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Research Article

Adjuvant Phytotherapy in Breast Cancer: A New Player in Conventional and Innovative Treatment Strategies?

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Abstract

Breast cancer remains a major public health concern worldwide, with high incidence and mortality rates among women. While conventional treatments such as surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapy have significantly improved patient outcomes, limitations including resistance, recurrence, and adverse effects persist.

This review aims to explore the current landscape of breast cancer therapies both conventional and innovative and to assess the potential role of phytotherapy as an adjuvant in treatment strategies.

A comprehensive literature analysis was conducted, focusing on the mechanisms, efficacy, and limitations of standard and emerging therapeutic approaches. Special attention was given to plant-derived compounds with demonstrated anti-breast cancer activity in preclinical and clinical studies.

Innovative therapies, including immunotherapy, gene therapy, and nanotechnology-based treatments, offer promising avenues for more personalized and effective care. In parallel, several medicinal plants and their bioactive compounds such as *Pistacia lentiscus, Curcuma longa,* and *Camellia sinensis* have shown potential in enhancing therapeutic efficacy, reducing side effects, and targeting cancer pathways.

Phytotherapy, when integrated with evidence-based medicine, holds promise as a complementary strategy in breast cancer treatment. Further clinical research is essential to validate its safety, efficacy, and optimal use alongside conventional and innovative therapies.

Keywords: Breast Cancer; Chemotherapy; Radiotherapy; Innovative Therapy; Phytotherapy; Adjuvant Treatment; Medicinal Plants

Introduction

Breast cancer remains the most frequently diagnosed cancer and one of the leading causes of cancer-related deaths among women worldwide [1]. Despite significant advances in early detection and conventional treatment modalities: including surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapies, challenges such as drug resistance, toxicity, tumor recurrence, and patient quality of life persist [2,3]. As a result, there is a growing interest in integrative and supportive approaches that may enhance therapeutic outcomes while minimizing adverse effects [4].

In recent years, innovative therapies such as immunotherapy, gene therapy, and nanomedicine have emerged as promising strat-

egies to overcome limitations of standard treatments. Concurrently, the role of phytotherapy, using plant-derived compounds for medicinal purposes, has gained attention as a potential adjuvant in cancer therapy [5]. Numerous plant extracts and bioactive compounds have demonstrated anti-cancer effects through antioxidant activity, apoptosis induction, inhibition of angiogenesis, and modulation of key molecular pathways involved in tumor progression [6-8].

This review aims to provide an overview of conventional and innovative therapeutic strategies used in breast cancer management, with a particular focus on the potential role of phytotherapy as an adjuvant. By highlighting both preclinical and clinical evidence, this article seeks to underscore the relevance of integrating scientifically validated phyto-therapeutic agents into multidisciplinary breast cancer care.

Standard therapy of breast cancer

The treatment of breast cancer varies depending on the stage, type, and molecular classification of the disease. Each case may present individual characteristics that require specific evaluation by the medical team. Treatment options include surgery, radiotherapy, chemotherapy, hormone therapy, and immunotherapy.

Surgery

Surgical intervention in breast cancer management may serve multiple purposes, including tumor removal, staging of the disease (its extent), and, in certain cases, the reduction of recurrence risk [2,3]. The main types of surgical procedures employed in the treatment of breast cancer include:

- **Tumor excision**, encompassing lumpectomy or partial mastectomy, involves the removal of the tumor while preserving as much healthy breast tissue as possible.
- **Total mastectomy**, in which the entire breast is removed, may also include the nipple and sentinel lymph nodes depending on the clinical context.
- **Risk-reducing surgery** may be considered for women at high risk, such as prophylactic breast reduction, to diminish their likelihood of developing breast cancer.
- **Lymph node surgery** involves the excision of sentinel lymph nodes to assess the spread of the disease. A more extensive lymph node dissection may be required if metastatic cancer cells are detected.
- **Breast reconstruction surgery** can be performed to restore the aesthetic appearance of the breast following mastectomy.
- **Surgery aimed at lowering the risk of recurrence** may involve additional procedures, such as:
- **Oophorectomy (ovary removal)** in women with a predisposition to hormone-dependent breast cancer.

Following surgery, additional treatments: such as radiotherapy, chemotherapy, or hormone therapy, may be indicated depending on the individual clinical profile of the patient.

Chemotherapy

Anticancer drug therapy, commonly referred to as **chemotherapy**, is a treatment strategy aimed at destroying or slowing the growth of cancer cells in the breast and preventing their spread to other parts of the body [2,3]. When administered prior to surgery, **neoadjuvant chemotherapy** may help reduce tumor size, thereby facilitating its surgical removal. Conversely, **adjuvant chemotherapy**, given after surgery, seeks to eliminate residual cancer cells and lower the risk of recurrence.

In cases of advanced or metastatic breast cancer, chemotherapy may be employed to control disease progression, alleviate symptoms, and improve quality of life. A variety of chemotherapeutic agents may be delivered intravenously, orally, or by injection, with the choice of administration depending on the clinical context. Among the most commonly used drug classes

- **Anthracyclines**, including doxorubicin and epirubicin, are potent agents effective against various cancers, including breast cancer. They act by inhibiting DNA-associated enzymes and blocking DNA synthesis.
- **Taxanes**, such as paclitaxel and docetaxel, are frequently used in breast cancer therapy. These agents interfere with the mitotic process by stabilizing micro-tubules, thereby preventing cell division.
- **Antimetabolites**, such as methotrexate, disrupt DNA synthesis and cellular replication by mimicking natural metabolites.
- **Platinum-based agents**, particularly carboplatin and cisplatin, form platinum-DNA adducts, leading to DNA crosslinking and cytotoxicity. These are classified as alkylating agents due to their DNA-damaging effects.

Chemotherapy may lead to a range of side effects, including hair loss, fatigue, nausea, vomiting, hematologic disturbances, and increased susceptibility to infections. These adverse effects underscore the need for careful monitoring and supportive care throughout the course of treatment.

Radiotherapy

Radiotherapy involves the use of ionizing radiation (high-energy X-rays or gamma rays) to target and destroy cancerous cells within the breast tissue [2,3]. It can be employed at various stages of breast cancer treatment, depending on factors such as tumor size, disease stage, the type of surgery performed, and patient-specific clinical considerations.

In certain cases, **neoadjuvant radiotherapy** may be administered prior to surgery with the aim of reducing tumor volume and thereby facilitating surgical resection. For patients undergoing **breast-conserving surgery** (partial or total mastectomy), **adjuvant radiotherapy** may be recommended to eradicate residual malignant cells in the breast region following surgery.

Post-mastectomy, **radiation therapy to the chest wall** may be indicated, particularly in cases where the primary tumor was large, lymph node involvement was confirmed, or other high-risk features were present. **Irradiation of the axillary lymph nodes** may also be required if there is known or suspected metastatic involvement, or if these nodes are considered at high risk of harboring malignant cells [3].

In selected patients with small, localized tumors, **partial breast irradiation** may be considered, focusing radiation solely on the tumor bed rather than the entire breast. Another modern approach, **hypo-fractionated radiotherapy**, delivers higher doses per session over a shorter overall treatment period, offering logistical and therapeutic advantages in specific contexts [2]. Radiotherapy, while effective, may produce adverse effects such as fatigue, skin redness or irritation, localized pain, and, more rarely, long-term changes in skin texture or breast tissue consistency. These potential side effects must be carefully managed within a multidisciplinary framework to ensure optimal patient outcomes.

Immunotherapy

Immunotherapy represents a groundbreaking therapeutic strategy in the management of breast cancer. Its principal objective is to activate or enhance the patient's immune system to identify and eliminate malignant cells. Although immunotherapy is not yet as widely established in breast cancer treatment as it is in certain other malignancies, significant advances are being made to explore its efficacy and expand its clinical applications [2,3].

An overview of current and emerging immunotherapeutic approaches in breast cancer includes.

Immune Checkpoint Inhibitors (ICIs), such as PD-1 inhibitors (e.g., pembrolizumab) and PD-L1 inhibitors (e.g., atezolizumab), function by lifting the immune "brakes" that prevent T cells from recognizing and attacking cancer cells. These agents have demonstrated promising results, particularly in certain subtypes of breast cancer, including **triple-negative breast cancer (TNBC)**, which is considered more immunogenic.

Therapeutic cancer vaccines are designed to provoke a targeted immune response against specific tumor-associated antigens expressed by breast cancer cells. Ongoing clinical trials are investigating the potential of these vaccines to enhance immune-mediated tumor eradication.

CAR-T cell therapy (Chimeric Antigen Receptor T-cell therapy) involves the genetic modification of a patient's T lymphocytes to express synthetic receptors that specifically target cancer cells. While still in early stages for breast cancer, this approach has revolutionized the treatment of hematologic malignancies and holds promise in solid tumors.

Dendritic cell therapy uses the patient's own dendritic cells, which are harvested and manipulated ex vivo to present tumor-specific antigens, thereby stimulating a robust and specific anti-timor immune response upon reinfusion.

It is important to note that immunotherapy is not universally effective across all breast cancer subtypes or in all patients. Its success appears to be particularly pronounced in subtypes such as TNBC, which tend to exhibit greater immune responsiveness [2].

Hormonotherapy

Hormone therapy is a widely used strategy in the treatment of so-called **hormone receptor-positive breast cancer**, in which tumor growth is at least partially driven by hormones such as estrogen and/or progesterone. The goal of hormone therapy is to block or reduce the action of these hormones in order to slow or halt tumor progression [2,3].

Goserelin and leuprolide are **luteinizing hormone-releasing hormone (LHRH) analogues**, employed to suppress ovarian estrogen production in premenopausal women. These agents are typically administered in combination with other hormonal therapies. In rare cases where breast cancer progression may be influenced by **androgens** (male sex hormones), **anti-androgen therapy**: such as **bicalutamide**, may be considered [9,10].

In other scenarios, **progesterone receptor inhibitors**: such as **megestrol acetate**, can be used to block progesterone-mediated stimulation of breast cancer cell proliferation. **Anti-estrogens**, on the other hand, act by preventing estrogen from binding to its receptors on cancer cells. The two main classes of estrogen-blocking agents include: **tamoxifen**: a selective estrogen receptor modulator (SERM), often prescribed to **premenopausal** women [11], and a**romatase inhibitors**: such as **anastrozole, letrozole**, and **exemestane**, which are primarily indicated in **postmenopausal** women [9].

Innovant therapy of breast cancer

The field of breast cancer treatment is constantly evolving, with new therapies continually being developed and evaluated through clinical trials.

Targeted therapy

Targeted therapies represent a significant advancement in the treatment of breast cancer, particularly by focusing on specific molecular pathways involved in tumor growth and progression.

Among these, **CDK4/6 inhibitors**: such as **palbociclib**, **ribociclib**, and **abemaciclib**, are commonly used in the management of hormone receptor-positive breast cancer, in combination with endocrine therapy [12]. These agents function by inhibiting cyclin-dependent kinases 4 and 6, thereby arresting the cell cycle and limiting tumor proliferation.

PI3K inhibitors, such as **alpelisib**, are also employed in hormone receptor-positive breast cancer, specifically in patients harboring **PIK3CA mutations** [13]. These agents interfere with the PI3K/AKT/mTOR signaling pathway, which is frequently dysregulated in breast cancer.

Another important class includes **PARP inhibitors** (poly [ADP-ribose] polymerase inhibitors), such as **olaparib** and **talazoparib**. These targeted agents are particularly effective in **triple-negative breast cancer (TNBC)** patients with **BRCA mutations**, especially in advanced or metastatic settings. PARP inhibitors exploit the tumor cells' heightened susceptibility to DNA damage by impairing their ability to repair single-strand breaks, ultimately leading to cell death [14].

Personalized therapies

Personalized therapies represent a growing frontier in breast cancer management, aiming to tailor treatment strategies to the individual molecular and genetic profile of each patient's tumor.

One of the key tools in this approach is **advanced genomic sequencing**, which enables a deeper understanding of the tumor's specific genetic alterations, thereby facilitating the development of highly targeted therapeutic strategies [15].

Another promising avenue involves **CAR-T cell therapy** (Chimeric Antigen Receptor T-cell therapy). In this approach, T lymphocytes are genetically engineered to express synthetic receptors that specifically recognize tumor-associated antigens. While this technology has shown remarkable success in hematologic malignancies such as leukemias and lymphomas, ongoing research is investigating its applicability to solid tumors, including breast cancer [16].

Several tumor-specific antigens-such as **HER2**, **MUC1**, and others, are currently being explored as potential targets for **breast cancer-specific CAR-T cells** [17]. These efforts aim to develop immunotherapies with enhanced specificity and efficacy against malignant breast tissue while minimizing off-target effects.

Other therapies

Researchers are investigating the benefits of combining different targeted therapies to enhance treatment efficacy. In particular, there has been considerable development of **mRNA-based therapies**, including **mRNA vaccines**, which aim to stimulate a robust antitumor immune response [18].

Plant proven effective against breast cancer

Research has confirmed the relevance of certain empirical methods. It is likely that early plant-based medicine, beyond the almost instinctive use of the anticancer properties of plants, laid the foundation for this understanding. This awareness has gradually sparked a renewed interest in the use of medicinal plants.

Plant proving effect against breast cancer

Turmeric, which contains curcumin, is a compound endowed with anti-inflammatory and antioxidant properties. Preliminary research suggests that curcumin may offer potential benefits in the prevention and treatment of breast cancer by inhibiting cancer cell growth [19].

Green tea contains catechins, natural antioxidants that have been studied for their ability to inhibit the proliferation of breast cancer cells [20].

Ginseng, a plant widely used in traditional Chinese medicine, may have a positive effect on the quality of life of breast cancer patients by reducing fatigue and enhancing immune function [20].

Maitake mushrooms are often used as dietary supplements alongside cancer treatments. They are believed to stimulate the immune system and possess anticancer potential [21].

Fenugreek is rich in bioactive compounds and antioxidants and has been studied for its potential to reduce breast cancer cell growth.

Furthermore, **milk thistle** is sometimes used as a complementary treatment to help mitigate side effects of conventional cancer therapies, such as hepatic toxicity [22].

Certain studies have also indicated the potential of **Ginkgo biloba** to improve the quality of life for breast cancer patients by reducing fatigue and other treatment-related symptoms [23].

Pistacia lentiscus, commonly known as mastic tree, is a Mediterranean plant recognized for its rich content of bioactive compounds with potent antioxidants, anti-inflammatory, and anticancer properties. Recent studies have highlighted its promising role in breast cancer management due to its ability to inhibit tumor cell proliferation, induce apoptosis, and modulate key molecular pathways involved in cancer progression. The extracts of *Pistacia lentiscus* have demonstrated synergistic effects when combined with conventional therapies, enhancing their efficacy while potentially reducing side effects. Given the increasing interest in natural products as adjuncts to standard cancer treatments, *Pistacia lentiscus* represents a valuable candidate for further investigation as a complementary therapeutic agent in breast cancer prevention and treatment [4,5].

Mechanisms of Action

Phytochemicals exert anticancer effects through multiple mechanisms, including

Antiproliferative activity by inhibition of cancer cell growth and induction of cell cycle arrest (e.g., genistein from soy, curcumin from turmeric) [24], and p**ro-apoptotic effects, through t**riggering programmed cell death in malignant cells (e.g., resveratrol, epigallocatechin gallate [EGCG] from green tea) [20]. **Also, anti-angiogenic effects by i**nhibiting the formation of new blood vessels that support tumor growth [25], with a**ntioxidant and anti-inflammatory actions** which contribute to cancer progression [5]. **Some plant was known as hormonal modulation, e**specially relevant in hormone-sensitive breast cancer; for instance, phytoestrogens may compete with endogenous estrogens for receptor binding [20].

It is important to note that some plants may interact with medical treatments or cause undesirable side effects. Therefore, they should never be used as substitutes for standard medical therapies but rather as complementary or adjunctive options.

Potential benefits

Some phytochemicals can enhance the efficacy of chemotherapy (e.g., curcumin with paclitaxel or doxorubicin) or hormone therapy (e.g., resveratrol or lignans with tamoxifen) [24]. Although, phytotherapy may alleviate side effects like mucositis, fatigue, nausea, or cardiotoxicity [8]. Moreover, certain plants may reduce the risk of metastasis by modulating the tumor microenvironment [7]. Many medicinal plants have immunomodulatory effects that help strengthen host defenses [5].

Research has confirmed the relevance of certain empirical methods. It is likely that the earliest plant-based medicines, beyond the almost instinctive use of therapeutic plant properties existing since antiquity and still maintained by some communities, have contributed to this understanding. This growing awareness has led to a renewed interest in medicinal plants, due to their ability to treat many conditions without causing adverse side effects [8].

Clinical evidence and challenges

While many pre-clinical studies show promise, robust clinical data are still limited. Some trials report improved outcomes or symptom relief, but more high-quality RCTs are needed. **Looking for standardization issues, the v**ariability in plant extracts (source, preparation, dose) complicates reproducibility and efficacy assessment. Although, some plant compounds may interact with chemotherapeutic agents, affecting drug metabolism (e.g., via cytochrome P450 enzymes) [6].

Phytotherapy should be considered **adjunctive,** not alternative. Must be **evidence-based** and **supervised by healthcare professionals**. Requires **personalized approaches**, considering tumor subtype, patient health status, and concurrent treatments. **Network pharmacology and systems biology** approaches may help elucidate multitarget effects of phytochemicals. **Nanotechnology** can enhance bioavailability of poorly soluble compounds (e.g., nano-curcumin). **Synergistic combinations** of phytochemicals with drugs could reduce required dosages and toxicity.

Limitation and Future Perspectives

Despite the growing interest in phytotherapy as a supportive strategy in breast cancer treatment, several limitations hinder its integration into standard clinical practice. One major challenge is the limited number of well-designed human clinical trials evaluating the safety, efficacy, optimal dosage, and long-term effects of plant-based compounds [5,26]. Most current data are derived from in vitro or in vivo preclinical studies, which, while promising, are not sufficient to establish clear clinical recommendations. Additionally, potential interactions between phytotherapeutic agents and conventional cancer treatments, such as chemotherapy or hormone therapy, may alter drug metabolism, reduce treatment efficacy, or increase toxicity. These concerns highlight the need for a multidisciplinary approach involving oncologists, pharmacologists, and researchers in integrative medicine to ensure that phytotherapy is used safely and effectively. Future research should prioritize rigorous clinical trials and standardized guidelines to better define the role of phytotherapy as an adjuvant in comprehensive cancer care.

Conclusion

Phytotherapy undoubtedly holds substantial promise as a complementary approach in the management of breast cancer, offering potential benefits in enhancing therapeutic efficacy and mitigating adverse effects. However, it is imperative to emphasize that its application should remain strictly adjunctive to established conventional and innovative treatments. To fully harness the therapeutic potential of plant-derived compounds, their use must be rigorously regulated within the framework of well-designed scientific protocols and robust clinical trials. Only through such meticulous investigation can safety, efficacy, and standardized integration of phytotherapy into multidisciplinary cancer care be ensured, ultimately improving patient outcomes and advancing the frontier of oncological therapeutics.

Conflict of Interest

No conflict of interest exists.

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