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REVIEW ARTICLE

Phytotherapeutic Potential of *Desmostachya bipinnata* (L.) Stapf. - A Narrative Review

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Abstract

Oral cancer is one of the most prevalent cancers in India. It is mostly caused by radiation exposure, genetics, alcohol and cigarette use, and Human Papillomavirus (HPV) infections, along with other factors. Even with the latest developments in the identification and management of oral cancer, patients' quality of life is still gravely impaired. A potentially beneficial adjunctive therapy to lessen the side effects of conventional medicines is traditional medicine. For centuries, plant extracts have been employed in the treatment of numerous diseases, including cancer and conditions like diabetes and cardiovascular disorders. Numerous pharmacological activities of the *Dharba* plant, *Desmostachya bipinnate*, have been demonstrated, notably antioxidant, antibacterial, anticancer, and anti-inflammatory properties. Phytochemicals, found in these plants, are bioactive substances with therapeutic effects for a variety of ailments.

Keywords: Cancer, *Dharba*, *Desmostachya bipinnata*, Medicinal Plants, Phytochemicals, Phytotherapy

1. Introduction

Cancer is a genetic illness that is marked by specific body cells proliferating out of control and potentially spreading to other organs. It can affect any part of the body and is a leading cause of mortality[1,2]. Normally, human cells undergo mitosis to grow and divide and create new cells when the body needs them. New cells replace old ones when they age or sustain damage[3]. This well-organized mechanism is susceptible to disruption, which can result in the emergence and growth of aberrant or damaged cells. These cells can develop tumours, which can be benign or malignant (cancerous). As per Robins and Cotran's definition, neoplasia is a term used to describe any aberrant cell collection that grows faster than normal tissue and without proper coordination[3].

The development of cancer is triggered by mutations or alterations in the genetic material of the cell. These alterations might develop on their own or be brought on by substances known to cause cancer (carcinogens). Sunlight, radiation, chemicals, viruses, and tobacco are examples of carcinogens[4,5]. A genetic flaw in any living thing can make it more susceptible to cancer, even

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though not all exposed cells to carcinogens develop cancer. Persistent inflammation can also increase a cell's susceptibility to malignant growth. In the promotion phase, environmental chemicals or specific medications, such as hormones, can stimulate a cell which went through initiation to develop into cancer[6]. Malignant transformation is the process by which a pre-neoplastic cell becomes malignant. By encouraging the proliferation of started cells predisposed to malignant transformation, tumour promotion contributes to carcinogenesis. Tumour suppressor genes are inactivated during this process, while proto-oncogenes are activated. As the malignant phenotype develops more aggressive traits over time, it signifies the last stage, known as tumour progression. This phenotype is characterised by uncontrolled growth and genomic instability, as well as additional genetic and epigenetic modifications.

Epigenetic alterations play a crucial role in carcinogenesis by modulating gene expression without changing the DNA sequence. Key mechanisms include DNA methylation, histone modifications, and non-coding RNA regulation. Aberrant DNA methylation can silence tumour suppressor genes, while histone acetylation or deacetylation affects chromatin structure and gene transcription. Non-coding RNAs, such as microRNAs, further regulate oncogenes and tumour suppressor genes. These reversible changes contribute to genomic instability, uncontrolled growth, and the malignant phenotype of cancer cells[7,8].

Oral cancer, more precisely oral squamous cell carcinoma, is one of the most common cancers. It is mostly brought on by radiation, genetics, HPV infections, tobacco and alcohol usage, and other causes. Treatment options may include immunotherapy, surgery, radiation, chemotherapy, and targeted therapy, depending on the stage of the malignancy[7]. Though there have been encouraging developments recently in the detection and treatment of oral cancer, patient Quality of Life (QoL) is still a key problem[8]. Natural substances derived from plants are a valuable resource for treating a range of diseases, including cancer. To decrease the negative effects of conventional therapy, supplementary therapies such as herbal or traditional medicine might be employed[8,9].

Turmeric *Curcuma longa* (the spice)[10], the herb *Zingiber officinale* (ginger root)[11,12], *Ocimum sanctum*, (tulsi)[13,14], the species *Crocus sativus* (a golden colour, saffron)[15], and *Cinnamomum verum* (cinnamon)[16,17] are among the plants that have anti-tumorigenic potential. *Desmostachya bipinnata* (Db), commonly referred to as "big cord grass," "salt reed grass," "half grass," or "*Dharba* grass," is a tropical plant with long, pointed, linear leaves. Revered as a sacred grass since the Vedic period, it holds significant cultural and medicinal importance. It has historically been employed as an analgesic, diuretic, anti-inflammatory, and anti-diarrhea drug. Additionally, displaying hepatoprotective properties, *D. bipinnate* is beneficial in the treatment of menorrhagia, jaundice, and dysentery. Its anti-ulcerogenic[18,19] and antioxidant[20] qualities have also been reported by studies. This review examines and assesses Db's possible anti-cancer properties.

Desmostachya bipinnata, is a priceless medicinal plant with a wide range of therapeutic uses. Its ability to consume harmful radiation has been experimentally demonstrated, protecting the environment's sanctity and purity. Perennial *D. bipinnata* grass is found throughout South Asia, mostly by riverbanks (Figure 1).

Blue and UV light, which are supposed to have disinfecting qualities, can quickly multiply germs in food items during an eclipse, rendering them unfit for human consumption. In place of dangerous manmade



Figure 1. Distribution of *D. bipinnata,* both fresh and dried grass.

chemical preservatives, *D. bipinnata* functions as an environmentally benign food preservative and a natural disinfection that prevents radiation[18]. Numerous ailments have been treated with the entire plant. *Briza bipinnata* L., *Uniola bipinnata* (L), *Stapfiola bipinnata* (L.) *Kuntze, Eragrostis cynosuroides* (Retz.) P. Beauv., and *Poa cynosuroides* Retz can all be used in place of *D. bipinnata.* classification taxonomy: Within the order *Cyperales*, the genus *Desmostachya*, the family *Poaceae*, the class *Monocotyledonae*, phylum *Spermatophyta*, and the species *Bipinnata* are the kingdom *Plantae*[18,19].

Conventional treatments such as radiation, chemotherapy, and surgery can be somewhat helpful, but they can also have unfavourable side effects that lower patients' quality of life. As a result, numerous strategies leveraging phytochemical compounds have been extensively investigated, revealing their potent anti-cancer properties with minimal to no adverse side effects. These compounds, derived from natural plant sources, have demonstrated significant efficacy in targeting key cancer-related pathways, making them promising candidates for safer and more effective cancer therapies. *D. bipinnate* is a grass that possesses important medicinal qualities, such as the capacity to prevent damaging UV radiation-induced cancer and to exhibit antioxidant and anticancer activity. It has not received much attention in the field of cancer treatments, despite its potential. By combining *D. bipinnate* with metal nanoparticles, nanotechnology may be able to provide a better cancer therapy alternative with little to no side effects, thus enhancing patient quality of life[18]. The therapeutic qualities of *D. bipinnata* are the main topic of this review.

Plant description: Desmostachya bipinnate, often known as *D. bipinnate*, is a hardy perennial grass that grows huge, green tussocks with flaky, widely spread tubers. The stiff, pronged culms have fibrous sheaths covering them that have a yellowish hue. They reach a height of 80–100 cm and a diameter of 7-10 mm. *Technique for gathering plant and extract:* The entire plant, including the roots, is harvested. The roots are thoroughly washed under running water to remove any contaminants, then cut into small pieces and air-dried for ten days. Numerous methods are employed to analyse and study phytochemicals using the dried powder produced which includes Solvent Extraction, Chromatography (TLC, HPLC, GC, LC-MS), Spectroscopy (UV-Vis, FTIR, NMR), Quantitative Assays (Folin-Ciocalteu, Aluminum chloride method), Microscopic Analysis, Bioassays, Mass Spectrometry (Q-TOF, GC-MS), Electrochemical Analysis (Cyclic Voltammetry)[18,19].

2. Therapeutic Uses

Many pharmacological properties, including diuretic, antibacterial, anti-inflammatory, antioxidant, and anti-cancer properties, are displayed by *D. bipinnate.* These therapeutic effects are attributed to a multitude of bioactive substances (Figure 2, Table 1).

2.1 Anti-microbial Effects

A Minimal Inhibitory Concentration (MIC) in the range of 6 to 50 µg/ml, β-*sitosterol-D-glucopyranoside* in Db exhibits strong antibacterial activity and functions in concert with several antibiotics, most notably ciprofloxacin. Time-kill curves demonstrated that most infections were eradicated by β-sitosterol-D-glucopyranoside in 5-10 h[20] (Table 1). *Vibrio fischeri*, the *Staphylococcus aureus* bacteria, typhimurium of *Salmonella*, *Streptococcus pyogenes, K. pneumoniae, Bacillus subtilis, Enterobacter aerogenes, P. aeruginosa,* as well as *Candida albicans,* have all been shown to be susceptible to the antimicrobial properties of *D. bipinnata*'s ethanolic extract[21,22]. Furthermore, the growth of bacteria such as *Bacillus subtilis*, *Sarcina ventriculi, P. aeruginosa, Staphylococcus aureus,* and *Serratia marcescens* was suppressed by the ethanolic extract. The compound demonstrated antifungal activity against several fungal species, including *Aspergillus fumigatus*, *Candida albicans*, *Penicillium chrysogenum*, and *Aspergillus flavus*[23]. Agar diffusion

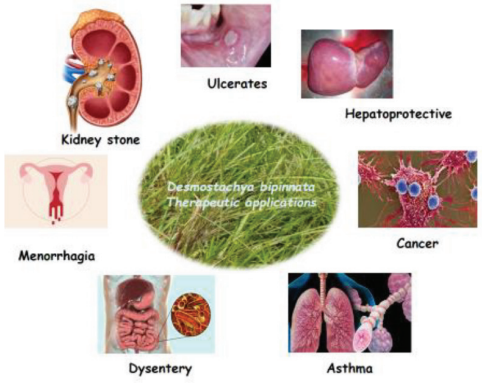


Figure 2. Therapeutic applications of *D. bipinnata*.

Table 1. Phytoconstituents found in various parts of *D. bipinnata* and their therapeutic uses[20]

S. No.	Plant part	Identified phytochemical compounds	Therapeutic activity
1	Leaves - methanol extract	Benzofuran 2,3-dihydro and octasiloxane 1,1,3,3,5,5,7,7,9,9,11,11,13,13,15, 15,- hexamethyl	Anti-ulcerogenic
		β-sitosterol-D-glucopyranoside	Anti-bacterial
		Flavonoids: kaempferol, quercetin, quercetin-3-glucoside, trycin, and trycin-7-glucoside	
		Sterols: stigmasterol, β-sitosterol, daucosterol, stigmast-5-en-3β,7β-diol, and stigmast-5-en-3β,7α-diol	
		2,6-dihydroxy-7-methoxy-3H-xanthen-3-one	Anti-cancer activity
		4′-methoxy quercetin-7-O-glucoside	Anti-helicobacter
2	Plant essential oils	β-eudesmol (11.2%), eseroline (25.1%), calarene (3.5%), camphene (16.8%), caryophyllene diepoxide (12.3%), isobornyl acetate (9.9%), tricyclene (4.3%)	Anti-bacterial
3	Rootstock	5-Hydroxymethyl 2-furfural, β-amyrin, β-sitosterol, β-sitosterol-glucoside, stigmasterol-glucoside	Anti-bacterial
		ρ-hydroxycinnamic acid ethyl ester (16.2%), palmitic acid (15.1%), palmitic acid ethyl ester (9.2%), linoleic acid (6.6%), oleic acid (6.5%), linoleic acid ethyl ester (7.5%) and 2-methoxy-4-formylphenol	

and broth dilution procedures were used to confirm the anti-bacterial properties of *D. bipinnata* root oil, and the results showed considerable suppression against a variety of microorganisms including *E. coli, S. aureus,* and *Klebsiella* species[24].

2.2 Anti-inflammatory, Antipyretic, and Analgesic Effects

Albino rats induced with pyrexia through yeast administration were utilized to evaluate the antipyretic effects of aqueous extracts derived from the whole *D. bipinnata* plant. Oral administration of these extracts resulted in a significant reduction in elevated body temperature, comparable to the effects of diclofenac sodium and paracetamol. Anti-inflammatory activity was assessed using a digital plethysmometer[25,26] (Table 2). The *D. bipinnate* extracts markedly decreased paw inflammation after carrageenan as the suspension was administered via the sub-plantar surfaces of an albino rat's hind limbs. The ethanol extract showed maximum inhibition (53.84%), while diclofenac sodium showed 32.30% inhibition. Utilising the tail immerse method, the analgesic efficacy of many *D. bipinnate* preparations was evaluated, and significant analgesic effects were found[27].

In a clinical study of paw oedema caused by carrageenan, the analgesic and anti-inflammatory properties of *D. bipinnata* roots were evaluated using hydro-alcoholic extracts. After three hours, these extracts significantly inhibited edema as compared to traditional treatments. In comparison to analgin, the analgesic action was also determined to be effective[25].

2.3 Anti-ulcerogenic Effects

Rats with stomach ulcers caused by ethanol were used to test *D. bipinnata's* anti-ulcerogenic qualities. Two additional groups were administered trycin and trycin-7-glucoside derived from the ethanolic extract of *D. bipinnata*[28]. The extracted whole and its separated constituents demonstrated strong anti-ulcerogenic properties. The most potent extract was *D. bipinnate* (DEM) methanolic, which demonstrated strong *in vitro* anti-helicobacter activity at a 40 µg/ml MIC. An ethyl Acetate portion with strong anti-helicobacter activity was obtained through filtration of the DEM extract. A flavonoid component known as 4'-methoxy quercetin-7-O-glucoside was recovered by subsequent fractionation and column chromatography, and it showed a favourable MIC value[29] (Table 2).

Rats were used to investigate the anti-diarrheal effects of alcohol and aqueous extracts of the roots of D. bipinnate at different dosages utilizing charcoal-based meal tests and castor oil-induced diarrhoea[30]. Both extracts, but particularly the alcoholic one, dramatically lowered the weight of the faeces and the amount of charcoal that passed through the digestive

system. The standard aqueous-methanolic extract of *D. bipinnata* resulted in a partial unwinding in the rabbit jejunum following the atropine-sensitive spasmogenic reaction. Following atropine pre-incubation, an inhibitory effect resembling verapamil was seen[31]. This result was comparable to the maximal contraction that acetylcholine could produce. The entire *D. bipinnate* plant was extracted hydroponically, however rats did not experience any laxative effects from it. Nonetheless, despite a dose of 500 mg/kg, a little increase in faecal production was observed, which was comparable to the conventional therapy[32].

2.4 Anti-cancer Effects

Using a brine shrimp lethality assay, the *in vitro* cytotoxicity in *D. bipinnate* aqueous extract with alcohol at four different doses was examined. With an LD50 level of 1215.929 ppm, the *D. bipinnata* plants cause 17.4 and 42% of deaths at 500 and 1000 ppm, respectively. The novel xanthene 2,6-dihydroxy-7-methoxy-3Hxanthen-3-one, produced by *D. bipinnata* methonolic extract with an IC50 value of 27.2 mM, inhibited the oxidation of low-density lipoprotein and the signalling transducer and activator of transcription 3 activity in the HCT-116 colon cancer cell line[33].

The cytotoxic properties of different doses of a seventy per cent methonolic extract were tested *in vitro* on human cervical tumour cell lines (HeLa), human laryngeal squamous carcinoma cell lines, and NIH 3T3 cells. Significant *in vitro* anti-cancer activity was shown by *D. bipinnata* methonolic extract, which inhibits every line of cells in a dose-dependent way between 25 and 400 g/ml[32] (Table 2).

2.5 Diuretic Activity and Anti-urolithiasis

Rats were used to test the diuretic properties of the whole hydroalcoholic extract of *D. bipinnata*. For a positive control of diuretics effect, furosemide was employed. The hydro alcoholic extract, at 500 mg/kg, led to a considerable increase in urine production when compared to the regularly used drug Frusemide. It was also shown that this extract was effective in raising the levels of the elements Na+, K+, and Cl- in the urine electrolytes[33].

D. bipinnata, both alone and in conjunction with *Brassica oleracea*, demonstrated an anti-urolithiatic effect when urolithiasis was experimentally induced in rats using a mixture of ethylene glycol and ammonium chloride in drinking water for ten days. Over ten days, urolithiatic rats were administered an aqueous extract of each herb, both alone and in combination, at a concentration of 400 mg/kg. When compared to the control group, daily oral extract treatments not only restored all biochemical abnormalities but also significantly decreased the quantity of calcium oxalate that accumulated in the kidneys[34] (Table 2).

2.6 Antioxidant Effect

After *D. bipinnata* roots were extracted in 70% methanol, the antioxidant effects of this extract at different doses were explored using a variety of models, such as DPPH, nitric oxide activity, hydrogen peroxide, and hydroxyl radical scavenging. The extract's antioxidant properties were up to par in all of the tests.

Another efficient hydrogen peroxide scavenger was *D. bipinnata*, whose IC50 value was 127.07 6.44 g/ml as opposed to 122.60 2.14 g/ml for traditional ascorbic acid[33,35].

The antioxidant and DNA damage protection capabilities of *D. bipinnata* hydro alcoholic extract were investigated (both *in vitro* and *in vivo*). In the H_2O_2 scavenging assay, the extract showed a substantial antioxidant action in a dose-dependent manner, with an IC_{50} value of 264.18 3.47 g/ml. At a certain concentration, it prevented DNA from becoming oxidatively damaged. Furthermore, in a spot experiment, the extract protected the yeast cells against the chemical that damages DNA in a dose-dependent manner. Moreover, the extract's presence showed strong antioxidant activity in living cells by protecting yeast cells from H_2O_2, a substance that induces oxidative stress[36] (Table 2).

2.7 Hepatoprotective Property

Hepatoprotective effects of the Polyphenolic Part of *D. bipinnata* roots (Pp *D. bipinnata*) were investigated in liver-damaged female Sprague-Dawley rats. The proportion of possibilities increased in a dose-dependent manner when BRL3A cells exposed to ethanol were administered Pp *D. bipinnata*. Following pre-treatment with Pp *D. bipinnata*, serum levels of creatinine, urea, uric acid, bilirubin, glutamic oxalo-acetic transaminase, triglycerides, alkaline phosphatase, and urea were all significantly lower in both treatment

groups, while serum protein levels were moderately restored. Additionally, in rats given tamoxifen, Pp *D. bipinnata* dramatically reduced the peroxidation of lipids in liver tissue and blocked antioxidant enzymes[37] (Table 2).

Histopathological analysis showed a reduction in liver cell necrosis, which validated the biochemical results. The potential of dried powdered roots of *D. bipinnata* to shield Wistar rat' livers from the hepatic damage caused by paracetamol was investigated. Rats administered a water-based extract of *D. bipinnata* showed dramatically enhanced levels of the antioxidant enzymes and much smaller amounts of the elevated blood enzyme markers the MDA, LH, and bilirubin when compared with rats with paracetamol damage. We looked into whether dried powdered roots of *D. bipinnata* could protect the livers of Wistar rats from damage caused by paracetamol. Animals administered a water-based extract of *D. bipinnata* showed dramatically enhanced levels of the antioxidant enzymes and significantly reduced levels of the elevated blood enzyme markers the MDA, LH, and bilirubin were compared with rats with paracetamol damage[38].

2.8 Anti-diabetic Effects

Rats without diabetes were used to test how the aqueous extract of *D. bipinnata* affected their blood glucose levels. The addition of hydroalcoholic extract didn't substantially alter euglycemic levels, according to the results. But when this extract was given to meals, the severity of the condition in hypoglycemic (food-deprived or exercise-induced) rats was dramatically reduced[39]. Additionally, the quantity of hyperglycemia brought on by the exogenous dose of dextrose was greatly decreased by this extract. In diabetic rats administered alloxan, the anti-diabetic effects of an *ethanolic extract* of the *D. bipinnata are* being investigated. The extract demonstrated a high degree of anti-diabetic activity; levels of cholesterol, urea, creatinine, triglycerides, blood glucose, uric acid, alkaline phosphatase, and SGOT were all dramatically lowered[40,41] (Table 2).

2.9 Respiratory Effects

Rabbit trachea contractions caused by carbachol (1 mM) were suppressed by *D. bipinnata* crude aqueous-methonolic extract. However, it additionally produced an atropine-sensitive emphasis on increased K^+-induced contractions, which was subsequently halted at a specific dose. The organic component and the stimulating effect that occurs in the aqueous fraction are the main causes of this negative impact on activity-directed fractionation[42].

2.10 Anti-allergic Activity

The effects of various *D. bipinnata* extracts on the contractile responses of guinea pig ileum induced by histamine were analyzed. The most successful extract was the alcoholic one, even though all of them could cause ileum in guinea pigs. The findings that demonstrated the extracts had a strong anti-histaminic effect were verified by histamine-induced lethality tests[43]. Histamine-induced mortality was prevented in guinea pigs when the extracts were administered prior to histamine injection[44].

According to research on the long-term toxicity of both alcohol and water air extracts from this plant, female albino mice could safely consume up to 2000 mg/kg of these extracts. When the mice were given alcoholic extracts at different dosages between 0.1 and 5 g/kg of body weight, no mortalities occurred. For prolonged fever, the roots or blossoms were boiled in 500 ml of water until the volume was reduced to 250 ml. The prepared decoction was consumed three times a day for three days. For loose stools, a few grams of flowers were boiled in 500 ml of water until the volume was reduced to half, and the solution was taken twice daily[44].

3. Chemical Constituents and Phytochemicals found in *D. bipinnata*

Phytochemicals, also known as phytonutrients, are plant-based compounds that naturally occur and offer health benefits to humans when used as nutrients and/or medicinal substances. Fruits and vegetables contain molecules called antioxidants that shield the body from the harm that free radicals can inflict. Phytochemicals, on the other hand, are biochemical complexes made by plants that function as anti-oxidants and neutralize free radicals[45]. The most common causes of free radicals are tobacco use, heavy metal exposure, smoking, metal poisoning, and prolonged radiation exposure.

Antioxidants play the important job of minimising the negative effects of these exposures and preserving the balance between oxidants and antioxidants. The primary cause of oxidative stress is any change in the aforementioned ratio which might cause cancer[45,46].

There are two categories for phytochemicals: Primary metabolites and secondary metabolites.

3.1 Primary Metabolites

They either directly or indirectly contribute significantly to the growth and development of plants. Lipids, proteins, amino acids, carbs, peroxidase, and catalase are a few examples. The majority of phytochemicals, including proteins, lipids, carbohydrates, and catalase, were present in the hydroalcoholic extract of *D. bipinnata*.

3.2 Secondary Metabolites

Although they function as biocatalysts and as a means of curing illnesses, these substances are involved directly in growth and development. Alkaloids, flavonoids, coumarins, statins, and phenols are a few examples.

3.3 Alkaloids

Alkaloids are a broad class of substances with cyclic structures and at least one fundamental nitrogen atom (Figure 3). Plants from families such as Loganiaceae, Leguminosae, Menispermaceae, and Papaveraceae as well as Ranunculaceae, which are extensively dispersed throughout the vegetative kingdom, contain the majority of these chemicals. A wide range of alkaloids, including tetrandrine, sanguinarine, evodiamine, piperine, berberine, vinblastine, camptothecin, and berberine matrine, are widely recognized for their potent chemotherapeutic effects. On a range of cancers, natural alkaloids show antiproliferative and antimetastatic properties[47,48].

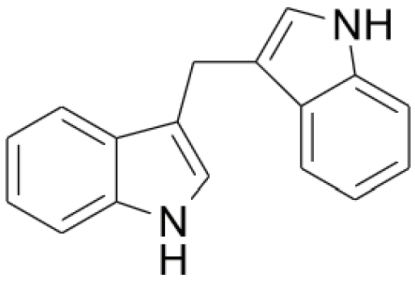


Figure 3. Chemical structure of alkaloid.

Many indole alkaloids, derived from various medicinal plants, had lethal effects on various cancer cell lines through inducing autophagy, inflammatory cell death, and apoptosis. These effects were mediated by multiple proteins implicated in the apoptotic cascade. Vinblastine, vincristine, and vindesine are three compounds that were identified and intensively studied as potential anticancer medicines from *Catharanthus roseus* (family: Apocynaceae). Cell development was suppressed by vinca alkaloids via changing the rates of tubule addition and removal at the tip of microtubules within the mitotic spindles[49]. Vinblastine and vincristine are commonly used in conjunction with other chemotherapy medications to treat lymphomas, breast cancer, leukaemia, testicular cancer, lung cancer, and Kaposi's sarcoma.

Together with autophagy inducer, vinblastine, potent autophagy maturation inhibitor, along with nano-liposomal C6-ceramide increased apoptotic cell death in HepG2 as well as LS174T cell lines by increasing the concentration of autophagic vacuoles and lowering cell autophagy maturation[50]. The combined therapy blocked Beclin-1, a protein associated with autophagy, from being eliminated.

The broad-spectrum anticancer drug camptothecin is derived from the Nyssaceae family plant *Camptotheca acuminata*. Treatment plans for colorectal, ovarian, and small-cell lung cancers include a number of camptothecin analogues. Topotecan and Irinotecan, two semi-synthesized camptothecin byproducts, are also used for the same purpose[47].

The isoquinoline alkaloids that are extracted from the perennial herb Chelidonium majus include allocryptopine, berberine and sanguinarine, chelerythrine, as well as 8-hydroxydihydrosanguinarine. It has been demonstrated that chelerythrine was cytotoxic to renal cancer cells from patients with von Hippel-Lindau mutations (SW-839) as well as human embryonic kidney cells (HEK-293). It caused apoptosis, which was then accompanied by an upregulation of p53 and Bax, a downregulation of PARP, Bcl-2, and caspase-3 expression, and a reduction in phosphorylation of ERK and Akt. Furthermore, it prevented the tumour from developing in a model of mice that used xenografts.

Reports state that sanguinarine was effective against melanoma and that it caused apoptosis in human lung cancer cells as well as pancreatic

carcinoma[51,52]. Its efficacy against drug-resistant experimental cervical cancer cell lines has also been reported[53,54]. When used as a cancer treatment, sanguinarine suppresses SW620 cells by binding to the G-quadruplex KRAS promoter, which is directly linked to KRAS mutations[55]. Liriodenine, a type of isoquinoline alkaloid obtained from *Enicosanthellum pulchrum*, triggered apoptosis via the mitochondrial signalling system and interrupted the progression of cell cycles at the S-phase to inhibit the proliferation of CAOV-3 human ovary cancer cells. Bax was increased while Bcl-2 and survivin protein were downregulated. Apoptosis, necrosis, and autophagy were demonstrated by pyrrole alkaloids as possible anticancer processes. When autophagy was stimulated, there was a change in Beclin-1 expression and an increase in LC3B formation. Numerous pyrrole alkaloids caused mitochondrial dysfunction upon treatment, which led to cellular death. Through the use of both an ultrasound-assisted technique and a bismuth nitrate catalyst, several N-substituted pyrrole derivatives were synthesized[56].

Tylophora indica, an *Asclepiadaceae* plant, produced tylophorine, an isolated chemical with anti-tumour properties. Tylophorine was found to be cytotoxic to leukaemia cells L1210 and P-388[57], Tylophorine stopped the cells at the G1 phase and inhibited the S-phase advancement in cancer of the gastric, human nasopharyngeal cancer (HONE-1), as well as hepatocellular cancer (HepG2) cell lines[58]. Tylophorinidine and pergularine were isolated from the herb *Pergularia pallida. Lactobacillus leichmannii* cell-derived dihydrofolate reductase enzyme suppressed these compounds, suggesting that they may have anticancer potential.

3.4 Flavanoids

Plants produce flavonoids, a compound of polyphenolics, as beneficial secondary metabolites. Green tea, chocolate, and fruits (plums, cherries, apples, and berries) are the primary sources. They function as strong antioxidants and shield the plants from a variety of harmful effects. 15 carbon the phenyl propanoid chains make up flavonoids, which also form two rings of aromatic compounds (Figure 4). They are divided further into anthocyanidins, flavanones, flavanols, and isoflavanoids[59-62].

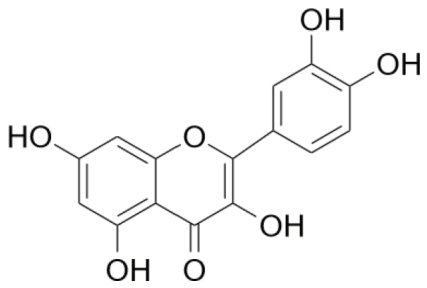


Figure 4. Chemical structure of flavonoids.

A B ring in isoflavonoids is joined to a chromane ring at C2 or C3. The most commonly occurring isoflavonoids are genistein and daidzein. The core structure of flavanones is the saturated, oxidized C-ring, also known as dihydroflavone. The two most commonly occurring flavanones are hesperetin and naringenin[63]. The unoxidized C ring with the C3 hydroxyl group is what makes up catechins. Flavanols are composed of an unsaturated C ring at positions C2 or C3, which is hydroxylated by C3 and oxidised near C4. Additionally, they include myricetin, fisetin, kaempferol, quercetin, and isorhamnetin. Anthocyanidins are the unsaturated flavonoids that are soluble in water found in plants. Delphinidin, cyaniding, peonidin, malvidin, and other anhocyanidins are among them[64,65].

Flavanoids are primarily glycosides that link sugars or aglycones. The flavanoids' lipophilicity allows them to cross cell or mitochondrial membranes despite their mild hydrophobic acidity. They can regulate cellular metabolism, scavenge free radicals, and shield against oxidative stress-related diseases[66,67]. Numerous studies have shown that flavonoids can control cellular metabolism, scavenge free radicals, and protect against diseases linked to oxidative stress. There is growing evidence that certain flavonoids have anticancer properties, even though the underlying mechanisms generating this action are still not completely known[68,69].

The multifaceted illness known as cancer is characterised by unchecked cell proliferation and a disrupted cell cycle, which allow aberrant cells to invade and spread to different sections of the body. Elevated anxiety, pollution, cigarette smoking, radiation, and UV light exposure are the main extrinsic variables linked to the development of cancer; oxidative damage, hypoxia, genetic alterations, and loss of apoptotic function are the main endogenous causes. The primary

internal causes of cancer are oxidative stress, hypoxia, which is caused by genetic alterations, and a lack of apoptotic function; the primary external causes are growing anxiety, pollution, tobacco use, radiation, and UV radiation exposure[70,71].

The synthesis of Reactive Oxygen Species (ROS), regulation of metabolism, cell death signals, and cellular energy production are all significant functions of mitochondria. enhanced production of ROS, unregulated pH, enhanced aerobic glycolysis, plus decreased enzyme activity are the primary metabolic changes in cancer cells. This results in an acidic extracellular environment that is more conducive to inflammation; glutamine-driven lipid biosynthesis escalates and expands the pathways involved in the initiation as well as metastasis of tumours, blocking enzyme activity; mitochondria become hyperpolarised; and these outcomes are associated with the invasiveness along with malignancy of cancer cells[72,73].

A wide range of anti-tumour effects is exhibited by flavonoids, including the inhibition of growth and invasiveness of malignant cells, the activation of autophagy and apoptosis, and changes in the roles of enzymes that scavenge ROS and aid in cell cycle arrest[74]. Isoflavone genistein encouraged G2/M arrest in breast cancer cells, which led to ROS-dependent cell death. Daizzein produced ROS, which caused MCF-7 breast cancer cells to undergo apoptosis[72]. By boosting ROS formation and starting a mitochondrial apoptosis pathway, flavanone hesperetin caused apoptosis in human mammary cancer MCF-7 cells, oesophageal cancer, and gall bladder carcinoma cells. Applying flavanone naringenin to the choriocarcinoma JAR or JEG 3 cell lines resulted in the production of ROS and the activation of signalling pathways with anti-cancer properties. Moreover, it triggered the human epidermoid carcinoma A431 cells' apoptotic cascade.

Naringenin decreased migration and proliferation and increased apoptosis and ROS formation in prostate cancer PC3 and LNCaP cell lines[75,76]. The pro-oxidant qualities of cocoa catechins or procyanidins have caused morphological alterations, DNA damage, and death in ovarian cancer epithelial cells. Glutathione peroxidase and reductase activities were elevated in HepG2 cells as a result of the cocoa polyphenolic extract's stimulation of the ERK1/2 pathway. ROS was inhibited by cocoa procyanidins and catechins, shielding Caco2 cells from oxidative stress and eventual cellular death. Cocoa flavanols protect against colon cancer by their antioxidant effects.

One powerful flavonoid that prevents cancer through chemotherapy is quercetin. According to recent studies, quercetin slowed the growth of HepG2 cells, which are cells that cause hepatocellular carcinoma, and also reduced the amount of intracellular ROS. It increased ROS formation and apoptotic cell percentage among human cancers of the stomach AGS and breast cancer MCF-7 cells. The formation of cancerous bladder cells was inhibited by flavanol kaempferol-mediated S phase arrest and death produced by ROS level manipulation. ROS generation in the colorectal tumour cell lines HCT15, SW480, and HCT116 induced apoptosis and activated caspases[77].

Ketofenrol caused fatal effects on hepatocellular cancer cells in rats by mitochondrial targeting via ROS. In ovary cancer cell lines, the flavones luteolin and apigenin have demonstrated anticancer effects that have been associated with modified ROS signalling and the induction of apoptosis. Moreover, apigenin-induced mitochondrial apoptosis in cell lines derived from human cervical cancer, SiHa (HPV 16-positive)[78], HeLa (humans papillomavirus/HPV 18-positive), C33A (HPV-negative), CaSki (HPV 16 and HPV 18-positive), and cells. Research has shown that flavone chrysin raises ROS and lipid peroxidation levels, which kills ovarian cancer (OV90), choriocarcinoma (JAR and JEG3), and cancers of the bladder (ES2 and OV90) cells[79-81].

3.5 Tannins

Most common polyphenol components with large molecular weights are found in tannins. They possess anti-inflammatory, anti-fibrotic, anti-cancer, and anti-oxidant properties.

Tannins are coloured from light yellow to light brown and have a non-crystalline structure. They dissolve readily in a variety of liquids. Based on their structural characteristics, tannins are categorised as gallotannins, ellagitannins, complicated tannins and condensed tannins. Unlike ellagitannins, which are recognized by the existence of a number of hexahydroxydiphenoyl (HHDP) subunits esters to a glucopyranose core, gallotannins are polymer of galloyl moieties connected to different polyol units (mostly glucose) (Figure 5). Complex tannins have a

catechin (flavan-3-ol) unit together with gallotannin or ellagitannin units 9 (Figure 5). To create novel compounds, one monomeric catechin's C-4 can be coupled to the C-8 and C-6 of another[82].

Procyanidins, prodelphinidin B-2 3'-O-gallate, proanthocyanidins, ellagitannins such as oenothein B, granatin, casuarinin, also geraniin A, and granatin B, gallic acid, and tannic acid. Many plants that are important to both the economy and the environment produce tannins, which are phenolic compounds, through secondary metabolism. Tannic Acid (TA), a hydrolyzable tannin, is present in many naturally occurring foods and beverages, such as coffee, green tea, and grapes. In terms of its chemical properties, TA has a molecular weight of 1701.2 g/mol, a strong astringent flavour, and weak acidic properties[82].

Using TA has a wide range of medical advantages, such as anti-inflammatory, antioxidant, anti-cancer, and neuroprotective effects. On the other hand, TA is a potentially useful medication due to its hydroxy and carboxyl groups, which allow it to interact with macromolecules through cross-linking. Recently, TA has come to be recognized as a possible polyphenolic phytochemical that plays a significant role in every phase of the carcinogenesis transition. Even so, it still shows a variety of pharmacological actions that point to the possibility that it works well as an anti-tumorigenic agent. The properties encompass antioxidant, radical scavenging, and anti-inflammatory activities. Furthermore, it demonstrated potent anti-angiogenic effects in non-small cell lung cancer cells[83,84].

Apoptosis is a highly regulated and conserved kind of cell death that is frequently identified by particular morphological characteristics and the activation of many signalling pathways. The homeostatic mechanism that keeps the population of cells in tissue intact during growth and ageing is frequently how it occurs. Apoptosis may occur as a protective response in cases where harmful substances or illnesses cause cell death[85]. Thus, maintaining a healthy state of cellular homeostasis requires strict regulation of apoptosis[86]. Apoptotic signalling pathways are altered when the equilibrium between cellular proliferation and apoptosis is upset, leading to the development of tumours[87]. Numerous triggers, such as ROS, DNA damage, as well as receptor-mediated signals, can cause apoptosis.

Apoptosis is governed by a select number of signalling pathways, including the Bcl-2 protein family, which regulates intrinsic pathways controlled by the mitochondria, and the TNF family death ligands (TRAIL/Apo2L), along with their corresponding cell surface death receptors (DcR1), which mediate extrinsic receptor-driven pathways.

The process through which cells divide and mature through the G1, S, G2, and M stages is known as the cell cycle. When this regulatory mechanism is disrupted, malignant cells multiply uncontrollably. The cell cycle's progression depends on serine/threonine protein kinases or CDKs. The capacity of several tannins to impede the advancement of the cell cycle is essential to their anti-cancer characteristics. Cancer cell growth was significantly reduced by the green tea catechin Epigallocatechin Gallate (EGCG) treatment, which induces a cell cycle halt at the G1, G0/G1, G2/M, and S/G2 checkpoints. In addition, cells entered the G0/G1 phase, G1 phase, S phase, and G0/G1 phase due to the effects of tannins such as prodelphinidin B-23'-O-gallate, grapes proanthocyanidins, casuarinin, geraniin, oenothein B and tannic acid[84].

Tumour growth and metastasis are caused by a variety of factors, including angiogenesis, invasiveness, and migration. The potential of tannins to impede the angiogenesis, invasion, and migration of lung cancer has not been thoroughly investigated. Reports state that endogenous nitric oxide activates the ERK1/2 and guanylate cyclase pathways in A549 and H1299 cells to control cell migration.

It has been demonstrated that the anti-tumour effects of pomegranate leaves, cranberries and maize bran, red rice, as well as cinnamon, cacao beverages, blackberries and Chinese gallnut tannins may be found in the lungs. Several signalling pathways and genes that control death, Epithelial Mesenchymal

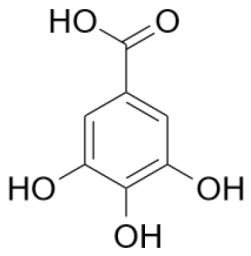


Figure 5. Chemical structure of tannins.

Transition (EMT), expansion, angiogenesis, migration, and invasion can be targeted by tannins. Tannins have an excellent likelihood of being used to treat lung cancer in experiments, but their clinical application is limited because of their rapid excretion through urine and faeces, significant biotransformation, poor gastrointestinal absorption, and possible adverse effects related to higher tannin consumption[84].

3.6 Terpenoids

Terpenoids are a broad group of secondary metabolites with a structural makeup based on isoprenoid bases that are found throughout the phyto-kingdom (Figure 6). There is increased interest in the biological uses and activities of terpenoids because of their diverse range and their anti-oxidative, anti-inflammatory, and anti-cancer properties. Triterpenes, tetraterpenes, diterpenes, triterpenes, monoterpenes, and polyterpenes are the different categories of terpenoids based on structural similarities. Inhibition of angiogenesis, and metastasis in the latter stages of tumor development through the control of numerous intracellular signalling pathways; and prevention of cancer development and growth by causing arrest of cell cycles, malignant cell differentiation, and apoptosis. Only a small number of terpenoids have been found to have anticancer effects[88].

Membrane damage is a part of cytotoxicity, several investigations have demonstrated that essential oils can damage proteins and lipids and induce cytoplasmic coagulation. Damage to cell walls and membranes can lead to macromolecule leakage. Terpenoids' cytotoxic properties made them useful chemotherapeutic agents for treating a range of carcinomas, such as those of the breast, prostate, colon, and liver[89].

Numerous trials have demonstrated the usefulness of dietary monoterpenes in cancer therapies[90]. D-limonene and perillyl alcohol were found to inhibit the development of breast, liver, skin, prostate, pancreatic lung, and colon cancers[91]. Oxygenated compounds such as D-limonene and carvone showed anti-tumorigenic qualities[92]. One aspect of monoterpenes' anticancer activity is their inhibition of post-translational isoprenylation, which controls the growth of cells. Human pancreatic cancer may respond to terpenes such as geraniol as a chemotherapeutic agent.

Research has demonstrated that betulinic acid is efficacious in inducing apoptosis in human cancers, including glioma and melanoma. Similarly, ursolic acid or oleanolic acid inhibited the formation of several transplantable tumours in both animals and leukaemia cells[93]. A diterpene paclitaxel, a potent antimitotic medication with exceptional efficacy against cancers of the breast and ovary, is also present in the bark of the yew tree.

3.7 Saponins

Many higher plants' roots, tubers, leaves, blooms, or seeds are common sources of saponins. According to Figure 7, the carbon skeletons of saponins were used to determine the subclasses of steroids and triterpenes. The majority of their glycone constituents were oligosaccharides, arranged either in a linear or branching fashion and connected to hydroxyl groups by means of an acetyl bond. The anti-tumorigenic activity of saponins on different cancer cells has been demonstrated by recent investigations[94]. Many saponins inhibit the development of cancer cells by causing cell cycle halting and death, with IC_{50} concentrations as small as 0.2 mM. Meanwhile, using saponins in addition to conventional cancer therapy techniques increases the therapeutic efficacy[95-97].

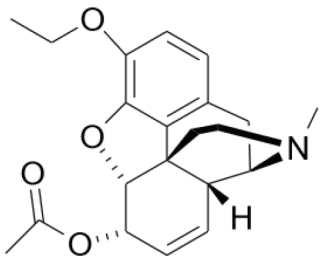


Figure 6. Chemical structure of terpenoids.

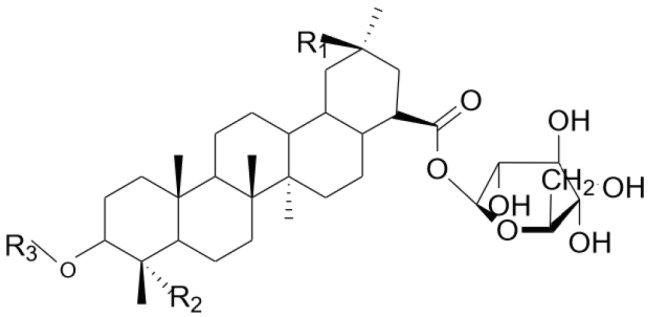


Figure 7. Chemical structure of saponins.

The plant families that have the largest concentrations of steroidal saponins are the *Agavaceae, Dioscoreaceae, Leguminosae, Solanaceae, Amaryllidaceae, Scrophulariaceae,* and *Rhamnaceae; Acanthopanax*, Legume family, *Araliaceae, Scrophulariaceae, Campanulaceae,* and *Caryophyllaceae* have the lowest amounts. There are over 11 main unique types of saponins, including dammaranes, taraxasteranes, ursanes, cycloartanes, lanostanes, tirucallanes, lupanes, hopanes, oleananes and cucurbitanes. Among these saponins, steroids, oleananes, dammaranes, cycloartanes, and lupanes have potent anti-tumour effects against numerous cancer types[96,97].

Cycloartane saponins may be used in addition to chemotherapy to treat malignancies, even though they have relatively limited anti-cancer activity. For example, whole Astragalus Saponins (AS) have a positive effect on human colon cancer cell lines and tumour xenografts. By inducing apoptosis and altering the ERK-independent NF-B signalling pathway, HepG2 cell growth is suppressed and the production of the HCC tumour marker, fetoprotein, becomes downregulated. AS can also be used as a supportive treatment to lessen the adverse effects of additional conventional chemotherapeutic medications. To reduce the synergistic effects of PI3K-Akt inhibitors, the NSAID-activated gene (NAG-1) would be the target. The knowledge gained could eventually help in the creation of innovative target-specific chemotherapy drugs with proven molecular pathways[98,99].

Cancer chemoprevention using phytochemicals like terpenoids may be one of the most effective ways to control cancer. Terpenoids have been demonstrated in preclinical investigations to reduce experimental carcinogenesis in several organs. They are easily obtained from fruits, vegetables, drinks, herbs, and medicinal plants. They are created by mixing molecules having five Carbon bases (C5), such as isoprene. All terpenoids are made up of two molecules comprising five carbon atoms each, according to a biochemical structural study. Terpenoids are categorised in the following order: monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes (C25), triterpenes (C30), tetraterpenes (C40) and polyterpenes, depending on the number of building units.

3.8 Dammaranes

The majority of dammarane saponins have antitumor properties. The naturally occurring OSW-1 compound from *Ornithogalum saudersiae* bulbs is highly cytotoxic to cancer cell lines. When non-cancerous cells were exposed to doses of OSW-1 that resulted in a larger loss of cell viability than those observed in malignant cells, their sensitivity to the drug was statistically different from that of cancerous cells. The membranes of the mitochondria and cristae of human leukaemia as well as pancreatic cancer cells were damaged by OSW-1, as demonstrated by electron microscopy as well as biochemical analyses[100,101]. Trans-membrane potential was disrupted, cytosolic calcium increased, and calcium-dependent apoptosis was triggered as a result.

Oleananes are a key source of saponins, which exhibit anti-tumour activity through various mechanisms such as chemoprevention, immunostimulation, anti-cancer effects, and anti-metastasis. Saikosaponins, soybean saponins, platycodigenins, avicins, tubeimoside, and *Pulsatilla koreana* saponins have demonstrated antitumor effects via distinct signalling pathways[102,103]. Notably, all except tubeimoside and *Pulsatilla koreana* saponins showed immunological activation. Platycodigenins and saikosaponins also possess anti-metastatic properties. Avicins, derived from Acacia victoriae, dephosphorylate Stat3 in various human tumour cell lines, reducing its transcriptional activity and regulating proteins such as c-myc, cyclin D1, Bcl2, survivin, and VEGF, leading to autophagic cell death[104,105].

One of the triterpenoid saponins present in *Bolbostemma paniculatum* (Maxim) Franquet's bulb, tubeimoside, shows promise as a cancer chemopreventive. It cytotoxically acts on HeLa cells via pathways connected to both mitochondrial dysfunction and ER stress-induced cell death. It can attach itself to tubulin's colchicine binding site, acting as an anti-microtubule agent. By increasing the release of TIMP-2 and reducing the synthesis of MMP-2 and MMP-9, soybean saponin prevents the growth of cancer cells. Researchers investigated the *in vivo* anticancer potential of saponins against BDF1 mice harbouring Lewis Lung Carcinoma (LLC), as well as their impact on human lung cancer cell lines, including HCT 15, SK-MEL-2, A-549, and SK-OV-3. A single dosage of 6.4 mg/kg of *Pulsatilla saponin D*, a potent anticancer component,

significantly inhibited tumour growth in BDF1 mice harbouring LLC cells (IR, 82%)[105].

The diosgenyl saponins dioscin, formosanin C, and Polyphyllin D (PD) have been shown to have positive immune-stimulatory and anti-cancer properties. The diosgenyl saponins dioscin, formosanin C, and PD have demonstrated significant immune-stimulatory and anti-cancer properties. Advances in manufacturing processes and the elucidation of their chemical structures have facilitated extensive research on the therapeutic effects of PD. It is a potent inducer of apoptosis via ER stress and mitochondrial dysfunction. Dioscin, a preclinical drug, showed potent anti-proliferative effects against most solid tumour and leukaemia cell lines. Proteomic investigations have reported that it induced apoptosis through both the mitochondrial and extracellular pathways[106-108].

Most furostanes exhibited negligible anti-tumor activity. As anticancer medications, protodioscin, protoneogracillin, and methyl protoneodioscin, methyl protodioscin, and methyl protoneogracillin have shown cytotoxic activity against the K562 cancer cell. The colon cancer line KM12, the CNS cancer line U251, the two melanoma lines MALME-3M and M14, the two cancers of the kidney lines 786-0 and UO-31 and the breast cancer line KM12, all demonstrated strong selectivity against methyl protogracillin. It showed cytotoxic action against a variety of examined cell lines from solid tumours (MDA-MB-231) and leukaemia within the NCI's cancer cell panel[109].

3.9 Phytosteroids

Phytosteroids are the name for plant steroids that may or may not act as active hormones in the body. Although they share an important ring structure with animal steroids (Figure 8), their chemical groups are attached to the core ring at different locations, therefore they cannot be substituted[110]. Mostly, they are used to treat issues related to reproduction, like treating sexually transmitted infections, facilitating easy labour and delivery, and boosting libido in men and women.

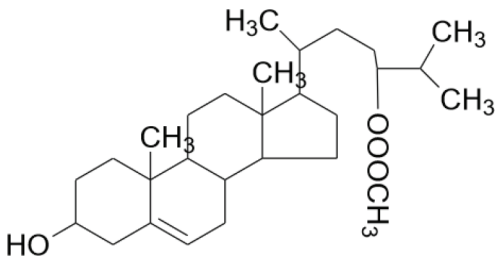


Figure 8. Chemical structure of phytosteroids.

They are potentially a source of contraceptives since they can be transformed into androgen or estrogen-like substances, which function as sex hormone derivatives[110,111]. Additionally, phytosteroids have antibacterial, analgesic, anti-inflammatory, and cholesterol-lowering qualities. They are also employed in the treatment of gastrointestinal diseases. Phytosteroids can prevent macrophage activation, which prevents the release of pro-inflammatory cytokines and the lethality caused by lipopolysaccharides. As a result, they are employed, like Physalins, as immunosuppressants[112-114].

4. Conclusion and Future Perspective

Plants are useful medical tools that are used to cure a wide range of illnesses. For prognosis and treatment, the mechanism underlying the development of cancer is significant. As a natural substance, plants can cause apoptosis, which stops cancer cells in their tracks. As a result, using herbal medicine boosts therapeutic benefits and decreases side effects. In order to lessen the negative effects of cancer therapies, herbal remedies must be revived. The WHO has also provided standards for evaluating the qualities of herbal medicines. One such herb is *D. bipinnata*, which has a variety of therapeutic uses but still needs further research for the treatment of oral cancer. Future research should ideally focus on the drug delivery of *D. bipinnata* extracts for the treatment of cancer via nanotechnology and drug carrier molecules like gold (Au), silver (Ag), and platinum (Pt).

It has been shown that the special physicochemical characteristics of nanoscale drug delivery, such as their ultra-small size, high reactivity, and tuneable practical change, are both extremely successful techniques for treating oral cancer and reliable diagnostic instruments for the disease. The oral cavity is the main barrier separating the oral environment from deeper tissues and is easily accessible. Because of its distinct topography, it is possible to visualise oral cancer, administer treatments to tumors selectively, and treat tumours with a variety of therapeutic approaches.

Table 2. Review of the literature on the phytochemical analysis and therapeutic use of *D. bipinnata*

S. No.	Parts of the plant and extract used	Experimental model	Outcome	Source
1	Leaf and roots, hydroalcoholic extract	*In vitro*	Leaves and root ethanolic extracts contain primary metabolites and show significant free radical scavenging activity. They also contain carbohydrates, proteins, lipids, and phenols.	115
2	Leaves, hydroalcoholic extract	*In vitro*	Gold nanoparticles synthesised *via* Db-mediated processes exhibit increasing scavenging activity against hydrogen peroxide. Maximum antibacterial activity was observed against *E. coli*, followed by *B. subtilis*.	116
3	Leaves, hydroalcoholic extract	*In vitro*	Db AgNPs demonstrate notable antimicrobial, antioxidant, and antiproliferative activities.	117
4	Leaves, alcoholic and aqueous extracts	Rodents	The elevated plus maze and actophotometer models indicate that Db leaf extracts have antianxiety properties. The alcoholic extract shows significantly higher activity compared to the aqueous extract.	41
5	Whole plant, methanolic extract	Wistar Albino rats	Db methanolic extract significantly enhances glucose absorption in isolated rat hemi-diaphragm, though less effective than Glibenclamide. The extract also helps normalize pathological abnormalities.	118
6	Root, hexane, acetone, methanol, water and methanol: Water extracts	*In vitro*	Acetone extract has the highest antioxidant activity, followed by methanol extract when compared to ascorbic acid. The root extracts also show promising antifungal and moderate antibacterial activities.	119
7	Root, hexane, ethyl acetate, acetone, methanol, water	*In vitro*	Root extracts display antibacterial activity against three gram-positive and one gram-negative bacteria, and antifungal activity against *A. niger* and *A. flavus*. Acetone extract exhibits antioxidant activity.	119
8	Roots, methanolic extract	Female Sprague-Dawley rats	Pretreatment with PFDB leads to a significant reduction in serum levels of enzymes like alkaline phosphatase, triglycerides, cholesterol, urea, uric acid, bilirubin, and creatinine.	37
9	Whole plant, ethanolic extract	Wistar Albino rats	The ethanolic extract of Db shows significant weight gain in diabetic rats, with high doses exhibiting notable antihyperglycemic activity.	40
10	Leaves, alcoholic extract	Ex-vivo	*Ex-vivo* evaluations of guinea pig ileum's contractile reactions to histamine show that the alcoholic extract is the most effective in preventing histamine-induced mortality.	44
11	Aerial part, aqueous extract	Wistar Albino rats	Aqueous extracts of *D. Bipinnata* and *Brassica oleracea* Gongylodes can dissolve urinary stones, potentially through diuresis and reducing urinary substances that cause stones.	34
12	Rootstock, ethanolic extract	*In vitro*	GC-MS analysis identifies lipid-like components such as palmitic acid, oleic acid ethyl ester, linoleic and oleic acid, and linoleic acid ethyl ester.	21
13	Leaves, hydroalcoholic extract	*In vitro*	Notable antibacterial activity was observed against *E. coli* and *Staph. aureus*, and *Klebsiella* species.	24
14	Whole plant, hydroalcoholic extract	Albino rats	The hydroalcoholic extract shows significant diuretic action, increasing urinary output and electrolyte concentration (Na+, K+, and Cl-).	35
15	Whole plant, hydroalcoholic extract	Albino mice	Dose-dependent antioxidant activity was observed, protecting yeast cells against oxidative stress.	31
16	Leaves, crude methanolic extract	Mice	Db crude extract protects mice against castor oil-induced diarrhoea and shows calcium antagonist activity, suggesting potential for treating gut and respiratory disorders.	42
17	Whole plant, hydroalcoholic extract	Wistar rats	Hydroalcoholic Db extract helps maintain euglycemic levels in hypoglycemic rats.	39

Table 2. Continued...

S. No.	Parts of the plant and extract used	Experimental model	Outcome	Source
18	Root, methanolic extract	*In vitro*	Methanolic extract of Db roots exhibits antioxidant properties and contains sterols, volatile oils, flavonoids, carbohydrates, glycosides, phenolic compounds, and amino acids.	33
19	Whole plant, hydroalcoholic extract	Brine shrimp	Db hydroalcoholic extract is non-toxic at high doses, with at least 50% survival rates at the highest concentration tested (1000 µg/ml).	35
20	Aerial part, hydroalcoholic extract	*In vitro*	Chemical components such as camphene, isobornyl acetate, tricyclene, trans-2,6-gamma-irone, caryophyllene diepoxide, β-eudesmol, eseroline, and calarene show significant antibacterial activity against gram-positive bacteria.	120
21	Leaves, methanolic extract	*In vitro*	Compound 2,6-dihydroxy-7-methoxy-3H-xanthen-3-one inhibits low-density lipoprotein oxidation and HCT-116 colon cancer cell line exhibits STAT3-dependent luciferase activity.	121
22	Root, alcoholic extract	Albino mice	Alcoholic extract significantly inhibits the gastrointestinal transit of charcoal in mice and decreases intestinal motility and prostaglandin synthesis.	122
23	Root, hydroalcoholic extract	Rat	Db hydroalcoholic extract shows good analgesic and anti-inflammatory effects by inhibiting prostaglandin synthesis.	25
24	Whole plant, aqueous and ethanolic extract	Albino rats	Both extracts significantly inhibit carrageenan-induced edema in a dose-dependent manner.	26
25	Whole plant, hydroalcoholic extract	Albino mice	Anti-helicobacter activity was confirmed, with quercetin showing therapeutic potential for peptic ulcers caused by *H. pylori* infection.	29
26	Aerial part, ethanolic extract	Wistar Albino rats	Trycin and trycin-7-glucoside show anti-ulcerogenic activity. Phytochemicals include quercetin-3-glucoside, quercetin, trycin, trycin-7-glucoside, and kaempferol.	123

Nanoparticle-based drug delivery systems offer enhanced solubility, improved bioavailability, reduced toxicity, increased pharmacological efficacy, greater stability, superior tissue macrophage distribution, extended drug release, and resistance to both chemical and physical degradation. Herbal-derived nanomaterials, including hydrogels, nanohydrogels, xanthan gums, polymeric micelles, liposomes, dendrimers, metallic nanoparticles, quantum dots, and crystalline nanoparticles, are utilized in these delivery systems. Consequently, nanomaterials derived from *D. bipinnata* can effectively integrate with various drug delivery platforms, providing versatility for numerous therapeutic applications.

Drugs delivered by nanoparticle size distribution have a larger surface area overall, which facilitates quicker blood breakdown and reduced toxicity while preserving therapeutic effects. To reduce toxicity concerns, there has been increased interest in the effectiveness of drug launching, drug dispersion, and targeted delivery of drug-based nanoparticles. These have primarily been utilised in conjunction with natural goods. The green chemistry approach is highly favoured for creating drug-loaded nanoparticles because it minimizes the potentially harmful components involved in the biosynthetic procedure.

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6. Author Contributions

Nitya K contributed to acquisition, analysis, or interpretation of data, drafted the manuscript; Ramya R, Pradeepkumar Y, Vikram SA, Kochli CN, Ashokkumar V critically revised the manuscript for important intellectual content, resources, substantially contributed to conception or design.

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