ROLE OF NATURAL PRODUCTS IN CANCER TREATMENT

Abstract

Cancer remains a substantial global health concern, and finding effective treatments stays a top priority in oncology research. In recent years, natural products have long been recognized as a valuable resource for discovering and developing cancer preventive and anticancer drugs. Natural products derived from plants, animals, and microorganisms exhibit an extensive array of bioactive compounds with diverse chemical structures. These compounds have demonstrated the ability to interfere with various molecular pathways in cancer initiation, progression, and metastasis. Furthermore, they often display selectivity for cancer cells, sparing normal cells from severe side effects commonly associated with conventional chemotherapeutic agents. Their diverse chemical structures and biological activities make them promising candidates for potential therapies in cancer treatment and prevention. In this chapter, we have examined the crucial role of organic substances in the realm of cancer therapy, drawing upon the insights presented in recent years' literature.

Keywords: Anticancer activity; Apoptosis; Bioactive compounds; Cancer treatment; Natural products.

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I. INTRODUCTION

Natural products are the compounds or substances that were produced naturallyby a living things and can be found in nature. These are broadly described as substances originating from living organisms.Additionally, natural compounds can be produced through chemical synthesisincluding semi-synthesis and total synthesis. Because of their intricate synthetic demands, they have played a crucial role in the advancement of the organic chemistry field.[1-3]. In the interest of commerce, the term "natural product" has been broadened to include goods such as natural-based foods, nutritional supplements, and cosmetics.

In the field of organic chemistry, the term" natural products" generally refers to organic compounds sourced from nature and produced through primary or secondary metabolic processes. The term is frequently further limited to secondary metabolites in the context of medicinal chemistry [4]. Secondary metabolites, also called specific biogenic compounds, provide an evolutionary advantage to the organisms creating them, even if they are not vital for existence.Many secondary biogenic compounds exhibit cytotoxic effects and have been selected and refined through evolution to serve as defensive "chemical warfare" mechanisms against prey, predators, and competing species.[5]. Due to their abundance of natural antioxidants like flavonoids, lignans, flavones, coumarins, isoflavones, anthocyanins, isocatechin and catechins, natural products demonstrate anti-cancer activity.

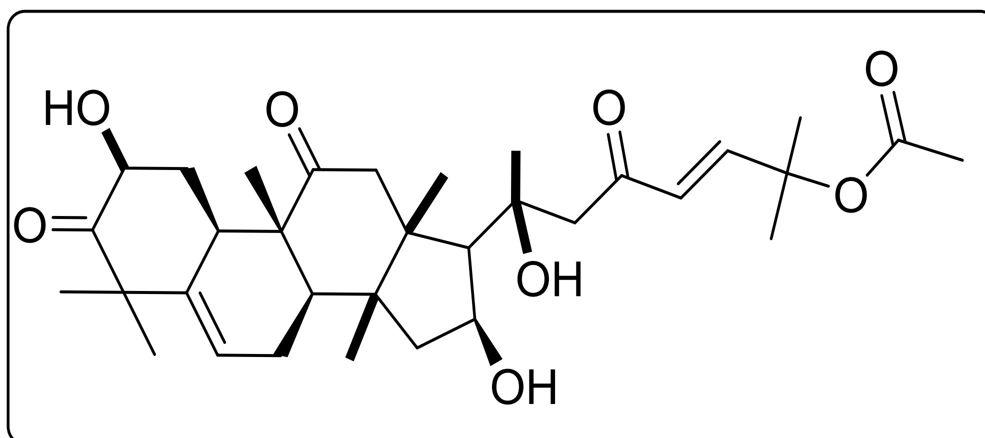
These elements serve as reducers, quenchers of singlet oxygen, and scavengers of free radicals, demonstrating their efficacy in the fight against cancer.[6,7]. Moreover, natural products can effectively mitigate and ease the toxic adverse effectslinked with radiation and chemotherapy treatments.Cancer encompasses a group of conditions distinguished by abnormal cell growth that has the potential to invade or spread to other areas of the body.Over the course of the last few decades,considerable efforts have been committed to isolating fresh natural products from a range of sources, including plants, microorganisms and other living organisms.

These efforts aimed to assess their anticancer properties and understand their mechanisms of action. As a result, a considerable number of anti-cancer drugs have been discovered. During the time span from 1981 to 2019, roughly a quarter of recently authorized anti-cancer drugs were sourced from natural products.Among all the anti-cancer agents, natural products play a crucial role as the most significant ones. In the field of medicine, approximately three-quarters of the anti-tumour compounds utilized are either natural products or derivatives closely associated with them [8,9].

II. CHEMISTRY OF NATURAL PRODUCTS AS ANTICANCER AGENTS

Jiaxin Xu et al. presented the role of Cucurbitacin B in gastric cancer treatment. Natural substance cucurbitacin B (CuB) has strong anti-cancer effects on solid tumors. Cucurbitacins, integral components of numerous traditional Chinese medicines (TCM), exhibit the characteristic bitterness associated with the Cucurbitaceae family.Extracted from the fruits of D.palmatus L., the substance is obtained. The fruit powder 1gram was continuously mixed with the suitable solvents to generate extracts, following a 72-hour over drying at 60^0C.after being filtered using Watsman No. 1 filter paper, the extracts underwent

concentration. They were then mixed with 1 mL of methanol and filtered through a 0.2-meter nylon filter (manufactured by HiMedia, India) before being used for HPLC analysis[10].



Structure of Cucurbitacin B

In this study, authors examined both in-vitro and in-vivo. theprimary molecular mechanisms through which CuB inhibits GC. At nanomolar levels, CuB hindered the expression of genes regulated by STAT3, like c-Myc and Bcl-xL and lowered the phosphorylation of STAT3 at TYR-705 in gastric cancer cell lines.CuB interacts with the DNA-binding domain of STAT3 at a number of hydrophobic sites, according to computational docking study. Additionally, pull-down tests demonstrated that CuB directly inhibits STAT3 through STAT3. CuB increased the cytotoxicity of the standard chemotherapy medication cisplatin in GC cells, probably as a result of potentiated suppression of STAT3 activity. Furthermore, a mouse model using xenografts verified the beneficial effects of CuB in vivo[11]

Wan-Ting Xu et al. discussed the finding focuses on the lung cancer cell-targeting effects of cytisine. Cytisine, a natural quinolizidine alkaloid found in substantial amounts within Cytisus laburnum seeds and the roots of Papilionaceae and Caesalpinioideae plants, has historical use in traditional Chinese medicine.During the process of extracting, one kilogram of seeds was thoroughly blended with 100grams of slaked lime and 500 cubic centimetres of water. The resulting mixture was kneaded into a rough powder and then subjected to a 20-hour extraction using chloroform.

The chloroform extract was eventually evaporated in a vacuum to remove the remaining traces of solvent, and the residue was mixed with 1 litre of light petroleum and left overnight. The mother-liquor was extracted with dilute acid after the majority of the alkaloid crystallized and was separated. The unrefined alkaloid underwent purification by boiling in a solution of diluted hydrochloric acid along with charcoal. Following filtration, the substance was then alkalized to a significant degree before undergoing extraction using chloroform. The chloroform solution was evaporated after being dried with sodium sulphate, to give the (yield 20 g.) [12]

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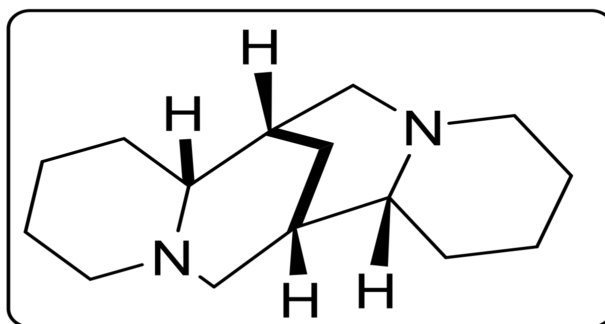
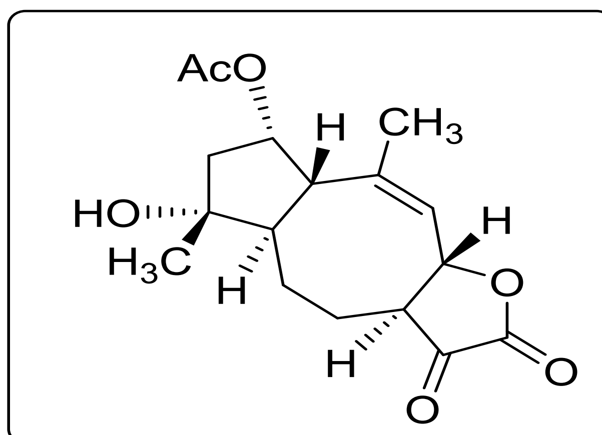


Structure of Cytisine

Through the initiation of apoptosis via elevated ROS levels and disruption of membrane potential, upregulating BAD, initiating PAR cleavage, and activating caspase-3, while concurrently downregulating Bcl-2, pro-PARP and pro-caspasse-2, cytisine induces notable cytotoxic impacts on lung cancer cells such as A549, NCl-h23 and NCl-H460 both in-vitro and in-vivo(rat model). Cytisine enhanced the levels of JNK, p38, and I-jB phosphorylation during apoptosis while decreasing the levels of ERK, STAT3, and NF-jB phosphorylation. Additionally, the inhibition of the Akt signaling pathway by cytisine resulted in the cell cycle being halted at the G2/M phase[13].

Afshin Karami et al. discussed the findings on antiproliferative effect of Gaillardin in human leukemic cells. Gaillardin (GLN) is a sesquiterpene lactone that was discovered in Inula oculus-christi's chloroform extract. 500 g of dried aerial portions of I. aucheriana were consecutively extracted with n-hexane and chloroform (each solvent for 3 days), with each extraction producing 9.4 g and 8.9 g of extract, respectively.The chloroform extract 5 grams underwent vacuum liquid chromatography(VLC) using silica gel(40-63Nm), employing a series of washes with ethyl acetate(EtOAc), ethyl acetate-methanol(EtOAc-MeOH) in ratios of 2:1 to 1:1 and pure methanol(MeOH) as the eluent. In this investigation, 5mg of GLN powder was dissolved in DMSO as stock solutions (16.3mM) and then diluted with new RPMI 1640 medium to attain the necessary concentration. Less than 0.1% of DMSO was ultimately present in the cells after treatment [14]



Structure of Gaillardin

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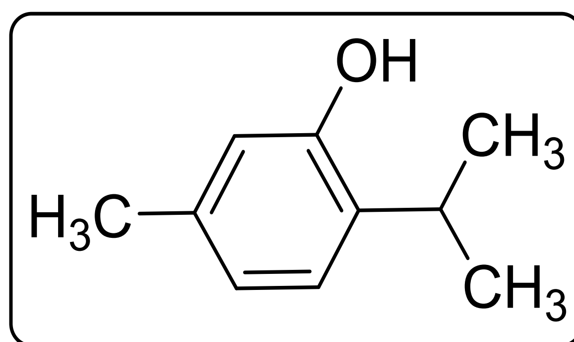
The impact of GLN in isolation and when combined with vincristine was assessed for cytotoxicity, apoptosis induction and modulation of cell cycle progression in cell lines representing acute lymphoblastic leukemia(ALL), namely NALM-6 and MOLT-4.This approach was adopted due to the neurotoxic nature of vincristine(VCR) in case of acute lymphoblastic leukemia(ALL). Demonstrating IC50 values of 7.3µM and 6.1µM correspondingly, GLN inducescytotoxic responses within MOLT-4 and NALM-6 cell lines. GLN prompts cell death by causing a halt in the G0/G1 phase, leading to apoptosis in a way that is influenced by the dosage[15].

Jorge J. De La Chapa et al. examined how thymol hinders the growth of oral Squamous cell carcinoma by utilizing mitochondria-mediated apoptosis. Thymol was extracted from Thymus vulgaris and it is a phenolic compound present in essential oils of various plants such as thyme, oregano, rosemary, bay laurel leaves, mandarin oranges, and cranberries .T. vulgaris leaves and air-dried aerial portions (stems and leaves) were hydrodistilated for 2.5 hours using a Clevenger-style device in accordance with the accepted practice. In the extraction burette, the volume of the essential oil was precisely quantified. The resulting essential oils were then dried with anhydrous sodium sulphate and kept at 4 °C in sealed, dark vials pending additional analysis. Volume (ml) of essential oil per 100 g of plant dry matter served as the unit of measurement for yield percentage [16]

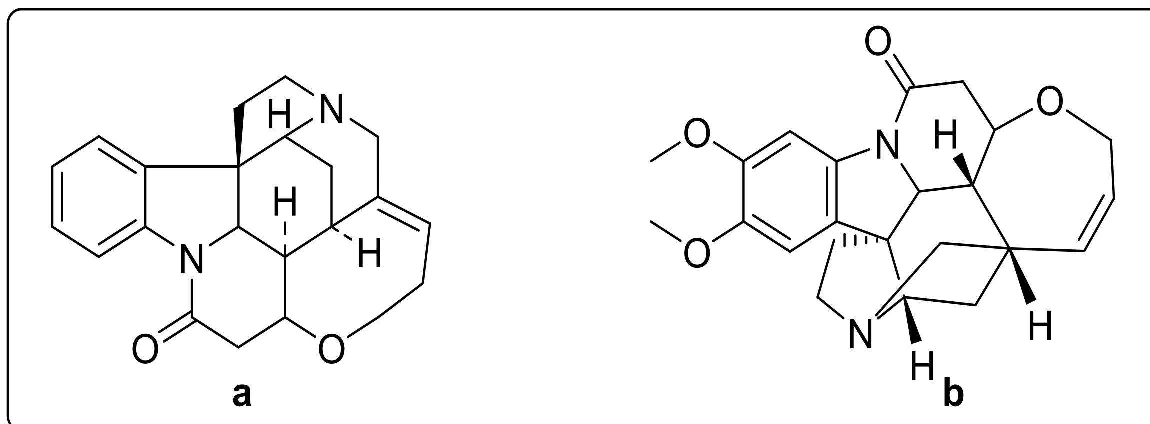


Structure of Thymol

MTS assays were used to identify thymol's antiproliferative effects in OSCC Cal27 cells. In vitro, thymol also exhibits cytotoxicity towards HL-60 cells, which are associated with acute promyelocytic leukemia. Thymol significantly inhibited the growth of Cal27-derived tumors in vivo. Thymol's anticancer properties were verified in xenografts made from HeLa cells, proving that its effects are not tumor-type-specific. Calcium imaging demonstrated calcium influx in Cal27 cells, which was inhibited by HC030031, a TRPA1 antagonist. However, HeLa cells did not exhibit calcium influx, demonstrating that TRP channels do not control the cytotoxicity of thymol. Using cell viability experiments, it was demonstrated that pre-treatment with HC030031 had no impact on the cytotoxicity of thymol[17].

Hua Ren et al. discussed the role of natural products brucine and Strychnine for the treatment of cancer. Strychnine and brucine are alkaloids extracted from the seeds of Strychnosnux vomica L. that have long been used in traditional medicine to cure tumors. Seeds from strychnosnux vomica weighing 500grams were subjected to air-drying and subsequentlyfinely ground into a powder with a particle size of 60 mesh. The resulting

powder underwent a triple extraction using 80% ethanol that had beenacidified to a pH range of 2.0-3.0. thecombinaed ethanol extracts were filtered and subjected to centrifugation. The resulting supernatant was thenraised to an alkaline state with a pH of 11.0-12.0 using a 10% NAOH solution, after which it was subjected to an extraction process using dichloromethane. To obtain crude total alkaloids, the dichloromethane fraction was evaporated. The crude alkaloids were then subjected to extensive chromatography on a silica gel column and eluted with a petroleum etherethyl acetate or ethyl acetatemethanol gradient solvent system to extract Brucine and Strychnine.



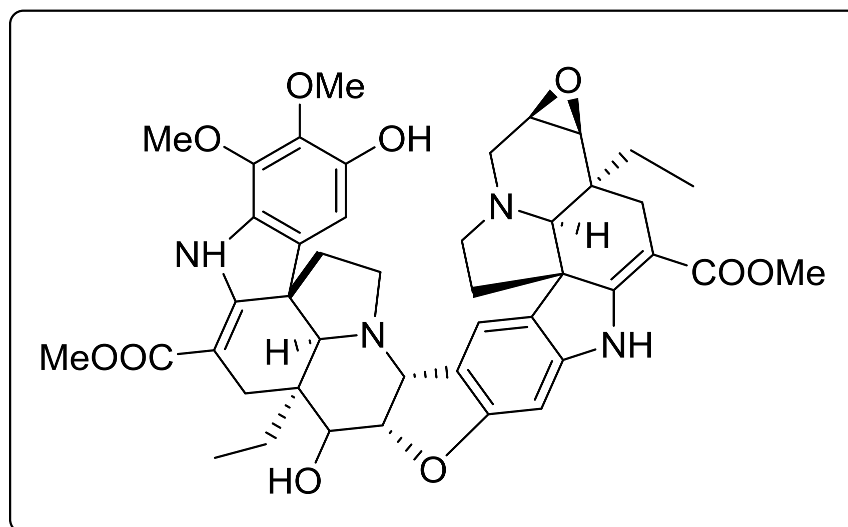
Structures of Strychnine (a) and Brucine (b)

Both brucine and strychnine inhibited the development of human colon cancer cells significantly. Flow cytometric studies revealed that the two alkaloids triggered cellular death. Furthermore, in the Brucine or Strychnine-treated groups, the growth of DLD1 xenografted tumors in nude mice was dramatically inhibited. Wnt/catenin signaling plays a role in this occurrence, characterized by notably heightened production of DKK1 and APC, coupled with diminished expression of catenin,cMyc and pLRP6 in both CRC cells and tumor tissues. Brucine and syrychnine demonstrate targeted inhibition of colon cancer proliferation both in-vitro andin-vivo, suggesting their promising potential for future development as effective agents against CRC[18].

Norihiro Ishii et al. elucidated the inhibitory impact of Conophylline on pancreatic cancer desmoplasia as well as cancer-promoting cytokines synthesized by cancer-associated fibroblasts. Conophylline (CnP), a vinca alkaloid sourced from the leaves of the tropical plant Ervatamia microphylla and Tabernaemontanadivaricata, has exhibited the capacity to stimulate the differentiation of β-cells within pancreatic precursor cells. Tabernaemontanadivaricata, which was gathered in Miyakojima, Okinawa Prefecture, Japan, provided the conophylline. Paper filters were used to filter the mixture of crushed dried leaves and 60% [v/v] ethanol. Crude Con- ophylline Preparation I (CCP-I) was created by lyophilizing the filtrate and vacuolizing it to concentrate it. The quantity of conophylline present was 2.3mg per gram. Employing our novel approach, 5kilograms of dried leaves were introduced into 500 litres of 0.025N hydrochloric acid and subjected to a gentle heating at 60°C for a duration of 30 minutes.

This process facilitated the filtration of the alkaloid with ease. After that, centrifugal filtration was used to produce a clean supernatant. Another three sets of extractions'

supernatants were combined and subjected to column chromatography employing an artificial adsorbent resin. Conophylline was then eluted with pure ethanol after the column had been washed with water and 30% [v/v] ethanol. Then, the final concentration of pure CnP was 0.05–1.0 g/mL, with a final methanol concentration of 0.1% (v/v), and it was employed in vitro. In vivo, crude CnP, which contains 22 mg/g of pure CnP, was diluted to 2 mg/mL in a 0.5% (v/v) Tween-80 solution[19].



Structure of Conophylline

CnP decreased CAF's stimulating effects on pancreatic cancer cells by reducing CAF activity and proliferation. Additionally, CnP significantly reduced the amount of cytokines generated by CAF, including interleukin (IL)-6, IL-8, CCL2 and CXCL12, which are all involved in the advancement of cancer. In vivo, in a mouse xenograft model, CAF enhanced tumor proliferation and desmoplastic development; CnP decreased desmoplasia of tumors made up of pancreatic cancer cells + CAF; and combination therapy with CnP and gemcitabine significantly reduced tumor growth[20].

Yuki Uchihara et al. discussed the process through which Taxodione triggers apoptosis in cells harboring the BCR-ABL mutation by initiating the generation of reactive oxygen species (ROS). Taxodione is a diterpene quinone methide extracted from Taxodium distichum. Taxodione was extracted from the cones of T. distichum obtained from Keio University's Medicinal Plant Garden. To obtain a fraction with a concentrated amount of taxodione, the cones of T. distichum (179 g) were treated twice with sequential additions of 2 L of hot acetone and stirred for 3 hours each time.

The resulting extracts underwent filtration and concentration under reduced pressure, resulting in a residue (13.4 g). This residue was then subjected to Diaion HP-20 column chromatography using a mixture of water, MeOH.

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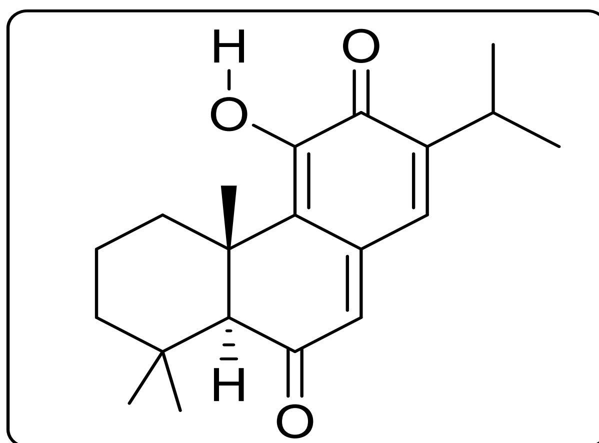

Structure of Taxodione

Taxodione triggered apoptosis in K562 cells derived from human myelogenous leukemia, which had undergone transformation by BCR-ABL. Taxodione diminished the functions of mitochondrial respiratory chain (MRC) complexes III and V, leading to the initiation of reactive oxygen species (ROS) generation. The antioxidant N-acetylcysteine (NAC) reversed the ROS production induced by taxodione, reinstated MRC activities, particularly complex V, and thwarted apoptotic cell death. Furthermore, upon the introduction of taxodione to K562 cells, the mitochondrial portion captured BCR-ABL along with crucial signalling components such as STAT5 and Akt. As a result, the shifted placement diminished their ability to incite cell growth, implying that these behaviors might serve as the fundamental process by which taxodione operates as a therapeutic agent against tumours. Taxodione caused apoptosis in transformed Ba/F3 cells, which was brought on by both BCR-ABL and BCR-ABL with the T315I mutation [21].

Heng Zhang et al. looked into the underlying molecular mechanisms of berbamine's possible anti-tumor actions in ovarian cancer. Berbamine is a naturally occurring substance derived from the plant Berberis amurensis and utilized in traditional Chinese medicine. Young leaves were dried by air drying and then pulverized with a mortar and pestle to a fine powder. Under dim lighting conditions lasting for a period of 24 hours at the ambient temperature, BIAa(benzylisoquinoline alkaloids)were acquired from dehydrated powdered samples through the utilization of 70% ethanol(1g/10mL).

Subsequently, the extract underwent dilution to achieve a concentration of 10,000 mg/L in preparation for High-performance Liquid Chromatography (HPLC) analysis, following filtration through a 0.22μm syringe filter. The analysis of berbamine was carried out using a Shimadzu Prominence HPLC system equipped with a diode array UV-visible detector,which monitored the substance at a wavelength of 290nm[22].

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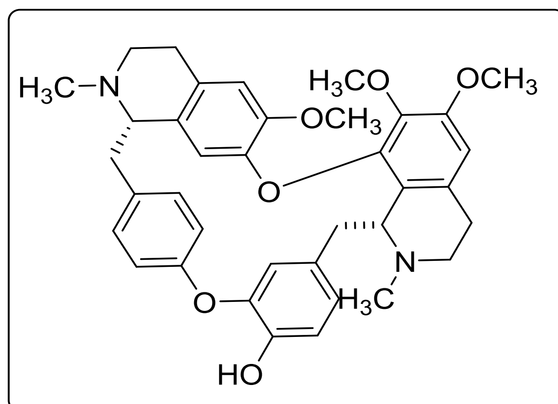
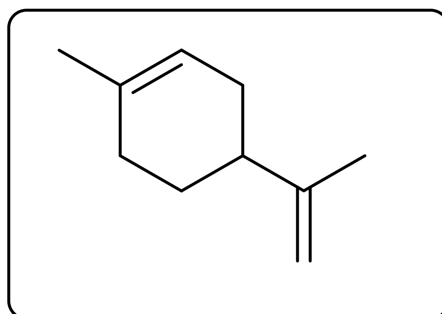


Structure of Berbamine

The methyl thiazolyl tetrazolium assay demonstrated that berbamine reduced the viability of ovarian cancer cells in a concentration-dependent manner. Additionally, as demonstrated by colony formation and cell invasion assays, berbamine inhibited the growth and invasion of ovarian cancer cells. According to flow cytometry tests, berbamine caused cell cycle arrest at the G0/G1 phase and boosted the rate of cell apoptosis in ovarian cancer cells. In ovarian cancer cells, berbamine enhanced the protein levels of cleaved caspase-3, cleaved caspase-9, and Bax while decreasing the protein levels of Bcl-2, according to a Western blot analysis. The Wnt/-catenin pathway in ovarian cancer cells was suppressed by berbamine therapy, as shown by quantitative real-time PCR and western blot analysis. Treatment with lithium chloride (LiCl) can partially counteract the inhibitory effects of berbamine on the viability and invasion of ovarian cancer cells. The berbamine-treated group had a significant inhibition of tumor growth, elevated caspase-3 and -9 cleavage, and decreased levels of -catenin protein in tumor tissues[23].

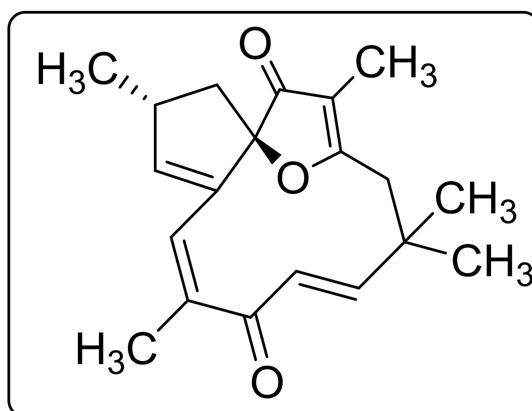
Xiao Yu et al. examined how d-limonene demonstrates anti-tumor properties by stimulating autophagy and apoptosis in lung cancer cells. D-limonene (1-methyl-4-isopropyl-cyclohexene) is a naturally occurring compound present in the essential oils of citrus fruits. The extraction of D-limonene involves utilizing orange peels, which are subjected to boiling in water. The resultant oil (D-limonene) is then distilled through steam at a temperature slightly below 100°C, well under its typical boiling point of 176°C[24]. For this experiment D-limonene was diluted with dimethyl sulfoxide in a 1:19 ratio, followed by dissolution in the cell culture medium.



Structure of D-Limonene

D-limonene impeded the proliferation of lung cancer cells and restrained the development of transplanted tumors in nude mice. Following treatment with d-limonene, there was an elevation in the expression of genes associated with apoptosis and autophagy within the tumors. Moreover, the employment of an autophagy inhibitor, chloroquine, along with the knockdown of the atg5 gene, hindered the apoptosis initiated by d-limonene[25].

Iram Fatima et al. elegantly analyzed the potential role of Jatrophone as a chemotherapeutic agent for highly chemoresistant triple negative breast cancers. Jatrophone was obtained from the plants Jatropha isabelli and Jatropha gossypiifolia, both of which belong to the Euphorbiaceae family. Jatrophone (JA) was extracted from the roots and stems (100 g) of 31 Jatropha gossypiifolia plants. The extraction process involved using a Soxhlet apparatus with refluxing ethanol (3 x 500 mL) for 48 hours. After filtration, the mixture was subjected to solvent evaporation, resulting in a dark green syrup. The unrefined blend underwent additional refinement through a standard silica gel column chromatography procedure in the normal-phase (using a mixture of 5% to 50% ethyl acetate and hexane). Afterward, the compounds with low polarity were subjected to another round of purification using a normal-phase silica gel column chromatography technique (employing a blend of 5% to 15% ethyl acetate and hexane)[26].



Structure of Jatrophone

JA disturbed the normal advancement of the cell cycle and led to the reduction in the activity of fundamental Wnt target genes like AXIN2, HMGA2, MYC, PCNA and CCND1. In terms of its mechanism, JA lowered the quantity of stable, unphosphorylated(activated) β-catenin protein, while having no impact on the overall levels of β-catenin. Additionally, JA led to the suppression of key epithelial-mesenchymal transition (EMT) markers and significantly impaired wound healing in scratch assays, indicating its direct involvement in inhibiting the migration of TNBC cells[27].

Liangqian Jian et al. detail the potential of Phycocyanin as a prospective candidate for cancer treatment. Phycocyanin, a bioactive nutritional component, is extracted and refined from various types of seaweeds. Phycocyanin has been isolated from different species including Aphanizomenon sp., Spirulina sp., Phormidium sp., Lyngbya sp., Synechocystis sp., and Synechococcus. A 500 ml sample of homogenized logarithmic phase (15 days old) culture underwent centrifugation at 4,000 rpm, resulting in a pellet formation. This pellet was then suspended in 100 ml of a 20 mM acetate buffer supplemented with 50 mM sodium

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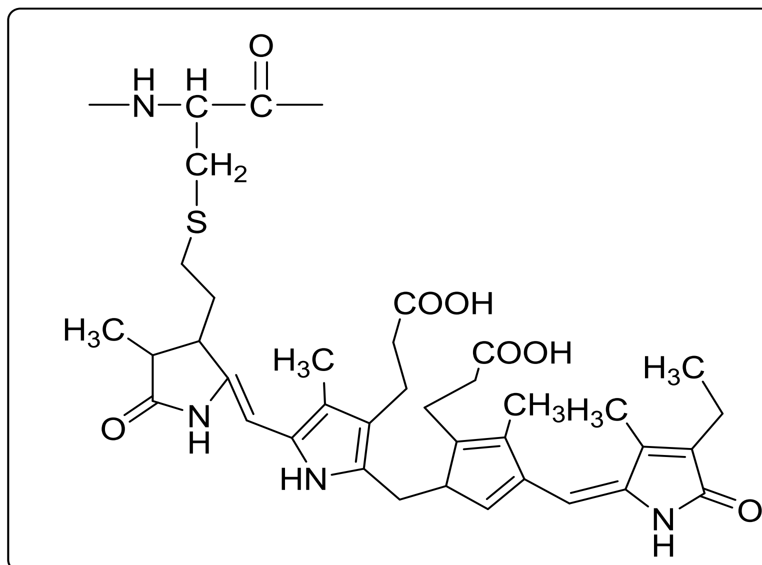
chloride and 0.002 M sodium azide, with a pH of 5.10. The extraction of C-Phycocyanin involved a procedure of repetitive freezing (at -20°C) followed by thawing at room temperature, until the blue color became evident in the acetate buffer (Step I). To eliminate cell debris, a centrifugation step was carried out at 5,000 rpm for 10 minutes, resulting in the obtained extract being referred to as the crude extract [28].



Structure of Phycocyanin

The engagement of NF-κB, MAPK, and PI3K-Akt-mTOR pathways was observed in the induction of both tumor cell apoptosis and autophagy by phycocyanin. These outcomes thus provide robust evidence for the anti-cancer properties of phycocyanin[29].

Shixin Xia et al. in their study investigated how oridonin suppresses the growth and metastasis of breast cancer by obstructing the Notch signaling pathway. Oridonin, a diterpenoid derived from Rabdosiarubescens, possesses significant anti-cancer properties. 500 grams of dried Rabdosiarubescen powder was introduced into an ultrasonic extractor, and subsequently subjected to two rounds of extraction using a 95% ethanol-water solution (5 L each time). The resulting solutions from the two extractions were pooled together and concentrated until their volume was reduced to one-third of the original. Activated carbon was then incorporated into the concentrated solution, and a 30-minute ultrasonic-assisted decolorization process was executed. Following filtration under reduced pressure, the decolorized extracted solution was acquired. Further concentration led to the attainment of the crude extract. Employing the oridonin standard as a reference substance, the thin layer chromatography technique was utilized to monitor the presence of oridonin within the elution solution. The desired elution solution was gathered and concentrated to a suitable volume, after which it was refrigerated at 4°C for a duration of 2 days, leading to the precipitation of crystals. Following filtration under reduced pressure, the crystals were procured. A gentle wash with a small quantity of acetone rendered the crystals white, and subsequent drying resulted in the attainment of the final oridonin product, possessing an HPLC purity of 97.42% [30].

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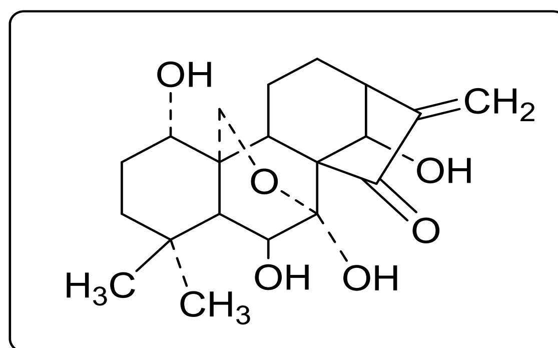


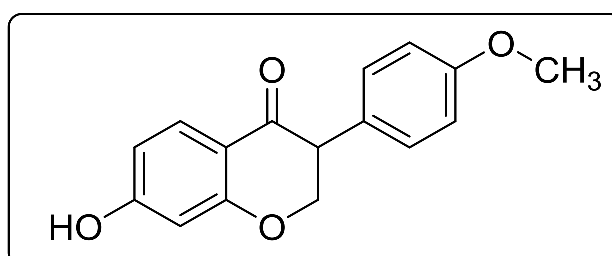
Structure of Oridonin

Oridonin's impact on proliferation was assessed through MTT assay, while its influence on cell migration and invasion was determined through transwell migration and invasion assays conducted on human breast cancer cells. The inhibitory effect of oridonin was further ascertained in an in vivo context by utilizing xenografted nude mice.

Oridonin displayed inhibitory effects on human breast cancer cells both in laboratory settings and within living organisms. Additionally, oridonin notably triggered apoptosis in human breast cancer cells. Moreover, the administration of oridonin not only suppressed the migration and invasion of cancer cells but also led to a more noteworthy reduction in the expression of Notch 1-4 proteins[31].

R. Zhou et al. elucidated the manner in which formononetin effectively inhibits the movement and incursion of breast cancer cells MDA-MD-231 and 4T1, originating from the brest formononetin, an herbal isoflavone is a notable component present in the roots of Astragalus membranaceus, Trifolium pratense, Glycyrrhiza glabra and Pueraria lobata. For extraction, dried Trifolium pratense L. (red clover) was pulverized into powder and subsequently immersed in 90% methanol at a ratio of 5 volumes to the powder.

This mixture underwent soaking for 24 hours followed by reflux boiling for 4 hours. This procedure was repeated twice more. After cooling, the extract was filtered, first through filter paper and then extracted with acetic ether. The acetic ether was subsequently removed, and the resulting extract was subjected to reflux with 6 mol/L HCl. Concentration of the extraction was achieved through rotary evaporation to yield crystals, which underwent recrystallization twice with 95% methanol. The refined crystals were ultimately dried, resulting in the production of a white powder [32].



Structure of Formononetin

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The impact of formononetin on the migration and invasion abilities of MDA-MB-231 and 4T1 breast cancer cells, both in vitro and in vivo was investigated.Our findings revealed that, within a 24-hour timeframe and at concentrations below 160 µmol/l, formononetin did not exhibit significant inhibition of cell viability in MDA-MB-231 and 4T1 cells. Following exposure to a safe concentration of formononetin, the ability of MDA-MD-231 and 4T1 cells to migrate and invade was significantly hindered. This was evident from the result of wound healing assays, chamber invasion assays and mouse metastasis model conducted in-vivo. Laboratory tests conducted in-vitro demonstrated that formononetin caused a reduction in the levels of matrix metallooroteinase-2(MNP-2) and MMP-9 coupled with an increase in the expression of tissue inhibitor of metalloproteinase-1(TIMP-1) and TIMP-2. Moreover, insights obtained through immunofluorescence and immunoblotting experiments strongly suggested that formononetin possessed a potent ability to effectively suppress the activation of Akt and PI3K. In a collective interpretation, these findings propose that formononetin exerts inhibition on the migration and invasion of breast cancer cells by modulating the expression of MMP-2 and MMP-9 through the PI3K/AKT signalling pathway[33].

Conflict of Interest: The authors affirm that they have no conflicting interests related to this study.

III. LIST OF ABBREVIATIONS

- JA-Jatrophone
- Crc- colon cancer cell
- GC- Gastric cancer
- CuB-Cucurbitacin B
- STAT3-Signal transducer and activator of transcription
- GLN-Gaillardin
- OSCC-Oral Squamous Cell Carcinoma
- TRP- Transient Receptor Potential Channel
- TRPA1-Transient Receptor Potential Channel Ankyrin Subtype 1
- CnP-Conophylline
- CAF- cancer-associated fibroblasts

IV. ACKNOWLEGDEMENT

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V. CONCLUSION

Nowadays, natural products have shown a promising role in the treatment of cancer. Their diverse compounds, such as antioxidants, phytochemicals, and polyphenols, possess anti-cancer properties that can inhibit tumor growth, induce apoptosis, and even boost the efficacy of conventional medications. However, rigorous scientific research, clinical trials, and collaboration between traditional medicine and modern healthcare are essential for maximizing their potential and providing cancer patients with valuable alternatives. This

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chapter is a valuable resource for researchers seeking to innovate and develop novel approaches for cancer treatment through natural products.

CONSENT FOR PUBLICATION

The authors have formally consented to include their work as a chapter within the book titled "Emerging Directions in Chemical, Material Sciences and Nanotechnology".

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