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Medicinal Plants as Adjuvants in Chemotherapy

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ABSTRACT

Chemotherapy remains a cornerstone of cancer treatment but is often constrained by severe adverse effects, drug resistance, and limited therapeutic efficacy. In recent years, medicinal plants and their bioactive constituents have gained attention as promising adjuvants to conventional chemotherapy. Phytochemicals such as curcumin, ginsenosides, withaferin A, epigallocatechin gallate (EGCG), and silymarin exhibit diverse anticancer mechanisms, including apoptosis induction, cell cycle arrest, inhibition of angiogenesis, and immune modulation. Clinical and preclinical studies demonstrate that these compounds not only enhance the efficacy of chemotherapeutic drugs but also mitigate their toxic side effects, thereby improving patient outcomes and quality of life. Widely studied medicinal plants such as Curcuma longa, Panax ginseng, Withania somnifera, Camellia sinensis, and Silybum marianum exemplify this therapeutic potential. Despite encouraging evidence, challenges remain in the integration of medicinal plants into standard oncology practice, including issues of standardization, safety, herb-drug interactions, and regulatory approval. This review highlights the pharmacological mechanisms, clinical applications, and safety considerations of medicinal plants as adjuvants in chemotherapy, emphasizing their role in shaping future integrative cancer care strategies.

Keywords: Medicinal plants; Chemotherapy; Phytochemicals; Cancer treatment; and Adjuvant therapy.

INTRODUCTION

Chemotherapy involves the use of chemicals to treat cancer and constitutes a major method within clinics. Medicinal plants have played a fundamental role in cancer treatment, historically and presently [1-4]. A challenge in this context is the incompatibility of many chemotherapy drugs with two treatment pathways, which limits the information available to physicians responsible for patient care, potentially leading to severe toxicities. Nonetheless, several plants are commonly used for cancer care, such as Curcuma longa, Ginseng, Withania somnifera, green tea, and milk thistle. These species demonstrate interesting anticancer effects with specific mechanisms of action complementary to those of chemotherapy drugs [5-8]. Chemotherapy, derived from the Greek words 'chemo' for chemical and 'therapy' for treatment, represents the use of chemical agents to treat diseases, predominantly cancer. Several chemotherapeutic agents, including asbestos, arsenic, benzene, beryllium, and cadmium, are classified as human carcinogens [9-14]. Despite their wide application, chemotherapy is limited in effectiveness and often accompanied by severe adverse effects such as myelosuppression, mucositis, neutropenia, thrombocytopenia, alopecia, and immunosuppression. These limitations underscore the need for adjuvants that can enhance therapeutic outcomes and mitigate side effects [15-16].

Role of Medicinal Plants in Cancer Treatment

Cancer is a major health concern worldwide. Chemotherapy remains a key treatment modality despite its limitations, including side effects and tumor cell interactions. Medicinal plants have long been integrated into oncology, offering anticancer properties attributed to phytochemicals with pharmacological activity [17-19]. These plants provide accessible, cost-effective sources of adjuvant therapy, potentially enhancing chemotherapy efficacy while mitigating adverse effects. Early medicinal plants of interest include Curcuma longa, Ginseng, Withania somnifera, Green tea, and Aloe vera, which are widely used in modern anticancer applications [20-24]. Plant metabolites, or secondary metabolites, contribute significantly to therapeutic effects. Even established natural antitumor agents such as paclitaxel and camptothecin were originally isolated from plants. Curcumin from Curcuma longa, Panax ginseng, Paeonia lactiflora, Boswellia serrata, and Artemisia annua exemplify key

anticancer phytochemicals with supportive clinical evidence. Clinical data and ongoing trials affirm the role of anticancer medicinal plants in traditional chemotherapy, underscoring the potential to reduce cancer-associated side effects and alleviate chemotherapy burdens [25-28].

Mechanisms of Action of Medicinal Plants

Medicinal plants produce a variety of pharmacologically bioactive phytochemicals such as flavonoids, saponins, tannins, terpenoids, and alkaloids whose consumption is connected to a reduced risk of cancer [29-32]. More specifically, these natural agents mediate multiple cancer pathways and reduce tumour growth through the induction of reactive oxygen species, apoptosis, immune modulation, and the inhibition of PD-L1 and STAT3 expression [33-37]. They also act synergistically with chemotherapeutic agents to augment the tumouricidal capacity of immune cells and decrease proinflammatory responses. Since phytochemicals have wide natural sources, lower toxicity, and diverse immunomodulatory activities, they represent particularly attractive adjuvants; yet, their targets and molecular mechanisms related to tumour immunity remain insufficiently characterised. Harnessing natural biomolecules and derivatives for clinical applications, therefore, requires a better understanding of cancer immunity as well as the development of advanced drug delivery technologies and computer-aided drug design. The use of medicinal plants in cancer treatment is well known, and many pharmaceutical medicines originate from plants with anti-cancer effects; some of these natural products can have the capacity to mitigate chemotherapy and radiotherapy side effects [2]. Some plant species found in the Himalayas, which are utilised in cancer management, contain active constituents responsible for anti-proliferative activity. A range of medicinal plants have in vitro and in vivo anti-proliferative activity, but a number of phytocompounds remain uninvestigated. Many of these plants, which are widely distributed in the Himalayan region and surround the upper regions of India, Nepal, and Bhutan, therefore warrant further studies [3].

Phytochemicals and Their Effects

In the field of oncology, medicinal plants have been commonly used for the prevention and treatment of various diseases, including cancer. A major drawback of conventional chemotherapy is its toxicity towards both cancerous and normal cells. In recent years, an alternative approach has been found in medicinal plants and their active ingredients [3, 4]. Scientific evidence obtained from in vitro and in vivo studies shows that complementary medicines can help to cure cancer and reduce the toxic effects of chemotherapy. Medicinal plants can act in cancer treatment through various mechanisms of action, and when combined with chemotherapy drugs. These mechanisms include induction of apoptosis and cell cycle arrest in cancer cells, inhibition of angiogenesis, suppression of pathways involved in tumour growth and survival, reduction of chemotherapy and radiotherapy-caused toxicities, as well as activation of the immune system in cancer patients. Among the highly active phytochemicals, curcumin, ginsenosides, withaferin A, epigallocatechin gallate (EGCG), and silymarin are of particular interest because of their potential tumor-inhibiting effect when administered alone or in combination with anticancer drugs in cancer patient care. As several clinical trial studies using these phytochemicals have been recently conducted for different types of cancer, this overview focuses primarily on the reported plant extracts and phytochemical components [4]. These compounds are well acknowledged as anticancer agents with protective effects against chemotherapy and radiotherapy-induced toxicity [3, 4].

Synergistic Effects with Chemotherapeutics

Chemotherapy is a primary cancer treatment that uses synthetic drugs to target rapidly growing tumour cells, but toxic side effects and drug resistance limit its efficacy [4]. Medicinal plants and their bioactive derivatives are increasingly employed as complementary treatments in combination with chemotherapy to potentiate the overall anticancer response, control drug toxicity, and sensitize cancer cells to chemotherapeutic agents [5]. Several phytochemicals, such as polyphenols, polysaccharides, and saponins, demonstrate potent anticancer activities by inducing apoptosis and arresting the cell cycle at specific phases. Human cancer cell lines also exhibit enhanced responsiveness to different chemotherapeutic drugs after sequential treatment with these compounds [4, 5].

Common Medicinal Plants Used in Chemotherapy

Medicinal plants, with high levels of phytochemicals and bioactive agents, have a long history of use in health promotion and the management of various diseases, including cancer [2]. They continue to pave the way in herbal remedies to combat cancer. Many medicinal plants provide novel therapeutic options in chemotherapy due to the bioactive agents extracted for use as adjuvants for drug delivery and targeted therapy [1, 6]. Medicinal plants such as Curcuma longa, Ginseng, Withania somnifera, tea, and Silybum marianum, which are frequently used during chemotherapy, have been shown to contain active compounds with anticancer potential.

Curcuma longa (Turmeric)

Curcuma longa (turmeric) is a widely employed medicinal plant in chemotherapy protocols undergoing clinical study. Curcuma longa is conventionally used in cuisine, in Ayurvedic and Traditional Chinese Medicine, and in other herbal medical systems [7]. Modern clinical investigation of turmeric began with the identification of the

active component curcumin in 1910. Curcumin, a polyphenol distinguished by a vibrant yellow colour, exhibits anticancer properties against multiple tumor types [8]. Curcumin inhibits tumor progression through global mechanisms including proliferation suppression, downregulation of transcription factors, suppression of inflammatory and metastatic enzymes, blockade of growth factors and metastatic kinases, and inhibition of stem-like properties [7, 8].

Ginseng

Ginseng is a widely reproduced and harvested plant that is commonly consumed worldwide. Among the 13 plants under the genus Panax, the roots of three species of plants (P. ginseng, P. japonica, and P. vietnamensis) have received significant attention for their beneficial health effects [9]. The roots of the plants collected from the fields are usually air-dried and referred to as white ginseng, whereas the roots that are steamed before drying are called red ginseng (PG). Both white and red ginsengs are used for medicinal purposes [10]. Ginseng induces regeneration of immune cells through the stimulation of the bone marrow and possesses anti-inflammatory properties. Furthermore, ginseng protects cells against cytotoxic factors. Therefore, it is used as an adjuvant in cancer chemotherapy [9]. A systematic review and meta-analysis of 34 articles analyzed the efficacy of ginseng and its active components as adjuvant therapy for non-small cell lung cancer (NSCLC). Increased chemotherapy efficacy and improvements in quality of life were recognized in NSCLC patients receiving ginseng adjuvant therapy [9, 10].

Withania somnifera (Ashwagandha)

Withania somnifera, also known as Ashwagandha, is a renowned medicinal plant that has attracted considerable attention for its immunomodulatory and antitumour activities. The herb contains bioactive phytochemicals such as withaferin A and ashwagandhanolide, which exert multiple pharmacological effects [11]. Its properties include inhibition of lipid peroxidation, antioxidant and neuroprotective effects, anxiolytic, antidepressant, adaptogenic, and antiulcer activities. In in vivo models of Parkinsonism, the extract has shown neuroprotection by preventing depletion of dopamine and its metabolites, exerting anti-inflammatory effects, enhancing the growth of dopaminergic neurons, and reducing oxidative stress by improving glutathione peroxidase and glutathione reductase activities. In the context of cancer therapy, Withania somnifera has demonstrated anti-inflammatory, antitumour, radiosensitizing, and analgesic properties. It is able to downregulate nuclear factor _B and tumour necrosis factor, while enhancing apoptotic signalling [12]. Animal studies have shown that administration of Ashwagandha can significantly reduce tumour size and sensitize tumours to radiation. An evaluation of its in vitro cytotoxicity against human breast cancer cell lines revealed that methanolic and ethanolic extracts possess potent activity, with IC50 values below 100 μg/ml [11, 12].

Green Tea

The Camellia sinensis plant comprises three distinct varieties: black tea, oolong tea, and green tea, which owe their beneficial qualities to polyphenols [13]. Green tea extracts and compounds therefore exhibit potential antioxidant, anti-inflammatory, and anti-hepatotoxic activities. These results help to explain why green tea constituents are prepared as tea extracts and catechins and investigated for their anticancer properties. Camellia sinensis continues to offer natural-product leads for the development of drug candidates for preventing colon cancer and potentially other cancers. Green tea extracts and compounds possess anticancer properties that justify further studies of these botanical formulations as potential anti-inflammatory agents. An investigation with patients demonstrated that combining green tea with FOLFOX chemotherapy significantly improved overall survival for subjects with metastatic colorectal cancer [13]. The potential benefit of the addition of green tea to FOLFOX chemotherapy in advanced colorectal cancer led to its use at other referring hospitals. Results confirm that Camellia sinensis provides a rich source of bioactive agents and documents the antioxidant potential of these compounds. Green tea extracts and compounds, therefore, provide promising therapeutic tools with anticancer potency and chemopreventive properties or as an adjuvant in the chemotherapy of colorectal cancer. A study with the widely studied human breast cancer cell line MCF-7 demonstrates that polyphenols, flavonols, and methoxy flavones contribute toward the observed anticancer effects from Camellia sinensis [12, 13].

Milk Thistle

Silybum marianum Gaertn. (milk thistle) It is a medicinal plant used to treat chronic liver disorders, cancer, and inflammation. Milk thistle has attracted a lot of attention during the last decade. It is well documented that it protects the liver against toxic substances from chemotherapeutics [14]. The species was chosen for the present review because of its apotogenetic mechanisms. The plant's seeds contain a mixture of flavonolignans known as silimarin. They include silibin A, silibin B, silychristin, isosilybin A, isosilybin B, taxifolin, silidianin, and silandrin; their quantity varies according to the extraction method. Silibin was discovered in 1959 and has been extensively studied [14]. It exhibits significant modulation ability against tumor cells and encourages apoptosis. Silimarin acts as an anti-tumor agent by inhibiting the proliferation of tumor cells. Its apotogenetic ability was highlighted

in vivo by studying the influence of the compounds on tumor angiogenesis biomarkers (CD31 and nestin) [13]. The biomarker inhibition was explained by the suppression of linked molecules, such as VEGF, VEGFR1, VEGFR2, phospho-Akt, and HIF-1α. Other pathways were studied and highlighted (Wnt/β-catenin pathway, cyclin-dependent kinases, MAPK). Silibin induces apoptosis in breast cancer cells and leads to an increase in those cells' UVB-mediated apoptosis. In prostate cancer cells, silibin reduces PSA levels significantly and triggers G1-phase cell cycle arrest. It is capable of producing an efficient apotogenetic response and represents a highly promising anti-cancer agent [14].

Clinical Studies on Medicinal Plants

Growing evidence from experimental studies and clinical cases in vivo and in vitro indicates the effectiveness of several plant products as antitumor agents [15]. Although the use of medicinal plants by cancer patients undergoing chemotherapy is prohibited by oncologists, the practice persists, often driven by desires for enhanced efficacy and accelerated healing, as well as social and traditional influences [1, 13]. In a Moroccan survey, 30 medicinal plants were identified, with Euphorbia honey, garlic, turmeric, fenugreek, and thyme among the most widely used. Euphorbia honey contains phenolic compounds such as syringic acid, coumaric acid, and caffeic acid, which confer antioxidant, anticancer, and antidiabetic properties. Curcumin, the principal bioactive constituent of turmeric, exhibits anticancer activity by inhibiting carcinogenesis and tumor growth. Thyme contains active compounds including carvacrol, thymol, borneol, and p-cymene; thyme extract has been shown to induce necrotic cell death in lung cancer cells and suppress inflammatory cytokine release. Garlic is recognized as a potent anticarcinogen that induces apoptosis and autophagy in cancer cells and enhances the efficacy of chemotherapy [1, 14]. The most frequently utilized plant parts are seeds and leaves. Reported side effects are generally minor and include gastric burns, abdominal pain, gastritis, and sweating. Despite the potential for adverse reactions, medicinal plants are regarded as highly important by patients undergoing chemotherapy, with many seeking them primarily for disease cure [1].

Case Studies

Medicinal plants and natural products have been an integral part of the treatment of chronic diseases, including cancer. Although chemotherapy is the most effective tool in the treatment of cancer, it has several shortcomings, such as drug resistance and adverse effects. To overcome these problems and to increase the therapeutic index, adjuvants are often used in the chemotherapeutic regimen. Many clinical studies attest to the beneficial effects of some medicinal plants and the usefulness of their phytochemical constituents [15]. The use of medicinal plants as adjuvants in chemotherapy in the Northwest of Morocco was studied in a cross-sectional survey. Despite advice from oncologists, patients continued to use these remedies, possibly to achieve more efficient healing results rapidly, potentially influenced by social circles and media [1]. Thirty medicinal plants were identified; the most commonly used included euphorbia honey (40%), garlic (13%), turmeric (11%), fenugreek (11%), and thyme (11%). These plants have demonstrated anticancer effects: euphorbia honey contains phenolic compounds such as syringic acid, coumaric acid, and caffeic acid with antioxidant and anticancer properties; curcumin from turmeric inhibits carcinogenesis and tumor growth; thyme's compounds carvacrol, thymol, borneol, and p-cymene can induce necrotic cancer cell death and reduce inflammatory cytokines; garlic acts as a potent anticarcinogen triggering apoptosis and autophagy and reduces viability in multiple myeloma and prostate cancer cell lines while enhancing chemotherapy efficacy. Seeds (27%) and leaves (24%) were the most used plant parts. Reported adverse effects were low (5%), including gastric burns, abdominal pain, gastritis, and sweating. For 37% of patients, medicinal plants are very important, with 60% seeking cures for their diseases [1, 15].

Clinical Trials

Cancer is characterised by the uncontrollable growth and spread of abnormal cells that acquire the ability to invade adjoining tissue and metastasise to distant sites. One of the most common treatment modalities of cancer is the use of chemotherapeutic drugs, which are toxic to rapidly proliferating cancerous cells. Chemotherapy is widely accepted as an effective treatment option for cancer; however, using chemotherapeutic drugs alone can be toxic and mostly ineffective in later-stage cancer [15]. Improving treatment outcomes and survival rate in patients under chemotherapy has been the focus of several research efforts, and medicinal plants have received much attention over the past years. Medicinal plants have been widely used in various aspects of cancer treatment, including prevention, supportive care, chemotherapy, and as a source for the discovery of novel anti-cancer agents [1]. Over the years, several clinical studies have reported on the anticancer effects of medicinal plants used during chemotherapy. Adopting medicinal plants as adjuvants in chemotherapy can thus assist in addressing the toxic side-effects and poor curative capacity faced by the use of chemotherapeutic drugs during cancer treatment. Here, a scholarly overview of clinical trials involving medicinal plants in chemotherapy is presented [1, 15].

Safety and Efficacy of Medicinal Plants

Chemotherapy is a primary therapeutic modality for localized and disseminated cancers that eradicates rapidly dividing cells and induces cell death by either apoptosis or necrosis [1]. However, its use is constrained by multiorgan toxicity, drug resistance, and high costs. To overcome these challenges, numerous medicinal plants and natural products with anticancer activities that complement chemotherapy have been pursued in cancer drug discovery research [1]. Many phytochemicals from medicinal plants exert anticancer effects by modulating a wide range of molecular apoptotic and anti-apoptotic signalling proteins that promote chemoprevention, apoptosis, and minimize chemotherapeutic drug resistance; however, the clinical application of these medicinal plants as adjuvants has yet to be fully exploited [1, 15].

Toxicity Concerns

While medicinal plants may offer benefits when used as adjuvants in chemotherapy, their potential to cause toxicity and adverse effects should be considered [16]. Patients receiving chemotherapy are prone to symptoms like nausea and abdominal pain, the intensification of which may reduce medication dosage and limit therapeutic efficacy [17]. Toxicity can derive from directly cytotoxic components or from interaction effects [1]. Certain compounds, such as laetrile, contain inherently toxic substances (in this case, cyanide) and can have fatal consequences when used by cancer patients.

Drug Interactions

Medicinal plants may impact anticancer efficacy and chemotherapy-induced toxicity by affecting key aspects of absorption, distribution, metabolism, and excretion (ADME) processes or by modulating chemotherapeutic targets [18]. To optimize their use during chemotherapy, understanding the underlying pharmacokinetic and pharmacodynamic mechanisms is critical [19]. Both processes are relevant because naturally occurring phyto-compounds can alter transporter and enzymatic activities. Such modulation extends beyond ADME since transporters and enzymes participate in various cellular functions that influence key signal transduction pathways targeted by antineoplastic agents. Consequently, interference across these pathways or a compensatory cellular response may further contribute to adverse pharmacodynamic interactions. Some interactions attenuate anticancer efficacy, while others may be exploited to diminish chemotherapy-related adverse effects. Phytosome-loaded with curcumin inhibits five cytochrome P450 members, and extract of Trigonella foenum-graecum induces CYP3A4 and P-glycoprotein (P-gp) in vitro. Combining WH-1 and cisplatin synergistically reduces the viability of A549 cells, and turmeric administration slows the clearance of docetaxel. Therefore, the potential for herb–drug interactions warrants careful consideration, and clinical evaluation is essential to ascertain safety and efficacy [17].

Regulatory Aspects

Phytotherapy drugs, also known as phytopharmaceuticals, are defined in the European Union as Herbal Medicinal Products (HMPs); they are distinguished from dietary supplements and functional foods [1, 2]. For the phytopharmaceutical approval, it is necessary to provide monographs that demonstrate the efficacy and the safety. Other than national monographs, the ESCOP and HPMC monographs constitute the basis for the regulation at the EU level [1]. The ESCOP monographs follow the SmPC guideline, illustrating the efficacy and the safety, while the HPMC monographs specify the category of "well-established use" and "traditional use". The WHO develops monographs on efficacy, safety, and quality, but these monographs constitute only recommendations. As rational phytotherapy gains importance, particularly in tumour diseases, it deserves increased attention [1].

Guidelines for Use

The increasing integration of medicinal plants as chemotherapy adjuvants necessitates the establishment of rigorous guidelines to govern their use. Despite oncologists' prohibitions, patients frequently employ these remedies to expedite healing, influenced by the media and social environments. A Moroccan cross-sectional study identified thirty medicinal plants commonly used by chemotherapy patients: Euphorbia honey (40%), garlic (13%), turmeric, fenugreek, and thyme (11% each) [1, 17]. These species exhibit documented anticancer effects; Euphorbia honey contains phenolic compounds with antioxidant, anticancer, and antidiabetic properties; curcumin from turmeric inhibits carcinogenesis and tumor growth; thyme derivatives induce necrotic cell death and decrease inflammatory markers; garlic acts as a potent anticarcinogen by inducing apoptosis and autophagy, while enhancing chemotherapy efficacy. Seeds (27%) and leaves (24%) constitute the most utilized parts; reported adverse effects remain low (5%), primarily gastric burns and abdominal pain. Patients regard medicinal plants as crucial during chemotherapy, with 60% seeking them for disease cure [1]. Numerous international authorities have introduced guidelines for herbal and traditional medicines addressing cancer symptoms. Historically, botanical medicine has served palliative care providers for centuries, prompting the formulation of rules for controlled employment. The World Health Organization's strategy on traditional medicine consolidation mandates standardized regulatory frameworks encompassing registration, licensing, and pharmacovigilance. National standards encompass multiple regulatory phases: those established in 2004; India's standards for

Ayurvedic, Siddha, and Unani medicines since 1978; Sri Lanka's specifications effective prior to 2000 that contributed to the WHO 2005 guidelines; Zimbabwe's 2009 traditional medicines decree; and South Africa's, Sri Lanka's, and Vietnam's regulatory processes. Local guidelines align with national laws and international recommendations for traditional and complementary medicinal products [17].

Approval Processes

Approval processes for medicinal plants focus on detailed evaluation of therapeutic potential, mechanisms of action, and efficacy against resistant cancer cell lines. Phytochemical studies demonstrate cytotoxicity and anticancer activities, with natural compounds such as benzophenones, flavonoids, xanthones, and alkaloids exhibiting activity against both sensitive and multidrug-resistant cancer cells [19].

Future Directions in Research

The incorporation of medicinal plants into conventional chemotherapy represents a promising strategy for optimizing cancer treatment [2]. These natural sources of medicinal agents have long been employed in complementary health practices to enhance host resistance, and their integration into orthodox medicine is increasingly recognized. Phytochemicals from medicinal plants can act alone or synergistically with conventional drugs to enhance therapeutic efficacy and overcome limitations such as drug resistance and organ toxicity. Consequently, contemporary research efforts are dedicated to identifying, isolating, and evaluating potent phytocompounds suitable as adjuvants in chemotherapy, either alone or combined with synthetic drugs [2]. Established chemotherapeutic adjuvants have their limitations; hence, there is a continuous search for new agents derived from plants with proven anti-proliferative activity across diverse cancer types [20]. Notably, Phyllanthus emblica has demonstrated significant promise as an adjuvant in experimental chemotherapy and radiation therapy. Analyses of phytomedicine databases, incorporating systems biology and transcriptome-wide association studies, have further facilitated the rapid identification of potential anticancer agents. Long-standing clinical evidence supports the beneficial impact of medicinal plants and their phytochemicals as adjuvants in chemotherapeutic protocols. Certain plants exhibit superior activity when combined with chemotherapeutic drugs, providing enhanced clinical outcomes and patient survival. Among the most documented medicinal plants utilized in combination chemotherapy are Curcuma longa, Panax ginseng, Withania somnifera, Camellia sinensis, and Silybum marianum. These herbs are readily accessible and qualified for adjuvant use, each possessing unique phytochemical profiles that confer therapeutic advantages. Overall, the pursuit of novel combined chemotherapeutic regimes continues to underscore the relevance of medicinal plants as key contributors to future treatment paradigms [2, 20].

Emerging Trends

Cancer is a set of diseases with any change in the normal cellular process resulting in improper cell functioning, uncontrolled cell division, tissue or organ damage, and blockage of normal physiological functions leading to death. According to the cancer report of the WHO, the total number of cancer deaths recorded worldwide was estimated to be 9.6 million in 2018 [1]. Various cancer therapies such as chemotherapy, immunotherapy, and radiotherapy have been developed to prevent and treat cancer. However, currently, chemotherapy remains one of the most effective therapies for cancer treatment. Chemotherapy mainly uses chemical drugs to inhibit cell division or kill cancer cells; substances used in chemotherapy cause several side effects during the treatment. Medicinal plants and other natural products are considered effective adjuvants to reduce the side effects of chemotherapy and enhance the effectiveness of chemotherapy drugs [1].

Potential New Adjuvants

Medicinal plants widely serve as adjuvants in cancer chemotherapy, designated to improve the safety and efficacy of conventional treatment strategies. Newly emerging candidates with prospective clinical uses include Aristolochia baetica, Artemisia annua, Coptis chinensis, Curcuma longa, Fagonia indica, Morus alba, and Plumbago zeylanica. In chemotherapy, chemical substances, plant extracts, or biological agents prevent, inhibit, or arrest the development of malignant cells [19]. Therapeutic treatments, however, suffer from a range of side effects that ultimately inhibit their usefulness in the clinic. The use of medicinal plants extends back to before the Egyptian and Sumerian civilizations [3]. Current treatments for cancer include the integration of herbal medicine at various stages of therapy [6]. Because active phytochemicals derived from medicinal plants possess unique mechanisms of action that exert a range of effects on cellular proliferation, survival, invasion, angiogenesis, metastasis, and drug resistance, research has now shifted toward understanding such bioactivities to construct new therapies or improve conventional chemotherapeutic options in a more holistic manner [3, 19].

Challenges in Integrating Medicinal Plants

The integration of medicinal plants into chemotherapy faces several critical challenges, most notably issues of standardization and controlling adverse effects [1]. Many medicinal plants are unstandardized, which makes their effective use in traditional medicine problematic due to potential toxicity when consumed in concentrated doses.

Although many plants used during chemotherapy have been shown to reduce certain side effects or enhance the efficacy of anticancer drugs, a few can produce undesired effects. Alongside scientific concerns, public perception also constitutes a major barrier. The transition towards a strong integrative medicine practice requires a clear organisation of the care pathway to help guide the patients, therapists, and prescribers [1, 17].

Standardization Issues

Medicinal plants can be used alongside chemotherapy to increase efficacy and mitigate side effects 6. Significant obstacles remain before broader adoption can occur. Because herbal and dietary supplements are often purchased without consulting medical professionals, the potential for problems arises [17]. In many regions, the sale of dietary supplements does not require proof of clinical efficacy. The products must only be free from toxic substances, and manufacturers can avoid claims of therapeutic effects by explicitly disclaiming such on the labels. Legislation generally does not regulate the quality and quantity of active components in herbal products. A survey of ginseng products from reliable manufacturers in Germany found no active ginsenosides. Standardization of herbal components is complicated, especially when multiple herbs are combined in formulas. Herbal preparations usually comprise numerous substances, leading to a relatively low side-effect profile, but side effects and interactions with conventional therapies can occur. Bioavailability is often low but can be increased by natural or synthetic analogues [1]. Phytopharmaceuticals are defined as Herbal Medicinal Products (HMPs) in the European Union and are distinguished from dietary supplements. Five products contain only the dried herbal substance, while eight products are related to phytopharmaceuticals and hold marketing authorization. Monographs demonstrating efficacy and safety are issued by authorities such as the ESCOP and the HPMC; their consideration is imperative but not mandatory for regulatory approval. The World Health Organization develops monographs on herbal medicines that address efficacy, safety, and quality, although these documents are recommendations without official status. The importance of rational phytotherapy in tumor disease management is likely to increase, underscoring the need for continued investigation [17].

Public Perception

Despite an increasing number of reports indicating the safety of medicinal plants as adjuvants, they are often still perceived as dangerous. D. L. Seigler emphasized that no natural product is entirely safe and all must be tested for safety [1]. Various investigational methods, including genomics, proteomics, metabolomics, bioinformatics, DNA microarrays, synthetic modification/medicinal chemistry, combinatorial synthesis, high-throughput screening, and clinical trials, help determine the safety of phytoproducts. Numerous reports affirm the safety of medicinal plants in chemotherapy, as these natural compounds have been part of the human diet and used for symptoms of ailments for thousands of years [1, 19]. Their widespread consumption under unrestricted conditions suggests they are generally nontoxic. However, overdosage and adverse drug–drug interactions can lead to deleterious effects. Detailed investigations into the toxic effects of currently used medicinal plants remain scarce [18, 17].

CONCLUSION

Medicinal plants represent a valuable complement to conventional chemotherapy, offering both therapeutic enhancement and toxicity reduction. Their bioactive phytochemicals act through multiple pathways modulating immune responses, sensitizing cancer cells, suppressing tumor progression, and protecting normal tissues from chemotherapeutic damage. Clinical evidence increasingly supports their role in improving survival and quality of life among cancer patients. However, widespread clinical adoption is hindered by insufficient standardization, variability in bioactive content, safety concerns, and limited large-scale randomized trials. Future directions must focus on rigorous clinical validation, pharmacovigilance, and the development of standardized formulations to ensure efficacy and safety. With advancing research, medicinal plants have the potential to move from supportive remedies to validated therapeutic adjuvants, thereby strengthening the effectiveness of chemotherapy and advancing holistic approaches to cancer treatment.

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