



Review Article

APPLICATIONS OF BIOACTIVE COMPOUNDS OF TRADITIONAL CHINESE MEDICINE IN BREAST CANCER MANAGEMENT

Saumya Srivastava¹, Vijay Jagdish Upadhye², Madhulika Esther Prasad³, Pallavi Singh^{1*}

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ABSTRACT

Background: Over the past few decades, the prevalence of breast cancer has been rapidly increasing, making it one of the most prevalent malignancies diagnosed in women globally. Traditional Chinese Medicine (TCM) has gained attention as a potential approach for managing breast cancer by boosting immune response, inhibiting cancer-related gene activity, and alleviating the adverse effects of radiotherapy and chemotherapy. TCM offers a valuable framework for therapeutic systems and scientific exploration that is widely practiced in many regions worldwide, primarily in China, Korea, and Japan. The herbal components of TCM exhibit complex biological activities that influence multiple aspects of cancer progression, including cell proliferation, programmed cell death (apoptosis), immune modulation, and tumor-host interactions. **Methodology:** A systematic literature review was conducted using peer-reviewed articles published between 2017 and 2024. Relevant data were collected from publicly available scientific databases. Non-English, Conference papers, and duplicate studies were excluded to ensure the inclusion of high-quality and relevant research findings. **Result and Discussion:** Analysis revealed that specific bioactive compounds in TCM exhibit significant anti-cancer effects. For example, ginsenoside Rg3 inhibited tumor growth by 45% in vivo, while curcumin reduced MDA-MB-231 breast cancer cell viability by 60% at 20 μ M. **Conclusion:** The promise of TCM, especially its bioactive components and medicinal herbs in the treatment of breast cancer, is the main highlight of this paper. Additionally, it highlights the key scientific databases that provide critical insights into TCM research while exploring the therapeutic mechanisms of Chinese herbs and their bioactive components in mitigating breast cancer progression.

INTRODUCTION

Cancer is currently the second leading cause of death globally, taking the lives of around 9.6 million people annually [1].

According to estimates from GLOBOCAN 2022, nearly 19,976,499 new cancer cases were diagnosed globally in 2022. Almost 24.2% of these cases were reported in China, comprising

¹Department of Biotechnology, Graphic Era Deemed to be University, Dehradun, Uttarakhand 248002, India.

²Research and Development cell, Parul Institute of Applied Sciences (PIAS), Parul University, Vadodara 391760, Gujarat, India.

³Department of Biochemistry and Biotechnology, School of Life Sciences, Sardar Bhagwan Singh University, Dehradun, Uttarakhand 248002, India.

***For Correspondence:** fsdasankop@gmail.com

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2,290,797 females. The breast cancer statistics pertain to 33.0 per 100,000 population [2]. Breast Cancer is the most frequent cancer among women worldwide, accounting for 17.1% of all cancer diagnoses [3]. This data reflects the severe impact of cancer on a global level, leading researchers to focus on the area due to critical health concerns. Among all other cancers, breast cancer ranks as the 5th most prevalent cancer affecting women with an increasing rate [4,5]. Traditional treatments for breast cancer include surgeries, chemotherapies, targeted and endocrine therapies, etc. Although these treatments aid in breast cancer removal, they are accompanied by drawbacks such as

recurrence, metastases, postoperative complications, and many other side effects [6,7]. Unlike conventional treatments, Traditional Chinese Medicine (TCM) and Chinese Herbs play a significant role in cancer treatment (as shown in Figure 1) by addressing multiple factors and sites affected during the condition. The progression of Breast Cancer is associated with several aspects, such as genetic variations, familial cancer history, ethnicity, chronic alcohol consumption, as well as early onset of menstruation, delayed pregnancy, and many other female reproductive variables [8,9].

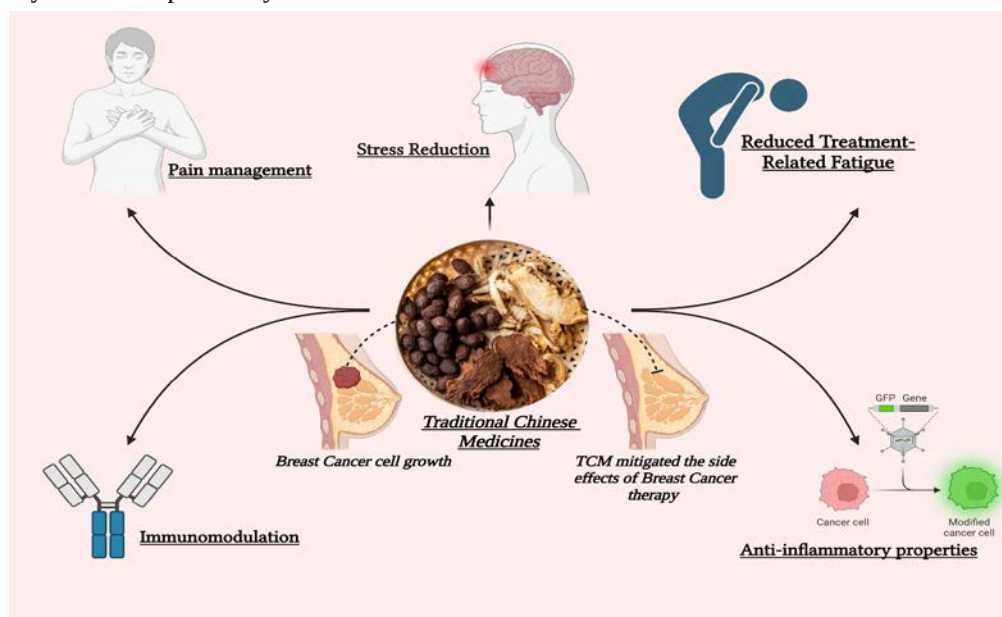


Figure 1: Pharmacological Importance of Traditional Chinese medicine in the treatment of breast cancer.

Figure 1 depicts the significance of traditional Chinese medicine in the treatment of Breast Cancer. The central image depicts a collection of TCM herbs, symbolizing the diverse bioactive compounds used in traditional Chinese medicine (TCM) treatments. Further arrows indicate the key therapeutic effects of TCM, including pain management, stress reduction, reduced treatment-related fatigue, immunomodulation, etc.

Traditional Chinese medicine (TCM) operates within its medical framework, employing distinctive terminology to describe human diseases and physiology. TCM has a robust theoretical foundation and is widely used in the clinical treatment of breast cancer, with a global practitioner population of over a million. Recognized by the State Administration of TCM, breast cancer is included among the 95 illnesses or conditions that can be properly treated with Traditional Chinese Medicine, mainly involving herbal medications, massage, acupuncture, and moxibustion.

Over centuries, TCM has evolved within Asian countries, particularly China, establishing a unique framework of concepts,

diagnoses, and treatments. Its popularity has surged in recent decades due to its significant role in both cancer treatment and prevention. Medical practitioners, including TCM doctors, extensively employ TCM to address symptoms, manage side effects, and mitigate the toxicity associated with cancer treatments. This not only improves patients' quality of life but also prolongs the time before cancer recurrence and enhances overall survival rates [10,11].

Chinese medicine's effectiveness in the treatment of breast cancer extends to all types of clinical stages, which presents a holistic approach with fewer or no side effects [12]. The work bridges the gap between customary wisdom and modern science,

in contrast to conventional evaluations that often focus solely on the theoretical framework or clinical application of TCM in breast cancer. It examines how bioinformatics methods can accelerate the search for novel drug candidates to treat breast cancer and improve the understanding of the therapeutic advantages of TCM.

Overall, this study provides a comprehensive analysis of the therapeutic potential of TCM's bioactive ingredients in managing breast cancer, highlighting the crucial role bioinformatics plays in enhancing the therapeutic benefits of conventional medicine. By fusing insights from both contemporary technologies & traditional knowledge, it aims to open the way for innovative approaches to treat breast cancer that take advantage of the synergistic benefits of bioactive compounds produced from TCM.

METHODOLOGY

The data were collected using scientific databases, including Google Scholar, ScienceDirect, the Chinese Biomedical Literature Database (CBM), PubMed, and the Chinese National Knowledge Infrastructure (CNKI), to gather data that supported our plan to conduct a comprehensive review. Articles released between 2017 and 2024 were cited. The majority of references consisted of personal anecdotes from healthcare practitioners or case studies detailing individual physicians' experiences.

Additionally, several citations were derived from laboratory experiments investigating the efficacy of herbal medicine.

Inclusion/Exclusion Criteria

The study selection criteria were explicitly defined. Only peer-reviewed articles in English were cited, while non-English and duplicate studies were excluded. Additional filters applied included studies with full-text availability and experimental data relevant to breast cancer treatment using Traditional Chinese Medicine. Articles were filtered out from inclusion through meticulous assessment of their relevance, accuracy, potential duplications, and ethical considerations.

Figure 2 demonstrates the PRISMA flow diagram for meta-analysis applied in this systematic review. Conversely, the inclusion of cited articles is predicated on the articles' demonstration of high quality, depth of insight, originality, and ability to contribute to a diverse and inclusive representation of perspectives. Additionally, editorial judgments are also kept into consideration, ensuring that the review maintains coherence, relevance, and scholarly significance. The search strategy employed Boolean operators, such as AND and OR, to refine the results. The keywords used were “Traditional Chinese Medicine AND Breast Cancer”, “Chinese herbs AND Breast Cancer”, and “Bioactive compounds AND Breast Cancer”.

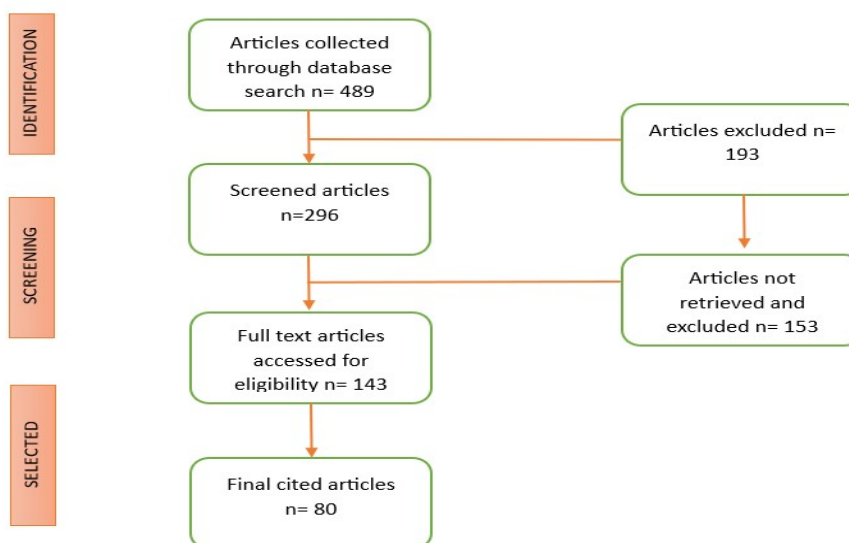


Figure 2: PRISMA for Meta-Analysis

Diagnosis of breast cancer in TCM

Traditional Chinese Medicine (TCM) uses a combination of pathology identification & differentiation to diagnose breast cancer (BC). The main features of the condition include skin

abnormalities, nipple discharge, tumors, and modifications in the nipple-areola region. In TCM, the stomach, liver, kidney, and spleen are more closely related to breast cancer. The TCM theory suggests that abnormal physiological activities in the

breast arise from the invasion of external pathogens, internal qi deficiency, bodily fluid imbalance, and a shortage of vital qi [13]. The etiology encompasses six external factors that contribute to the development of pathogenic toxins and diseases, including inadequacies in healthy qi, deficiencies in blood and qi, interior injuries resulting from the 7 emotions, congenital endowment, the buildup of poisonous heat, and improper diet.

Based on pathological anomalies related to viscera, yin and yang, qi and blood, liver qi stagnation, toxic heat accumulation, and imbalance of Chong and Ren, patients are categorized into different categories [14].

Bioactive compounds and Chinese herbs

Although Traditional Chinese Medicine (TCM) has a long history of use, it is essential to acknowledge that there is not much scientific proof confirming the effectiveness of particular bioactive compounds within TCM for BC treatment. Moreover, TCM typically employs intricate formulations rather than isolated compounds.

Nevertheless, several studies have investigated the potential therapeutic effects of specific TCM herbs concerning breast cancer. Here are some bioactive compounds and Chinese herbs within TCM that have been the subject of research for their potential advantages.

Tanshinone - They are the dried roots or rhizomes of *SM Bunge* that hold a significant place in Traditional Chinese Medicine across China and several Asian nations. *Tanshinone* is valued for having an extensive list of therapeutic benefits and an exceptional safety record [15]. According to studies, *tanshinone* exhibits promising effects for various illnesses, including cancer [16], inflammation [17], cardiac issues such as myocardial ischemia [18], oxidative stress [19], and the formation of blood clots [20]. It also shows promise in preventing left ventricular hypertrophy, enlarging blood vessels [21], preventing atherosclerosis [22], protecting brain cells [23], improving blood flow in small vessels [24], inhibiting pulmonary fibrosis [25], and enhancing the immune system [26].

Triptolide- This compound is found in the plant *Tripterygium wilfordii*, which has been used for generations in TCM. Triptolide exhibits several therapeutic properties, including anti-cancer, immunosuppressive, and anti-inflammatory effects.

Triptolide has shown promise against several malignancies, including neuroblastoma, lung, breast, and pancreatic cancer, in both laboratory and animal tests. Its ability to inhibit cancer cell proliferation, induce tumor cell death, and prevent metastasis is one of the key functions of its anti-cancer properties [27].

Artemisinin- It's a bioactive compound that has been derived from sweet wormwood, often known for its anti-cancer properties, and also exhibits some anti-cancer properties. Derivatives like artesunate and dihydroartemisinin (DHA) alert cancerous cells to traditional treatments. When combined with other anticancer drugs, these derivatives enhance efficacy without additional side effects. The broad anticancer effects of artemisinin-based combination treatments (ARTs) have been reported in several investigations [28]. Importantly, because of their high selectivity, ARTs have become attractive options for cancer therapy, even though large dosages of the drug have been shown to cause neurotoxicity in clinical trials [29].

Berberine- Berberine, commonly derived for research and pharmaceutical applications, has been extensively investigated for its potential anticancer properties. It demonstrates the ability to neutralize free radicals, trigger apoptosis, halt the cell cycle, and inhibit angiogenesis and inflammation. It also modulates diverse cell signaling pathways, including the MAPK/ERK, PI3K/AKT/mTOR, and Wnt/ β -catenin pathways. Alkaloid berberine (BBR) showed promising effectiveness against breast cancer (BC) [30].

Quercetin-Quercetin, a pentahydroxy flavone with a hydroxy group located at 3-, 3', 4', 5-, and 7- end positions, is among one of the most prevalent flavonoids found in edible vegetables, fruits, and wine serving various roles, acting as an antioxidant agent, antibacterial, antineoplastic agent, protein kinase inhibitor, phytoestrogen, chelator, radical scavenger and aurora kinase inhibitor.

Quercetin is classified as a pentahydroxy flavone and a 7-hydroxyflavonol, and is recognized for its ability to inhibit the proliferation of many cell lines associated with human breast cancer. Its pro-oxidant characteristics benefit in preventing the formation of tumour cells. One of the primary goals of cancer treatment is to induce apoptosis, and quercetin is a suitable candidate for this purpose due to its inherent apoptotic properties [31].

Paeonol - Identified chemically as 2-hydroxy-4-methoxy acetophenone, possesses a modest molecular weight of 166.17 g/mol with a melting point of 52°C [32]. Its anti-tumour effects are evident through diverse molecular mechanisms, and numerous derivatives of paeonol have been identified and synthesized, demonstrating the significant anticancer potential and serving as structural models for the innovation and creation of novel anticancer agents [33].

Epigallocatechin gallate (EGCG)- The formal condensation of gallic acid with the 3R-hydroxy group of (-) epigallocatechin yields epigallocatechin gallate, a gallate ester. Its actions include Hsp90 inhibition, serving as an antineoplastic agent, inducing apoptosis, and acting as an antioxidant. EGCG can influence several signalling pathways due to its prophylactic anticarcinogenic effects. Moreover, EGCG enhances the therapeutic response when combined with natural or synthetic medications, which lessens the negative effects of non-targeted therapy [34].

Salidroside - One of the most potent substances found in *Rhodiola rosea* is salidroside, which exhibits a range of biological properties. In addition to its antioxidant and anti-inflammatory properties, it exhibits anticancer properties by inhibiting the proliferation of human breast cancer cells. Salidroside helps prevent tumor growth in breast cancer cells MCF-7 [35].

Astragaloside IV- They exhibit a variety of roles such as encouraging autophagy and apoptosis, controlling reactive oxygen species, causing cell cycle arrest, and inhibiting the invasiveness of cancer cells. Its significant anti-cancer properties extend to liver, breast, gastric, and lung cancer [36-39].

Curcumin- The anticancer, antioxidant, and anti-inflammatory effects of curcumin have been demonstrated. It holds the potential to inhibit the growth and proliferation of cancer cells of several sorts, including breast, prostate, pancreatic, colorectal, head and neck, and brain cancers. Its mechanisms of action involve the modulation of various cellular targets. Curcumin regulates signaling pathways crucial for breast cancer progression, including the NF- κ B, COX-2, and pSTAT3 pathways. Research indicates that curcumin can boost the effectiveness of standard chemotherapy medications like doxorubicin and paclitaxel in treating breast cancer [40,41].

Ginsenosides- *P. notoginseng* is a medicinal plant frequently employed in traditional Chinese medicine. Its diverse pharmacological effects encompass immunity enhancement, antioxidant properties, anti-tumor activities, and anti-aging benefits. The primary active constituents of *P. notoginseng* consist of *Panax notoginseng saponins* (PNS). Protopanaxadiol (containing Ginsenosides Ra1, Ra2, Ra3, etc.), protopanaxatriol (containing ginsenosides Re, Rf, Rg1, etc.), C17 side-chain varied (containing Rg5, Rk1, Rh4, etc.), and oleanolic acid (containing ginsenosides R0, Rh3, R1, etc.) are the four main groups into which these ginsenosides are usually divided. Ginsenosides hold a great deal of promise for treating breast cancer, according to several studies [42,43]. Table 1 outlines the bioactive compounds and Chinese herbs, prominently featured in TCM, their sources, chemical structures, and therapeutic actions against Breast cancer.

Role of bioinformatics in TCM data management and analysis of TCM data

Traditional Chinese Medicine (TCM) boasts thousands of years of experience in clinical practices and is essential to maintaining public health, especially in Asian countries. Breast cancer is a complex disease with significant morbidity and mortality rates worldwide, possessing challenges to existing therapies mainly in advanced stages [55]. The realm of Traditional Chinese Medicine (TCM) research is witnessing a surge in data, thanks to advancements in analytical tools and integrative bioinformatics methods. This growing body of data is being managed, accessed, and analysed more effectively by bioinformatics, which is a fusion of biology and computer science. To enhance our understanding and explore potential treatments, various bioinformatics tools, including DAVID, BATMAN-TCM, SwissTargetPrediction, KEGG, and SystemsDock, are commonly employed. KEGG is a knowledge database for the systematic analysis of gene function, linking genomic information with higher-order functional information. These tools aid in identifying relevant pathways, key genes, and proteins associated with human diseases, thereby facilitating the prediction of potential therapeutic targets [56]. Abundant databases are currently accessible for searching information on components and bioactivity, categorized by single compounds, herbs, or frequently utilized formulas. Table 2 above describes the prominent databases that give detailed information about traditional Chinese medicines, their potential targets, drug targets, and disease networks.

Table 1: Different Bioactive compounds present in TCM showing Therapeutic Action against Breast Cancer

Bioactive compounds and herbs	Source	Therapeutic action	IC50 (μM)	Ref.
<i>Tanshinone</i>	Found in <i>Salvia miltiorrhiza</i> (SM)	Tanshinones inhibit the adhesion, migration, invasion, and metastasis of cancer cells, which are pivotal stages in cancer progression, and have the potential to regulate inflammatory and immune responses, suppress telomerase activity, and trigger the activation of tumor suppressor proteins such as p53. Tanshinone IIA prompts MDA-MB-231 breast cancer cell death by boosting Bax and lowering Bcl2 levels.	0.75	44
<i>Triptolide</i>	Active diterpenetriepoxide from the Chinese herb <i>T. wilfordii</i> Hook f.	Triptolide has been shown to cause cell death in breast cancer cells via a lysosome-regulated mechanism. Additionally, it has established the capacity to inhibit the expansion and proliferation of breast cancer cells by targeting genes associated mainly with inflammation and tumor progression. Triptolide has been shown in studies to have anticancer effects by inducing apoptosis in breast cancer cells & inhibiting their growth, motility & invasion.	0.008	45, 85
<i>Artemisinin</i> (Qinghaosu)	Artemisinin is a sesquiterpene lactone obtained from sweet wormwood	Through the production of reactive oxygen species (ROS), artemisinins cause apoptotic cell death in breast cancer. Additionally, they initiate nonapoptotic processes such as ferroptosis, autophagy, and necrosis. They also affect cancer stem cells, immunosuppression, and cancer metabolism. Artemisinins affect medication response, interactions, and resistance by modulating important pathways and variables in breast cancer, such as NFκB and survivin. Artemisinins induce autophagy by a variety of molecular processes, such as the buildup of reactive oxygen species and the activation of certain pathways in distinct cancer cell type.	Not specified	46
<i>Berberine</i>	<i>Berberine</i> is an isoquinoline alkaloid extracted from the medicinal herb <i>Rhizoma coptidis</i> .	Berberine promotes apoptosis, inhibits angiogenesis, and scavenges free radicals. Moreover, it lessens the expression of TNF-α and IL-6, which are linked to the advancement of breast cancer, and suppresses NF-κB activation. It is suggested that berberine and silver nanoparticles be used as a possible treatment for breast cancer. By upregulating the CDK inhibitors p21 and p27, berberine induces apoptosis and cell cycle arrest in breast cancer cells, leading to the inhibition of various cyclins. Through direct interactions with miRNA, transcriptional regulatory elements, effector proteins, and several signaling pathways, it has strong anticancer potential against breast cancer.	4.14±0.35	47, 86
<i>Quercetin</i>	Quercetin, a bioactive flavonoid, can be naturally sourced from a variety of sources like	Quercetin induces apoptosis and stops the cell cycle in tumor cells, decreasing the Bcl-2/Bax ratio, increasing caspase-3 expression, and inhibiting MMP-2 protein linked to cancer metastasis.	55	48, 87

Bioactive compounds and herbs	Source	Therapeutic action	IC50 (μM)	Ref.
	fruit, vegetables & grains. It is abundant in foods like apples, berries, onions, citrus fruits, broccoli, and leafy greens.			
<i>Paeonol</i>	Paeonol is a naturally occurring active substance derived from traditional Chinese medicine <i>Cortex Moutan</i> (CM).	Paeonol prompts apoptosis, suppresses cell proliferation, invasion, and migration, and regulates angiogenesis and cell cycle arrest in breast cancer cells. It also improves radiosensitivity, serving as a potential complementary approach in breast cancer treatment. Paeonol influences various signaling mechanisms, such as NF-κB and PI3K/AKT in breast cancer.	1500.27	49, 88
<i>Epigallocatechin gallate (EGCG)</i>	EGCG belongs to the catechin category present in green tea. Green tea, derived from the leaves of <i>Camellia sinensis</i> , stands among the globally consumed beverages	EGCG delays the formation and growth of breast cancer cells, suppressing angiogenesis crucial for tumor nutrient supply, triggers cell death in breast cancer cells. The anticancer actions of EGCG are linked to the regulation of reactive oxygen species (ROS) production and inhibition of nuclear factor-B (NF-B) signaling. It also suppresses the expression of Epidermal growth factor receptors (EGFR or ErbB), including ErbB1 and ErbB2, that are frequently overexpressed in breast cancer, mainly in epidermoid carcinoma (A-431) and SK-BR3 cell lines.	83	50, 89
<i>Salidroside</i>	Salidroside is a compound that is extracted from the <i>Rhodiola rosea</i> plant	Salidroside inhibits the growth of human breast cancer cells (MCF-7) by limiting their proliferation, migration, colony formation and invasion that leads to apoptosis and halts the cell cycle at the G0/G1 phase in BC cells and also inhibits the production of ROS and activation of MAPK pathway. The downregulation of Bcl-2 and p53 as well as the overexpression of caspase 3 and Bax may be part of the mechanism of action. Tumour cells eventually undergo apoptosis because of this process, which increases the production of pro-apoptotic proteins.	6.2	51, 88
<i>Astragaloside IV</i>	This compound is considered the main active ingredient of the dried root of <i>Astragalus membranaceus</i>	AS-IV has been shown to regulate the activities of enzymes that scavenge reactive oxygen species, leading to a reduction in oxidative stress and offering protection against the progression of breast cancer. Additionally, it exhibits the capability to inhibit the metastasis of breast cancer cells, potentially impeding the spread of the disease.	12.57	52, 89, 90
<i>Curcumin</i>	The active ingredient found in the <i>Curcuma longa</i> plant is commonly known as turmeric.	Curcumin primarily works against cancer by stimulating apoptotic pathways in cancer cells and inhibiting angiogenesis, metastasis, and inflammation—processes that promote cancer growth. It targets multiple signaling pathways important for	30.78	53

Bioactive compounds and herbs	Source	Therapeutic action	IC ₅₀ (μM)	Ref.
		cancer therapy, including those mediated by mammalian target of rapamycin, p53, Ras, phosphatidylinositol 3-kinase, protein kinase B, and Wnt-β-catenin.		
Curcumin	The active ingredient found in the <i>Curcuma longa</i> plant, is commonly known as turmeric.	Curcumin primarily works against cancer by stimulating apoptotic pathways in cancer cells and inhibiting angiogenesis, metastasis, and inflammation—processes that promote cancer growth. It targets multiple signaling pathways that are important for cancer therapy, such as those mediated by mammalian targets of rapamycin, p53, Ras, phosphatidylinositol-3-kinase, protein kinase B, and Wnt-β catenin.	30.78	53
Ginsenosides	They are the main bioactive component of the Chinese herb <i>Panax notoginseng</i>	Ginsenosides have the potential to induce apoptosis in endometrial cancer cells, and this effect may be associated with elevated levels of apoptosis markers such as cleaved poly ADP-ribose polymerase (PARP) and caspase 3 proteins. Moreover, apoptosis and the Bcl-2/Bax/Caspase-3 signaling pathway are closely related. Ginsenosides affect the Bcl2/Bax/Caspase-3 signaling pathway, which causes breast cancer cells to undergo apoptosis.	Not specified	54

Table 2: Prominent databases for gathering information about TCM

Database Name	Country	Description	Ref.
TCM- Mesh Database	China	The current world's most extensive and comprehensive freely available small molecular database for virtual screening in traditional Chinese medicine is the TCMMesh database, which comprises extensive data including nearly 6,235 herbs, 383,840 compounds, 14,298 genes, 6,204 diseases, and many more. It's one of the earliest Chinese medicine databases, and is now widely acknowledged as one of the most reputable repositories for Chinese medicine chemical components. URL: http://tcm.cmu.edu.tw/	57
TCMID	Singapore	TCM-ID is one of the key resource centers on TCM data research. In 2005 TCM-ID was first launched and maintained by: Bioinformatics & Drug Design (BIDD) group in the Department of Pharmacy, National University of Singapore. In TCMID 2.0, the original dataset has been significantly expanded, with the inclusion of two new data fields- prescription ingredients and MS spectra. TCMID has included nearly 46,929 prescriptions, 8,159 Chinese medicinal materials. URL: https://bidd.group/TCMID/	58
TCM Gene database	China	A specialized database that automatically extracts and consolidates association details between traditional Chinese medicines (TCMs), diseases, effects genes, and ingredients from extensive biomedical	59
		literature. Additionally, it includes integrated information on protein-protein interactions and biological pathways sourced from public databases, offering a comprehensive repository of diverse TCM-related associations. URL: https://ngdc.cncb.ac.cn/databasecommons/database/id/3846	

Database Name	Country	Description	Ref.
BATMAN – TCM	China	An improved integrated database has been created to house established and anticipated connections between traditional Chinese medicine (TCM) ingredients and the target proteins involved in T cell death in breast cancer. BATMAN-TCM database is uniquely tailored for deciphering TCM pharmacological mechanisms and pinpointing active ingredients for treating various diseases. BATMAN-TCM 2.0 version provides a broader set of possible targets for drug development by including 3,279 identified and 9,493 predicted target proteins for TCM. URL: https://bionet.ncpsb.or.g.cn/batman-tcm/	60
CHEMTCM	UK	The database encompasses information on chemicals, targets, drug-target networks, and the corresponding drug-target-disease networks. Additionally, it provides pharmacokinetic properties for natural compounds, encompassing aspects such as oral bioavailability, drug-likeness, intestinal epithelial permeability, blood-brain barrier permeability, aqueous solubility, and other relevant parameters. This database is distinguished by its classification of the skeletal structures of Chinese medicine compounds, which comprise main categories such as aliphatics, alkaloids, phenols, and terpenoids. URL: http://www.chemtcm.com/	61

Neural network-based approaches for the assessment of the activity of bioactive compounds

TCM

Due to the complex nature of Traditional Chinese Medicine (TCM), explaining its mechanism through one or two pathways is a challenging task. Consequently, many TCM researchers are shifting from traditional target-based studies to embrace network pharmacology research. Network pharmacology aims to model disease processes and the interaction between medicine and the organism from a systems biology perspective. This approach investigates mechanisms and encourages medical innovation through extensive data capture research, molecular data from the internet, and computer analysis [62].

Databases Used in Network Pharmacology

Many reliable databases in the medical field are used in network pharmacology research. These databases are primarily sourced from pharmaceuticals and chemicals derived from herbs or herbal formulations used in Traditional Chinese Medicine (TCM). The relationships between different diseases or syndromes and medications can be easily identified using network pharmacology [63]. Neural network-based algorithms, such as DeepAffinity and VISAR, can be utilized by scientists in TCM research to quickly examine the binding patterns of drug proteins and predict the affinity of medicines for their targets [64,65]. By using both labeled and unlabeled data, the algorithms can help analyze how a compound's substructures affect its overall activity and predict drug-protein interactions.

Network pharmacology in Traditional Chinese Medicine holds the capability to enhance the research quality and incorporation in related fields by fusing experimental methodologies with neural network tools. The molecular basis of TCM herbal formulations, the identification of targets for various compounds, and the evaluation of biomolecule networks underlying disease could be investigated using TCM network pharmacology [66,67].

Some additional databases are

TCMGeneDIT: Contains data and information on TCM chemicals, herbs, functions, and disorders, as well as genes [68], which facilitates the investigation of possible TCM mechanisms by examining the correlations between gene regulation.

ETCM (Encyclopaedia of Traditional Chinese Medicine) database: This database predicts the compound targets based on chemical fingerprint similarity with prevailing medications, shedding insights into TCM botanicals, formulations, and their chemical constituents [69].

SymMap: It's a TCM database that mainly focuses on the correlation of syndromes. The database includes TCM syndromes, herbs, diseases linked to syndromes, and TCM chemical and pharmacological targets.

Moreover, some visualization tools are also essential for determining and assessing TCM data, enabling scientists to investigate the complex relationships related to TCM [70,71].

Among the datasets used for TCM and molecular research, TCMID contains over 20,000 compounds, providing a broad spectrum of data, whereas CHEMTCM focuses on approximately 8,000 highly characterized molecules, ensuring a more curated dataset. BATMAN-TCM 2.0 includes 3279 known and 9493 predicted TCM target proteins, providing more potential targets for drug discovery [72]. The choice between these databases depends on the research priority, whether a comprehensive or highly validated dataset is required.

BI tools play a crucial role in analyzing and validating the therapeutic potential of TCM compounds. Still, their accuracy and reliability vary depending on the quality of the database, experimental validation, and prediction algorithms. While databases like TCMID provide extensive records of compounds, they often lack experimental confirmation for certain molecular interactions. In contrast, CHEMTCM offers a more curated selection but may have fewer available compounds. A practical example where bioinformatics played a crucial role is in identifying tetrandrine as a promising TCM compound for breast cancer treatment. A network pharmacology study revealed that tetrandrine exerts anticancer effects by targeting multiple key signalling pathways, including mTOR, PI3K-Akt, MAPK, and Jak-STAT. The study identified 37 protein targets involved in the re-regulation of deregulated genes/proteins, with primary targets such as Jun, MAPK, Ras, p53, and Myc. These findings provide valuable insights into the development of tetrandrine-based drugs against these crucial oncogenic proteins. This demonstrates how bioinformatics can accelerate the discovery of effective TCM compounds, although experimental validation remains essential for clinical relevance [73].

RESULT

This review highlights several key findings regarding the integration of Traditional Chinese Medicine (TCM) in breast cancer treatment. The incorporation of TCM along with the traditional treatments of breast cancer is initially focused. This curve represents a robust response to the potential benefits of enhancing treatment outcomes and mitigating side effects. Additionally, the review aims to focus on the therapeutic actions of the bioactive compounds present in TCM for minimizing the side effects of conventional treatments. These actions comprise apoptosis, inhibiting metastasis, regulating cell cycle progression, modulating immune responses, and many more, which play fundamental roles in impeding breast cancer

progression. The review primarily exemplifies the numerous bioactive compounds ranging from Tanshinone to Ginsenosides, outlining how each of these compounds has a therapeutic mechanism that impedes the growth of breast cancer cells and modifies the signaling pathways involved. Secondly, the essential role of bioinformatics in advancing traditional Chinese medicine (TCM) was also highlighted. By utilizing advanced software, such as BATMAN-TCM, and databases like TCMID and CHEM-TCM, scientists can easily identify complex pathways and potential therapeutic targets. Algorithms like Deep Affinity support network pharmacology, which aids in understanding TCM's complex interactions. By using bioinformatics tools, the analysis and practical implementation of the TCM could be made very easier.

Bioavailability and Pharmacokinetics of TCM Compounds

The therapeutic efficacy of TCM-derived bioactive compounds is significantly influenced by their bioavailability and pharmacokinetics. Many herbal constituents suffer from poor solubility and low systemic absorption, which limits their effectiveness in clinical applications. For instance, Curcumin, despite its potent anticancer properties, has extremely low bioavailability due to rapid metabolism and systemic elimination [74]. Future research should focus on improving the delivery mechanisms of these bioactive compounds to enhance their therapeutic potential in the treatment of breast cancer.

Regulatory challenges in integrating TCM with conventional medicines

Despite the growing interest in TCM for cancer treatments, many regulatory challenges hinder its integration with conventional medicines. One of the major concerns is variability in quality control and standardization of herbal formulations. Differences in preparation methods, potential contaminants, and active ingredient concentrations raise concerns regarding safety and efficacy. Another concern is the lack of large-scale clinical trials that meet global regulatory standards, which limits widespread acceptance. Regarding ethical standards, it is crucial to address the moral issues raised by cutting-edge technologies, such as AI, that are incorporated into TCM research and diagnosis. Upholding these ethical norms in medical research requires careful consideration of issues such as data privacy and algorithmic transparency [75]. Addressing these challenges requires collaborative efforts to establish standardized protocols, conduct rigorous clinical trials, and ensure regulatory

harmonization, thereby facilitating the integration of TCM into mainstream oncology care [76].

CONCLUSION

Through this review, we have investigated the promising potential of traditional Chinese medicine (TCM) in breast cancer management, with a focus on the key role of bioactive compounds and various herbs in TCM, including Tanshinone and Ginsenosides. It also explores the prospective potential of TCM in this area. The broad range of biological activities possessed by herbal derivatives highlights the urgent need for ongoing research and validation of TCM with established cancer treatment procedures. Gaining a thorough understanding of TCM's therapeutic mechanisms requires a combination of traditional knowledge with modern scientific approaches, especially with the use of bioinformatics TCM databases. The area of TCM research is advancing through considerable breakthroughs, thanks to the increased data generated by advancements in analytical tools and bioinformatics methodologies. Numerous bioinformatics tools, such as Swiss Target Prediction, DAVID, BATMAN-TCM, System Dock, and KEGG, aid in identifying essential genes, proteins, and pathways associated with diseases, thereby facilitating the prediction of potential therapeutic targets. Furthermore, well-known databases such as the TCM-Mesh database, TCMID [91], TCM Gene database [92], BATMAN-TCM, and CHEM-TCM provide extensive archives of TCM-related relationships, which aid in clarifying pharmacological processes and identifying active components for treating a range of illnesses, including breast cancer.

In addition, the use of neural network-based algorithms, such as DeepAffinity and VISAR, to enhance network pharmacological techniques presents a promising path toward comprehending the intricate nature of TCM and its interactions with biological systems. These results showed how bioinformatics can revolutionize TCM research and its uses in treating diseases like breast cancer. Despite these promising results, several obstacles remain. The lack of extensive clinical trials, variability in bioactive compound concentrations, and the standardization of herbal formulations are significant hurdles to the widespread therapeutic use of TCM. To sum up, the investigation of TCM in the treatment of breast cancer presents a vibrant and developing area with significant potential to improve treatment outcomes and patient satisfaction. Besides the theoretical aspect,

TCM's practical applications in clinical areas show considerable promise for addressing the unmet needs and complementing current treatment technologies. Future research efforts should prioritize rigorous clinical studies, mechanistic investigations, and the development of integrative protocols to solidify TCM's role within the broader landscape of breast cancer care. Pre-clinical studies and small-scale clinical trials suggest the potential benefits of TCM in breast cancer treatment; large-scale clinical trials are essential to establish its safety and efficacy. Integrating TCM with modern clinical methodologies such as pharmacokinetics will provide insights into the mechanism of action and optimize treatment strategies. By harnessing the combined wisdom of traditional healing practices and modern scientific advancements, we can pave the way for innovative and effective approaches to breast cancer treatment, ultimately benefiting patients worldwide.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Saumya Srivastava contributed to the methodology, data curation, and writing of the original draft. Vijay Jagdish Upadhye handled conceptualization and manuscript review. Madhulika Esther Prasad supported resources, figure formatting, and manuscript review. Pallavi Singh was responsible for conceptualization, methodology, resources, supervision, and funding. All authors read and approved the final manuscript.

REFERENCES

- [1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians*, **68**, 394–424 (2018) <https://doi.org/10.3322/caac.21492>.
- [2] Diao X, Guo C, Jin Y, Li B, Gao X, Du X, Chen Z, Jo M, Zeng Y, Ding C, Liu W, Guo J, Li S, Qiu H. Cancer situation in China: an analysis based on the global epidemiological data released in 2024. *Cancer Communications*, **45**, 178–97 (2024) <https://doi.org/10.1002/cac2.12627>
- [3] Lei S, Zheng R, Zhang S, Wang S, Chen R, Sun K, Zeng H, Zhou J, Wei W. Global patterns of breast cancer incidence and mortality: A population-based cancer registry data analysis from

- 2000 to 2020. *Cancer Communications*, **41**, 1183–94 (2021) <https://doi.org/10.1002/cac2.12207>.
- [4] Cao W, Chen H-D, Yu Y-W, Li N, Chen W-Q. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chinese Medical Journal*, **134**, 783–91 (2021) <https://doi.org/10.1097/cm9.0000000000001474>
- [5] Feng R-Q, Li D-H, Liu X-K, Zhao X-H, Wen Q-E, Yang Y. Traditional Chinese Medicine for Breast Cancer: A Review. *BCTT*, Volume **15**, 747–59 (2023) <https://doi.org/10.2147/bctt.s429530>.
- [6] Waks AG, Winer EP. Breast Cancer Treatment. *JAMA*, **321**, 288 (2019) <https://doi.org/10.1001/jama.2018.19323>.
- [7] Spronk I, Schellevis FG, Burgers JS, de Bock GH, Korevaar JC. Incidence of isolated local breast cancer recurrence and contralateral breast cancer: A systematic review. *The Breast*, **39**, 70–9 (2018) <https://doi.org/10.1016/j.breast.2018.03.011>.
- [8] Coughlin SS. Epidemiology of Breast Cancer in Women, *Springer International Publishing*, 9-29 (2019) https://doi.org/10.1007/978-3-030-20301-6_2.
- [9] Akram M, Iqbal M, Daniyal M, Khan AU. Awareness and current knowledge of breast cancer. *Biol Res*, **50**, (2017) <https://doi.org/10.1186/s40659-017-0140-9>.
- [10] Zhang X, Qiu H, Li C, Cai P, Qi F. The positive role of traditional Chinese medicine as an adjunctive therapy for cancer. *BST*, **15**, 283–98 (2021) <https://doi.org/10.5582/bst.2021.01318>.
- [11] Wang Y, Zhang Q, Chen Y, Liang C-L, Liu H, Qiu F, Dai Z. Antitumor effects of immunity-enhancing traditional Chinese medicine. *Biomedicine & Pharmacotherapy*, **121**, 109570 (2020) <https://doi.org/10.1016/j.biopha.2019.109570>.
- [12] Zia FZ, Olaku O, Bao T, Berger A, Deng G, Yin Fan A, Garcia MK, Herman PM, Kaptchuk TJ, Ladas EJ, Langevin HM, Lao L, Lu W, Napadow V, Niemtzow RC, Vickers AJ, Shelley Wang X, Witt CM, Mao JJ. The National Cancer Institute's Conference on Acupuncture for Symptom Management in Oncology: State of the Science, Evidence, and Research Gaps. *JNCI Monographs*, (2017) <https://doi.org/10.1093/jncimonographs/lgx005>.
- [13] Yiming ZH, Xinchun TI, Yufei WA, Haochen WA, Heran ZH, Yonghong WA, Shulong JI. Exploring traditional Chinese medicine-based diagnosis and treatment of breast cancer based on molecular typing. *Journal of Beijing University of Traditional Chinese Medicine*, **1**, 46(7), (2023) <https://doi.org/10.3969/j.issn.1006-2157.2023.07.022>.
- [14] Guo Q, Coyle ME, Zhang AL, Xue X, Bian W, Song A, Xie X, Hong R, Lyu G, Liu L, Chen Q, Xue CC. Chinese Medicine Syndrome Differentiation for Early Breast Cancer: A Multicenter Prospective Clinical Study. *Front. Oncol.*, **12**, (2022) <https://doi.org/10.3389/fonc.2022.914805>.
- [15] Fang Z, Zhang M, Liu J, Zhao X, Zhang Y, Fang L. Tanshinone IIA: A Review of its Anticancer Effects. *Front. Pharmacol.*, **11**, (2021) <https://doi.org/10.3389/fphar.2020.611087>.
- [16] Jin Z, Chenghao Y, Cheng P. Anticancer Effect of Tanshinones on Female Breast Cancer and Gynecological Cancer. *Front. Pharmacol.*, **12**, (2022) <https://doi.org/10.3389/fphar.2021.824531>.
- [17] Ye T, Xiong D, Chen L, Li Y, Gong S, Zhang L, Li B, Pan J, Qian J, Qu H. Effect of Danshen on TLR2-triggered inflammation in macrophages. *Phytomedicine*, **70**, 153228 (2020) <https://doi.org/10.1016/j.phymed.2020.153228>.
- [18] Zhu P-C, Shen J, Qian R-Y, Xu J, Liu C, Hu W-M, Zhang Y, Lv L-C. Effect of tanshinone IIA for myocardial ischemia/reperfusion injury in animal model: preclinical evidence and possible mechanisms. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1165212>.
- [19] Wu Y-T, Xie L-P, Hua Y, Xu H-L, Chen G-H, Han X, Tan Z-B, Fan H-J, Chen H-M, Li J, Liu B, Zhou Y-C. Tanshinone I Inhibits Oxidative Stress-Induced Cardiomyocyte Injury by Modulating Nrf2 Signaling. *Front. Pharmacol.*, **12**, (2021) <https://doi.org/10.3389/fphar.2021.644116>.
- [20] Feng J, Liu L, Yao F, Zhou D, He Y, Wang J. The protective effect of tanshinone IIA on endothelial cells: a generalist among clinical therapeutics. *Expert Review of Clinical Pharmacology*, **14**, 239–48 (2021) <https://doi.org/10.1080/17512433.2021.1878877>.
- [21] Lu Y, Yan Y, Liu X. Effects of alprostadil combined with tanshinone IIA injection on microcirculation disorder, outcomes, and cardiac function in AMI patients after PCI. *Ann Palliat Med*, **10**, 97–103 (2021) <https://doi.org/10.21037/apm-20-2147>.
- [22] Wen J, Chang Y, Huo S, Li W, Huang H, Gao Y, Lin H, Zhang J, Zhang Y, Zuo Y, Cao X, Zhong F. Tanshinone IIA attenuates atherosclerosis via inhibiting NLRP3 inflammasome activation. *Aging*, **13**, 910–32 (2020) <https://doi.org/10.18632/aging.202202>.
- [23] Wang X, Wang W-M, Han H, Zhang Y, Liu J-L, Yu J-Y, Liu H-M, Liu X-T, Shan H, Wu S-C. Tanshinone IIA protected against lipopolysaccharide-induced brain injury through the protective effect of the blood-brain barrier and the suppression of oxidant stress and inflammatory response. *Food Funct.*, **13**, 8304–12 (2022) <https://doi.org/10.1039/d2fo00710j>.
- [24] Qin C, Liu S, Zhou S, Xia X, Hu J, Yu Y, Ma D. Tanshinone IIA promotes vascular normalization and boosts Sorafenib's anti-hepatoma activity via modulating the PI3K-AKT pathway. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1189532>.
- [25] Feng F, Cheng P, Xu S, Li N, Wang H, Zhang Y, Wang W. Tanshinone IIA attenuates silica-induced pulmonary fibrosis via Nrf2-mediated inhibition of EMT and TGF- β 1/Smad signaling. *Chemico-Biological Interactions*, **319**, 109024 (2020) <https://doi.org/10.1016/j.cbi.2020.109024>.

- [26] Chen H, Shu H, Su W, Li B, Zhang H, Li L, Lin C, Yi W, Zhan X-Y, Chen C, Li X, Yang Y, Zhou M, Yang M. Tanshinone IIA Has a Potential Therapeutic Effect on Kawasaki Disease and Suppresses Megakaryocytes in Rabbits With Immune Vasculitis. *Front. Cardiovasc. Med.*, **9**, (2022) <https://doi.org/10.3389/fcvm.2022.873851>.
- [27] Liu Q, Wang W, Li F, Yu D, Xu C, Hu H. Triptolide Inhibits Breast Cancer Cell Metastasis Through Inducing the Expression of miR-146a, a Negative Regulator of Rho GTPase. *oncol res*, **27**, 1043–50 (2019) <https://doi.org/10.3727/096504019x15560124931900>.
- [28] Xu C, Zhang H, Mu L, Yang X. Artemisinins as Anticancer Drugs: Novel Therapeutic Approaches, Molecular Mechanisms, and Clinical Trials. *Front. Pharmacol.*, **11**, (2020) <https://doi.org/10.3389/fphar.2020.529881>.
- [29] von Hagens C, Walter-Sack I, Goeckenjan M, Storch-Hagenlocher B, Sertel S, Elsässer M, Remppis BA, Munzinger J, Edler L, Efferth T, Schneeweiss A, Strowitzki T. Long-term add-on therapy (compassionate use) with oral artesunate in patients with metastatic breast cancer after participating in a phase I study (ARTIC M33/2). *Phytomedicine*, **54**, 140–8 (2019) <https://doi.org/10.1016/j.phymed.2018.09.178>.
- [30] Zhong X-D, Chen L-J, Xu X-Y, Liu Y-J, Tao F, Zhu M-H, Li C-Y, Zhao D, Yang G-J, Chen J. Berberine as a potential agent for breast cancer therapy. *Front. Oncol.*, **12**, (2022) <https://doi.org/10.3389/fonc.2022.993775>.
- [31] Jeong J, An JY, Kwon YT, Rhee JG, Lee YJ. Effects of low dose quercetin: Cancer cell-specific inhibition of cell cycle progression. *J. Cellular Biochemistry*, **106**, 73–82 (2008) <https://doi.org/10.1002/jcb.21977>.
- [32] Latif S, Choi S-H, Gyawali A, Hyeon SJ, Kang Y-S, Ryu H. Antioxidant and Neuroprotective Effects of Paeonol against Oxidative Stress and Altered Carrier-Mediated Transport System on NSC-34 Cell Lines. *Antioxidants*, **11**, 1392 (2022) <https://doi.org/10.3390/antiox11071392>.
- [33] Cai M, Shao W, Yu H, Hong Y, Shi L. &p>Paeonol Inhibits Cell Proliferation, Migration and Invasion and Induces Apoptosis in Hepatocellular Carcinoma by Regulating miR-21-5p/KLF6 Axis<p><p>CMAR, Volume **12**, 5931–43 (2020) <https://doi.org/10.2147/cmar.s254485>.
- [34] Marín V, Burgos V, Pérez R, Maria DA, Pardi P, Paz C. The Potential Role of Epigallocatechin-3-Gallate (EGCG) in Breast Cancer Treatment. *IJMS*, **24**, 10737 (2023) <https://doi.org/10.3390/ijms241310737>.
- [35] Sun A-Q, Ju X-L. Inhibitory effects of salidroside on MCF-7 breast cancer cells in vivo. *J Int Med Res*, **48**, (2020) <https://doi.org/10.1177/0300060520968353>.
- [36] Xia D, Li W, Tang C, Jiang J. Astragaloside IV, as a potential anticancer agent. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1065505>.
- [37] Li L, Li G, Chen M, Cai R. Astragaloside IV enhances the sensibility of lung adenocarcinoma cells to bevacizumab by inhibiting autophagy. *Drug Development Research*, **83**, 461–9 (2021) <https://doi.org/10.1002/ddr.21878>.
- [38] Ye Q, Su L, Chen D, Zheng W, Liu Y. Astragaloside IV Induced miR-134 Expression Reduces EMT and Increases Chemotherapeutic Sensitivity by Suppressing CREB1 Signaling in Colorectal Cancer Cell Line SW-480. *Cell Physiol Biochem*, **43**, 1617–26 (2017) <https://doi.org/10.1159/000482025>.
- [39] Zheng Y, Dai Y, Liu W, Wang N, Cai Y, Wang S, Zhang F, Liu P, Chen Q, Wang Z. Astragaloside IV enhances taxol chemosensitivity of breast cancer via caveolin-1-targeting oxidant damage. *Journal Cellular Physiology*, **234**, 4277–90 (2018) <https://doi.org/10.1002/jcp.27196>.
- [40] Tomeh MA, Hadianamrei R, Zhao X. A Review of Curcumin and Its Derivatives as Anticancer Agents. *IJMS*, **20**, 1033 (2019) <https://doi.org/10.3390/ijms20051033>.
- [41] Alibeiki F, Jafari N, Karimi M, Peeri Dogah H. Potent anti-cancer effects of less polar Curcumin analogues on gastric adenocarcinoma and esophageal squamous cell carcinoma cells. *Sci Rep*, **7**, (2017) <https://doi.org/10.1038/s41598-017-02666-4>.
- [42] Wei G, Zhang G, Li M, Zheng Y, Zheng W, Wang B, et al.. *Panax notoginseng*: panoramagram of phytochemical and pharmacological properties, biosynthesis, and regulation and production of ginsenosides. *Horticulture Research*, **11**, (2024) <https://doi.org/10.1093/hr/uhae170>.
- [43] Ratan ZA, Haidere MF, Hong YH, Park SH, Lee J-O, Lee J, Cho JY. Pharmacological potential of ginseng and its major component ginsenosides. *Journal of Ginseng Research*, **45**, 199–210 (2021) <https://doi.org/10.1016/j.jgr.2020.02.004>.
- [44] Zhang P, Liu W, Wang Y. The mechanisms of tanshinone in the treatment of tumors. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1282203>.
- [45] Liu Q, Wang W, Li F, Yu D, Xu C, Hu H. Triptolide Inhibits Breast Cancer Cell Metastasis Through Inducing the Expression of miR-146a, a Negative Regulator of Rho GTPase. *oncol res*, **27**, 1043–50 (2019) <https://doi.org/10.3727/096504019x15560124931900>.
- [46] Xu C, Zhang H, Mu L, Yang X. Artemisinins as Anticancer Drugs: Novel Therapeutic Approaches, Molecular Mechanisms, and Clinical Trials. *Front. Pharmacol.*, **11**, (2020) <https://doi.org/10.3389/fphar.2020.529881>.
- [47] Zhong X-D, Chen L-J, Xu X-Y, Liu Y-J, Tao F, Zhu M-H, Li C-Y, Zhao D, Yang G-J, Chen J. Berberine as a potential agent for breast cancer therapy. *Front. Oncol.*, **12**, (2022) <https://doi.org/10.3389/fonc.2022.993775>.
- [48] Ezzati M, Yousefi B, Velaei K, Safa A. A review on anti-cancer properties of Quercetin in breast cancer. *Life Sciences*, **248**, 117463 (2020) <https://doi.org/10.1016/j.lfs.2020.117463>.

- [49] Chang X, Feng X, Du M, Li S, Wang J, Wang Y, Liu P. Pharmacological effects and mechanisms of paeonol on antitumor and prevention of side effects of cancer therapy. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1194861>.
- [50] Marín V, Burgos V, Pérez R, Maria DA, Pardi P, Paz C. The Potential Role of Epigallocatechin-3-Gallate (EGCG) in Breast Cancer Treatment. *IJMS*, **24**, 10737 (2023) <https://doi.org/10.3390/ijms241310737>.
- [51] Sun A-Q, Ju X-L. Inhibitory effects of salidroside on MCF-7 breast cancer cells in vivo. *J Int Med Res*, **48**, (2020) <https://doi.org/10.1177/0300060520968353>.
- [52] Ye Q, Su L, Chen D, Zheng W, Liu Y. Astragaloside IV Induced miR-134 Expression Reduces EMT and Increases Chemotherapeutic Sensitivity by Suppressing CREB1 Signaling in Colorectal Cancer Cell Line SW-480. *Cell Physiol Biochem*, **43**, 1617–26 (2017) <https://doi.org/10.1159/000482025>.
- [53] Song X, Zhang M, Dai E, Luo Y. Molecular targets of curcumin in breast cancer (Review). *Mol Med Report*, (2018) <https://doi.org/10.3892/mmr.2018.9665>.
- [54] Deng X, Wang J, Lu C, Zhou Y, Shen L, Ge A, Fan H, Liu L. Updating the therapeutic role of ginsenosides in breast cancer: a bibliometrics study to an in-depth review. *Front. Pharmacol.*, **14**, (2023) <https://doi.org/10.3389/fphar.2023.1226629>.
- [55] Expansion of the Gene Ontology knowledgebase and resources. *Nucleic Acids Res*, **45**, D331–8 (2016) <https://doi.org/10.1093/nar/gkw1108>.
- [56] Li Y, Wang J, Lin F, Yang Y, Chen S-S. A Methodology for Cancer Therapeutics by Systems Pharmacology-Based Analysis: A Case Study on Breast Cancer-Related Traditional Chinese Medicines. *PLoS ONE*, **12**, e0169363 (2017) <https://doi.org/10.1371/journal.pone.0169363>.
- [57] Wang Y, Liu M, Jafari M, Tang J. A critical assessment of Traditional Chinese Medicine databases as a source for drug discovery. *Front. Pharmacol.*, **15**, (2024) <https://doi.org/10.3389/fphar.2024.1303693>.
- [58] Song Z, Chen G, Chen CY-C. AI empowering traditional Chinese medicine? *Chem. Sci.*, **15**, 16844–86 (2024) <https://doi.org/10.1039/d4sc04107k>.
- [59] Fang Y-C, Huang H-C, Chen H-H, Juan H-F. TCMGeneDIT: a database for associated traditional Chinese medicine, gene and disease information using text mining. *BMC Complement Altern Med*, **8**, (2008) <https://doi.org/10.1186/1472-6882-8-58>.
- [60] Liu Z, Guo F, Wang Y, Li C, Zhang X, Li H, Diao L, Gu J, Wang W, Li D, He F. BATMAN-TCM: a Bioinformatics Analysis Tool for Molecular mechANism of Traditional Chinese Medicine. *Sci Rep*, **6**, (2016) <https://doi.org/10.1038/srep21146>.
- [61] Zhai Y, Liu L, Zhang F, Chen X, Wang H, Zhou J, Chai K, Liu J, Lei H, Lu P, Guo M, Guo J, Wu J. Network pharmacology: a crucial approach in traditional Chinese medicine research. *Chin Med*, **20**, (2025) <https://doi.org/10.1186/s13020-024-01056-z>.
- [62] Miao R, Meng Q, Wang C, Yuan W. Bibliometric Analysis of Network Pharmacology in Traditional Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine*, 2022, 1–11 (2022) <https://doi.org/10.1155/2022/1583773>.
- [63] Xu T, Chen W, Zhou J, Dai J, Li Y, Zhao Y. NPBS database: a chemical data resource with relational data between natural products and biological sources. *Database*, 2020, (2020) <https://doi.org/10.1093/database/baaa102>.
- [64] Wang X, Wang Z-Y, Zheng J-H, Li S. TCM network pharmacology: A new trend towards combining computational, experimental and clinical approaches. *Chinese Journal of Natural Medicines*, **19**, 1–11 (2021) [https://doi.org/10.1016/s1875-5364\(21\)60001-8](https://doi.org/10.1016/s1875-5364(21)60001-8).
- [65] Li S, Wan F, Shu H, Jiang T, Zhao D, Zeng J. MONN: A Multi-objective Neural Network for Predicting Compound-Protein Interactions and Affinities. *Cell Systems*, **10**, 308-322.e11 (2020) <https://doi.org/10.1016/j.cels.2020.03.002>.
- [66] Zhang L, Chen W-X, Li L-L, Cao Y-Z, Geng Y-D, Feng X-J, Wang A-Y, Chen Z-L, Lu Y, Shen A-Z. Paeonol Suppresses Proliferation and Motility of Non-Small-Cell Lung Cancer Cells by Disrupting STAT3/NF- κ B Signaling. *Front. Pharmacol.*, **11**, (2020) <https://doi.org/10.3389/fphar.2020.572616>.
- [67] Ding Q, Hou S, Zu S, Zhang Y, Li S. VISAR: an interactive tool for dissecting chemical features learned by deep neural network QSAR models. *Bioinformatics*, **36**, 3610–2 (2020) <https://doi.org/10.1093/bioinformatics/btaa187>.
- [68] Öztürk H, Özgür A, Ozkirimli E. DeepDTA: deep drug–target binding affinity prediction. *Bioinformatics*, **34**, i821–9 (2018) <https://doi.org/10.1093/bioinformatics/bty593>.
- [69] Karimi M, Wu D, Wang Z, Shen Y. DeepAffinity: interpretable deep learning of compound–protein affinity through unified recurrent and convolutional neural networks. *Bioinformatics*, **35**, 3329–38 (2019) <https://doi.org/10.1093/bioinformatics/btz111>.
- [70] Cheng F, Desai RJ, Handy DE, Wang R, Schneeweiss S, Barabási A-L, Loscalzo J. Network-based approach to prediction and population-based validation of in silico drug repurposing. *Nat Commun*, **9**, (2018) <https://doi.org/10.1038/s41467-018-05116-5>.
- [71] Xu H-Y, Zhang Y-Q, Liu Z-M, Chen T, Lv C-Y, Tang S-H, Zhang X-B, Zhang W, Li Z-Y, Zhou R-R, Yang H-J, Wang X-J, Huang L-Q. ETCM: an encyclopaedia of traditional Chinese medicine. *Nucleic Acids Research*, **47**, D976–82 (2018) <https://doi.org/10.1093/nar/gky987>.
- [72] Wu Y, Zhang F, Yang K, Fang S, Bu D, Li H, Sun L, Hu H, Gao K, Wang W, Zhou X, Zhao Y, Chen J. SymMap: an integrative database of traditional Chinese medicine enhanced by symptom mapping. *Nucleic Acids Research*, **47**, D1110–7 (2018) <https://doi.org/10.1093/nar/gky1021>.

- [73] Guo J-C, Zhang P, Zhou L, You L, Liu Q-F, Zhang Z-G, Sun B, Liang Z-Y, Lu J, Yuan D, Tan A-D, Sun J, Liao Q, Dai M-H, Xiao GG, Li S, Zhang T-P. Prognostic and predictive value of a five-molecule panel in resected pancreatic ductal adenocarcinoma: A multicentre study. *eBioMedicine*, **55**, 102767 (2020) <https://doi.org/10.1016/j.ebiom.2020.102767>.
- [74] Kong X, Liu C, Zhang Z, Cheng M, Mei Z, Li X, Liu P, Diao L, Ma Y, Jiang P, Kong X, Nie S, Guo Y, Wang Z, Zhang X, Wang Y, Tang L, Guo S, Liu Z, Li D. BATMAN-TCM 2.0: an enhanced integrative database for known and predicted interactions between traditional Chinese medicine ingredients and target proteins. *Nucleic Acids Research*, **52**, D1110–20 (2023) <https://doi.org/10.1093/nar/gkad926>.
- [75] N B. Network pharmacology based investigation on the mechanism of tetrandrine against breast cancer. *Phytomedicine Plus*, **3**, 100381 (2023) <https://doi.org/10.1016/j.phyplu.2022.100381>.
- [76] Hua H, Tang J-Y, Zhao J-N, Wang T, Zhang J-H, Yu J-Y, Yang C-M, Ai Y-L, Luo Q-X. From traditional medicine to modern medicine: the importance of TCM regulatory science (TCMRS) as an emerging discipline. *Chin Med*, **20**, (2025) <https://doi.org/10.1186/s13020-025-01152-8>.
- [77] Huang N, Huang W, Wu J, Long S, Luo Y, Huang J. Possible opportunities and challenges for traditional Chinese medicine research in 2035. *Front. Pharmacol.*, **15**, (2024) <https://doi.org/10.3389/fphar.2024.1426300>.
- [78] Zhu L, Mou W, Lai Y, Lin J, Luo P. Language and cultural bias in AI: comparing the performance of large language models developed in different countries on Traditional Chinese Medicine highlights the need for localized models. *J Transl Med*, **22**, (2024) <https://doi.org/10.1186/s12967-024-05128-4>.
- [79] Liu W, Yang B, Yang L, Kaur J, Jessop C, Fadhil R, Good D, Ni G, Liu X, Mosaib T, Yi Z, Wei MQ. Therapeutic Effects of Ten Commonly Used Chinese Herbs and Their Bioactive Compounds on Cancers. *Evidence-Based Complementary and Alternative Medicine*, 2019, 1–10 (2019) <https://doi.org/10.1155/2019/6057837>.
- [80] Almatroodi SA, Alsahli MA, Rahmani AH. Berberine: An Important Emphasis on Its Anticancer Effects through Modulation of Various Cell Signaling Pathways. *Molecules*, **27**, 5889 (2022) <https://doi.org/10.3390/molecules27185889>.
- [81] Fu J, Yu L, Luo J, Huo R, Zhu B. Paeonol induces the apoptosis of the SGC-7901 gastric cancer cell line by downregulating ERBB2 and inhibiting the NF- κ B signaling pathway. *Int J Mol Med*, (2018) <https://doi.org/10.3892/ijmm.2018.3704>.
- [82] Deeken JF, Wang H, Hartley M, Cheema AK, Smaglo B, Hwang JJ, He AR, Weiner LM, Marshall JL, Giaccone G, Liu S, Luecht J, Spiegel JY, Pishvaian MJ. A phase I study of intravenous artesunate in patients with advanced solid tumor malignancies. *Cancer Chemother Pharmacol*, **81**, 587–96 (2018) <https://doi.org/10.1007/s00280-018-3533-8>.
- [83] Liu X, Cao J, Huang G, Zhao Q, Shen J. Biological Activities of Artemisinin Derivatives Beyond Malaria. *CTMC*, **19**, 205–22 (2019) <https://doi.org/10.2174/1568026619666190122144217>.
- [84] Varghese E, Samuel SM, Varghese S, Cheema S, Mamtani R, Büsselberg D. Triptolide Decreases Cell Proliferation and Induces Cell Death in Triple Negative MDA-MB-231 Breast Cancer Cells. *Biomolecules*, **8**, 163 (2018) <https://doi.org/10.3390/biom8040163>.
- [85] Sun Y, Zhou Q, Chen F, Gao X, Yang L, Jin X, Wink M, Sharopov FS, Sethi G. Berberine inhibits breast carcinoma proliferation and metastasis under hypoxic microenvironment involving gut microbiota and endogenous metabolites. *Pharmacological Research*, **193**, 106817 (2023) <https://doi.org/10.1016/j.phrs.2023.106817>.
- [86] Maugeri A, Calderaro A, Patanè GT, Navarra M, Barreca D, Cirimi S, Felice MR. Targets Involved in the Anti-Cancer Activity of Quercetin in Breast, Colorectal and Liver Neoplasms. *IJMS*, **24**, 2952 (2023) <https://doi.org/10.3390/ijms24032952>.
- [87] Wang Y, Li B-S, Zhang Z-H, Wang Z, Wan Y-T, Wu F-W, Liu J-C, Peng J-X, Wang H-Y, Hong L. Paeonol repurposing for cancer therapy: From mechanism to clinical translation. *Biomedicine & Pharmacotherapy*, **165**, 115277 (2023) <https://doi.org/10.1016/j.biopha.2023.115277>.
- [88] Banerjee S, Mandal AKA. Role of epigallocatechin-3- gallate in the regulation of known and novel microRNAs in breast carcinoma cells. *Front. Genet.*, **13**, (2022) <https://doi.org/10.3389/fgene.2022.995046>.
- [89] Ren M, Xu W, Xu T. Salidroside represses proliferation, migration and invasion of human lung cancer cells through AKT and MEK/ERK signal pathway. *Artificial Cells, Nanomedicine, and Biotechnology*, **47**, 1014–21 (2019) <https://doi.org/10.1080/21691401.2019.1584566>.
- [90] Chen L, Zhuo D, Yuan H. Clinical effect of astragaloside IV on breast carcinoma cells based on MDR1: A randomised trial. *Trop. J. Pharm Res*, **20**, 2311–6 (2021) <https://doi.org/10.4314/tjpr.v20i11.12>.
- [91] Xue R, Fang Z, Zhang M, Yi Z, Wen C, Shi T. TCMID: traditional Chinese medicine integrative database for herb molecular mechanism analysis. *Nucleic Acids Research*, **41**, D1089–95 (2012) <https://doi.org/10.1093/nar/gks1100>.
- [92] Chen CY-C. TCM Database@Taiwan: The World's Largest Traditional Chinese Medicine Database for Drug Screening In Silico. *PLoS ONE*, **6**, e15939 (2011) <https://doi.org/10.1371/journal.pone.0015939>.