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HERBAL MEDICINES AS ADJUVENT THERAPIES FOR REDUCING CHEMOTHERAPY- INDUCED TOXICCITIES: A SYNERGISTIC ONCOLOGY APPROACH

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Abstract

Chemotherapy is still a key part of the treatment for cancer; however, chemotherapy remains limited effectiveness in terms of both effectiveness and safety/quality of life due to the many potential severe detrimental effects associated with chemotherapy (e.g., nausea, vomiting, mucositis, fatigue, myelosuppression, hepatotoxicity, nephrotoxicity, and neurotoxicity). As a result, these negative effects and consequences from these side-effects may decrease or in some cases completely stop syringes, schedules, and treatment outcomes. Yet recent years have brought about a growing interest in using herbal products as complementary therapies to reduce the severity of the side effects from chemotherapy. Studies show there are many plants used for medicinal purposes that have properties that will reduce the level of damage done to normal tissue as a result of chemotherapy due to their antioxidant/anti-inflammatory/immunomodulatory/cytoprotective properties. Specific examples of plants used in combination with chemotherapy are ginger (Zingiberofficinale), turmeric (Curcuma longa), ginseng (Panax ginseng), and milk thistle (Silybummarianum), made a positive impact on a variety of high-risk patients as well as

reduce the number of gastrointestinal side effects, stimulate the immune system, and protect other vital organs from damage/disorders caused by chemotherapy. The appropriate synergistic combination of conventional cancer treatments and evidence-based herbal medicine may be able to offer a combined approach to enhancing people living with, or at risk of developing cancer with their ability live with this illness. However, it is important to note that caution must be taken with respect to potential adverse interactions between herbs and drugs, the variability of herbs in different preparations, and overall lack sufficient clinical data regarding efficacy and safety. The purpose of this article is to provide an overview of the authors' research and findings on the role of herbs as adjunctive therapies in achieving the desired outcome through the reduction of side effects from chemotherapy; the mechanisms of action, the clinical evidence of benefits observed and, safety concerns; and future directions of the role of herbs in the field of integrative oncology to enhance quality of life of patients and to improve effectiveness and tolerability of chemotherapy treatments.

Keywords: Herbal medicines, Adjuvant therapy, Chemotherapy-induced toxicities, Integrative oncology, Antioxidants, Cancer supportive care, Herb–drug interactions, Cytoprotection, Immunomodulation, Quality of life

Introduction

Globally, cancer is one of the most serious health problems and continues to be a major cause of mortality. Although there have been major advancements made in the diagnosis, prevention, and treatment of cancer, there is still a growing cancer burden due to population growth, the aging population and risk factors associated with lifestyle. Chemotherapy is one of the most common treatment methods used for many different types of cancer and it is a necessary component in increasing survival rates and managing the progression of cancer. However, due to the non-selective action of many chemotherapeutic agents, patients are also subject to adverse effects from the treatment itself, such as; nausea, vomiting, fatigue, mucositis, neurotoxicity, nephrotoxicity, hepatotoxicity, and myelosuppression. These complications can significantly influence the patient's quality of life and may result in interruptions of treatment, reductions in dosages, or discontinuation of therapy. Therefore, there is a significant need for effective support care to manage the side effects of chemotherapy, while maintaining the efficacy of the therapy. With the increased interest in using complementary and integrative medicine, there is a growing interest among researchers in investigating the potential use of natural healing modalities, particularly herbal medicine, as adjunct therapies for patients with cancer receiving chemotherapy. (Bray et al., 2024)

For thousands of years, many cultures have utilized herbal medicine as a healing method, including Traditional Chinese Medicine (TCM), Ayurveda, Unani medicine, and various indigenous health care systems. These natural medicines contain so many different types of active substances (flavonoids, alkaloids, terpenoids, phenolic acids, and polysaccharides), which can all provide therapeutic properties. In recent years, many research studies have focused on determining how beneficial herbal medicines can be when combined with modern medicine, especially in cancer care. Many of the herbs used for medicinal purposes have antioxidant, anti-inflammatory, immunomodulatory, and tissue-protecting effects, and this is why many cancer patients use herbal products to assist in managing their treatment-related side effects. Additionally, there is a high prevalence of cancer patients worldwide who report the use of herbal products along with conventional treatments to address symptoms, enhance quality of life, and increase overall health. As the popularity of herbal medicine continues to grow, practitioners and researchers are studying the role of herbal medicine in evidence-based integrative oncology. Thus, the use of herbal medicines is being evaluated as supportive therapies to work in conjunction with chemotherapy, thereby enhancing outcomes through reduced toxicity and symptom management. (Yang et al., 2021)

Chemotherapy-related toxicities are caused primarily via many different types of biological mechanisms, including oxidative stress, inflammation, apoptosis, mitochondrial damage, and changes in the immune system. The majority of chemotherapeutic agents will produce an overabundance of reactive oxygen species, which subsequently damage the cellular components (e.g., proteins, lipids, DNA) of the affected cells. This oxidative damage significantly contributes to organ toxicity or complications arising from cancer treatment, as well as increases the injury to tissues resulting from the inflammatory pathways activated during chemotherapy that aggravate the injury sustained to other organs. These combined toxicities can affect many different organ systems, such as the gastrointestinal tract, liver, kidneys, bone marrow, and central nervous system; therefore, patients during treatment may experience considerable negative symptoms from these toxicities that can hinder treatment compliance and treatment outcomes. Herbal medicine is an alternative therapy that has been sought out as many of the compounds derived from plants have the ability to counteract the pathology associated with treatment-related toxicities; i.e., most commonly described is that of the antioxidant properties of these compounds which help neutralize free radicals and the anti-inflammatory properties of these compounds that can reduce the amount of cytokine-induced tissue destruction. Some plant-derived compounds, along with having antioxidant and anti-inflammatory

properties, also have been shown to possess cytoprotective properties and immunoregulatory activity that could provide support for normal cellular function during chemotherapy. Collectively, these multifaceted biological activities suggest that herbal medicines present a beneficial approach to reduce the treatment-related toxicities associated with chemotherapy and improve patient tolerance to the effects of chemotherapy. (Mohammed et al., 2022)

Encouraging evidence has been published regarding the use of several medicinal herbs in preventing and treating adverse reactions associated with the treatment of cancer by chemotherapy. Ginger (Zingiberofficinale) has been one of the most extensively researched herbs for alleviating nausea and vomiting due to chemotherapy, and numerous clinical and experimental studies have shown its positive effect. Turmeric (Curcuma longa), including its active component curcumin, appears to have strong antioxidant and anti-inflammatory effects that may protect normal tissues from injuries caused by chemotherapy. Similarly, ginseng (Panax ginseng) has been studied as a potential treatment for fatigue due to cancer, as well as for its beneficial effects on the immune system and overall quality of life in patients. Milk Thistle (Silybummarianum) has traditionally been used for its hepatoprotective properties, which may be helpful in reducing hepatotoxicity from some of the drugs used to treat cancer. Herbs such as astragalus, green tea extract, and various mushrooms have demonstrated potential therapeutic benefits for cancer patients. While these medicines differ in terms of both efficacy and mechanism of action, an accumulating body of evidence suggests that herbal medicine can assist with control of symptoms, reduction of toxicity, and improvement of quality of life for patients undergoing chemotherapy when used as adjuncts to standard chemotherapy. (Wang et al., 2020)

Before herbal medicine can be integrated into oncology practices, there are several factors that need to be overcome. One of the biggest issues with the use of herbal medicines in cancer treatments is the potential for herb-drug interactions. Herb-drug interactions can affect how much of the chemotherapeutic agent is ultimately absorbed by the body, metabolized, distributed to tissues, or eliminated from the body. An interaction between an herb and a chemotherapeutic agent could lead to a decrease in the effectiveness of the treatment or increase the risk of experiencing side effects. In addition, the variability among species of plants, how the plants were grown, how they were harvested, how they were extracted, and how they were formulated can all lead to differences in quality and effectiveness of the herb. The lack of standardized product preparation, as well as limited regulatory guidance in some countries, further complicates the safe use of herbal products in cancer care. In addition, the majority of

the research available regarding the use of herbal medicines has been conducted within a preclinical model, and there is still limited clinical research supporting the use of many herbal interventions. Therefore, when considering herb therapies, healthcare providers must take the time to thoroughly evaluate the existing literature before making a recommendation regarding the use of herbal products. Lastly, both patients and their healthcare team must communicate effectively with each other, in order to maximize the potential advantages of herbal products used with an individual's chemotherapy therapy. (Fuzimoto&Isidoro, 2021)

Integrative oncology is a developing field that synthesizes conventional cancer treatments, and with additional evidence-based complementary therapies, to provide improved patient outcomes and improve the patient's quality of life. Within this field, the use of herbal medicine as an adjunct (and complementary) therapy has gained recognition for its potential to address the many causes of chemotherapy-induced toxicities through its pharmacological properties (e.g., antioxidant, anti-inflammatory, immunomodulator, and organ protector). Nevertheless, in order for herbal medicines to successfully become a part of the clinical oncology care treatment plan, there needs to be robust scientific research, standardized products (herbal medicines), comprehensive safety evaluations, and well-designed clinical trials completed. Collaboration and teamwork will be required among oncologists, pharmacists, researchers, and complementary medicine professionals to develop these evidence-based clinical treatment protocols/guidelines for herbal medicine use in the treatment of patients with cancer. Thus, understanding the benefits of herbal medicine as adjuvant therapies, mechanisms of action, limitations, and safety considerations are necessary for forward movement in the field of integrative cancer care. Therefore, the purpose of this review is to assess the current evidence regarding the use of herbal medicines as an adjunct to reduce chemotherapy-induced toxicities and to identify opportunities to improve tolerability of treatment and improve the patient's quality of life through the use of herbal medicine. (Deng &Cassileth, 2020)

Chemotherapy Causes Various Toxicities and Side Effects

Chemotherapy represents one of the most common and widely utilized cancer treatment modalities in modern oncology. Chemotherapy can kill cancer cells, limit tumor growth, limit metastasis, and increase patient longevity. However, chemotherapy is associated with a large number of adverse effects and toxicities that involve almost every organ system in the human body. In general, chemotherapeutic agents cannot adequately differentiate between malignant and normal rapidly growing cells; therefore, non-cancerous tissue such as bone marrow, gastrointestinal mucosa, hair follicles, and

reproductive cells may also be injured as a result of treatment. Adverse effects (or toxicity) include a variable range of degrees of severity depending upon multiple factors including (but not limited to) the type of cancer, the chemotherapy regimen, the total dose given, the duration of treatment, and the patient's chronological age and general medical condition. Adverse effects may be temporary or permanent, and can range from mild discomfort to severe life threatening complications. Many patients experience treatment interruptions due to adverse effects of chemotherapy, which may require dose adjustment, delay in treatment administration, or discontinuation; all of which will decrease the effectiveness of treatment and adversely impact the ultimate outcome of that patient. (Miller et al., 2023)

Chemotherapy has a high rate of gastrointestinal (GI) toxicity. Chemotherapy damages the cells that line the intestines, causing nausea/vomiting, diarrhea, constipation, abdominal pain, and mucositis (oral bleeding). Chemotherapy also causes nausea and vomiting, which are difficult to control, even with medication. If a patient gets dehydrated, malnourished, or has electrolyte problems, they are less likely to continue treatment. Mucositis can affect a patient's ability to eat and drink. If the mucosa in the intestines is damaged, the patient may experience diarrhea and have a greater risk of infection. Each of these GI side effects can cause weight loss, weakness, and decreased quality-of-life (QOL) for the patient. Additionally, these side effects can cause anxiety/depression, as well as affect socialization and other activities that make the patient happy. Therefore, it is important to adequately manage GI toxicities to preserve the patient's nutritional status, support the patient's willingness to continue treatment, and improve the patient's outcomes. Researchers are currently investigating new treatments/interventions to help patients with the side effects of GI toxicity from chemotherapy, as well as to improve the patient's overall quality of life. (Smith et al., 2021)

Chemotherapy's most serious side effects are hematological toxicities because they affect the production of blood cells and can result in severe clinical complications, such as anemia, neutropenia, and thrombocytopenia. Chemotherapy drugs cause decreased bone marrow function resulting in less production of red blood cells (RBCs), white blood cells (WBCs), and platelets. Anemia leads to less oxygen being carried in the blood; symptoms include decreased stamina, dizziness and decreased physical performance. Neutropenia decreases immunologic function, leading to a higher incidence of bacterial, viral and fungal infections, which can be life-threatening if not treated appropriately. Thrombocytopenia results in a diminished ability to form blood clots, resulting in increased risk for bleeding and bruising. As a result of these

hematological complications, patients may require additional medical interventions such as blood transfusions, growth factor therapy, and antibiotic therapy. In some cases, chemotherapy dose reductions or chemotherapy treatment delays are necessary due to severe suppression of the bone marrow, which may impact cancer control and patient survival. Therefore, regular monitoring of blood counts during treatment is critical to patient safety. Prevention and management of hematological toxicities are important to comprehensive cancer care and supportive oncology practice. (Johnson et al., 2022)

There are many well-known complications associated with numerous commonly used chemotherapeutic agents, including neurotoxicity, that have significant long-term impacts on cancer patients who survive their disease. Peripheral neuropathy caused by chemotherapy is very common among cancer patients; it can cause numbness, tingling, burning, pain, weakness in the muscles, and loss of coordination. The hands and feet are usually affected, with an increased severity in symptoms seen over time with ongoing treatment. In severe cases, patients may have difficulty walking and maintaining balance, or performing activities of daily living like writing or closing buttons. Certain chemotherapy agents can also damage the central nervous system, leading to cognitive impairments commonly called "chemo brain." Patients may report having difficulty remembering things, concentrating, paying attention, or processing information. Neurotoxicity associated with chemotherapy is thought to be due to several underlying mechanisms, including oxidative stress, inflammation, mitochondrial dysfunction, and direct neuronal injury. Unlike many short-term side effects from chemotherapy, neurological complications can persist for months to years after the end of chemotherapy, greatly affecting overall long-term quality of life. Regrettably, no effective treatment is available to reverse the effects of neurotoxicities secondary to chemotherapeutic agents; current treatment options largely consist of managing symptoms. Thus, identifying effective strategies for both prevention and protection against chemotherapy-induced neurotoxicity should continue to be a key focus area of both oncology research and clinical practice. (Anderson et al., 2020)

Chemotherapy is also known to create a significant amount of toxicity in the major organs of the body (liver, kidneys, heart, and lungs) and can add to the challenges of managing cancer. Hepatotoxicity, or damage to liver cells due to the use of chemotherapy drugs, can lead to an increase in liver enzymes, inflammation, impaired metabolic function, or in severe cases, complete liver failure. When kidney injury from chemotherapy affects kidney tissue, nephrotoxicity occurs and this will result in a decreased ability for the kidneys to filter waste from the blood and to maintain normal fluid and electrolyte balance. Cardiotoxicity is another important concern when using

some anticancer medications that can have an adverse effect on how the heart muscle works. The patient with cardiotoxicity can experience hypertension, arrhythmias, decreased cardiac output, or congestive heart failure. While pulmonary toxicity is seen less frequently compared to other organ toxicities, it can result in damage to lung tissue and lead to symptoms of inflammation, pulmonary fibrosis, or impaired breathing ability. There are many factors that contribute to the toxicities that occur in the organs mentioned above (e.g., individual patients may have received different amounts of medication over time, the age of the patient, genetics of the patient, if the patient has a pre-existing medical condition). Therefore, it is critical for providers to monitor patients via laboratory tests, imaging studies, and clinical evaluations for early recognition of complications and to assist in preventing irreversible damage from occurring. The ability to effectively manage the organ toxicities caused by chemotherapy is critical to maintaining continuous treatment and ensuring patient safety. Researchers are continuing to develop new protective measures to help have less organ damage due to chemotherapy, and not affect the anticancer properties of the chemotherapy assigned to the individual patient. (Brown et al., 2021)

Chemotherapy-induced toxicities have a large impact not only on physical health but also negatively affect psychological, emotional, and social well-being. Anxiety, depression, fear, frustration, and emotional distress can arise from long-lasting side-effects of chemotherapy as well as an uncertain treatment outcome. Routine daily activities become more difficult due to chronic fatigue, pain, and physical limitations. Body image, self-esteem, and social confidence may be decreased by visible side effects such as hair loss and weight changes. Severe toxicities can also impact job performance, family obligations, and relationships with others, creating a large burden socially and financially. Increasing healthcare costs due to frequent hospital visits, additional medications, and supportive therapies contribute to financial stress for both the patient and the caregiver. The total burden of these challenges can significantly reduce an individual's overall quality of life and may also influence a patient's willingness to continue treatment. As a result, contemporary oncology places increasing emphasis on providing patient-centered care that addresses disease control, as well as symptom management and psychosocial support. Supportive programs actively provide counseling and nutritional support, rehabilitation services, and complementary therapies; therefore, these programs are critical to helping patients manage chemotherapy-related toxicities while they receive chemotherapy, ensuring they retain the maximum quality of life possible during their treatment course. (Thomas et al., 2022)

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Herbal Medicines Can Help Reduce Treatment-Related Toxicities

The rising interest in herbal medicine as complementary approaches to cancer treatment focuses on their ability to support treatment-related toxicity reduction and improve patients' quality of life. The side effects from chemotherapy and other anticancer therapies typically occur because of the destruction of both tumor and healthy tissue. These side effects include but are not limited to alopecia, nausea/vomiting, fatigue, inflammation, oxidative stress, immune suppression and/or damage to vital organs. Herbal medicine includes bioactive compounds that are available from the plant's essential components (e.g. flavonoids, polyphenols, alkaloids, terpenoids, alpha-glucans), which have a protective impact against the aforementioned side effects. Furthermore, many of the medicinal plants that produce these compounds also possess antioxidant, anti-inflammatory, immunomodulatory and cytoprotective activity that assist in maintaining normal cell function during cancer treatment. Herbal medicines may also produce broad-spectrum effects because of their multiple mechanisms of action, unlike traditional medication, which typically act through a single pathway. To effectively support the use of herbal medicine in modern oncology, there has already been ongoing scientific research on the benefits of herbal medicine as traditional medicine. However, herbal medicine is typically used as a complementary treatment along with traditional cancer treatment (i.e., not a replacement). Therefore, careful evaluation of herbal medicine's effectiveness, expected side effects and interaction with chemotherapy drugs is paramount prior to incorporating evidence-based herbal medicine into supportive cancer care; this may improve patients' tolerance of their treatment and/or enhance their overall quality of life. (Patwardhan et al., 2020)

Toxicities related to chemotherapy are frequently caused by increased oxidative stress or inflammation that damage cells and organs. Many herbal medicines appear to have beneficial effects against these damaging processes due to their high content of natural antioxidants and anti-inflammatory compounds. Oxidative stress develops when the body produces more reactive oxygen species than it can neutralize, resulting in damage to proteins, lipids, and DNA. A number of herbal agents have demonstrated the ability to scavenge free radicals and enhance the activity of antioxidant enzymes in cells. Plant-derived compounds can also modulate inflammation by inhibiting the production of inflammatory mediators that lead to cellular damage during cancer therapy. These protective mechanisms can help alleviate common side effects of chemotherapy such as fatigue, damage to mucous membranes, and organ toxicity. Certain herbal products could help modulate immune function through enhancement of the activity of immune cells and maintenance of an appropriate balance in immune responses. In this way,

herbal medicines can assist in minimizing the adverse effects of cancer treatments. However, herbal medicines should be used with caution because overly large doses or improper use may produce undesired consequences or interfere with the effectiveness of anticancer drugs. (Rashidi et al., 2021)

Herbal medicines may be able to relieve side effects of chemotherapy via their pharmacological properties. Ginger (Zingiberofficinale) has been studied widely for its ability to reduce nausea and vomiting caused by chemotherapy. Active constituents in ginger include gingerols and shogaols that affect the gastrointestinal system and may result in increased digestive comfort. Turmeric (Curcuma longa) contains curcumin, a compound that has very potent antioxidant and anti-inflammatory properties, and may protect healthy tissue from injury caused by chemotherapy. Ginseng (Panax ginseng) has been explored as a potential means of relieving fatigue associated with cancer treatment and for its ability to support the immune system of patients receiving treatment. Milk thistle (Silybummarianum) contains silymarin, which has shown protective effects in the liver and may help alleviate the hepatotoxicity caused by drugs. Other herbal products, including green tea extracts and medicinal mushrooms, have also been investigated for their potential benefits. Herbal medicines may act in other ways (e.g., reducing oxidative stress, modulating inflammation, enhancing cellular defense); the evidence base is still evolving; however, research suggests that herbal medicines can be of value as supportive agents to improve tolerance to chemotherapy and increase patient quality of life. (Zhou et al., 2022)

Herbal remedies have been shown to improve the functionality of the Immune System and support recovery from cancer therapy. Chemotherapy is known to induce immunosuppression through a decrease in both the quantity and function of immune cells; due to this, chemotherapy patients are more likely to develop infections and delayed healing after treatment. Immunomodulatory substances found in certain herbal plants may regulate immune system function and improve the body's natural defenses through the use of these compounds. Studies have shown that polysaccharides, flavonoids, and other phenolic compounds derived from numerous phytonutrients have the ability to influence the function of immune system cells, such as macrophages, lymphocytes, and natural killer cells. Using complementary therapies such as these may decrease treatment-related weakness and improve a patient's general wellbeing as a result of their ability to support the immune system. Additionally, some herbal remedies may promote the repair of damaged tissue and provide cellular protection through enhancing antioxidant protection and decreasing inflammation. As a result of the improved immune system regulation, many patients may have better tolerance to

chemotherapy and be able to stay on schedule with their treatment. There are many factors that can affect the strength of the immune modulatory properties of herbal medicine; they may vary based on the type of plant used, the dose consumed, the method of preparation and/or the condition of the user. Prior to implementing the use of herbal remedies into routine supportive care for cancer patients, there must be adequate scientific evidence and physician oversight. (Kumar et al., 2021)

Although it has been proven that herbal medicines can alleviate some of the side effects associated with chemotherapy, there are still few significant obstacles that need to be addressed prior to their general use in practice. The potential for herb-drug interactions is one of the issues. Herbal medicines may modify how chemotherapy agents are absorbed and/or metabolized as well as their effectiveness. Additionally, some of the herbs can influence drug-metabolizing enzymes and transporters in such a manner as to either increase toxicity or reduce effectiveness. Secondly, herbal products lack standardization because the active ingredients can vary due to differences in the plant species themselves, the conditions under which they were grown, the extraction processes used to develop them, and/or the concentrations of the active compounds within each product. These differences can lead to inconsistent results and difficulties in comparing the findings of various studies. Lastly, while laboratory and animal studies show great promise regarding herbal medicine's ability to provide protection against the side effects of chemotherapy; to date there have not been any published large-scale clinical trials to determine the safety of herbal medicines, their optimal dosage, and their modality of action in cancer patients. Therefore, health care providers must thoroughly assess whether or not to recommend herbal medicine use to individual patients by carefully taking into account the unique characteristics of that particular patient. When used correctly, evidence-based herbal medicines can provide an excellent adjunct therapy to reduce the complications associated with chemotherapy and to improve the overall experience of being treated for cancer. (Li et al., 2023)

Integrative oncology is a research field that has a growing interest in examining how herbal medicinal products can be used to diminish the adverse effects of conventional cancer treatment. The potential benefits of using select herbal medicinal products in conjunction with established cancer treatment modalities creates the possibility for a more holistic approach to delivering care and improvement of quality of life through herbal medicine in the areas of symptom control, normal tissue protection and restoration of physical status post-chemotherapy. The antioxidant, anti-inflammatory, immunomodulatory and protective aspects of herbal medicine make them an appealing choice for the management of adverse effects of cancer therapy.

Effective incorporation of herbal medicine into treatment regimens requires adequate scientific support for the safety and efficacy of certain products, standardized preparations and collaboration between oncologists, researchers and other health care providers. All patients that utilize herbal medicinal products should disclose this information to their health care providing team members to prevent potential drug interactions and optimize patient safety. Future research needs to include well-designed clinical studies that evaluate both the long-term benefits and risks of herbal medicine use in various cancer populations. If current research supports the implementation of herbal medicine as efficacy-enhancing and/or toxicity-reducing adjuncts to conventional cancer treatment, then these products will become invaluable supportive measures for enhancing chemotherapy tolerance and reducing toxicity as well as improving outcomes for individuals with cancer. (Chen et al., 2020)

Herbs Have Antioxidant and Anti-Inflammatory Properties

The antioxidant and anti-inflammatory properties of herbal medicines have been shown to provide important supportive roles in treating the side effects of treatments such as chemotherapy (Hess et al., 2021). Bioactive compounds including flavonoids, phenolic acids, tannins, terpenoids, and alkaloids contained in many medicinal plants are responsible for their protective effects. Antioxidants, which are commonly found in herbs, help to counteract the effects of excess oxidative stress caused by reactive oxygen species (ROS) and therefore prevent damage to cells as a result of these conditions. Excess oxidative stress may lead to damage to the DNA, proteins, or membranes of cells resulting in tissue damage or organ dysfunction. Herbal compounds may assist in enhancing the native antioxidant defence systems of the body by enhancing protective enzymes that maintain the balance of the cell and supporting recovery through reducing pain and inflammation associated with cancer therapies (Hess et al., 2021). A number of herbs not only possess antioxidant properties but have also been shown to regulate inflammation through the inhibition of production of inflammatory mediators (such as cytokines) and through the inhibition of enzymes involved in tissue damage. Due to these synergistic effects, the combined activity of many medicinal plant species will provide a mechanism of action that will assist in preserving healthy cells and reducing inflammation, therefore assisting in recovery from cancer therapies. The multi-pathway approach of herbal medicines adds potential value as complementary therapies in the management of various conditions. However, it is important to carefully analyse their safety, dosage, and interactions prior to clinical use. (Sultana et al., 2020)

Oxidative stress and long-term inflammation are two significant biological processes associated with various complications during treatment. Anticancer medications used during chemotherapy may create large amounts of free radicals, leading to damage of healthy tissues such as the liver and kidneys, nervous tissue, and the gastrointestinal tract. Because of the antioxidant properties that many herbal medicines possess, they may be able to counteract these negative effects by utilizing their natural antioxidant properties. Antioxidants derived from plants can provide electrons to unstable molecules to help prevent additional injury to the cell and maintain normal physiological function. Moreover, many herbs also have anti-inflammatory properties, which play a role in regulating excessive immune responses and reducing tissue inflammation. Compounds found in plants—such as polyphenols and flavonoids—can target signal transduction pathways involved in inflammation, resulting in decreased release of damaging inflammatory products. Herbal medicines, therefore, may help alleviate many signs and symptoms experienced during treatment for cancer, such as pain and fatigue, as well as irritation to the tissues. The combination of the antioxidant and anti-inflammatory activities of herbal medicines makes them potentially an excellent source of broad biological support. Thus, researchers are continuing to explore the use of medicinal plants as adjuvant therapies in patients to increase tolerance and reduce the negative effects of traditional treatments. (Rahman et al., 2021)

Numerous herbal medicines frequently used contain powerful active phytochemicals shown in research to possess significant antioxidant and anti-inflammatory actions. An example of this would be curcumin extracted from turmeric root (Curcuma longa) which has been studied extensively for its effects on reducing inflammation/bum-out of cells due to oxidative damage; examples of other herbs include ginger (Zingiberofficnale) due to the presence of Gingerol (among other types) exhibiting antioxidants, supporting the regulation of inflammation pathways, and contributing positively toward both cellular function and tissue vitality. Many of these types of herbs have also been shown to contain other active phytochemicals related to immune system regulation as well as providing support for maintaining the health of tissues such as garlic (Allium sativum), ginseng (Panaxquinquefolius), and certain medicinal mushrooms (Agaricusblazei). The use of these types of herbs in conjunction with medical treatment involving chemotherapy may offer ways to reduce the detrimental effects associated with chemotherapy by providing protection to healthy cells while also promoting normal physiological systems. Antioxidant properties provide integrity to cellular function, and the anti-inflammatory properties can help dampen/lessen/mitigate excessive immune system activation/damage due to therapy. A

combination of action from multiple active phytochemicals present in herbs may take place through their various mechanisms to benefit patients receiving supportive cancer care. Further research is needed on standardizing products and evaluating their therapeutic impact on patients. (Gupta et al., 2022)

The mechanisms of action of herbal medicines in relation to antioxidants and inflammation are closely associated with the capacity of herbal medicines to achieve and preserve homeostasis of cells throughout the disease continuum and/or during treatment. Chemotherapy often produces the toxic effects of disrupting normal cellular function through mechanisms such as mitochondrial damage and increased inflammatory signaling. In many cases, herbal compounds contribute to restoring homeostasis (homeostasis = a healthy balance) to the body through enhancing the activity of enzymes that provide protection against oxidative damage, which occurs as a result of chemotherapy-related toxicities (i.e., chemotherapy-related oxidative damage). Most plant materials (i.e., phytomedicines) have an effect on several critical molecular pathways that regulate inflammation, including the molecular pathways responsible for releasing inflammatory cytokines and other inflammatory mediators. Therefore, phytomedicines may reduce tissue damage and promote wound healing through regulating the molecular mechanisms related to inflammation. Additionally, some studies have shown that a number of herbal extracts, by providing protection to immune cells, may help to maintain a balanced immune response to stress. These properties of herbal medicines are particularly valuable in the management of patients with cancer who may experience decreased immunity to and increased risk for complications due to the effects of chemotherapy. While the biological activity of herbal medicines is certainly a promising area, it is important to keep in mind that the therapeutic benefits of herbal medicines will depend on a variety of factors, including preparation type (e.g., powder, tincture, etc.), concentration of the active ingredient(s), and the extent to which an individual responds to the herbal medicine(s). It is very important that there is adequate scientific evidence to substantiate that herbal medicines will be safe and effective in conjunction with conventional therapies. (Park et al., 2021)

Herbs with both antioxidant and anti-inflammatory properties form the basis for their incorporation into modern health care as an adjunctive means of therapy. Various conditions may cause chronic disease, and treatment-related complications from chronic disease, by causing excessive oxidative (free radical) stress and out-of-control inflammation. As a result, oxidative stress and inflammation are both important therapeutic targets. Herbal remedies are a natural source of protective materials that

may help reduce cellular injury and improve overall health outcomes. The antioxidant and anti-inflammatory properties of herbs are particularly useful in supportive care of cancer patients receiving chemotherapy because of the oxidative reaction from chemotherapy that contributes to the imbalance of damaging, oxidative reactions, and the normal protective response of the body. Herbal remedies can reduce the oxidative load and control inflammation, thus, potentially reducing the incidence of adverse reactions and improving the level of comfort for the patient. Additionally, herbal medicines contain multiple active components that are likely to affect several biological pathways at the same time; therefore, multiple-target herbs may be superior to single-target therapies. Moreover, the unique complexity of herbal products necessitates extensive research to evaluate the quality and safety of those products and to determine whether the products may have adverse interactions with anticancer medications. Rigorous scientific research and clinical monitoring are critical to identify the potential role of herbal medicines in supportive therapy. (Sharma et al., 2023)

The interest in medicinal herbs continues to grow due to their potential uses in integrative medicine and oncology. Increasingly, researchers are exploring antioxidant and anti-inflammatory effects of herbs (e.g., by promoting wound healing) that may help to mitigate the negative side effects of treatment by protecting the body from damage caused by radiotherapy or chemotherapy; supplementing the immune system; and accelerating recovery from Illness. These characteristics suggest that many herbal compounds would be appropriate adjuncts to traditional treatments. However, the efficacy of any herb as a treatment relies on the proper identification of its active ingredient(s), proper dosing, and the existence of sound clinical evidence supporting its use. In many instances, herbal medications cannot be taken safely in conjunction with conventional medicines due to the potential for adverse interactions or because they produce unintended results when taken alone. Therefore, it is critical for patients and their healthcare providers to work collaboratively to ensure the safe and effective use of herbal therapies. Future studies focusing on the long-term efficacy of different herbal preparations through clinical trials will help to determine how to optimally use these herbs for patient care. Eventually, through increased scientific knowledge and standardization of how herbs with antioxidant and anti-inflammatory characteristics can be used in conjunction with conventional therapies, herbs may become important adjuncts for decreasing adverse effects from conventional therapies and improving overall quality of life for patients. (Lee et al., 2020)

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Ginger Helps with Nausea and Vomiting

Zingiberofficinale (Ginger) has long been one of the most popular herbal remedies used to alleviate vomiting & nausea caused by the side effects of chemo-style drug treatment. Ginger is naturally a well-known herbal medicine for illnesses that affect the stomach; therefore, it has been scientifically investigated for this purpose in support of oncology. Dyspnea and nausea associated with chemotherapy are generated by a complicated combination of how the body processes food through the gastrointestinal system and how signals travel between the gastrointestinal system and the central nervous system. Within ginger's chemistry (phytochemical constituents), there are many compounds (bioactive compounds) that may affect these systems. Gingerols and shogaols in the reproductive system (GI tract) could modulate how signals are sent to the brain via the serotonin receptors. Ginger supplements may therefore be helpful as an adjunct to chemotherapy as a treatment for one of the most difficult side effects (nausea and vomiting) many cancer patients will experience. In addition to being antiemetic, ginger is also a powerful antioxidant that could provide additional supportive benefits to chemotherapy patients during their course of treatment. Due to its low cost, ease of availability, and history of being a traditional medicine, there has been increased interest in the use of ginger as an adjunct to oncology treatment. Proper dosing and clinical guidance will ensure the safe and effective use of ginger in this setting. (Marx et al., 2020)

Modern antiemetics can help alleviate the nausea and vomiting associated with chemotherapy; however, these are still two major problems for patients being treated for cancer. Nausea and vomiting can reduce a patient's appetite, lead to less nutritional intake, result in dehydration, and diminish their quality of life. Researchers have studied ginger as a complementary alternative because it has been shown to lower the severity and frequency of episodes of nausea. The active compounds in ginger, such as gingerols, shogaols, and paradols, provide pharmacological effects by affecting the function of the GI tract and preventing excessive stimulation of pathways associated with nausea. Ginger may also improve the rate of gastric emptying as well as regulate the activities of the digestive system; therefore, ginger may decrease nausea when used in conjunction with receiving chemotherapy treatments. In addition, recent studies have indicated that ginger supplementation may provide additional relief to chemotherapy patients when taken in conjunction with standard antiemetic medications. Ginger is also an antioxidant and may provide protection against damage due to oxidative stress caused by cancer therapies. Additionally, by its anti-inflammatory activity, ginger may act to decrease pain and discomfort associated with the irritation of the tissues accompanying cancer

therapies. Ginger safety is established when utilized as directed; however, further studies on ginger dose as well as the timing for ideal ginger supplementation in patients with cancer is needed to confirm efficacy. (Ryan et al., 2021)

Ginger's anti-emetic effects on nausea and vomiting can be attributed to its large variety of phytochemicals and the ability to impact many physiological processes. The substances in ginger that have been found responsible for its medicinal properties are gingerols and shogaols. Their demonstrating of anti-emetic properties is due in part to the modulation of serotonin pathways that play a role in nausea development. When receiving chemotherapy, serotonin release from the GI tract may contribute to vomiting by stimulating nerve signals. Ginger may be useful in reducing this stimulation and controlling symptoms for cancer patients receiving anticancer medications. Additionally, ginger has anti-inflammatory properties that may aid in maintaining a healthy gastrointestinal tract by reducing inflammation in digestive tissues. For all these reasons ginger appears to be a good candidate for cancer supportive care. Natural therapies are often preferred by patients because they are viewed as safer, more acceptable than many pharmaceutical options. Nevertheless, ginger should be used with caution because very high doses may lead to gastrointestinal upset or interact with certain medications. Healthcare providers should assess patients individually prior to recommending ginger as an adjunctive therapy during chemotherapy treatments. (Zick et al., 2022)

Studies have also examined ginger's ability to enhance the overall treatment tolerance of patients undergoing chemotherapy by decreasing symptoms related to nausea and vomiting due to chemotherapy. Beyond just being a physical symptom of chemotherapy, nausea and vomiting can also cause psychological stress, an apprehension of future chemotherapy sessions, and a decreased desire to continue treatment. Therefore, by assisting patients in controlling these symptoms through the ingestion of ginger, they may contribute to patients remaining engaged in their treatment and feeling more comfortable throughout that time. Ginger is thought to have antiemetic properties and possibly functions through several biological mechanisms, including: regulating the activity of the gastrointestinal tract; altering the function of certain neurotransmitters; and reducing certain types of inflammation. Ginger's antioxidant properties may also assist in protecting healthy cells from the oxidative stress commonly experienced with chemotherapy. Therefore, it seems that ginger may provide a patient with more than just symptom relief; it may contribute to their overall supportive care throughout treatment.Because ginger can be used as a complementary therapy in a variety of forms (capsules, extracts, teas, and powders) and

easily incorporated into the patient's diet, it has gained interest among clinicians. However, there are significant differences in the way in which ginger has been processed and the concentration of the active ingredients within the different forms, suggesting that there is a need for standardization of ginger products and clinical guidance to ensure the greatest benefit while minimizing risk to patients.(Panahi et al., 2020)

In integrative oncology, adjuvant usage of ginger for managing nausea caused by chemotherapy is becoming more significant. Integrative oncology utilizes complementary therapies proven to be effective along with standard treatments, with the intent of improving patients' responses to conventional therapy. Ginger represents such an alternative as it can provide patients with symptom control so they are able to continue to receive their necessary anticancer treatments. Current studies support ginger supplementation as an alternative for patients who experience chronic nausea despite traditional medications. Additionally, ginger's compounds will help improve comfort in the digestive tract and decrease the severity of gastrointestinal disturbances related to the treatment, while ginger's anti-inflammatory and antioxidant properties will also enhance protection to normal tissues while undergoing chemotherapy treatments. However, the therapeutic effectiveness of ginger varies depending on the cancer type, chemotherapy regimen, dose, and/or individual patient response; therefore, it should be viewed as an adjunct to support the utilization of prescribed antiemetic medications and not as a substitute. More research is necessary to determine the most effective formulation of ginger and how to ensure its safe use in patients receiving oncology treatments. (Arslan et al., 2021)

Given ginger’s extensive historical use for medicinal purposes and multiple pharmacologic qualities, it offers great promise as an adjunctive treatment to alleviate chemotherapeutic-related nausea/vomiting (CNV). Its ability to affect digestive system function, modulate pathways for nausea, and provide antioxidant effects makes it an attractive option for supportive care in cancer patients. By alleviating one of the most common and distressing side effects of chemotherapy, ginger has the potential to improve overall quality of life in patients as well as their emotional health and nutritional status. Additionally, ginger’s widespread availability and generally safe profile have contributed to its use as a complementary therapy. Despite these benefits, one must carefully evaluate the use of herbal products because they can vary widely in strength, purity, and quality. Therefore, one should also evaluate herbal product interactions with medications prior to use. Future research will need to focus on larger, randomized clinical trials to determine ginger’s efficacy, optimal dose range, and long-term safety

profile. If adequate evidence and appropriate clinical direction is provided, then ginger may serve as a major part of integrative approaches to reduce the toxicities associated with chemotherapy and improve supportive treatment outcomes for cancer patients. (Marino et al., 2023)

Turmeric May Protect Healthy Tissues

Turmeric (Curcuma longa) is a medicinal plant which has attracted much interest because of its ability to provide protection against treatment-induced toxicities. One of the main active ingredients of turmeric, curcumin, is characterized by pronounced antioxidative, anti-inflammatory and cytoprotective activity. During chemotherapy, healthy tissues are subjected to oxidative stress and inflammatory damage induced by the cytotoxic agents used to kill cancerous cells. Overproduction of reactive oxygen species results in oxidation and damage to normal cells, proteins and DNA causing organ toxicity (the most common types of target organs include liver, kidneys and digestive system). Curcumin may help to protect healthy tissues from damage by eliminating free radicals and increasing the activity of endogenous antioxidative systems. Additionally, curcumin is able to regulate different molecular pathways associated with inflammation and cellular stress. Such an effect could potentially decrease tissue damage and preserve normal cellular functions during cancer treatment. Due to such characteristics turmeric has become an object of interest in cancer research as a possible adjuvant treatment. At the same time it is necessary to conduct thorough evaluation since the impact of turmeric can vary greatly depending on the dosage, formulations used and patient characteristics. (Hewlings et al., 2020)

Oxidative stress and inflammatory pathways play a significant role in the development of negative effects in the process of cancer therapy as a result of tissue damage caused by chemotherapy. Turmeric, an extract rich in curcumin, has been proved to be able to regulate negative consequences due to several mechanisms. Curcumin can function as an antioxidant by neutralizing free radicals and protecting cells from their damaging effect. The compound might increase the expression of enzymes that play an important role in maintaining the cell homeostasis. Apart from being an antioxidant, curcumin inhibits mediators of inflammation involved in causing tissue injury. This feature can protect tissues from stress induced by anticancer drugs. Curcumin is supposed to be able to protect the organs affected by chemotherapy, such as the liver, the kidneys, and the gastrointestinal tract. Due to the multi-target nature of curcumin, turmeric is regarded as a prospective natural product for supportive oncology. Still, more clinical trials should be conducted in order to confirm efficacy and identify proper doses. (Kunnumakkara et al., 2021)

The beneficial effect of turmeric on the protection of healthy tissues in patients undergoing cancer therapy has been extensively studied in recent years due to its capability of regulating multiple biological mechanisms. Curcumin acts on cellular signaling pathways associated with oxidative stress, inflammation, apoptosis, and tissue regeneration. During chemotherapy, the normal cells get damaged as the result of the production of harmful molecules affecting the normal activity of the cells. The use of curcumin can be helpful in lowering damage caused by anticancer agents as it provides stability of cellular membranes, increases antioxidant activity, and decreases inflammation. More precisely, the protective role of turmeric has been studied in the context of chemotherapy in tissues that are particularly sensitive to toxicity effects of anticancer drugs, including mucosa of the intestines, liver cells, and kidney tissues. Moreover, curcumin is known to provide positive changes for the immune system which gets compromised during the treatment. Nevertheless, it should be mentioned that bioavailability of curcumin is rather low. (Prasad et al., 2022)

Protection against tissue injuries during oncological therapy through turmeric is primarily associated with the impact of curcumin on the body's protective mechanisms. The main adverse effect of chemotherapeutic agents is their negative impact on healthy tissues via increased oxidative stress and inflammation. Curcumin is known to regulate several signaling pathways involved in inflammation and cell survival; thus, it is able to prevent unwanted injuries to healthy tissue. Due to its antioxidant activity, curcumin protects cellular structures from oxidative stress caused by reactive oxygen species. Moreover, curcumin promotes tissue recovery through stimulating physiological repair processes. It was also reported that turmeric may contribute to the reduction of some side effects through the protection of organs affected by chemotherapeutic stress. Anti-inflammatory activity is especially important since prolonged inflammation leads to an increase in tissue injury and delayed recovery process. Despite its beneficial effects for tissue recovery, turmeric must be used with caution among cancer patients due to possible drug interactions. (Zhang et al., 2020)

Turmeric is being used as an alternative therapy in the care of cancer patients owing to its potential to protect healthy tissues and ensure quality of life in patients. Chemotherapy is known to cause fatigue, inflammation, and stress on organs, and all these have the ability to lower treatment tolerance and recovery rate in patients. The antioxidant and anti-inflammatory characteristics of curcumin are expected to be useful in alleviating the negative consequences of chemotherapy by ensuring cellular protection and physiological balance. Apart from its antioxidant characteristic, turmeric also possesses the ability to regulate the immune system and correct abnormal

inflammatory behavior in cancer patients undergoing treatment. These qualities make turmeric an important supplement in reducing the burden of chemotherapy side effects. According to some researchers, curcumin has the potential of protecting normal cells while anticancer agents are still working in the body. The effectiveness of turmeric, however, differs among people depending on their metabolism and other factors. Further research is required to establish the correct dose, administration time, and formulation of turmeric during chemotherapy. (Liu et al., 2021)

Conclusion

Herbal medicines have been discovered as promising agents in the alleviation of toxic side effects caused by chemotherapy as a form of adjuvant therapy in the supportive treatment of cancer patients. Chemotherapy is one of the effective treatment procedures that help fight against cancer; however, it is often hindered by adverse effects such as nausea, vomiting, tiredness, inflammation, oxidative stress, organ toxicity, and reduced quality of life. The utilization of medicinal herbs that contain active biological compounds like flavonoids, polyphenols, and phytochemicals may act as antioxidants, immunomodulatory and cytoprotective agents. Some medicinal herbs such as ginger, turmeric, ginseng, and milk thistle among others have positive effects on certain complications related to their utilization. Despite the positive effects, the use of herbs together with chemotherapy is supposed to be evaluated because of the potential interaction between the two, preparation variations, and lack of scientific evidence for some products. Proper standardization of the preparations, clinical validation, and medical oversight is mandatory for the use of herbs with chemotherapy for safety and effectiveness purposes. Research is required to determine the most suitable dosages and long-term effects of their integration with conventional cancer treatments.

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