Texila International Journal of Public Health
Special Issue-2025
DOI: 10.21522/TIJPH.2013.SE.25.01.Art006

Therapeutic Implications of Medicinal Plants in Combatting Gastric Cancer

Heera Maheswari Jayaveeran[1], Savitha Niren[2], Shiny Paul[3], Manju Parthiban[1], Krithika C[4], Sureka Varalakshmi V[5], Sridevi Gopathy[6], Arunima Padmakumar Reshma[7], Ponnulakshmi Rajagopal[1]*

[1]*Central Research Laboratory, Meenakshi Ammal Dental College and Hospital, Meenakshi Academy of Higher Education and Research (Deemed to be University), Chennai, 600095, India*

[2]*Department of Physiology, Chettinad Institute of Medical Sciences, Chettinad Academy of Research and Education, Manami- Nallur, India*

[3]*Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, India*

[4]*Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College and Hospital, (Deemed to be University), Chennai-600 095*

[5]*Meenakshi Academy of Higher Education and Research, West K.K. Nagar, Chennai, India*

[6]*Department of Physiology, SRM Dental College, Bharathi Salai, Ramapuram, Chennai, Tamil Nadu, India*

[7]*Department of Periodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai India*

Abstract

Cancer ranks as the second most prevalent cause of mortality globally. More specifically, gastric cancer holds the second position in terms of cancer-related fatalities and is the fourth most frequently diagnosed cancer worldwide. A malignant condition called gastric carcinoma begins in the stomach. Despite decreased incidence, all malignancies continue to be second leading cause mortality around the globe. The majority of the stomach cancer aren't discovered until they're become rather large or have migrated outside the stomach in nations where routine screening for the disease is not practised. Loss of appetite, weight loss, stomach pain, feeling of fullness after eating a small amount. The Epstein-barr virus, in addition to H.pylori infection, is the second component linked to the development of GC. The treatment of gastric cancer is a complex process that typically involves in surgery, chemotherapy, radiation therapy, and targeted therapies. While plants and natural compounds have been explored for their potential in cancer treatment, it's important to note that there is no single plant or herbal remedy that can serve as a standalone cure for gastric cancer. Instead, various plants and their derivatives may play supportive roles in managing symptoms, improving the overall well-being of patients, and potentially enhancing the effectiveness of conventional treatments. In this review mainly focus of the medicinal plant such as Curcuma Mangga Rhizomes, Curcuma Zedoaria Rhizomes, Zanthoxylum Nitidum, Perilla Frutescens, Bamboo Shavings, Hericium Erinaceus Mycelium, Liang Jing mushroom, Turmeric.

Keywords: *Cytotoxic Effect, Epstein - Barr Virus, Gastric Carcinoma, Health and Well-being, H.pylori Infection, Novel Methods.*

Introduction

A malignant condition called gastric carcinoma begins in the stomach. Despite

Received: 18.07.2024 ***Accepted: 13.10.2024*** ***Published on: 31.01.2025***

****Corresponding Author: drponnulakshmi.researchscientist@madch.edu.in***

decreased incidence, all malignancies proceed to be the leading cause of mortality around the globe. Stomach adenocarcinoma is still a serious health issue. The incidence of this malignancy has decrease globally. however, the extent of this decline differs greatly between different geographical area. GC ranks as the second leading cause of cancer-related mortality worldwide and stands as the 4th most prevalent cancer on a global scale. Over 50% of newly diagnosed cases occur in developing nations. The prognosis for gastric cancer diagnosed at >T1N0 is poor. Geographical differences in gastric prevalence exist. The prevalence of gastric cancer has steadily decreased during the past few decades. The mucosa, submucosa, muscularis propria and subserosa make up the stomach wall [1]. By inducing apoptosis and targeting apoptotic pathways, β-sitosterol has substantial therapeutic potential as an anticancer drug against oral cancer KB cells [2].

Gastric cancer holds the fifth position among the most prevalent cancers globally, with it being the 4th most common cancer among males and the 7th most common among females. In 2020, over 1 million new cases of breast cancer were diagnosed. The 10-month mortality rates, with a 95% confidence interval between 19.20% and 21.03%, vary significantly based on the cancer stage. Stage III (42.6%) and Stage IV (36%) patients experience considerably higher mortality, exceeding that of Stage I (1.6%) and Stage II (19.7%) patients. Moreover, mortality is substantially elevated at 70.5% for patients who did not undergo surgery.

Helicobacter pylori, a bacterium known to be a significant factor in the development of gastric cancer, employs a complex molecular mechanism. This mechanism involves several virulence factors, such as the CagA (cytotoxin-related gene A), VacA (vacuolating cytotoxin A), and various oncogenic outer membrane proteins. These factors influence gastric carcinogenesis through multiple pathways. These virulence factors stimulate cell signalling pathways that regulate cell proliferation, including PI3-kinase/Akt, JAK/STAT, ERK, Ras and Raf signalling which leads to uncontrolled proliferation in the host organism [3]. Higher DMFT scores, more severe caries, and a plaque ecology that favors Streptococcus mutans are all associated with the presence of *H. pylori* in severe carious lesions [4].

To the prevention and treatment of GC diet plays a crucial role. Epidemiological research is increasingly pointing to the potential anti-cancer properties of foods such as fruits, grains, vegetables, soy, spices and edible macro fungi. Including, many previous researches has shown that there is a positive correlation between natural product consumption and cancer risk. Phytochemicals, as demonstrated by clinical studies, exhibit anti-cancer properties through various mechanisms, which encompass the suppression of cell proliferation, induction of apoptosis and autophagy, anti-angiogenesis, and inhibition of cell metastasis. Additionally, using phytochemicals as an adjuvant therapy for stomach cancer could be quite effective. With a thorough study of the mechanism of action, the sim of the study is to document the bioavailability and safety of phytochemicals [5]. By preventing the proliferation, migration, invasion, and aerobic glycolysis of HSC-3 oral squamous carcinoma cells, calotropin has anti-cancer effects [6]. Phytochemicals have the potential to boost the immune system's reactivity, thereby increasing the body's impervious against infections and diseases. and phytochemicals can be a valuable part of a balanced and healthy diet, contributing to overall well-being and potentially complementing medical treatments when appropriate.

Phytochemical Benefits

The term “phytochemical” is a general one that refers to a large number of substances that naturally occur in plants. In the next section,

many phytochemicals have antioxidant properties that protect the body's cell from oxidative damage, and the phytochemicals support the immune system, limit the number of tumor cancer cells that can proliferate and prevent DNA damge that can lead to cancer. They are considered as bioactive substances because they have the ability to regulate an array of physiological processes, including decreasing cholesterol synthesis, reducing inflammation, controlling cell differentiation, and preventing oxidative damage to organelles and cellular DNA. Extensive research, encompassing *In vitro*, *In vivo* and clinical studies, has been carried out to assess the influence of phytochemicals on various types of cancer. In order to summarise the numerous phytochemicals' methods of action, metabolism, doses examined, and sources for the treatment of cancer, this chapter has been created.

Medicinal Plants And Products

Medicinal plants are those plants which are used to treat various types of disease and have medicinal properties. Some medicinal plants are rich sources of ingredients which are used for synthesis of drug developments. Medicinal herbs can have three main benefits: health benefits for drug users; financial benefits for those who collect, process and sell them; and benefits to the wider community such as employment, tax revenue and employee productivity. But a lack of strong scientific backing, subpar drug development procedures, and inadequate funding stifle the development of plants or extracts with potential medical use. In modern times, the significance of medicinal plants plays a vital role in pharmaceutical research and development. Many commonly used drugs are derived from plant sources or have been synthesized based on plant compounds.

Curcuma Zedoaria Rhizomes

Curcuma zedoaria is a dried or fresh rhizomes belonging to the family *Zingiberaceae*. They generally known as white turmeric. It also contains components like starch, grains, volatile oil Curcuminoids and resins [7]. The biological profile of rhizome oil from *Curcuma zedoaria* (CZ) is characterized by its potent antioxidant properties. Additionally, the extract from the tuber of CZ demonstrates strong antimicrobial activity against pneumonia, Aspergillus niger, and Klebsiella. NGS analysis helps with minimal intervention techniques and individualized therapy planning by identifying a variety of genetic alterations in different stages of OSCC [8].

Curcuzedoalide, a compound derived from the turmeric plant, has gained attention in cancer treatment due to its potential therapeutic properties. Research indicates that curcuzedoalide exhibits anti-inflammatory, antioxidant, and anti-cancer activities. It may help inhibit the growth of cancer cells, induce apoptosis, and reduce angiogenesis, which is essential for tumor development. Moreover, curcuzedoalide has shown the ability to enhance the efficacy of certain chemotherapy drugs while mitigating their side effects. While these findings are promising, more extensive clinical trials are needed to fully understand its effectiveness, optimal dosage, and safety in cancer treatment, potentially offering a valuable addition to conventional therapies.

Phytochemical Composition of *C. Zedoaria*: *Curcuma zedoaria* is rich in phytochemicals, many of which have been studied for their potential health-promoting properties. Some of the key phytochemicals found in this plant include.

Sesquiterpenes: Zedoary oil extracted from *Curcuma zedoaria* rhizomes contains sesquiterpenes, such as zingiberene and curzerenone. These compounds contribute to the plant's aromatic properties and may have therapeutic effects.

Curzerenone: Curzerenone, a sesquiterpene found in *Curcuma zedoaria*, has anti-inflammatory attributes and potential for treating inflammatory disorders are evident.

Starch: The rhizomes of *Curcuma zedoaria* also contain a high amount of starch, which can serve as a source of dietary energy.

Proteins and Amino Acids: The plant contains various proteins and amino acids, which play essential roles in human nutrition and health.

Curcuminoids: Curcuminoids are a clump of polyphenolic compounds that include curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Curcumin, in particular, is known for its anti-inflammatory and antioxidant properties. It has been extensively studied for its potential health benefits, including its anti-oxidative effects, anti-inflammatory, and anti-cancer.

Curcuzedoalide: Curcuzedoalide is a relatively lesser-known compound derived from *Curcuma zedoaria*. The potential of curcuzedoalide in the treatment of various properties, which include: apoptosis induction, anti-inflammatory, Anti-Angiogenic Properties, Immune Modulation and anti-oxidative. Especially the compound has gained attention for its potential role in the treatment of gastric cancer.

"*Curcuma zedoaria*, also known as zedoary, is under investigation for its potential effects on the viability of human AGS cells and its role in modulating the molecular mechanisms involved in the apoptosis pathway. AGS cells serve as a valuable model for studying gastric cancer pathogenesis, drug testing, and the development of targeted therapies. AGS cells retain the characteristics of gastric cancer cells and are widely used to investigate molecular mechanisms involved in cancer progression, invasion, and metastasis.

Apoptosis, a critical process in the regulation of cellular death, is of significant interest in the context of cancer research. The aims to elucidate the impact of *C.zedoaria* on AGS cell viability and its potential influence on the apoptosis pathway, shedding light on its potential therapeutic relevance in gastric cancer treatment.

The anticancer activity and cytotoxic effect of a medicinal plant on AGS human colon cells were assessed through an *In vitro* cell viability test [9-11]. The cleavage of caspase-8 and initiating caspase in the extrinsic apoptosis pathway Death receptors bind to it, activating downstream effector caspases in the process shown in [Figure 1]. Apoptosis results from the proteolytic cascade that is started by caspase-8 cleavage, caspase-9. when mitochondrial damage occurs, the intrinsic apoptosis pathway's initiator caspase, caspase-9, is activated [12].

Its cleavage is necessary for the caspase cascade to be activated, which triggers apoptosis, caspase-3 Apoptosis is carried out by the effector caspase caspase-3, which cleaves different cellular substrates to cause cell death. The morphological and biochemical alterations observed in apoptotic cells are caused by the cleavage of caspase-3, which is a characteristic feature of apoptosis [13], and PARP Nuclear enzyme PARP is involved in genomic stability maintenance and DNA repair. Caspases, especially caspase-3, break PARP during apoptosis, which inactivates PARP and DNA repair pathways, promoting cell death [14]. In this molecular focal point for conducting cell viability experiments using human gastric cancer cell lines [Table 1].

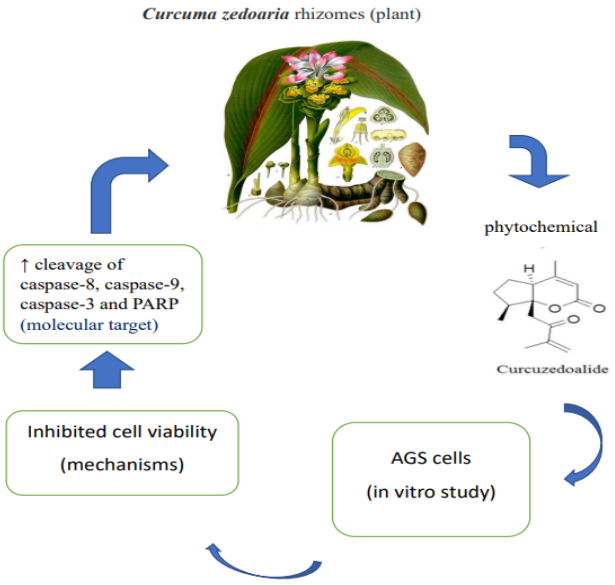


Figure 1. Curcuzedoalide Significantly Reduced Cell Viability in the AGS Cell Line. Anti-Cancer Agent, as Demonstrated by its Inhibition of Cell Viability in the AGS Cell Line.

Hericium erinaceus Mycelium

Hericium erinaceus mycelium is edible mushroom or medicinal mushroom sometimes known as lion's mane, and is quite popular in Asia [15,16]. *H.erinaceus* has been shown to enhance the effects of mycelium and biological chemicals such as erinacines and hericanones produced from liquids and substances in fermentation without any harm. Numerous bioactive extracts, known for their significant biological properties, are obtained from either the mycelium or the fruit bodies of *H. erinaceus*. This species exhibits a diverse range of medicinal attributes, such as antioxidant, hypolipidemic, hemagglutinating, antibacterial, anti-aging, and anticancer activities, as indicated in research. Erinacine A, a compound renowned for its anticancer effects, and anti-inflammatory has been extensively investigated and is suggested to contribute to reduced cell viability and cell death in various cancer cell types [17]. During orthodontic treatment stages, salivary levels of IL-17A and 1-25dihydroxycholecalciferol correlate, indicating that vitamin D administration may hasten tooth movement with little tissue injury [18].

Phytochemical Composition of *Hericium erinaceus* Mycelium:

Polysaccharides: Lion's Mane mushroom has a high content of bioactive polysaccharides, including β-glucans and heteropolysaccharides. These compounds have immunomodulatory properties and can enhance the body's immune response, making them potentially used in supporting the treatment of many diseases, including cancer.

Hericenones: Hericenones are another class of compounds found in Lion's Mane mushrooms. Anti-inflammatory and antioxidant properties, suggesting their potential role in treating conditions related to oxidative stress and inflammation.

Aromatic Compounds: *Hericium erinaceus mycelium* also contains various aromatic compounds, such as hericenone C and hericenol. These compounds may contribute to the mushroom's unique flavor and aroma, and they have potential therapeutic applications in the food and beverage industry.

Phytosterols: Lion's Mane mushroom contains phytosterols, including ergosterol. Phytosterols have cholesterol-lowering properties, which can be beneficial for

individuals with hypercholesterolemia or those at risk of cardiovascular diseases.

Erinacines A: Erinacines are unique bioactive compounds found in *Hericium erinaceus*, especially in the mycelium. These compounds have been studied for their neuroregenerative properties, making them potential candidates for the treatment of neurological disorders like Alzheimer's and Parkinson's disease. And also, Erinacines are bioactive compounds that have garnered attention for their potential role in the treatment of GC

In vitro study *H. erinaceus* with MKN-28 epidermal growth factor cell, The MKN-28 human GC cell line has played an important part in comprehending the function of epidermal growth factor (EGF) in the progression of cancer. Strongly acting on cell growth, proliferation, and differentiation, EGF is a mitogen. Research using MKN-28 cells has demonstrated that EGF activates multiple intracellular signalling pathways, most notably the Ras-Raf-MEK-ERK pathway that promotes the growth of cancer cells.

These studies, along with that conducted by Y. Park et al., have shed light on the molecular mechanisms underlying EGF signalling in gastric cancer, paving the way for possible targeted treatments [19] which are well-differentiated stomach adenocarcinoma cell suppressing the proliferation of TSGH-9201, a human gastric carcinoma cell line. A number of essential signalling proteins are involved in different cellular processes, including Focal Adhesion Kinase (FAK), Protein Kinase B (Akt), p70S6K (p70 S6 Kinase), and PAK1 (p21-Activated Kinase 1). FAK acts as a mediator between integrin signals to control cell adhesion and migration. The PI3K/Akt signalling pathway's essential component, Akt, is essential for cell survival, growth, and proliferation shown in [Figure 2]. p70S6K regulates protein synthesis and cell division and is located downstream of Akt. Cell motility and cytoskeletal dynamics are regulated by PAK1. Since these proteins' dysregulation is linked to cancer, cancer therapies are drawn to them as potential targets [20-23] [Table 1].

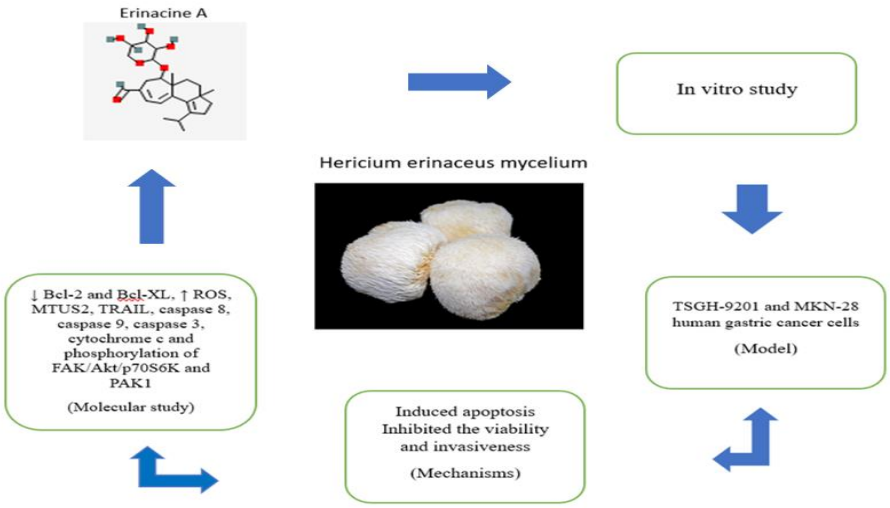


Figure 2. Erinacine A-Induced Apoptosis Suppressed Viability and Invasiveness in Human Gastric Cancer Cells TSGH-9201 and MKN-28

Curcuma Mangga Of Rhizomes

C. mangga belonged to the *Zingiberaceae* family. In Malaysia, mango ginger, or curcuma mangga, is reffered to as temu peuh, while in Thailand, it is called temu manga or kunir putih. Breast cancer, lung cancer and gastric cancer have all been shown to be resistant to the cytotoxic activity and anti-proliferative

(anticancer) effects of *C.mangga* rhizomes and leaves. [24,25].

Phytochemical Composition of *Curcuma mangga* of Rhizomes:

Curcuminoids: *Curcuma mangga* contains curcuminoids, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin. These compounds are well-known for their potential anti-cancer properties, antioxidant and anti-inflammatory. They have been extensively studied for their role in the prevention and treatment of various diseases, including cancer, neurodegenerative conditions and diabetes.

Curdione: Curdione is a sesquiterpene present in *Curcuma mangga*, and it has been investigated for its antioxidant properties and anti-inflammatory. It may have potential applications in managing inflammatory conditions and oxidative stress-related diseases.

Zerumbone: Zerumbone is a sesquiterpene present in *Curcuma mangga* with anti-inflammatory, anti-cancer, and anti-oxidative properties. Its potential role in cancer prevention and therapy has been the subject of study.

6-Gingerol: While more commonly associated with ginger (Zingiber officinale), 6-gingerol is also found in *Curcuma mangga*. It is known for its antioxidant properties and anti-inflammatory, which may have applications in mitigating inflammatory diseases.

Kaempferol: Kaempferol is a flavonoid found in *Curcuma mangga* with antioxidant and anti-inflammatory properties. It has been investigated for its potential role in preventing chronic diseases and its anti-cancer effects.

Labdane diterpenes: Labdane diterpenes are a class of natural compounds with a diverse range of biological activities, and they have gained attention in the context of gastric cancer treatment. including its ability to inhibit the growth and proliferation of gastric cancer cells by interfering with various signalling pathways and promoting apoptosis, the programmed cell death of cancer cells.

Labdane diterpenes, a phytochemical component is a class of natural compounds found in *Curcuma mangga*. Their pharmacological properties are diverse, encompassing anti-inflammatory, anticancer, and antimicrobial effects. And they employed in the study in-vitro in the model AGS cell line have been instrumental in drug screening and testing, aiding in the development of potential anti-cancer therapies [26] [Table 1]. Studies has shown that a range of substances and therapies can considerably reduce the viability of AGS cells, a cell line that represents stomach adenocarcinoma in humans. Despite its chemical and biological activity, limited research has explored the cytotoxic effects of *Curcuma mangga* on human cancer cells [Figure 3]. [27].

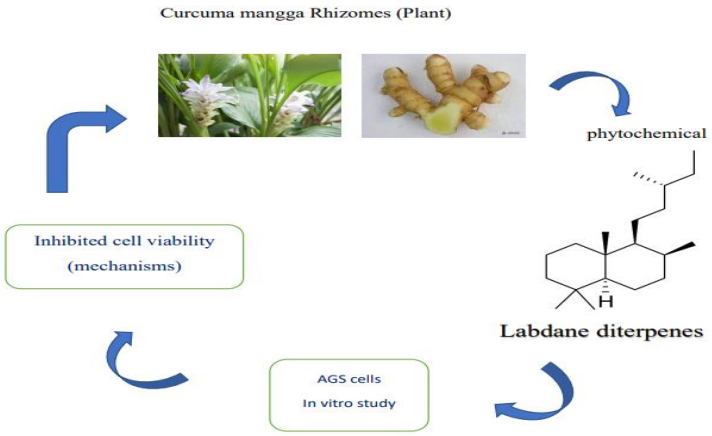


Figure 3. Labdane Diterpenes as Novel Agents for the Inhibition of Cell Viability in the AGS Cell Line

Zanthoxylum nitidum

Zanthoxylum nitidum, commonly known as shiny-leaf prickly ash, bears the botanical identity of belonging to the *Rutaceae* family, and it's a notable flowering plant. In China, it is referred to as "liang mian zhen," while in Assam, it goes by the name "tez-mui." This plant has garnered attention in the realm of natural medicine due to its remarkable properties.

One of the key discoveries associated with *Zanthoxylum nitidum* is the isolation of nitidine chloride, a naturally occurring bioactive phytochemical alkaloid. Nitidine chloride has garnered interest for its multifaceted potential in various medical domains. Its antioxidant properties make it valuable in combating oxidative stress, while it also demonstrates antifungal characteristics. Furthermore, its anti-inflammatory and analgesic attributes underline its therapeutic promise.

Zanthoxylum nitidum is just one among many Zanthoxylum species that have a long history of utilization in traditional medicine across the globe. The properties and compounds found in this plant family have piqued the interest of researchers and traditional healers alike [28, 29].

Phytochemical Composition of Zanthoxylum Nitidum:

Zanthoxylum nitidum contains a diverse array of phytochemicals, many of which contribute to its medicinal properties. Some of the prominent phytochemicals found in this plant include:

Alkaloids: *Zanthoxylum nitidum*, known for its alkaloid content such as berberine, has been the subject of research due to its antimicrobial, anti-inflammatory, and anticancer properties.

Flavonoids: Flavonoids such as quercetin and rutin are present in the plant and are known for their antioxidant and anti-inflammatory properties.

Lignans: Compounds like sesamin and asarinin are lignans found in the plant, and they have shown potential for various health benefits, including cardiovascular protection.

Terpenoids: Terpenoids like limonin and β-sitosterol contribute to the plant's medicinal properties. Limonin has been explored for its anticancer potential, while β-sitosterol has cholesterol-lowering and anti-inflammatory effects.

Essential Oils: *Zanthoxylum nitidum* also contains essential oils with various constituents, including alpha-pinene and beta-pinene, which have demonstrated antimicrobial properties.

Phenolic Compounds: Phenolic compounds, such as gallic acid, are found in the plant and are known for their antioxidant and anti-inflammatory effects.

Nitidine chloride: Nitidine chloride, a natural alkaloid compound extracted from the *Zanthoxylum nitidum* plant, has garnered significant interest in cancer research for its potential therapeutic properties. Studies have demonstrated that nitidine chloride displays considerable anti-cancer potential, as it can inhibit cell proliferation, induce apoptosis, and blocking the migration and invasion of gastric cancer cells.

Modelling SGC-7901 The well-known human gastric adenocarcinoma cell line SGC-7901 is important for both drug development and cancer research. SGC-7901 cells are derived from gastric tumour tissue and are useful models for researching drug response, disease progression, and the molecular mechanisms of gastric cancer. They are especially helpful in determining how different genes and signalling pathways contribute to the development of stomach cancer. Research utilising SGC-7901 cells has aided in the identification of possible anti-cancer drugs and therapeutic targets [30] and AGS cells using the STAT3, cyclin D1, Bcl-2, Bcl-xL, and VEGF are important players in gastric cancer, according to AGS cell line research. Cell survival and proliferation are enhanced by STAT3 activation. Cell cycle progression is

regulated by cyclin D1. Inhibiting apoptosis, Bcl-2 and Bcl-xL improve cell survival. VEGF promotes angiogenesis, which aids in the growth of tumours. Potential indicators for determining the risk of malignant transformation in individuals with leukoplakia, OSMF, and OSCC include circulating exosomal miRNAs miRNA 21, miRNA 184, and miRNA 145 [31].

Targeting these factors in AGS cells has been shown by researchers, as in the work by Y. Zhang et al., to inhibit the progression of gastric cancer and provide potential therapeutic strategies. Z. nitidum *In vitro* method and induced apoptosis P-STAT3, Bcl-xL, cyclin D1, VEGF's and Bcl-2 molecular targets were able to inhibit cell survival and angiogenesis, antitumor and immunomodulatory effects of Z. nitidum. However, specific molecular targets and stimulation of the immune system. In order to diminish the tumor's affinity for STAT-3 and VEGF, we extracted total RNA from SGC-7901 cancer cells subjected to varying durations of treatment with echinacea chloride (30 mol/L) shown in [Figure 4]. Thermo Fisher Scientific's TRIzol reagent played a pivotal role in our laboratory procedures, serving as the foundation for RNA extraction. To ensure precision and consistency, we meticulously followed the manufacturer's instructions throughout the extraction process. This step is of paramount importance, as it directly impacts the quality and integrity of the RNA samples obtained, a crucial factor in downstream molecular biology applications.

Following the successful RNA extraction, our next critical task was RNA purification. To accomplish this, we utilized a well-suited RNA purification kit. This kit's design and components were chosen to efficiently remove impurities and contaminants, resulting in highly purified RNA. High-quality RNA is essential for dependable and reproducible results in subsequent experiments, such as gene expression analysis. For the conversion of RNA into complementary DNA (cDNA), we adopted a reverse transcriptase PCR (RT-PCR) kit from Invitrogen, a subsidiary of Thermo Fisher Scientific. This kit, designed for accurate and efficient cDNA synthesis, was utilized in accordance with its instructions. The transformation of RNA into cDNA represents a pivotal step in molecular biology, as it allows for the further exploration of gene expression, gene function, and various other molecular processes [32] [Table 1].

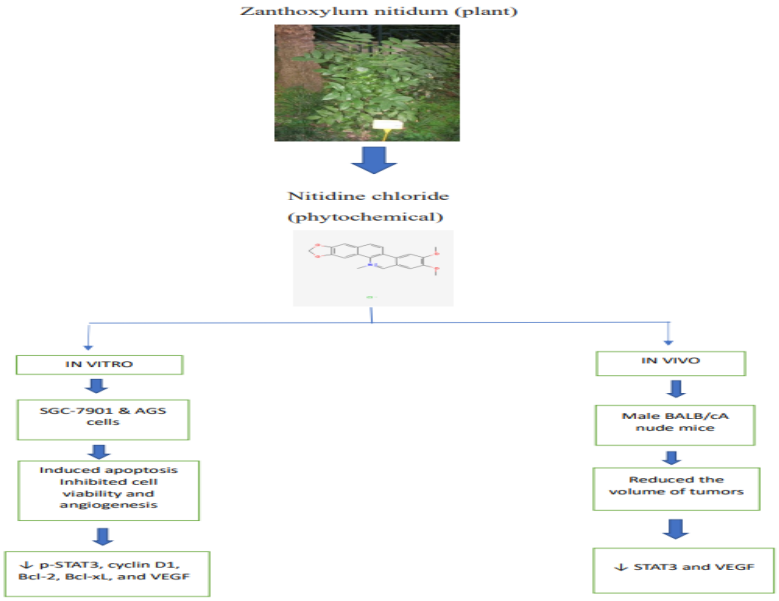


Figure 4. Nitidine Chloride Triggered Apoptosis and Suppressed Cell Viability, Angiogenesis, as Well as Tumor Volume in sgc-7901 and Ags Cell Lines

Perilla frutescens

Perilla frutescens also commonly known as deulkkae or Korean perilla. This is the species of *P.frutescens* order of lamiales and kingdom of plantae. Perilla is a weed that grows wild in the United States and is poisonous to cattle when consumed. In southeast Asia, perilla is used as a traditional medicine and food, for example: As a spice, in masala sauce, in rice, vegetables and soups. As well as add color and flavor to many dishes. Because of its recognized medicinal properties, *Perilla frutescens* is also used for skin cream, soaps and medicinal preparation. The plant is used to cure cancer, lung ailments, the common cold, stomach pain, and asthma.

Phytochemical Composition of *Perilla frutescens:*

Perilla frutescens is renowned for its rich content of bioactive phytochemicals, which contribute to its numerous health benefits. Some of the major phytochemicals found in perilla include:

Perillaketone: Perillaketone is another volatile compound found in perilla, which has demonstrated anti-inflammatory and antioxidant properties.

Flavonoids: Perilla contains abundant flavonoids like luteolin and apigenin, renowned for their ability to provide antioxidant and anti-inflammatory benefits. These compounds possess the capacity to alleviate oxidative stress and reduce inflammation within the body.

Phenolic Compounds: Perilla contains various phenolic compounds, including rosmarinic acid and caffeic acid, known for their antioxidant and anti-inflammatory properties. These compounds play a crucial role in reducing the risk of chronic diseases.

Omega-3 Fatty Acids: Perilla oil, rich in alpha-linolenic acid (ALA), which is an omega-3 fatty acid, is an excellent source. ALA is known for its cardiovascular benefits, including reducing the risk of heart disease.

Triterpenoids: Perilla contains triterpenoids, such as ursolic acid and oleanolic acid, which have shown potential in cancer prevention and anti-inflammatory activities.

Vitamins and Minerals: Perilla boasts a wealth of vital nutrients, including essential vitamins such as A, C, and K, as well as minerals like calcium and iron, which are vital for overall health.

Essential Oils: The essential oils in perilla are used in aromatherapy and traditional medicine for their soothing and stress-reducing effects.

Perillaldehyde: Perillaldehyde, a natural compound found in the *Perilla frutescens* plant, has gained attention in recent years for its potential role in the treatment of gastric cancer. Studies have suggested that perillaldehyde exhibits anti-cancer effects against gastric cancer cells through several mechanisms. It has been found to induce apoptosis, or programmed cell death, in cancer cells, thereby preventing their uncontrolled growth and spread. Moreover, perillaldehyde can inhibit the proliferation of cancer cells by interfering with their cell cycle progression. It also exerts its antioxidant properties and anti-inflammatory, which may help to reduce the risk of GC development and progression.

Perillaldehyde is a phytochemical substance that has been used in research on *P. frutescens* have been done both *In vitro and In vivo study*. *In vitro*, the induction of autophagy by Microbial fuel cells (MFCs) things on the molecular target are bio-electrochemical devices that use microbiological activity to transform organic matter into electricity. One cell line used to study stomach cancer is GC9811-P. The field of bio-electrochemical therapy for cancer has examined these two seemingly unrelated entities in tandem. MFCs were used in a study by Li et al. to administer chemotherapeutic medications to GC9811-P cells, exhibiting a novel method of treating cancer [33-34]. Salivary MMP-9 is a possible marker for early detection and prognosis since

it correlates with the severity of OSCC and malignant transformation [35].

P-AMPK. In an *In vivo* context, utilizing a female BALB/c nude mouse model, this experimental model in biomedical research. These mice are useful for research involving the transplantation and xenografting of human tissues, especially tumours, because they are immunodeficient due to the absence of a functioning thymus. Because of its weakened immune system, the BALB/c nude mouse is a valuable model for preclinical testing of anti-cancer treatments because it can engraft and support the growth of different cancer cell lines.

Researchers have used this model, as in the study by Yan Gao et al., to assess the effectiveness of cutting-edge therapeutic approaches for the treatment of cancer [36]. miRNAs exhibit potential as therapeutic targets and biomarkers for the early identification and management of OPMDs [37]

The inhibition of stomach tumor growth through the induction of autophagy is achieved by the presence and activity of various key proteins and molecules. Notably, beclin-1, LC3-II, cathepsin, caspase-3, p53, Bcl-2, Bcl-xL, Bid, Mn-superoxide dismutase, catalase, and GSH play pivotal roles in this process. Beclin-1 and LC3-II are essential components of the autophagic machinery, promoting the degradation of cellular components. Cathepsin and caspase-3 are involved in apoptosis, a mechanism that contributes to tumor cell death. p53 acts as a tumor suppressor by regulating cell cycle arrest and apoptosis. Bcl-2, Bcl-xL, and Bid influence apoptosis regulation. Mn-superoxide dismutase, catalase, and GSH help counteract oxidative stress, a factor in tumor development [Figure 5]. Together, these elements effectively hinder the progression of autophagy-induced stomach tumors, presenting promising prospects for therapeutic interventions [38] [Table 1].

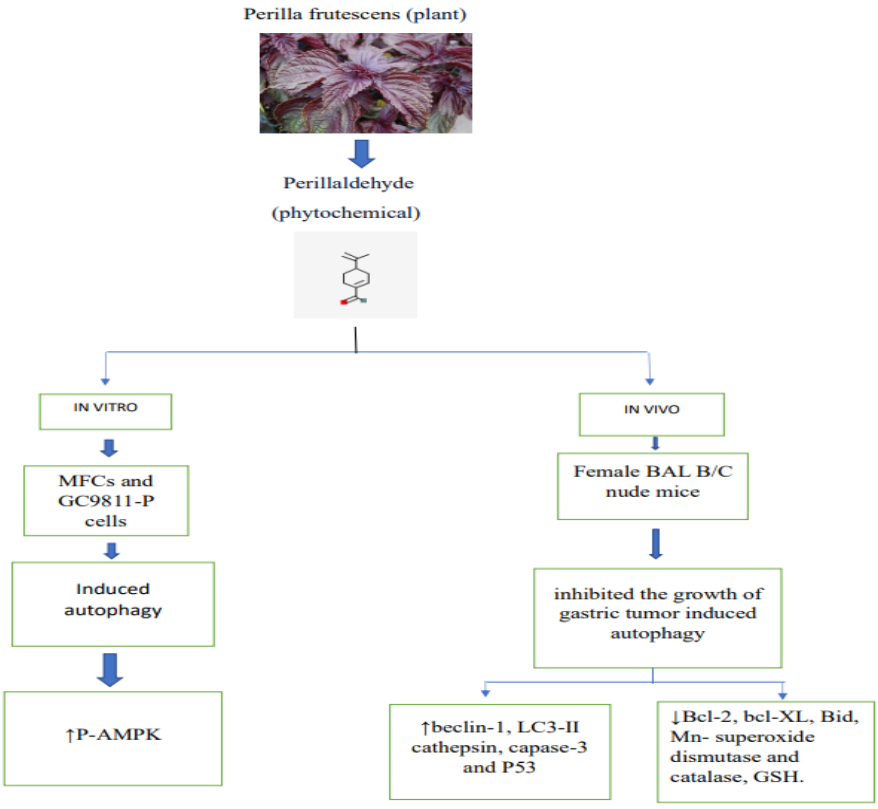


Figure 5. Perillaldehyde Induced Autophagy and Inhibited Gastric Tumor Growth In Female Bal B/C Nude Mice, Gc981-P Cells, and Mfcs

Bamboo Shaving

For more than a thousand years, Chinese medicine and food have both used bamboo leaves and shavings. Due to their potential health benefits, a increasing amounts of study on the biological properties of bamboo shavings and leaves. Several bioactive compounds, such as lignans, phenolic acids, saponins, sterols, and triterpenoids, are present in bamboo shaving extract (BSE). Previous research on the bamboo shaving extract's safety revealed that it had a low level of toxicity. The use of bamboo shavings as herbal supplement or food additive as well as a potential low-cost natural antioxidant source are also possibilities [39-41].

Phytochemicals in bamboo shavings:

Phytochemicals, which are naturally found bioactive compounds in plants, have been linked to numerous health benefits. Bamboo shavings contain several classes of phytochemicals, each with its own unique properties:

Phenolic Compounds: Bamboo shavings are rich in phenolic compounds such as flavonoids and phenolic acids, which are well-known for their antioxidant properties. These compounds protect cells from oxidative damage and reduce the risk of chronic diseases. (Zhang, X et al., 2013)

Silica: Bamboo shavings are a significant source of silica, a mineral essential for maintaining healthy skin, hair, and nails. Silica is also known to support bone health and may play a role in collagen formation. (Puri, A et al., 2012)

Lignans: Bamboo shavings contain lignans, which are known for their potential anti-cancer properties. Some lignans have been studied for their ability to inhibit the growth of cancer cells.(Yang, Z et al.,2012)

Alkaloids: Some bamboo species have alkaloids that may possess anti-inflammatory properties and analgesic. These compounds have been traditionally used in pain management. (Hua, J et al., 2008)

Sterols: Bamboo shavings also contain sterols, which have been associated with cholesterol-lowering effects. These compounds may help maintain heart health. (Khushboo, M et al.,2016)

Polysaccharides: Bamboo shavings contain polysaccharides, which have immune-modulating properties. They can help regulate the immune system and may have applications in the treatment of autoimmune diseases. polysaccharides show promise in the treatment of gastric cancer by harnessing their immunomodulatory, anti-inflammatory, and anti-tumor properties. While research in this field is ongoing, these natural compounds represent a potential adjunctive therapy that can complement conventional treatments and improve the overall outcomes for gastric cancer

In the syngeneic murine stomach cancer model, polysaccharides were employed as a phytochemical to suppress tumor growth and lengthen survival by targeting cascape 3, Bax and BIK in an *In vivo* model [42] [Table 1]. A major enzyme in the apoptotic process, caspase-3 cleaves a variety of cellular substrates to start the cell death cascade. Pro-apoptotic proteins called Bax and BIK are essential for controlling the intrinsic or mitochondrial apoptotic pathway. When BIK upsets the balance of mitochondria, it causes apoptosis, whereas Bax encourages the release of cytochrome c from mitochondria. "The prognosis of non-small cell lung cancer is significantly correlated with caspase-3, Bax, and BIK. These three proteins' expression profiles can be useful prognostic indicators for a number of diseases, including cancer [43] [Figure 6].

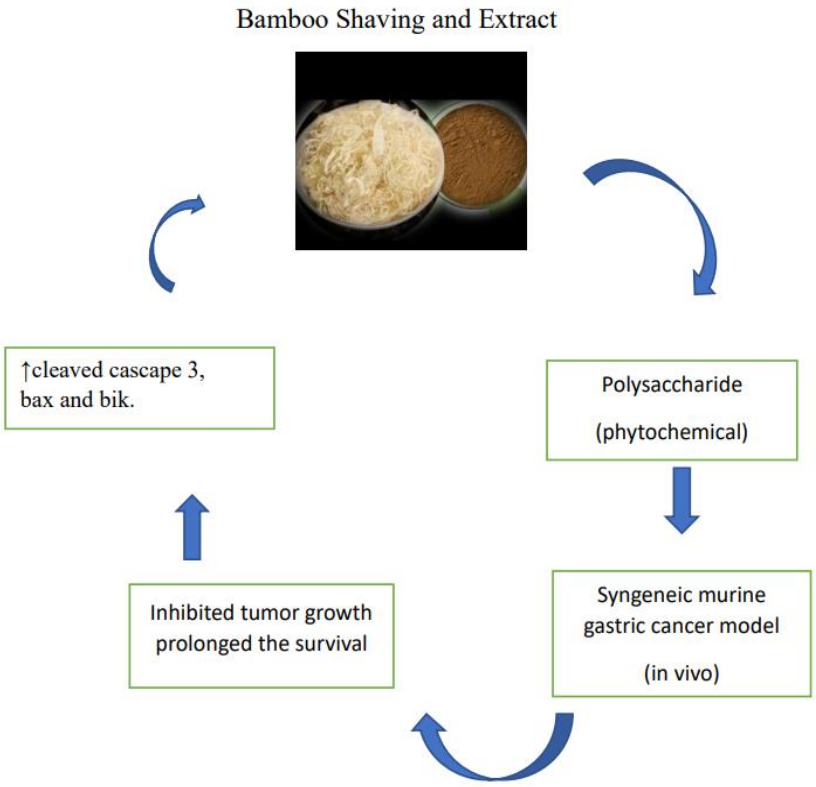


Figure 6. In A Syngeneic Murine Gastric Cancer Model, The Polysaccharide Inhibited Tumor Growth And Extended Survival

Liang Jing Mushroom

Crystal mushroom was supplied by Fuzhou Huasheng Food Co.,China. The active RNA-protein complex FA-2-b, obtained from the Liang Jing fungus, has been isolated and thoroughly examined. It exhibits dual properties: it not only demonstrates inhibitory effects on cancer cells but also shows promise in reducing the toxicity of chemotherapy drugs. When employed in tandem with chemotherapy drugs, it enables the use of lower doses and mitigates the adverse side effects, all without compromising their therapeutic efficacy. The experimental data from our study has been made available for additional studies. For all the above reasons, FA-2-b and AZT could functional simultaneously to create a synergistic effect [44].

Phytochemical Composition of Liangjing Mushroom:

Liang Jing Mushroom is a rich source of phytochemicals, many of which have been studied extensively for their health benefits. Some of the key phytochemicals found in Liang Jing Mushroom include:

Polysaccharides: *Liang Jing Mushroom* contains a high number of water-soluble polysaccharides, which have shown immunomodulatory and antioxidant properties. They can enhance the immune system's function and help combat oxidative stress.

Beta-glucans: These are a type of polysaccharide known for their immune-enhancing effects. They can activate immune cells and promote overall immune system health. (Wasser, 2017)

Tremellin: A specific protein found in Liang Jing Mushroom that exhibits antitumor properties and may help in cancer prevention.

Ergosterol: This compound can be converted into vitamin D2 when exposed to UV radiation, contributing to vitamin D intake.

Nucleosides: Liang Jing Mushroom contains adenosine and uridine, which have

demonstrated anti-inflammatory and neuroprotective effects.

Terpenoids: Some studies suggest that terpenoids found in Liang Jing Mushroom may have anti-inflammatory and antitumor activities.

Vitamins and Minerals: The mushroom is a source of various vitamins (B vitamins) and minerals (potassium, calcium, and iron), which are essential for overall health.

3'-azido-3'-deoxythymidine (AZT) is specifically used in the gastric cancer treatment. *In vitro* studies that combine phytochemicals isolated from the RNA-protein complex (FA-2-b) with 3'-azido-3'-deoxythymidine (AZT) have demonstrated encouraging outcomes in inducing apoptosis in the MKN-45 cell line. Antiretroviral medication AZT is well-known for its potential in cancer treatment. It has been discovered that the combination of AZT and FA-2-b compounds causes MKN-45 cells to enter an apoptotic state, which results in programmed cell death. This study emphasises how pharmacological agents and natural compounds can be combined to improve the effectiveness of anti-cancer therapies. Additionally, these compounds exhibit the inhibition of cell proliferation with the specific aim of targeting tumor-associated molecular pathways. They demonstrate that MKN-45 cells are subjected to a complex response to the combined treatment of 3'-azido-3'-deoxythymidine (AZT) and phytochemicals derived from the RNA-protein complex (FA-2-b) [Figure7]. This mixture seems to affect Bcl-2 expression and

cellular telomerase activity, both of which are frequently linked to improved cell survival in cancer. In addition, it encourages a rise in caspase-3 levels, which is a crucial apoptotic effector. These complementary effects point to a possible mechanism by which compounds AZT and FA-2-b cause programmed cell death while blocking mechanisms that support unchecked cell proliferation and survival [45] [Table 1].

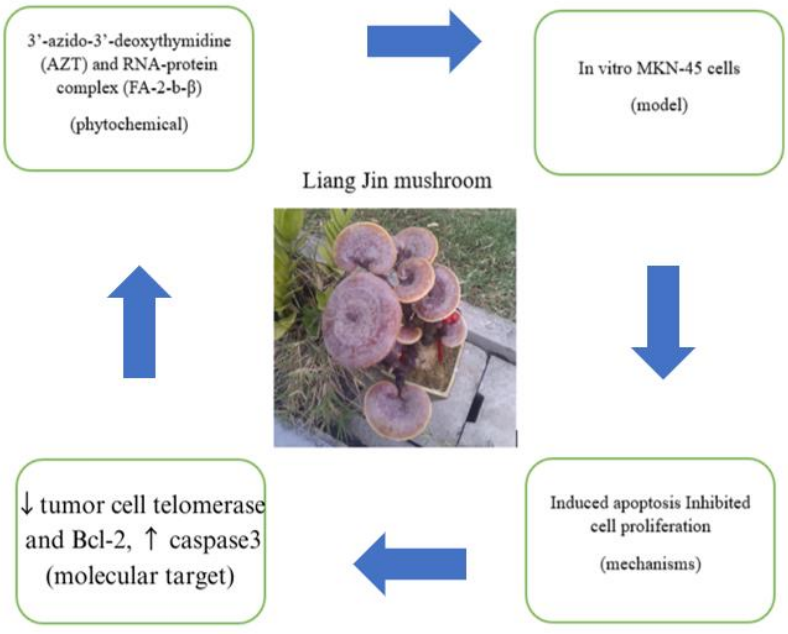


Figure 7. Cell Proliferation in the Mkn-45 Cell Line was inhibited by 3'-Azido-3'-Deoxythymidine (Azt) and the RNA Protein Complex-Induced Apoptosis

Turmeric

Turmeric is an herb from the ginger family native to southeast Asia, where it is grown commercially mainly in India, curcuminoids is the active ingredient in turmeric. According to the studies, curcumin has numerous health benefits, including the ability to fight cancer cells. It may be effective in treating lung, breast, prostate and gastric cancer in some experimental studies. Others suggest that curcumin might boost the effectiveness of chemotherapy. Curcuminoids are a phytochemical found in the *Curcuma longa* plant. It has the power to alter

specific biochemical pathways as well as stop the growth and spread of cancer cells. A popular chemotherapy medicine used regularly to treat cancer is called doxorubicin (DOX). Cancer cells, similar to those that can be targeted with various chemotherapeutic drugs like cisplatin, paclitaxel, docetaxel, etoposide, and oxaliplatin, can develop resistance to these treatments. which decreases the efficiency of DOX. Increasing the dosage for cancer treatment results. Etoposide is the only effective single agent in patients with untreated gastric cancer. Oncologists are becoming more and more interested in the use of etoposide in conjunction with drugs like doxorubicin, cisplatin and 5-flurouracil with or without leucovorin [46] [Table 1].

Phytochemical composition of turmeric:

Curcumin: Curcumin is the most well-known and extensively studied phytochemical in turmeric. It is a polyphenolic compound responsible for the spice's characteristic yellow colour. Curcumin is considered a promising agent in the management of various chronic diseases, including arthritis, cardiovascular diseases, and neurodegenerative disorders, due to its potent anti-inflammatory, antioxidant, and anti-cancer properties.

Turmerones: Turmerones are a group of sesquiterpenes found in turmeric, with aromatic turmerone and curcumin being the most prominent. They have demonstrated neuroprotective effects, showing promise in the treatment of neurodegenerative conditions such as Alzheimer's disease.

Curcuminoids: Aside from curcumin, turmeric contains other curcuminoids like demethoxycurcumin and bisdemethoxycurcumin, which contribute to its medicinal properties. These compounds possess anti-inflammatory, antioxidant, and anti-cancer activities, extending the therapeutic potential of turmeric.

Caffeic Acid: Caffeic acid, found in turmeric, is a hydroxycinnamic acid with antioxidant properties. It plays a role in reducing oxidative stress and preventing cellular damage.

Gingerols: While ginger and turmeric are distinct plants, they belong to the same botanical family and share similar bioactive compounds. Gingerols, found in both ginger and turmeric, exhibit anti-inflammatory and antioxidant effects, contributing to the overall health benefits of turmeric.

Zingiberene: Zingiberene is another sesquiterpene present in turmeric, contributing to its unique aroma. This compound has demonstrated anti-inflammatory and analgesic effects, showcasing its potential in pain management.

Beta-carotene: Turmeric, containing beta-carotene, a precursor to vitamin A, plays a crucial role in preserving healthy vision, supporting immune function, and promoting skin health. Additionally, it functions as an antioxidant, safeguarding cells against oxidative damage.

Niacin: Niacin, also known as vitamin B3, is found in turmeric and is essential for various metabolic processes in the body. It plays a critical role in maintaining cardiovascular health and supporting overall energy metabolism.

Iron: Turmeric contains trace amounts of iron, an essential mineral for the formation of red blood cells and oxygen transport in the

body. Adequate iron intake is crucial to prevent anemia and maintain overall health.

Curcuminoids: Curcuminoids the bioactive compounds found in turmeric, Anti-cancer properties of curcuminoids, particularly curcumin, in gastric cancer. These compounds have demonstrated several mechanisms that can inhibit the growth and progression of cancer cells. and also, have shown promising potential in the treatment of GC.

The SGC-7901 cell line was utilised in an *In vitro* investigation to augment the anti-tumor efficaciousness of doxorubicin and etoposides. The goal of this study was to identify important molecular variables linked to cancer cell resistance and survival. Along with decreased levels of the anti-apoptotic proteins Bcl-2 and Bcl-xL, the study showed a significant reduction in the activity of NF-κB, a transcription factor linked to cell survival and proliferation [Figure 8]. These results imply that etoposides and doxorubicin together may be able to block these pro-survival factors efficiently, which could lead to better therapeutic results when treating cancer [47].

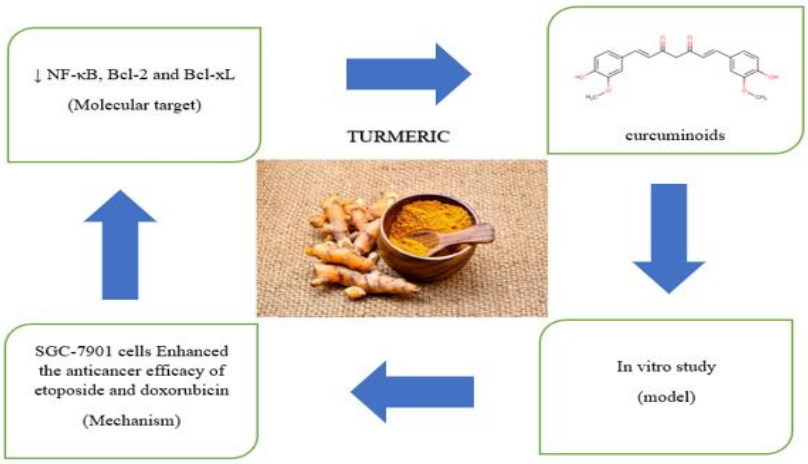


Figure 8. Curcuminoids Enhanced The Efficacy Of Etoposide And Doxorubicin In Inhibiting The Cells' Nf-Kb, Bcl-2, And Bcl-Xl

Table 1. Experimental Studies Have Explored The Impact Of Phytochemicals On Gastric Cancer

S.No	Medicinal Plant	Phytochemical	Study Method	Target Molecular	Activity	Reference
1.	*Curcuma zedoaria rhizomes*	Curcuzedoalide	*In vitro*	↑cleavage of caspase-3, caspase-8, caspase-9, and PARP	Inhibited cell viability	[14]

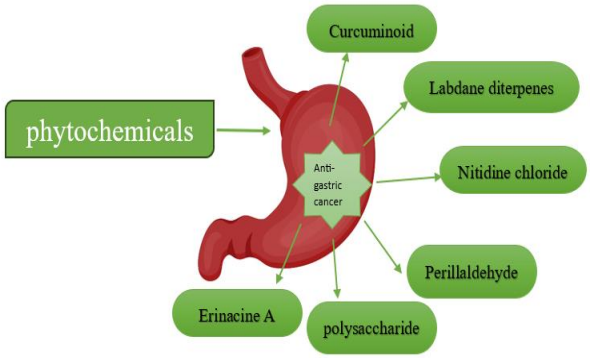
						
2.	*Hericium erinaceus mycelium* 	Erinacine A	*In vitro*	↓Bcl and Bcl-xL, ↑ROS, MTUS2, TRAIL, Caspase-8, Caspase-9, Caspase-3, Cycochrome c and phosphorylation of FAK/Akt/p70s6K and PAK1	Induced apoptosis inhibited the viability	[17]
3.	*Curcuma mangga of rhizomes*  	Labdane diterpenes	*In vitro*	Inhibited cell viability	Inhibited cell viability	[26]
4.	*Zanthoxylum nitidum* 	Nitidine chloride	*In vitro*	↓p-STAT3, cyclin D1, Bcl-2, Bcl-xL and VEGF	Induced apoptosis inhibited cell viability and angiogenesis.	[29]
	Zanthoxylum nitidum	Nitidine chloride	*In vivo*	↓STAT3 and VEGF	Reduced the volume of tumors	[29]

5.	*Perilla frutescens* 	Perillaldehyde	*In vitro*	↑P-AMPK	Induced autophagy	[38]
	Perilla frutescens	Perillaldehyde	*In vivo*	↑Beclin-1, LC3-II Cathepsin, capase-3 and P53 ↓Bcl-xL, Bid, Mn-superoxide dismutase and catalase, GSH	Inhibited the growth of tumor and induced autophagy	[38]
6.	Bomboo shaving 	Polysaccharide	*In vivo*	↑Cleaved Cascape 3, Bax and BIK	Inhibite growth of tumor prolonged the survival	[42]
7.	*Liang jing mushroom* 	3'-azido-3'-deoxythymidine (AZT)	*In vitro*	↓tumor cell telomerase and Bcl-2, ↑ caspase-3	Induced apoptosis inhibited cell proliferation	[45]
8.	Turmeric 	curcuminoids	*In vitro*	Bcl-2, ↓NF-kB and Bcl-xL	Inhibited cell survival and proliferation	[46]

Conclusion

Medicinal plants have shown promising potential in the treatment of gastric cancer. Research has revealed that various plant-derived compounds, such as curcumin from turmeric and resveratrol from grapes, possess anti-cancer properties, including inhibiting tumor growth and inducing apoptosis. These natural remedies often exhibit fewer side effects compared to conventional treatments, offering a more holistic approach. However, while preliminary findings are encouraging, more extensive clinical studies are required to establish their effectiveness, safety, and optimal dosages for gastric cancer therapy. In conclusion, medicinal plants hold great promise as complementary or alternative treatments, but further research is essential for their integration into mainstream medical care.

Graphical Abstract



Conflict of Interest

The authors hereby declare that there is no conflict of interest.

Acknowledgement

The author expresses their gratitude to Department of Science and Technology-Science and Engineering Research Board – DST-SERB under Engineering Research Council (ECR/2016/000415) is greatly acknowledged.

References

[1]. Sitarz, R., Skierucha, M., Mielko, J., Offerhaus, G. J. A., Maciejewski, R., Polkowski, W. P., 2023, Gastric cancer: epidemiology, prevention, classification, and treatment, 239-248 10.2147/CMAR.S149619.

[2]. Jayaraman, S., Natarajan, S. R., Ponnusamy, B., Veeraraghavan, V. P., & Jasmine, S. 2023, Unlocking the potential of beta-sitosterol: Augmenting the suppression of oral cancer cells through extrinsic and intrinsic signalling mechanisms. *The Saudi Dental Journal*, 35(8), 1007-1013.

[3]. Alipour, M., 2021, Molecular Mechanism of *Helicobacter pylori*-Induced Gastric Cancer. *J Gastrointest Cancer*, 23-30.10.1007/s12029-020-00518-5.

[4]. Sruthi, M. A., Mani, G., Ramakrishnan, M. and Selvaraj, J., 2023, Dental caries as a source of Helicobacter pylori infection in children: An RT-PCR study. *International Journal of Paediatric Dentistry*, 33(1), pp.82-88.

[5]. Mao, Q. Q., Xu, X. Y., Shang, A., Gan, R. Y., Wu, D. T., Atanasov, A. G., Li, H. B., 2020,

Phytochemicals for the Prevention and Treatment of Gastric Cancer: *Effects and Mechanisms*, 10.3390/ijms21020570.

[6]. Jayaraman, S., Natarajan, S. R., Veeraraghavan, V. P. and Jasmine, S., 2023, Unveiling the anti-cancer mechanisms of calotropin: Insights into cell growth inhibition, cell cycle arrest, and metabolic regulation in human oral squamous carcinoma cells (HSC-3). *Journal of Oral Biology and Craniofacial Research*, 13(6), pp.704-713.

[7]. Mustapha, N. M., 2010, ASEAN herbal and medicinal plants ASEAN Secretariat, Jakarta, Indonesia, 336(p).

[8]. Krishnan, R. P., Pandiar, D., Ramani, P. and Jayaraman, S., 2025, Molecular profiling of oral epithelial dysplasia and oral squamous cell carcinoma using next generation sequencing. *Journal of Stomatology, Oral and Maxillofacial Surgery*, 126(4), p.102120.

[9]. Jung, E. B., Trinh, T. A., Lee, T. K., Yamabe, N., Kang, K. S., Song, J. H., Choi, S., Lee, S., Jang, T. S., Kim, K. H., Hwang, G. S., 2018, Curcuma zedoalide contributes to the cytotoxicity of Curcuma zedoaria rhizomes against human gastric cancer AGS cells through induction of apoptosis, 213, 48–55. 10.1016/j.jep.2017.10.025.

[10]. Eun Bee Jung, Tuy An Trinh, Kyoung Lee, et al.: Curcuma zedoalide contributes to the cytotoxicity of Curcuma zedoaria rhizomes against human gastric cancer AGS cells through induction of apoptosis *Journal of Ethnopharmacology*. 2018, 48-55. 10.1016/j.jep.2017.10.025

[11]. Salvesen, G. S., Dixit, V. M., 1997, Caspases: intracellular signalling by proteolysis, 443-446. 10.1016/s0092-8674(00)80430-4.

[12]. Li, P., Nijhawan, D., Budihardjo, I., Srinivasula, S. M., Ahmad, M., Alnemri, E. S., Wang, X., 1997, Cytochrome c and dATP-dependent formation of Apaf-1/caspase-9 complex initiates an apoptotic protease cascade, 479-489. 10.1016/s0092-8674(00)80434-1.

[13]. Earnshaw, W. C., Martins, L. M., Kaufmann, S. H., 1999, Mammalian caspases: structure, activation, substrates, and functions during apoptosis. Annual Review of Biochemistry, 383-424. 10.1146/annurev.biochem.68.1.383.

[14]. Broker, L. E., Kruyt, F. A., Giaccone, G., 2005, Cell death independent of caspases: a review, 10.1158/1078-0432.ccr-04-2223.

[15]. Zhang, C. C., Cao, C. Y., Kubo, M., Harada, K., Yan, X. T., Fukuyama, Y., Gao, J. M., 2017, Chemical Constituents from Hericium erinaceus Promote Neuronal Survival and Potentiate Neurite Outgrowth via the TrkA/Erk1/2 Pathway, 10.3390/ijms18081659.

[16]. Kuo, H. C., Kuo, Y. R., Lee, K. F., Hsieh, M. C., Huang, C. Y., Hsieh, Y. Y., Lee, K. C., Kuo, H. L., Lee, L. Y., Chen, W. P., Chen, C. C., Tung, S. Y., 2017, A Comparative Proteomic Analysis of Erinacine a's Inhibition of Gastric Cancer Cell Viability and Invasiveness, 195-208, 10.1159/000480338

[17]. Cordeiro, Y., Machado, F., Juliano, L., Juliano, M. A., Brentani, R. R., Foguel, D., 2001, *Journal of Biological Chemistry*, 276(24), 21887–21893.

[18]. Sagar, S., Ramani, P., Moses, S., Gheena, S. and Selvaraj, J., 2024, Correlation of salivary cytokine IL-17A and 1, 25 dihydroxycholecalciferol in patients undergoing orthodontic treatment. *Odontology*, pp.1-10.

[19]. Schaller, M. D., 2004, FAK and paxillin regulators of N-cadherin adhesion and inhibitors of cell migration, 157-169. 10.1083/jcb.200406151.

[20]. Manning, B. D., Cantley, L. C., 2007, AKT/PKB signalling: navigating downstream, 1261-1274. 10.1016/j.cell.2007.06.009.

[21]. Weng, Q. P., Kozlowski, M., Belham, C., Zhang, A., Comb, M. J., Avruch, J., 1998, Regulation of the p70 S6 kinase by phosphorylation *In vivo*. Analysis using site-specific anti-phosphopeptide antibodies, 16621-16629. 10.1074/jbc.273.26.16621

[22]. Bokoch, G. M., 2003, Biology of the p21-activated kinases. Annu Rev Biochem, 743-781. 10.1146/annurev.biochem.72.121801.161742

[23]. Liu, Y. B., Nair, M. G., 2011, Labdane diterpenes in Curcuma mangga rhizomes inhibit lipid peroxidation, cyclooxygenase enzymes and human tumour cell proliferation. *Food Chem*, 124, 527–532. 10.1016/j.foodchem.2010.06.064

[24]. Malek, S. N., Lee, G. S., Hong, S. L., Yaacob, H., Wahab, N. A., Faizal Weber, J. F., Shah, S. A., 2011, Phytochemical and cytotoxic investigations of Curcuma mangga rhizomes *Molecules*, 4539-4548. 10.3390/molecules16064539

[25]. Liu, Y., Nair, M., 2012, Curcuma longa and Curcuma mangga leaves exhibit functional food property Food Chem, 135 (2), 634-640. 10.1016/j.foodchem.2012.04.129

[26]. Keum, Y. W., 2011, Differential Modulation of Helicobacter pylori Drug Susceptibility by Specific Fatty Acids," *Antimicrobial Agents and Chemotherapy*, 2867-2875. 10.1128/AAC.01432-10

[27]. Yunbao Liu, Muraleedharan G. Nair: Labdane diterpenes in *Curcuma mangga* rhizomes inhibit lipid peroxidation, cyclooxygenase enzymes and human tumour cell proliferation. 2011.10.1016/j.foodchem.2010.06.064

[28]. Xu, Q., Li, Z. X., Ye, Z. M., 2011, Nitidine chloride-induced apoptosis of human osteosarcoma cells and its mechanism]. Nan Fang Yi Ke Da Xue Xue Bao. PMID: 21354931

[29]. Hu, J., Zhang, W. D., Liu, R. H., Zhang, C., Shen, Y. H., Li, H. L., Liang, M. J., Xu, X. K., 2006, Benzophenanthridine alkaloids from Zanthoxylum nitidum (Roxb) DC, and their analgesic and anti-inflammatory activities, 10.1002/cbdv.200690108.

[30]. An, R., Hou, Z., Li, J. T., Yu, H. N., Mou, Y. H., Guo, C., 2018, Synthesis and Biological Evaluation of Novel 4-Substituted Coumarin Derivatives as Antitumor Agent,10.3390/molecules23092281.

[31]. Yasothkumar, D., Ramani, P., Jayaraman, S., Ramalingam, K. and Tilakaratne, W.M., 2024, Expression Profile of Circulating Exosomal microRNAs in Leukoplakia, Oral Submucous Fibrosis, and Combined Lesions of Leukoplakia and Oral Submucous Fibrosis. *Head and Neck Pathology*, 18(1), p.28.

[32]. Yang, Y., Cao, Y., Chen, L., Liu, F., Qi, Z., Cheng, X., Wang, Z., 2018, Cryptotanshinone suppresses cell proliferation and glucose metabolism via STAT3/SIRT3 signaling pathway in ovarian cancer," *Journal of Cellular Physiology*, 10.1002/cam4.1691.

[33]. Chen, J., Wang, J., Lin, L., He, L., 2011, Inhibition of STAT3 Signaling Pathway by Nitidine Chloride Suppressed the Angiogenesis and Growth of Human Gastric Cancer, 10.1158/1535-7163.MCT-11-0648

[34]. Cui, Y., Lai, B., Tang, X., 2019, Microbial Fuel Cell-Based Biosensors, 10.3390%2Fbios9030092

[35]. Gao, Y., Lyu, L., Feng, Y., Li, F., Hu, Y., 2021, A review of cutting-edge therapies for hepatocellular carcinoma (HCC): Perspectives from patents, 3066-3081. 10.7150/ijms.59930.

[36]. Zhang, Y., Liu, S. S., Feng, Q., Huang, X., Wang, X., Peng, Y., Zhao, Z., Liu, Z., 2019, Perillaldehyde activates AMP-activated protein kinase to suppress the growth of gastric cancer via induction of autophagy, 1716–1725. 10.1002/jcb.27491

[37]. Pazhani, J., Chanthu, K., Jayaraman, S. and Varun, B. R., 2023, Evaluation of salivary MMP-9 in oral squamous cell carcinoma and oral leukoplakia using ELISA. *Journal of Oral and Maxillofacial Pathology*, 27(4), pp.649-654.

[38]. Lu, B. Y., Wu, X. Q., Tie, X. W., Zhang, Y., Zhang, Y., 2005, Toxicology and safety of anti-oxidant of bamboo leaves. Part 1: Acute and subchronic toxicity studies on anti-oxidant of bamboo leaves. *Food Chem Toxicol*, 783–792. 10.1016/j.fct.2005.01.019.

[39]. Fathima, J. S., Jayaraman, S., Sekar, R. and Syed, N. H., 2024, The role of MicroRNAs

in the diagnosis and treatment of oral premalignant disorders. *Odontology*, pp.1-10.
[40]. Gong, J. Y., Wu, X. Q., Lu, B. Y., Zhang, Y., 2010, Safety evaluation of polyphenol-rich extract from bamboo shavings. *Afr J Biotechnol*, 77–86. http://www.academicjournals.org/AJB
[41]. Sreevarun, M., Ajay, R., Suganya, G., Rakshagan, V., Bhanuchander, V., & Suma, K., 2023, Formulation, Configuration, and Physical Properties of Dental Composite Resin Containing a Novel 2π + 2π Photodimerized Crosslinker - Cinnamyl Methacrylate: An In Vitro Research. *The Journal Of Contemporary Dental Practice*, 24(6), 364–371. https://doi.org/10.5005/jp-journals-10024-3480
[42]. Alam, M. K., Alqhtani, N. R., Alnufaiy, B., Alqahtani, A. S., Elsahn, N. A., Russo, D., Di Blasio, M., Cicciù, M., & Minervini, G., 2024, A systematic review and meta-analysis of the impact of resveratrol on oral cancer: potential therapeutic implications. *BMC Oral Health*, 24(1), 412. https://doi.org/10.1186/s12903-024-04045-8
[43]. Yadalam, P. K., Arumuganainar, D., Ronsivalle, V., Di Blasio, M., Badnjevic, A., Marrapodi, M. M., Cervino, G., & Minervini, G., 2024, Prediction of interactomic hub genes in PBMC cells in type 2 diabetes mellitus, dyslipidemia, and periodontitis. BMC Oral Health, 24(1), 385. https://doi.org/10.1186/s12903-024-04041-y
[44]. Sun, Y. Q., Guo, T. K., Xi, Y. M., Chen, C., Wang, J., Wang, Z. R., 2007, Effects of AZT and RNA-protein complex (FA-2-b-beta) extracted from Liang Jin mushroom on apoptosis of gastric cancer cells, 10.3748/wjg.v13.i31.4185
[45]. Olivas-Aguirre F. J, Rodrigo-Garcia J, Martinez-Ruiz N. D. R., Cardenas- Robles, A. I., Mendoza-Diaz, S. O., Alvarez-Parrilla, E., Gonzalez-Aguilar, G. A., De la rosa, L. A., Ramos- Jimenez, A., Wall-Medrano, A., 2016, Cyanidin-3-O-glucoside: Physical-chemistry, foodomics and health effects. *Molecules*, 10.3390/molecules21091264
[46]. Ashrafizadeh, M., Zarrabi, A., Hashemi, F., Zabolian, A., Saleki, H., Bagherian, M., Azami, N., Bejandi, K. A., Hushmandi, K., Ang, H. A., Makvandi, P., Khan, H., Kumar, A. P., 2020, Polychemotherapy with Curcumin and Doxorubicin via Biological Nanoplatforms Enhancing Antitumor Activity, 10.3390/pharmaceutics12111084
[47]. Yu, L. L., Wu, J. G., Dai, N., Yu, H. G., Si, J. M., 2011, Curcumin reverses chemoresistance of human gastric cancer cells by downregulating the NF-κB transcription factor. 26, 1197–1203. 10.3892/or.2011.1410