.
- 15. Pochet, S., et al., *Herb-anticancer drug interactions in real life based on VigiBase, the WHO global database.* Sci Rep, 2022. **12**(1): p. 14178.
- 16. Salm, S., et al., *Current state of research on the clinical benefits of herbal medicines for non-life-threatening ailments*. Front Pharmacol, 2023. **14**: p. 1234701.
- 17. Xue, Y., et al., *Protective effects of scutellaria-coptis herb couple against non-alcoholic steatohepatitis via activating NRF2 and FXR pathways in vivo and in vitro.* J Ethnopharmacol, 2024. **318**(Pt A): p. 116933.
- Yang, A.K., et al., *Herbal interactions with anticancer drugs: mechanistic and clinical considerations*. Curr Med Chem, 2010. 17(16): p. 1635-78.
- 19. Chantrill, L.A., et al., *Precision Medicine for Advanced Pancreas Cancer: The Individualized Molecular Pancreatic Cancer Therapy* (*IMPaCT*) *Trial.* Clinical Cancer Research, 2015. **21**(9): p. 2029-2037.
- 20. Swerdlow, S.H., et al., *The 2016 revision of the World Health Organization classification of lymphoid neoplasms*. Blood, 2016. **127**(20): p. 2375-90.
- 21. Weber, J., et al., Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. N Engl J Med, 2017. 377(19): p. 1824-1835.
- 22. Weber, J.S., et al., Adjuvant Therapy of Nivolumab Combined With Ipilimumab Versus Nivolumab Alone in Patients With Resected Stage IIIB-D or Stage IV Melanoma (CheckMate 915). J Clin Oncol, 2023. **41**(3): p. 517-527.
- 23. Agarwal, N., C. Majee, and G. Chakraborthy, *Natural Herbs as Anticancer Drugs*. International Journal of PharmTech Research, 2012. 4(3): p. 1-12.
- 24. Ali Abdalla, Y.O., et al., *Natural Products for Cancer Therapy: A Review of Their Mechanism of Actions and Toxicity in the Past Decade.* J Trop Med, 2022. 2022: p. 5794350.
- 25. Babamohamadi, M., et al., *Anti-CTLA-4 nanobody as a promising approach in cancer immunotherapy*. Cell Death Dis, 2024. **15**(1): p. 17.
- Brown, S.-A., N. Sandhu, and J. Herrmann, Systems biology approaches to adverse drug effects: the example of cardio-oncology. Nature Reviews Clinical Oncology, 2015. 12(12): p. 718-731.
- 27. Childs, R.W. and M. Carlsten, *Therapeutic approaches to enhance natural killer cell cytotoxicity against cancer: the force awakens*. Nature Reviews Drug Discovery, 2015. **14**(7): p. 487-498.
- Derynck, R., S.J. Turley, and R.J. Akhurst, *TGFβ biology in cancer progression and immunotherapy*. Nature Reviews Clinical Oncology, 2021. 18(1): p. 9-34.
- 29. Kalubai Vari, K. and B. Rajasekaran, *Natural Products for Treatment of Chronic Myeloid Leukemia*, in *Anti-cancer Drugs*, B. Jasna, Editor. 2016, IntechOpen: Rijeka. p. Ch. 1.
- 30. Kibble, M., et al., *Network pharmacology applications to map the unexplored target space and therapeutic potential of natural products*. Nat Prod Rep, 2015. **32**(8): p. 1249-66.
- 31. Meimetis, N., D.A. Lauffenburger, and A. Nilsson, *Inference of drug off-target effects on cellular signaling using interactome-based deep learning*. iScience, 2024. **27**(4): p. 109509.

- 32. Peyressatre, M., et al., *Targeting cyclin-dependent kinases in human cancers: from small molecules to Peptide inhibitors*. Cancers (Basel), 2015. 7(1): p. 179-237.
- Xu, C., et al., Comparative safety of immune checkpoint inhibitors in cancer: systematic review and network meta-analysis. BMJ, 2018.
 363: p. k4226.
- 34. Alberghina, L., et al., *A Systems Biology Road Map for the Discovery of Drugs Targeting Cancer Cell Metabolism.* Current Pharmaceutical Design, 2014. **20**(15): p. 2648-2666.
- Allavena, P., et al., *Pathways connecting inflammation and cancer*. Current Opinion in Genetics & Development, 2008. 18(1): p. 3-10.
- 36. Hanahan, D., Hallmarks of Cancer: New Dimensions. Cancer Discov, 2022. 12(1): p. 31-46.
- 37. Hanahan, D. and R.A. Weinberg, Hallmarks of cancer: the next generation. Cell, 2011. 144(5): p. 646-74.
- 38. Luo, J., N.L. Solimini, and S.J. Elledge, *Principles of cancer therapy: oncogene and non-oncogene addiction*. Cell, 2009. **136**(5): p. 823-37.
- Abollo-Jiménez, F., R. Jiménez, and C. Cobaleda, *Physiological cellular reprogramming and cancer*. Seminars in Cancer Biology, 2010. 20(2): p. 98-106.
- 40. Adams, J.L., et al., *Big opportunities for small molecules in immuno-oncology*. Nature Reviews Drug Discovery, 2015. **14**(9): p. 603-622.
- 41. Ahmed, S., et al., A Network-Guided Approach to Discover Phytochemical-Based Anticancer Therapy: Targeting MARK4 for Hepatocellular Carcinoma. Front Oncol, 2022. **12**: p. 914032.
- 42. Al-Ubaidi, F.L., et al., *Castration therapy results in decreased Ku70 levels in prostate cancer*. Clin Cancer Res, 2013. **19**(6): p. 1547-56.
- 43. Alexander, S. and P. Friedl, *Cancer invasion and resistance: interconnected processes of disease progression and therapy failure.* Trends in Molecular Medicine, 2012. **18**(1): p. 13-26.
- 44. Antonia, S.J., et al., *Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial.* Lancet Oncol, 2016. **17**(7): p. 883-895.
- 45. Atanasov, A.G., et al., *Natural products in drug discovery: advances and opportunities*. Nat Rev Drug Discov, 2021. **20**(3): p. 200-216.
- 46. Bai, L. and S. Wang, *Targeting Apoptosis Pathways for New Cancer Therapeutics*. Annual Review of Medicine, 2013. **65**(1): p. 139-155.
- 47. Balandrán, J.C., A. Lasry, and I. Aifantis, *The Role of Inflammation in the Initiation and Progression of Myeloid Neoplasms*. Blood Cancer Discovery, 2023. 4(4): p. OF1-OF13.
- 48. Baracos, V.E., et al., *Cancer-associated cachexia*. Nature Reviews Disease Primers, 2018. 4(1): p. 17105.
- 49. Khan, B., et al., *Nivolumab and Ipilimumab Acting as Tormentors of Advanced Tumors by Unleashing Immune Cells and Associated Collateral Damage.* Pharmaceutics, 2024. **16**(6).
- 50. Qahwaji, R., et al., Pharmacogenomics: A Genetic Approach to Drug Development and Therapy. Pharmaceuticals, 2024. 17(7).
- Adams, S., et al., A Multicenter Phase II Trial of Ipilimumab and Nivolumab in Unresectable or Metastatic Metaplastic Breast Cancer: Cohort 36 of Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors (DART, SWOG S1609). Clin Cancer Res, 2022. 28(2): p. 271-278.
- Baba, M.R. and S.A. Buch, *Revisiting Cancer Cachexia: Pathogenesis, Diagnosis, and Current Treatment Approaches.* Asia-Pacific Journal of Oncology Nursing, 2021. 8(5): p. 508-518.
- 53. Bosch, F. and R. Dalla-Favera, *Chronic lymphocytic leukaemia: from genetics to treatment*. Nat Rev Clin Oncol, 2019. **16**(11): p. 684-701.

- 54. Bousquet, J., et al., *Systems medicine and integrated care to combat chronic noncommunicable diseases*. Genome Medicine, 2011. **3**(7): p. 43.
- 55. Browne, B.C., et al., *Global characterization of signalling networks associated with tamoxifen resistance in breast cancer*. The FEBS Journal, 2013. **280**(21): p. 5237-5257.
- 56. Carreira, S., et al., *Tumor clone dynamics in lethal prostate cancer*. Science Translational Medicine, 2014. 6(254): p. 254ra125.
- 57. Chang, A.J., et al., *High-risk prostate cancer classification and therapy*. Nature Reviews Clinical Oncology, 2014. **11**(6): p. 308-323.
- 58. Cunningham, J.J., A call for integrated metastatic management. Nat Ecol Evol, 2019. 3(7): p. 996-998.
- 59. Fu, B., et al., Multi-Component Herbal Products in the Prevention and Treatment of Chemotherapy-Associated Toxicity and Side Effects: A Review on Experimental and Clinical Evidences. Front Pharmacol, 2018. 9: p. 1394.
- 60. Alarcón, T., et al., *Multiscale modelling of tumour growth and therapy: the influence of vessel normalisation on chemotherapy.* Computational and Mathematical Methods in Medicine, 2007. 7(2-3): p. 85-119.
- 61. Bhat, M., et al., *Targeting the translation machinery in cancer*. Nature Reviews Drug Discovery, 2015. **14**(4): p. 261-278.
- 62. Brown, J.M., *Tumor Hypoxia in Cancer Therapy*. Methods in Enzymology, 2007. **435**: p. 295-321.
- 63. Duesberg, P., R. Stindl, and R. Hehlmann, Origin of multidrug resistance in cells with and without multidrug resistance genes: Chromosome reassortments catalyzed by aneuploidy. Proceedings of the National Academy of Sciences, 2001. **98**(20): p. 11283-11288.
- 64. Ferrari, P., et al., *Molecular Mechanisms, Biomarkers and Emerging Therapies for Chemotherapy Resistant TNBC.* International Journal of Molecular Sciences, 2022. 23(3): p. 1665.
- 65. Helleday, T., et al., DNA repair pathways as targets for cancer therapy. Nature Reviews Cancer, 2008. 8(3): p. 193-204.
- 66. Khan, H.A., et al., *Antiproliferative effect of Solanum nigrum L. water extract on breast can-cer cells: potential roles of apoptosis and oxidative stress.* Cell Mol Biol (Noisy-le-grand), 2023. **69**(10): p. 136-142.
- 67. Khandelwal, E., et al., Profile of Cardiovascular Autonomic Dysfunctions in Breast Cancer Patients. Cureus, 2023. 15(10): p. e46773.
- 68. McCubrey, J.A., et al., *Roles of the RAF/MEK/ERK and PI3K/PTEN/AKT pathways in malignant transformation and drug resistance.* Advances in Enzyme Regulation, 2006. **46**(1): p. 249-279.
- 69. Ramakrishnan, R., et al., *Chemotherapy enhances tumor cell susceptibility to CTL-mediated killing during cancer immunotherapy in mice.* Journal of Clinical Investigation, 2010. **120**(4): p. 1111-1124.
- 70. Shurin, M.R., Dual role of immunomodulation by anticancer chemotherapy. Nature Medicine, 2013. 19(1): p. 20-22.
- 71. Chen, C., et al., *Pioneering therapies for post-infarction angiogenesis: Insight into molecular mechanisms and preclinical studies.* Biomed Pharmacother, 2023. **166**: p. 115306.
- 72. Galluzzi, L., et al., *Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death* 2018. Cell Death Differ, 2018. **25**(3): p. 486-541.
- 73. He, B., et al., Synthesis and antitumor activity evaluation of coumarin Mannich base derivatives. Chem Biol Drug Des, 2023.
- 74. Wen, J., et al., *Selaginellin derivatives from Selaginella tamariscina and evaluation for anti-breast cancer activity*. Phytochemistry, 2023: p. 113919.
- 75. Ding, Z., et al., *Exploring the Mechanism of Action of Herbal Medicine (Gan-Mai-Da-Zao Decoction) for Poststroke Depression Based on Network Pharmacology and Molecular Docking.* Evid Based Complement Alternat Med, 2021. **2021**: p. 2126967.
- 76. Hao, X., et al., *Antitumor effect of luteolin proven by patient-derived organoids of gastric cancer*. Phytother Res, 2023. **37**(11): p. 5315-5327.
- 77. Huang, M.-Y., et al., Anticancer drug discovery from Chinese medicinal herbs. Chinese Medicine, 2018. 13(1): p. 35.
- Fluegen, G., et al., *Phenotypic heterogeneity of disseminated tumour cells is preset by primary tumour hypoxic microenvironments*.
 Nature Cell Biology, 2017. 19(2): p. 120-132.

- 79. Gatenby, R.A., et al., *Cellular adaptations to hypoxia and acidosis during somatic evolution of breast cancer*. British Journal of Cancer, 2007. **97**(5): p. 646-653.
- 80. Granit Mizrahi, A., et al., *Valproic acid reprograms the metabolic aberration of cisplatin treatment via ALDH modulation in triplenegative breast cancer cells.* Front Cell Dev Biol, 2023. **11**: p. 1217149.
- 81. Sergeant, G., et al., *The prognostic relevance of tumor hypoxia markers in resected carcinoma of the gallbladder*. European Journal of Surgical Oncology (EJSO), 2011. **37**(1): p. 80-86.
- 82. Sun, L., et al., Crystal structure of a bacterial homologue of glucose transporters GLUT1–4. Nature, 2012. 490(7420): p. 361-366.
- Vordermark, D. and J.M. Brown, *Endogenous Markers of Tumor Hypoxia*. Strahlentherapie und Onkologie, 2003. 179(12): p. 801-811.
- 84. Benakashani, F., A.R. Allafchian, and S.A.H. Jalali, *Biosynthesis of silver nanoparticles using Capparis spinosa L. leaf extract and their antibacterial activity*. Karbala International Journal of Modern Science, 2016. **2**(4): p. 251-258.
- 85. Muzammil, K., et al., Methanol extract of Iraqi Kurdistan Region Daphne mucronata as a potent source of antioxidant, antimicrobial, and anticancer agents for the synthesis of novel and bioactive polyvinylpyrrolidone nanofibers. Front Chem, 2023. **11**: p. 1287870.
- 86. Schoenafinger, G. and M.A. Marahiel, Wiley Encyclopedia of Chemical Biology. 2013: p. 1-9.
- 87. Anwer, S.T., et al., Synthesis of Silver Nano Particles Using Myricetin and the In-Vitro Assessment of Anti-Colorectal Cancer Activity: In-Silico Integration. Int J Mol Sci, 2022. 23(19).
- 88. Huwait, E. and M. Mobashir, Potential and Therapeutic Roles of Diosmin in Human Diseases. Biomedicines, 2022. 10(5).
- Koosha, S., et al., An Association Map on the Effect of Flavonoids on the Signaling Pathways in Colorectal Cancer. International Journal of Medical Sciences, 2016. 13(5): p. 374-385.
- 90. Ma, L., et al., Discovery of Myricetin as a Potent Inhibitor of Human Flap Endonuclease 1, Which Potentially Can Be Used as Sensitizing Agent against HT-29 Human Colon Cancer Cells. Journal of Agricultural and Food Chemistry, 2019. **67**(6): p. 1656-1665.
- 91. Rahman, M.M., et al., *In silico investigation and potential therapeutic approaches of natural products for COVID-19: Computer-aided drug design perspective.* Front Cell Infect Microbiol, 2022. **12**: p. 929430.
- 92. Alam, M.N., M. Almoyad, and F. Huq, *Polyphenols in Colorectal Cancer: Current State of Knowledge including Clinical Trials and Molecular Mechanism of Action.* BioMed Research International, 2018. **2018**: p. 4154185.
- 93. Almowallad, S., R. Jeet, and M. Mobashir, *Systems-level understanding of toxicology and cardiovascular system*. Jour. Bas. Sci., 2024. 5(1): p. 1-16.
- 94. Almowallad, S., R. Jeet, and M. Mobashir, *A systems pharmacology approach for targeted study of potential inflammatory pathways and their genes in atherosclerosis.* Jour. Bas. Sci., 2024. **6**(1): p. 1-12.
- 95. Bajrai, L.H., et al., Understanding the role of potential pathways and its components including hypoxia and immune system in case of oral cancer. Sci Rep, 2021. **11**(1): p. 19576.
- 96. El-Kafrawy, S.A., et al., *Genomic profiling and network-level understanding uncover the potential genes and the pathways in hepatocellular carcinoma*. Front Genet, 2022. **13**: p. 880440.
- 97. Helmi, N., D. Alammari, and M. Mobashir, *Role of Potential COVID-19 Immune System Associated Genes and the Potential Pathways Linkage with Type-2 Diabetes.* Comb Chem High Throughput Screen, 2022. **25**(14): p. 2452-2462.
- 98. Khan, B., et al., *Deciphering molecular landscape of breast cancer progression and insights from functional genomics and therapeutic explorations followed by in vitro validation.* Scientific Reports, 2024. **14**(1).
- 99. Mobashir, M., *The Understanding of the Potential Linkage between COVID-19, Type-2 Diabetes, and Cancer(s) Could Help in Better Drug Targets and Therapeutics.* Comb Chem High Throughput Screen, 2022. **25**(14): p. 2370-2371.
- 100. Mobashir, M., et al., An Approach for Systems-Level Understanding of Prostate Cancer from High-Throughput Data Integration to Pathway Modeling and Simulation. Cells, 2022. **11**(24).

101. Mustafa, S. and M. Mobashir, *LC-MS and docking profiling reveals potential difference between the pure and crude fucoidan metabolites.* Int J Biol Macromol, 2020. **143**: p. 11-29.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of JBS and/or the editor(s). JBS and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

Copyright: © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).