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A Review on Phytochemical & Pharmacological Properties of Bidens Bipinnata

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Abstract

Bidens bipinnata Linn, also known as *B. bipinnata*, is a member of the Asteraceae family that has been utilized for various medicinal purposes for a very long time in a variety of different civilizations. The purpose of this research is to gather the most recent information that is currently available on the phytochemical components and pharmacological activities of *B. bipinnata*. It is believed that the range of bioactive components that it possesses, such as flavonoids, terpenoids, and phenolics, are responsible for the medicinal properties that it possesses. Studies in the field of pharmacology have demonstrated that *B. bipinnata* possesses many pharmacological activity, such as anticancer, antibacterial, anti-inflammatory, and antioxidant characteristics. In particular, the total flavonoids found in *B. bipinnata* have been shown to have significant neuroprotective qualities in brain damage models, which makes it a potential candidate for more pharmacological investigation. The present study provides preliminary data as well as recommendations for more research in the fields of science and clinical medicine pertaining to this plant.

Introduction

Plants have long been integral in treating diverse ailments globally. The demand for medicinal plants is rising in developed and developing nations alike, owing to their minimal adverse effects. Herbal medicine constitutes a significant component of both traditional and contemporary medical systems [1]. Medicinal plants are still important in healthcare systems in many different parts of the world, where 80 percent of people rely mostly on traditional medicine to meet their medical requirements. Over four billion people, or 80% of the world's population, live in poor countries and depend mostly on plant-derived products for their healthcare needs [2]. Moreover, a considerable portion of contemporary medications utilized in modern medicine for treating illnesses, including aspirin, codeine, and quinine, have roots in traditional herbal remedies and medicinal plants. Consequently, medicinal plants serve as crucial reservoirs of highly effective medicines for treating illnesses and promoting long-term human health [3].

The presence of many bioactive chemicals, including lignans, tannins, terpenoids, polyphenols, alkaloids, and other secondary metabolites, is what gives medicinal plants their therapeutic qualities [4].

Bidens bipinnata (*B. bipinnata*), a member of the Asteraceae family, holds significant importance due to its numerous ethnomedicinal and nutritional properties. Traditionally, *B. bipinnata* is extensively utilized for treating a range of conditions, such as asthma, laryngeal and bronchial diseases, as well as for its styptic and vermifuge qualities, effective in addressing conditions like sore throat and conjunctivitis. Additionally, it is applied topically for wound healing, exhibiting bactericidal properties and demonstrating antimalarial activity, thereby aiding in alleviating symptoms such as fever, cough, and asthma [5].

Bidens pilosa and *B. bipinnata* are two of the species of the species group Bidens that have been the subject of much scientific research in recent decades on their possible medical

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benefits. Numerous beneficial chemicals have been identified as a result of these research efforts, including β caryophyllene, β-carotene, sesquiterpenes, and germacrene-D [6].

Investigating *B. bipinnata's* potential therapeutic benefits requires tying in-depth scientific study with the plant's traditional medical usage. This review explores contemporary research on the phytochemistry, pharmacology, toxicity, traditional applications, and botany of the plant. The combined information demonstrates the possible benefits of *B. bipinnata* and its constituent parts and suggests directions for further study to produce strong medicinal molecules.

Botany

B. bipinnata is an annual plant predominantly found in the temperate biome. It serves various purposes such as animal fodder, a source of poison, medicinal applications, and as food for invertebrates. Additionally, it holds environmental significance and is utilized as human food. According to taxonomic classification Table 1 shows that it belongs to the Bidens genus (Asteraceae) [7]. There are thought to be 230-240 species in this genus globally [8]. *B. bipinnata* thrives in wetland, tropical islands, and various habitats including river bluffs, pine-oak forests, campsites, roadsides, and abandoned farms. It favors shady areas and wet sandy soils like sandy loam, red sandy clay, and loamy sand. In North Florida flatwoods forests, it remains unaffected by soil disturbance caused by clearcutting and chopping [9]. *B. bipinnata*, commonly known as Spanish Needles, is an annual herb that grows to be approximately 2 to 5 feet tall, almost glabrous in texture. Stem: 4-angled, frequently branching, roughly straight. The majority of the leaves are opposite and are long petiolate, with up to four pairs of strongly lobed pinnae and scanty hair on the veins underneath. The last segments might be whole or dentate, cuneate at the base, and ovate to rhombic-lanceolate. The centre of the flower head has tubular disc blooms, encircled by strap-shaped ray flowers that are either yellow or white in colour. During the flowering stage, the single, upright capitula measure 6-8.5 x 5-6.5 mm, and the peduncles vary in length from 2 to 10 cm. The outermost involucral bracts are herbaceous, linear-lanceolate to rectangular, and shorter than the inner ones. Shorter than achenes, receptacular scales have black longitudinal lines and are scarious and linear. The flowers are roughly the same length as the involucre and are made up of disc florets with yellowish corollas and 0-4 ligulate florets that are 2-3 mm long (Figure 1) [10]. Achenes are brown-blackish, ranging from 8-10 mm to 10-18 mm in length, linear in shape, with a pappus of (2) 3-4 bristles measuring 2-4 mm long. The plant flowers from August to October, with fruiting occurring from September to October. Commonly known as Spanish Needles, it is naturalized worldwide, probably native to the American continents [11,12].

Table 1: Taxonomy of *B.bipinnata.*

Kingdom:	Plantae
Clade:	*Tracheophytes*
Clade:	*Angiosperms*
Clade:	Eudicots
Clade:	Asterids
Order:	Asterales
Family:	Asteraceae
Genus:	*Bidens*
Species:	*B. bipinnata*

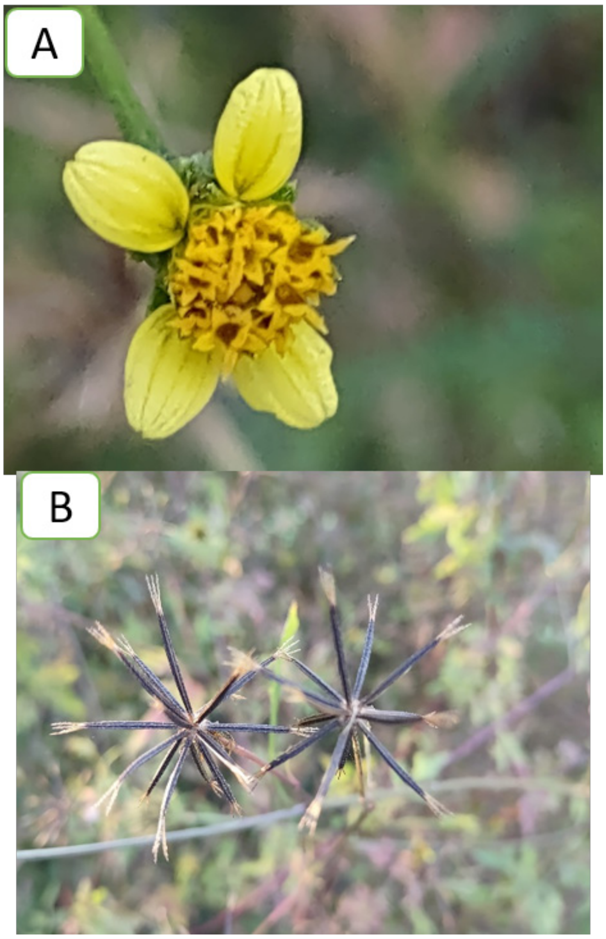


Figure 1: Bidens Bipinnata
(A): flower of B. Bipinnata.
(B): Needle-like seeds, hence the name "Spanish Needle.

Geographical distribution

The geographical distribution of *B. bipinnata* spans across North and South America. It is native to Mexico, Central America, United States, Canada, South America. Common in Eastern and central regions of the United States Extends into Canada, Brazil, Argentina, Colombia, Venezuela, and other countries in South America (Figure 2).

B. bipinnata thrives across Florida, Georgia, Maryland, Kentucky, Louisiana, North America, Mississippi, North Carolina, Eastern Canada, South Carolina, Tennessee, and Virginia. It extends its reach to various regions, including Cyprus in Western Asia, the United Kingdom in Northern Europe, and Belgium, Germany, and Hungary in Middle Europe, with further presence noted in Estonia within Eastern Europe, and Montenegro and Romania in Southeastern Europe, and Spain in Southwestern Europe. Naturalized populations have established in diverse locations across Africa, Ghana, Guinea, Nigeria, Sierra Leone, Togo, Malawi, Zimbabwe, Botswana, Lesotho, Eswatini, and Madagascar in the Western Indian Ocean. Additionally, it has naturalized in regions such as Yemen on the Arabian Peninsula, the Caucasus region including Ciscaucasia within the Russian Federation and Georgia, China, Korea, and Taiwan in Eastern Asia, and Bhutan, India, and Nepal within the Indian Subcontinent. Its reach extends into Southeast Asia, including Cambodia, Laos, Thailand, and Vietnam in Indo-China, and the Philippines in Malesia. Furthermore, it has been recorded in Australia, specifically in the state of Australia, and across Europe, including Switzerland in Middle Europe, and Bulgaria, Croatia, Italy (including Sicily), and Slovenia in Southeastern Europe, with

France in Southwestern Europe. In South America, it has been observed in Venezuela in Northern South America and Brazil, particularly in Rio Grande do Sul and Santa Catarina [13].

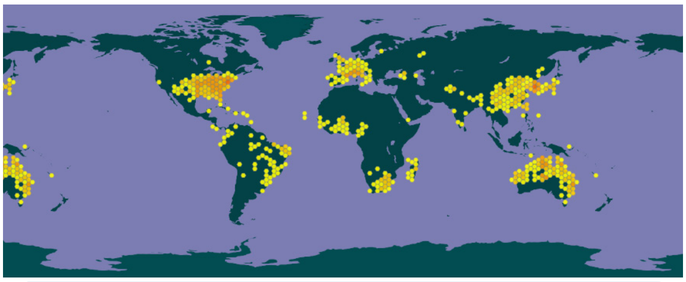


Figure 2: (Distribution of *B. bipinnata*) [14].

Ethnobotanical importance

B. bipinnata (Asteraceae) is traditionally utilized in China as an anti-inflammatory, antipyretic, and anti-rheumatic drugs, and it possesses a broad range of pharmacological applications [15]. As summarized in Table 1, *B. bipinnata* has been found to be beneficial in treating various diseases, including stomach ache, diarrhoea, dysentery, vaginitis, candidiasis, skin infections, and many others.

Table 1: Traditional uses of f *B.bipinnata.*

Diseases	*References*
Stomach Ache	[16]
Diarrhoea	[17]
Dysentery	[17]
Vaginitis	[18]
Candidiasis	[19]
Skin Infections	[17]

Phytochemical Composition of *B. bipinnata*

B. bipinnata exhibits a rich phytochemical profile, contributing to its diverse pharmacological applications. The analysis of its vegetative and reproductive parts reveals the presence of several bioactive compounds in significant quantities. The vegetative part contains 930±4.714 mg/100 g of tannins, which are known for their antioxidant properties. Alkaloids, which have therapeutic potentials such as analgesic and anti-inflammatory effects, are present at a concentration of 0.231%. Flavonoids, recognized for their role in reducing oxidative stress, are found at 5.09%. Saponins, which possess immunomodulatory and anti-cancer properties, are present at 7.09%. Oxalate content is measured at 2.97%, while cyanogenic glycosides, which can have both beneficial and toxic effects depending on the dose, are present at 520±0.275 mg/100 g. Phenols, essential for their antioxidant and anti-inflammatory activities, are found at 4.04±1.6750 mg/g, and lipids, which are vital for various physiological functions, are present at 6.4%.

In the reproductive part, tannins are slightly lower at 865±0.9428 mg/100 g, while alkaloids are present at 0.201%. Flavonoid content is higher at 8.2%, and saponins are also more abundant at 9.8%. Oxalate content decreases to 1.76%, and cyanogenic glycosides are measured at 465±1.3568 mg/100 g. Phenols increase to 5.98±0.7979 mg/g, while lipid content is slightly lower at 5.76% (Table 2) [20]. This phytochemical diversity underpins the medicinal value of *B. bipinnata* and supports its traditional use in treating various ailments [20].

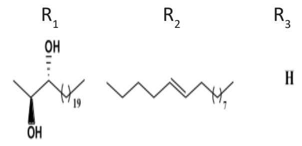
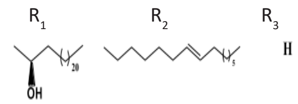
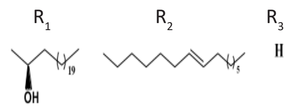
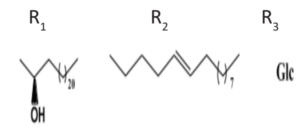
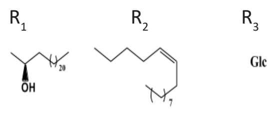
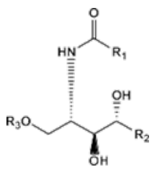
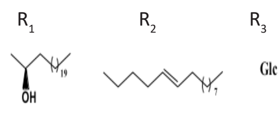
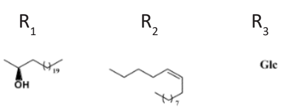
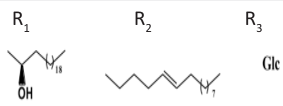
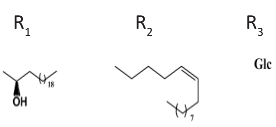
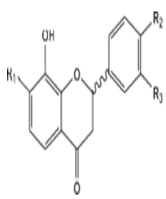
Table 2: Phytochemical Composition of *B. Bipinnata.*

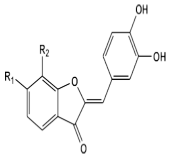
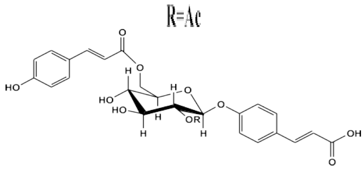
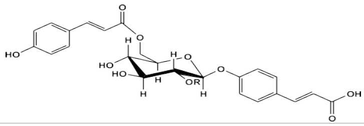
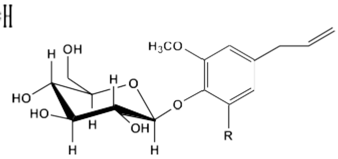
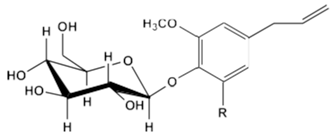
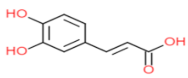
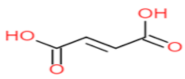
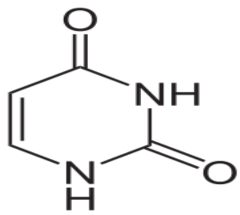
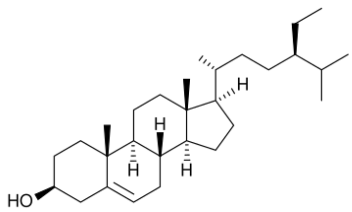
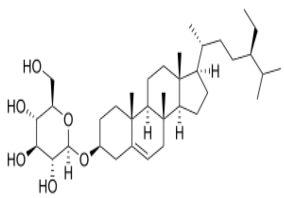
Plant	Tannin (mg/100 g)	Alkaloid (%)	Flavonoid (%)	Saponins (%)	Oxalate (%)	Cyanogenic Glycoside (mg/100 g)	Phenols (mg/g)	Lipid (%)
Vegetative part	930±4.714	0.231	5.09	7.09	2.97	520±0.275	4.04±1.6750	6.4
Reproductive part	865±0.9428	0.201	8.2	9.8	1.76	465±1.3568	5.98±0.7979	5.76

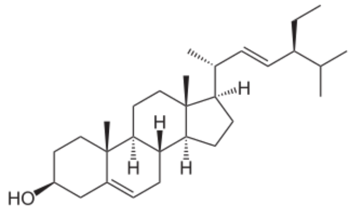
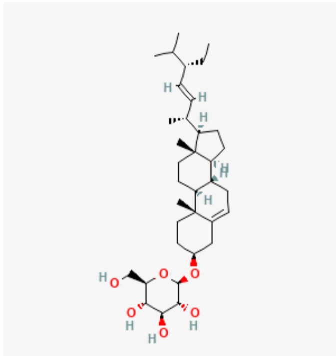
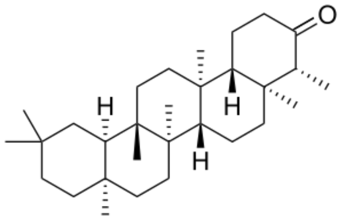
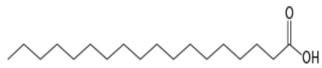
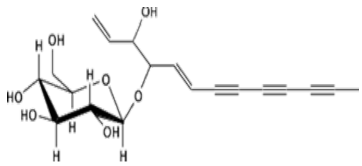
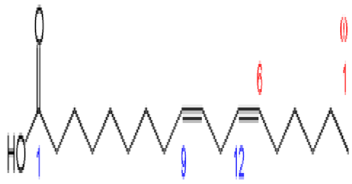
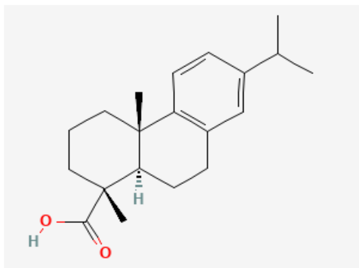
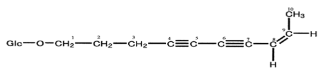
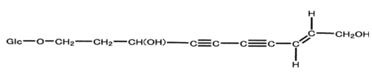
Compound isolation

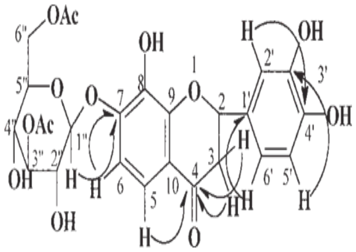
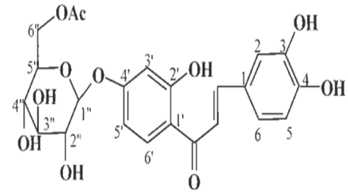
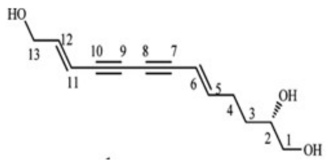
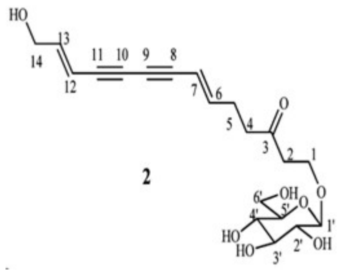
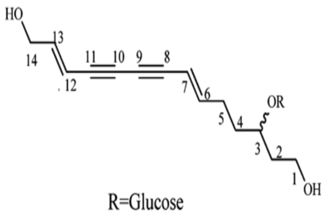
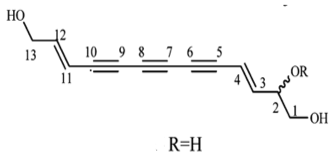
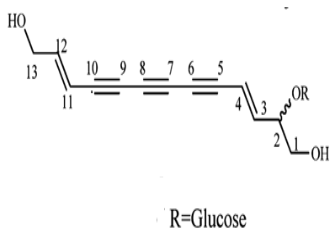
The mass spectrum of linoleic acid isolated from *B. bipinnata* shows a peak at m/z 280.4, which is consistent with the formula $C_{18}H_{32}O_2$. This polyunsaturated omega-6 fatty acid is mainly insoluble in water, however it is soluble in organic solvents and colourless or white. Dehydroabietic acid is another active molecule with the chemical formula $C_{20}H_{28}O_2$ with a molecular ion peak at m/z 300. It is a pyran-2,4-dione in which positions 3 and 6 have been replaced, respectively, with acetyl and methyl groups. Dehydroabietic acid belongs to the category of pyrone derivatives, which are heterocyclic substances made up of an oxygen atom, a ketone, and an unsaturated six-membered ring [20]. Linoleic acid is particularly significant for illness prevention, and it can prevent a number of allergic, depressive symptoms, cardiac, and some neurological conditions [21]. It has also been connected to improved membrane function and decreased blood cholesterol [22]. Linoleic acid has the most potent bactericidal effect against H. pylori, completely eliminating the germs via increasing the permeability of its outer membrane. This was validated by measuring released ATP, which indicated increased plasma membrane permeability and caused bacterial cell death. Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) revealed that linoleic acid altered the bacterial membrane's structure in under five minutes, affecting its integrity and resulting in cytoplasmic leakage [23]. One common chemical defence agent is dehydroabietic acid. It functions biologically in a variety of ways, including cytotoxic, antitumor, antiulcer, antiplasmodial, cardiovascular, antibacterial, antioxidant, and anti-inflammatory properties [24]. During the study on *B. bipinnata*, thirty-eight compounds were found and their structures were reported. These compounds included nine ceramides, thirteen flavonoids, five phenylpropanoids, four aliphatics, one pyrimidine, four steroids, one triterpenoid, and one polyacetylene. First, nine known compounds (4-9, 25, 26, 38) and five new compounds (1-3, 10-11) were taken out of the Bidens genus. Furthermore, new descriptions are provided for *B. bipinnata* Linn. compounds 12, 13, 16-21, and 30-34. The results are summarized in Table 3 [25]. A new flavanone glucoside named bidenoside F and a chalcone glucoside called bidenoside G have been isolated and structurally elucidated from *B. Bipinnata* [27]. The polyacetylenes that were isolated from *B. bipinnata* exhibited a range of characteristics and chemical makeups. Compound 1-also known as (2S)-(5E,11E)-tridecadiene-7,9-diyne-1,2,13-triol-displayed distinct spectrum characteristics that provided insight into its structure and composition. Compound 2, also known as (6E, 12E)-3-oxo-tetradecadiene-8,10-diyne-14-hydroxyl-1-O-b-D-glucopyranoside, had structural characteristics with the addition of a glucopyranose group. Both of these compounds and their recognized variants were subjected to in vitro testing to determine their cytotoxic and anti-inflammatory activities. Compounds 1, 5, and 6 had strong anti-inflammatory properties by reducing IL-1 and TNF-a levels, however none of them shown cytotoxicity against tested cancer cell lines [28]. Extract from *B. bipinnata* yielded a variety of chemicals with different structures. Compound 1 was recognized as a novel chlorinated flavonoid that is seldom seen in plants, namely 3,6,8-trichloro-5,7,3',4'-tetrahydroxyflavone. The unique chemical formula of compound 2, a phenylpropanoid glycoside, was C28H28O12. Compound 3, which exhibits unique structural properties, was identified as 8,3',4'-trihydroxyflavone-7-O-β-D-glucopyranoside. Furthermore, the compounds isolated from *B. bipinnata's* ethyl acetate fraction were tested for their capacity to impede α-amylase activity. Compound 6, isookanin, in particular, showed notable inhibitory action, with an IC50 value of 0.447 mg/ml [29]. The investigation into *B. bipinnata* effectiveness against hyperlipidemia involved analyzing its active components' tissue distribution and conducting molecular docking research. Compound isolation unveiled key molecules such as gallic acid, protocatechuic acid, rutin, hyperoside, Bipinnate Polyacetylenicloside (BPC), luteolin, and quercetin, recognized for their potential in treating hyperlipidemia. These compounds displayed significant distribution in liver tissue and exhibited binding affinity with multiple target proteins, suggesting their therapeutic promise against hyperlipidemia. Furthermore, the isolated polyacetylenes demonstrated noteworthy anti-inflammatory properties in vitro, underscoring their broader medicinal potential [30].

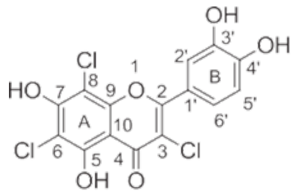
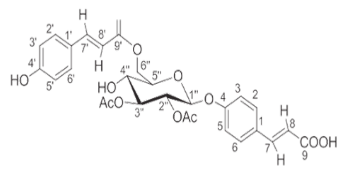
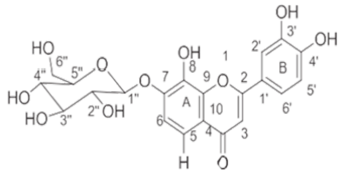
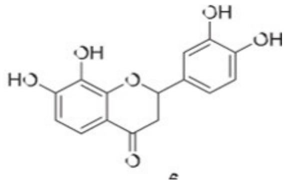
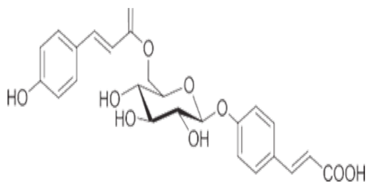
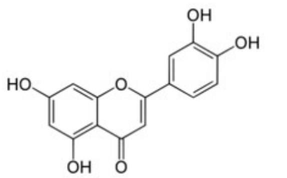
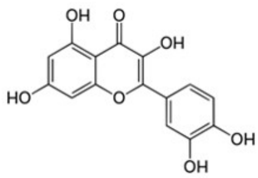
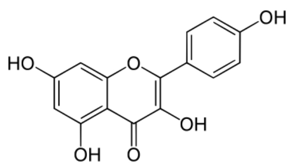
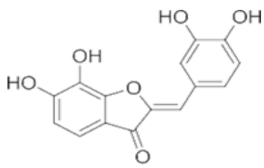
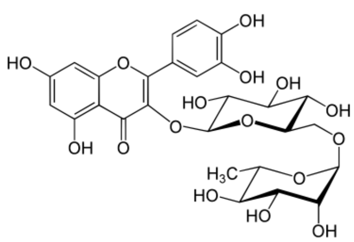
Table 3: Phytoconstituents of *B. Bipinnata.*

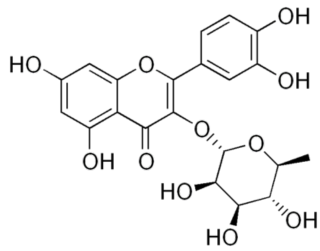
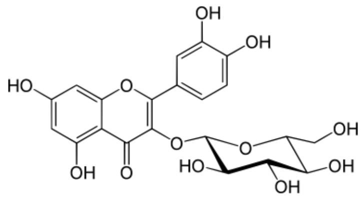
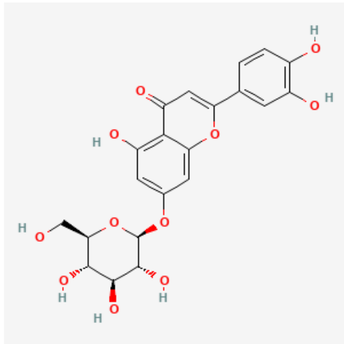
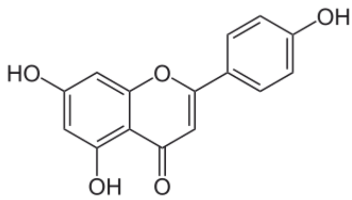
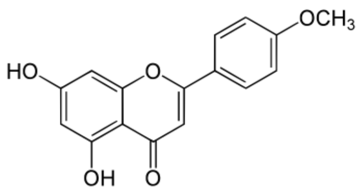
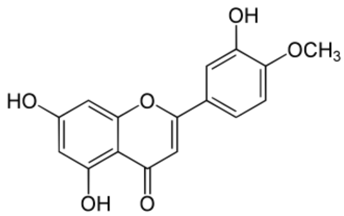
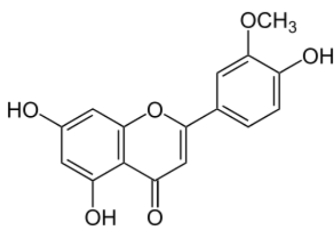
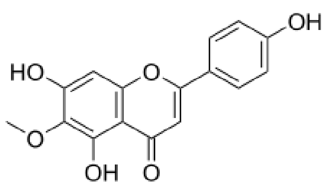
S.N.	Name	IUPAC Name	Class of Compound	Structure	References
1	-	(2S,3S,4R,8E)-2-(2'R,3'R-Dihydroxytricosanoylamino)-8-octadecene-1,3,4-triol			[25]
2	-	(2S,3S,4R,8E)-2-(2'R-Hydroxytetracosanoylamino)-10-octadecene-1,3,4-triol			[25]
3	-	(2S,3S,4R,8E)-2-(2'R-Hydroxytricosanoylamino)-10-octadecene-1,3,4-triol			[25]
4	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxytetracosanoylamino)-8-octadecene-1,3,4-triol			[25]
5	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxytricosanoylamino)-8-octadecene-1,3,4-triol			[25]
6	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxyheptadecanoylamino)-8-octadecene-1,3,4-triol	Ceramide 		[25]
7	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxydocosanoylamino)-8-octadecene-1,3,4-triol			[25]
8	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxyhexadecanoylamino)-8-octadecene-1,3,4-triol			[25]
9	-	1-O-β-D-Glucopyranosyl-(2S,3S,4R,8E)-2-(2'R-Hydroxyheptadecanoylamino)-8-octadecene-1,3,4-triol			[25]
10	-	(2R)-Isookanin-4'-methoxy-7-O-β-D-glucopyranoside	Flavonoid 	R_1 OGlc, R_2 OCH_3, R_3 OH	[25]
11	-	(2S)-Isookanin-4'-methoxy-7-O-β-D-glucopyranoside		R_1 OGlc, R_2 OCH_3, R_3 OH	[25]
12	-	(2R)-Isookanin-3'-methoxy-7-O-β-D-glucopyranoside		R_1 OGlc, R_2 OH, R_3 OCH_3	[25]

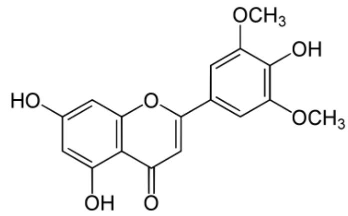
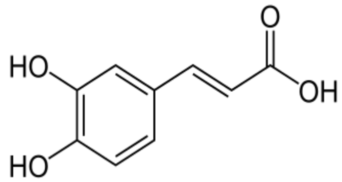
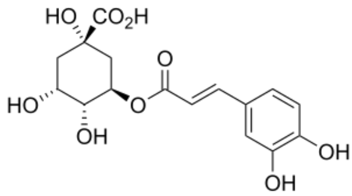
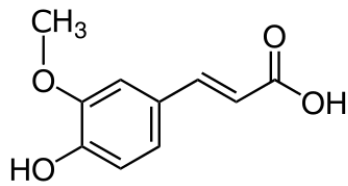
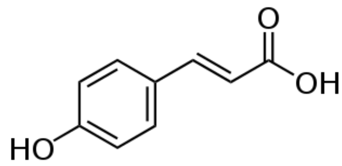
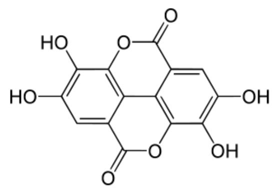
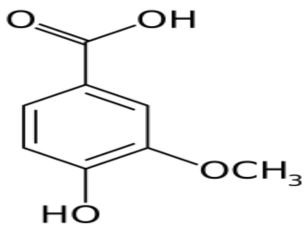
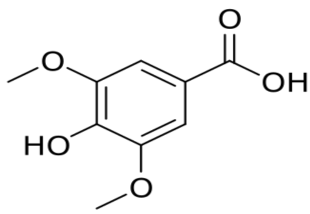
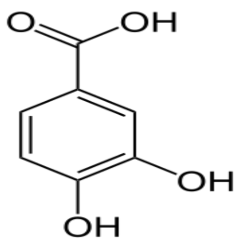
13	-	(2S)-Isookanin-3'-methoxy-7-O-β-D-glucopyranoside		R_1 R_2 R_3 OGlc OH OCH_3	[25]
14	-	(2R)-7,8,3',4'-Tetrahydroxyflavone-3'-methoxy-7-O-β-D-glucopyranoside		R_1 R_2 R_3 OH OH OH	[25]
15	-	(2S)-7,8,3',4'-Tetrahydroxyflavone-3'-methoxy-7-O-β-D-glucopyranoside		R_1 R_2 R_3 OH OH OH	[25]
16	-	E-6-O-β-D-Glucopyranosyl-6,7,3',4'-tetrahydroxyaurone	Flavonoid 	R_1 R_2 OGlc OH	[25]
17	-	7-O-β-D-Glucopyranosyl-6,7,3',4'-tetrahydroxyaurone		R_1 R_2 OH OGlc	[25]
18	Maritimetin	3',5-Dihydroxy-4',6,7-trimethoxyflavone		R_1 R_2 OH OH	[25]
19	-	E-4-O-(2''-O-diacetyl-6''-O-p-coumaroyl-β-D-glucopyranosyl)-p-coumaric acid	Phenylpropanoid	R=Ac 	[25]
20	-	4-O-(6''-O-p-Sementoncoacyl-β-D-glucopyranosyl)-p-coumaric acid	Phenylpropanoid	R=H 	[25]
21	Citrusin C	4'-Hydroxy-3,3',4',5,6,7-hexamethoxyflavone	Phenylpropanoid	R=H 	[25]
22	-	4-Allyl-2,6-dimethoxyphenyl glucoside	Phenylpropanoid	$R=OCH_3$ 	[25]
23	Caffeic Acid	3-(3,4-Dihydroxyphenyl)-2-propenoic acid	Phenylpropanoid		[25]
24	Fumaric Acid	(2E)-But-2-enedioic acid	Aliphatic		[25]
25	Uracil	2,4-Dioxopyrimidine	Pyrimidine		[25]
26	β-Sitosterol	(3β)-Stigmast-5-en-3-ol	Steroid		[25]
27	Daucosterol	(3β)-Stigmast-5-en-3-yl β-D-glucopyranoside	Steroid		[25]

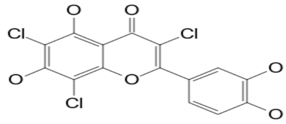
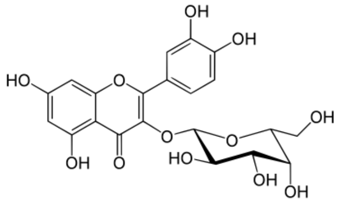
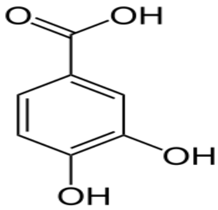
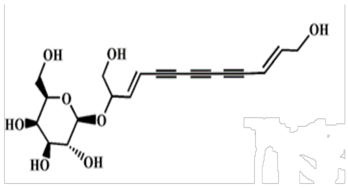
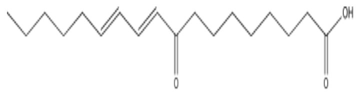
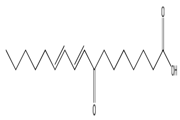
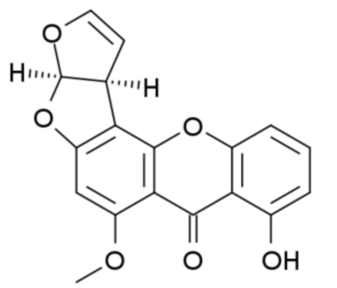
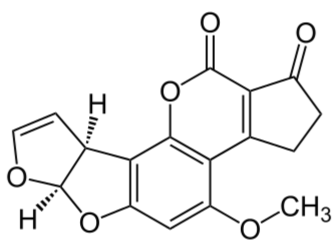
28	Stigmasterol	(22E)-Stigmasta-5,22-dien-3β-ol	Steroid		[25]
29	Stigmasterol-β-D-glucopyranoside	(3β,22E)-Stigmasta-5,22-dien-3-yl β-D-glucopyranoside	Steroid		[25]
30	Friedelin	Friedo-olean-3-one	Triterpenoid		[25]
31	Stearic Acid	Octadecanoic acid	Aliphatic		[25]
32	Hexadecanol	Hexadecan-1-ol	Aliphatic		[25]
33	n-Heneicosane	Heneicosane	Aliphatic		[25]
34	-	(5E)-Trideca-1,5-dien-7,9,11-triyne-3,4-diol-4-O-β-D-glucopyranoside	Polyacetylene		[25]
35	Linoleic Acid	cis, cis-9,12-Octadecadienoic acid	Fatty acid (Polyunsaturated omega-6 fatty acid)		[20]
36	Dehydroabietic Acid	4aS,10aS)-8,8-Dimethyl-4,4a,9,10,10a,10b-hexahydro-7-oxophenanthrene-2-carboxylic acid	Diterpenoid		[20]
37	Bidenoside C	(2Z)-deca-2-ene-4,6-diyn-1-O-β-D-glucopyranoside	Acetylenic Glucoside		[26]
38	Bidenoside D	(2E)-deca-2-ene-4,6-diyn-3,10-dihydroxy-1-O-β-D-glucopyranoside	Acetylenic Glucoside		[26]

39	Bidenoside F	5,7-dihydroxy-2-(4-hydroxyphenyl)-6-methoxy-8-(2,4-dihydroxyphenyl)-4H-1-benzopyran-4-one 7-O-(3',6'-di-O-acetyl)-β-D-glucopyranoside	Flavanone glucoside		[27]
40	Bidenoside G	3,4,2',4'-tetrahydroxychalcone-4'-O-(6''-O-acetyl)-β-D-glucopyranoside	Chalcone glucoside		[27]
41	(2S) (5E,11E)-Tridecadiene-7,9-diyne-1,2,13-triol	(2S,5E,11E)-Trideca-5,11-dien-7,9-diyn-1,2,13-triol	Polyacetylene		[28]
42	(6E,12E)-3-oxo-tetradecadiene-8,10-diyne-14-hydroxyl-1-O-β-D-glucopyranoside	(6E,12E)-3-Oxo-tetradeca-6,12-dien-8,10-diyn-14-yl β-D-glucopyranoside	Polyacetylene		[28]
43	(6E,12E)-Tetra-decadiene-8,10-diyne-1,3,14-triol	(6E,12E)-Tetradeca-6,12-dien-8,10-diyn-1,3,14-triol	Polyacetylene		[28]
44	(6E,12E)-Tetradecadiene-8,10-diyne-1,14-diol-3-O-β-D-glucopyranoside	(6E,12E)-Tetradeca-6,12-dien-8,10-diyn-1,14-diol-3-O-β-D-glucopyranoside	Polyacetylene		[28]
45	(3E,11E)-Tride-cadiene-6,8,10-atriyne-1,2,13-triol	(3E,11E)-Trideca-3,11-dien-6,8,10-triyn-1,2,13-triol	Polyacetylene		[28]
46	(3E,11E)-Tridecadiene-6,8,10-atriyne-1,13-diol-2-O-β-D-glucopyranoside	(3E,11E)-Trideca-3,11-dien-6,8,10-triyn-1,13-diol-2-O-β-D-glucopyranoside	Polyacetylene		[28]

47	3,6,8-Trichloro-5,7,3',4'-tetrahydroxyflavone	3,6,8-Trichloro-5,7,3',4'-tetrahydroxy-2-phenyl-4H-1-benzopyran-4-one	Chlorinated Flavonoid		[29]
48	p-Coumaroyl glucoside	1-O-(E)-4-hydroxycinnamoyl-6-O-(E)-4-hydroxycinnamoyl-2,3-di-O-acetyl-β-D-glucopyranose	Phenylpropanoid Glycoside		[29]
49	Apigenin-7-O-β-D-glucopyranoside	5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one 7-O-β-D-glucopyranoside	Flavone Glycoside		[29]
50	Luteolin	5,7,3',4'-Tetrahydroxyflavone	Flavonoid		[29,30]
51	5,7,3',4'-Tetrahydroxy-6-methoxyflavone	6-Methoxy-5,7,3',4'-tetrahydroxy-2-phenyl-4H-1-benzopyran-4-one	Flavonoid		[29]
52	3',4'-Dihydroxyflavone	3',4'-Dihydroxy-2-phenyl-4H-1-benzopyran-4-one	Flavonoid		[29]
53	Quercetin	2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one	Flavonol		[29]
54	Kaempferol	3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one	Flavonol		[29]
55	Isorhamnetin	3,5,7-Trihydroxy-2-(4-hydroxy-3-methoxyphenyl)-4H-1-benzopyran-4-one	Flavonol		[29]
56	Rutin	5,7,3',4'-Tetrahydroxyflavonol-3-rutinoside	Flavonol Glycoside		[29,30]

57	Quercitrin	5,7,3',4'-Tetrahydroxyflavonol-3-rhamnoside	Flavonol Glycoside		[29,30]
58	Isoquercitrin	5,7,3',4'-Tetrahydroxyflavonol-3-glucoside	Flavonol Glycoside		[25,29]
59	Luteolin-7-O-β-D-glucopyranoside	5,7,3',4'-Tetrahydroxyflavone 7-O-β-D-glucopyranoside	Flavone Glycoside		[29]
60	Apigenin	5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one	Flavone		[29]
61	Acacetin	5,7-Dihydroxy-4'-methoxyflavone	Flavone		[29]
62	Diosmetin	5,7,3'-Trihydroxy-4'-methoxyflavone	Flavone		[29]
63	Chrysoeriol	5,7,3'-Trihydroxy-4'-methoxyflavone	Flavone		[29]
64	Hispidulin	5,7,4'-Trihydroxy-6-methoxyflavone	Flavone		[29]

65	Tricin	5,7,4'-Trihydroxy-3',5'-dimethoxyflavone	Flavone		[29]
66	Caffeic acid	(E)-3-(3,4-Dihydroxyphenyl)prop-2-enoic acid	Phenolic Acid		[29]
67	Chlorogenic acid	(1S,3R,4R,5R)-3-{[(2Z)-2-(3,4-Dihydroxyphenyl)ethenoyl]oxy}-1,4,5-trihydroxycyclohexane-1-carboxylic acid	Phenolic Acid		[29]
68	Ferulic acid	(E)-3-(4-Hydroxy-3-methoxyphenyl)prop-2-enoic acid	Phenolic Acid		[29]
69	p-Coumaric acid	(E)-3-(4-Hydroxyphenyl)prop-2-enoic acid	Phenolic Acid		[29]
70	Gallic acid	3,4,5-Trihydroxybenzoic acid	Phenolic Acid		[29,30]
71	Vanillic acid	4-Hydroxy-3-methoxybenzoic acid	Phenolic Acid		[29]
72	Syringic acid	4-Hydroxy-3,5-dimethoxybenzoic acid	Phenolic Acid		[29]
73	Protocatechuic acid	3,4-Dihydroxybenzoic acid	Phenolic Acid		[29]

74	3,6,8-Trichloro-5,7,3',4'-tetrahydroxyflavone	3,6,8-Trichloro-5,7,3',4'-tetrahydroxy-2-phenyl-4H-1-benzopyran-4-one	Chlorinated Flavonoid		[29]
75	Hyperoside	3-(β-D-Galactopyranosyloxy)-3',4',5,7-tetrahydroxyflavone	flavonol glycoside		[25,30]
76	Protocatechuic acid	3,4-Dihydroxybenzoic acid	Phenolic		[30]
77	Bipinnat poly-acetylenicloside	-	-		[30]
78		9-oxo-(10E, 12E) octadecadienoic acid	Oxo fatty acid		[31]
79		8-oxo-(9E, 11E)-octadecadienoic acid	Oxo fatty acid		[31]
80	Sterigmatocystin	(3aR,12cS)-8-Hydroxy-6-methoxy-3a,12c-dihydro-7H-furo[3',2':4,5]furo[2,3-c]xanthen-7-one	Coumarin derivative (Furanocoumarin)		[31]
81	Aflatoxin B1	(6aR,9aS)-4-Methoxy-2,3,6a,9a-tetrahydrocyclopenta[c]furo[3',2':4,5]furo[2,3-h][1]benzopyran-1,11-dione	Coumarin derivative (Furanocoumarin)		[31]

Pharmacological Activity

Antibacterial activity

Antibiotic resistance has emerged as a major worldwide health concern in recent years, particularly in agricultural settings. In the current investigation, Campylobacter jejuni revealed 100% resistance to Ampicillin, which is consistent with earlier studies that have documented amoxicillin-resistant commensal Campylobacter. Amoxicillin alone was unsuccessful, while Co-amoxiclav revealed great activity against amoxicillin-resistant bacteria [32]. This underscores the importance of judicious antibiotic use in the cattle industry, as the emergence of high resistance necessitates careful management [33]. Similarly, Klebsiella species demonstrated resistance to ampicillin while remaining vulnerable to cephalosporins, aminoglycosides, and quinolones [34].

B. bipinnata demonstrated significant efficacy against various tested bacteria, particularly those isolated from cattle waste. This suggests its potential in preventing cattle infections caused by these organisms [35]. *B. bipinnata* exhibits notable antibacterial activity due to compounds such as caffeic acid [36], chlorogenic acid [37], ferulic acid [38], gallic acid [39], and quercetin [40]. *B. bipinnata* contains two significant antibacterial substances: 16-pregnenolone as well as 9-octadecenoic acid (Z)-methyl ester.16-Pregnenolone, a steroidal molecule, showed excellent antibacterial activity against Staphylococcus aureus, with a MIC50 of 72 µg/mL. In contrast, 9-Octadecenoic acid (Z)-methyl ester had a larger MIC50 value of nearly 250 µg/mL, suggesting decreased potency. Furthermore, the pharmacological efficiency of 16-pregnenolone is supported by its amphiphilic nature, which allows it to break bacterial membranes by targeting particular membrane components and thereby exerting its bactericidal effects [41].

Antitumor Activity

Human hepatocellular carcinoma (HepG2) and cervical cancer (Hela) cell lines were significantly inhibited by extracts of *B. bipinnata* in vitro. The MTT test was used to measure the extract's effect on cell growth at different concentrations, which led to the calculation of IC50 values. According to our findings, HepG2 and Hela cells are significantly inhibited, with the greatest suppression shown after 48 hours of therapy. One has an IC50 value of 14.80 µg/mL while the other is 13.50 µg/mL. The extract of *B. bipinnata* showed promising inhibitory effects on many cell lines, suggesting that it might be used in future studies [42]. In previous research, phytochemicals found in *B. bipinnata* were shown to have anticancer effects. Plant compounds that may have medicinal significance include maritimetin, citrusin C, fumaric acid, apigenin, luteolin, quercetin, kaempferol, dehydroabietic acid, and caffeic acid. The plant's effectiveness against cancer, and specifically U14 cells from cervical carcinoma, has been brought to light in recent investigations. The MTT test was used in in vitro research to show that *B. bipinnata* extract inhibits U14 cell growth in a way that is dependent on both dose and time. At 80µg/L, the inhibition rate was 70.44%. Extensive tumor growth inhibition and life extension advantages were shown in in vivo testing conducted on mice with U14 solid and ascites tumors. With a tumor suppression rate of 49.13% in high-dose groups and a life extension rate of 63.63% for ascites tumors, the extract clearly shows promise as an adjuvant therapy for cancer diagnosis and treatment [43]. One of the most well-known flavonoids found in *B. bipinnata*, isoquercitrin, has strong pharmacological effects, especially in the fight against liver cancer. Isoquercitrin has shown a dose- and time-dependent ability to inhibit the proliferation of HepG2 and Hep3B, two human liver cancer cell lines. At concentrations between 100 and 800 µM, there was a significant decrease in cell viability. A concentration-dependent increase in apoptotic cells was shown using Annexin V-FITC/PI double labelling flow cytometry, demonstrating that the chemical causes apoptosis. In addition to its antiproliferative effects, isoquercitrin causes cell cycle arrest in the G1 phase. The activation of caspases -3, -8, and -9 isoquercitrin's apoptotic action, suggesting that both intrinsic and extrinsic mechanisms are involved. And by increasing JNK phosphorylation and lowering ERK and p38MAPK phosphorylation, isoquercitrin modifies the MAPK transmission pathway. There is a reduction in the expression of protein kinase C (PKC), which is essential for the continued growth and survival of cells. Isoquercitrin significantly inhibited the growth of transplanted liver tumors in nude mice, lending credence to these results in in vivo research. The many paths that isoquercitrin can follow demonstrate its therapeutic potential and point to *B. bipinnata* as a plant that could provide bioactive compounds with strong anticancer effects [44].

Antidiarrhoeal Activity

B. bipinnata methanol extract showed significant antidiarrheal effectiveness in many pharmacological studies. *B. bipinnata* significantly reduced castor oil-induced diarrhoea in rats, according to a study that compared the antidiarrheal effects of several plant extracts. The number of soft faecal pellets was considerably reduced in the group that received the extract at dosages of 200 mg/kg and 400 mg/kg, in comparison to the control group. In addition, while measuring gastrointestinal motility with a charcoal meal, the longer the charcoal rods stayed in the test tube after consuming a higher dosage of *B. bipinnata* extract, suggesting less transit time through the intestines. To further demonstrate its antidiarrheal properties, the methanol extract dose-dependently reduced motility in isolated rabbit duodenum. The presence of tannins, flavonoids, carbohydrates, lactones, unsaturated sterols/triterpenes, and proteins/amino acids was shown by phytochemical analysis. These compounds are likely responsible for the antidiarrheal effects observed [45].

Anti-inflammatory Activity

Among the several pharmacological effects of *B. bipinnata* are its cytotoxic and anti-inflammatory properties. Flavonoids, sesquiterpene lactones, polyacetylenes, and other bioactive compounds are present in the plant and help explain its medicinal effects. Along with four other polyacetylenes that were previously reported, two more, (2S) (5E,11E)-tridecadiene-7,9-diyne-1,2,13-triol and (6E,12E)-3-oxo-tetradecadiene-8,10-diyne-14-hydroxyl-1-O-β-D-glucopyranoside, have demonstrated an impressive anti-inflammatory impact, joining four previously identified polyacetylenes. These substances block macrophage cells from responding to lipopolysaccharide (LPS) by releasing TNF-α and IL-1β, which means they have anti-inflammatory qualities. Even though these polyacetylenes were quite effective in reducing inflammation, they showed very little cytotoxicity when tested against human cancers of the cervical region (HeLa), human carcinomas of the liver (HepG-2), and human cancerous breast cells (MCF-7). Extensive research has shown that HUVECs, when exposed to serum from individuals with Henoch-Schönlein purpura (HSP), release many cytokines that promote inflammation, including Nitric Oxide (NO), interleukin-8 (IL-8), and Tumour Necrosis Factor-Alpha (TNF-α) [46]. Its significant anti-inflammatory activity is mainly due to the total flavonoid content (TFB) of *B. bipinnata*. Research has demonstrated that when stimulated with sera from Henoch-Schönlein purpura (HSP) patients, human umbilical vein endothelial cells (HUVECs) produce a number of pro-inflammatory cytokines, such as Nitric Oxide (NO), interleukin-8 (IL-8), and tumour necrosis factor-alpha (TNF-α). However, when treated with TFB, these cytokines are effectively inhibited. In addition, two important mediators of the inflammatory response, nuclear factor-kappa B (NF-κB) and fractalkine, are inhibited in their mRNA and protein production by TFB. According to these studies, TFB decreases inflammation by blocking NF-κB signalling pathways, which leads to cytokine production [47]. *B. bipinnata* flavonoids (BBTF) may have anti-inflammatory effects due to their capacity to reduce endothelial cell production of inflammatory mediators [48].

Antioxidant Activity

Recent pharmacological studies have highlighted the plant's diverse bioactivities, attributing its therapeutic potential primarily to its rich flavonoid content. The total flavonoids from *B. bipinnata* (BBTF) have demonstrated significant antioxidant activities [48].

B. bipinnata, possess antioxidative effects. The antioxidative properties of *B. bipinnata* are attributed to its ability to inhibit linoleic acid peroxidation and scavenge DPPH radicals. Five major flavonoids have been isolated from the plant's floral ethanol extract: sulfuretin, butein, 7,8,3',4' tetrahydroxyflavanone, maritimetin, and okanin. Sulfuretin and butein are highly effective chemicals that show significant antioxidative activity. These results validate the traditional usage of *B. bipinnata* in the management of oxidative stress by highlighting its potential as a natural source of antioxidants [49]. It has been demonstrated that the flavonoid-rich extract of *B. bipinnata* shields β-cells of the pancreas against oxidative stress-triggered apoptosis. The effect of the extract (BBTF) on INS-1 cells exposed to hydrogen peroxide (H2O2), a common oxidative stressor, was examined in this work. BBTF pretreatment increased β-cell viability, lowered ROS production, and decreased apoptosis. The underlying processes were unveiled by the modulation of apoptosis-related proteins: BBTF reduced levels of the pro-apoptotic protein Bax and increased levels of the anti-apoptotic protein Bcl-2. It also reduced the phosphorylation of stress-related kinases (JNK, ERK, and p38) and lowered the production of death receptor-related proteins (Fas and FasL), resulting in a reduction in caspase-8, caspase-9, and caspase-3 activity. The ability of the *B. bipinnata* extract, which is rich in flavonoids, to protect pancreatic β-cells from oxidative damage and ensure their survival and function might make it useful in managing diabetes [50].

Antidiabetic Activity

The phenolic components of *B. bipinnata* are primarily responsible for the significant anti-diabetic effects of its ethyl acetate extract. The enzyme α-amylase, which converts starch to glucose, is inhibited by isookanin. Isookanin can regulate postprandial blood glucose levels by inhibiting α-amylase, which makes it a useful treatment for diabetes. This study highlights the medicinal potential of *B. bipinnata*, opening the door for its application in the creation of functional foods and pharmaceutical formulations intended to manage diabetes and its related symptoms [51]. *B. bipinnata* (BBTF) flavonoids in their whole form have a regulating impact on insulin resistance through the PI3K/AKT1/GLUT4 signaling pathway [48].

Antihyperlipidemic Effect

B. bipinnata extracts have been proven to significantly low-density lipoprotein cholesterol (LDL-C) and lower blood total cholesterol (also known as TC), while increasing HDL-C. Furthermore, these extracts increase antioxidant enzyme activity, such as superoxide dismutase (SOD), while decreasing oxidative stress indicators including malonaldehyde (MDA) and Nitric Oxide (NO). The underlying processes involve modification of the PPAR signalling pathway, which is critical for regulating lipid metabolism. These findings imply that *B. bipinnata* may be an effective natural therapy for treating hyperlipidemia, with potential uses in decreasing the risk of cardiovascular disease [52]. *B. bipinnata* exhibits significant antihyperlipidemic activity, making it a promising candidate for managing hyperlipidemia, a major risk factor for cardiovascular diseases. Work has indicated that the whole extract of *B. bipinnata* is capable of efficiently controlling blood lipid levels. The extract significantly reduces blood levels of Triglycerides (TG), lower-density lipoprotein cholesterol (LDL-C), and Total Cholesterol (TC) in hyperlipidemic rat models, while increasing HDL-C levels. This lipid-regulating effect is primarily attributed to several active compounds, including gallic acid, protocatechuic acid, rutin, hyperoside, bipinnata polyacetylenicloside, luteolin, and quercetin. These compounds exhibit diverse chemical structures and are predominantly distributed in the liver, which is a key organ in lipid metabolism . Additionally, molecular docking studies have identified significant binding affinities between these compounds and target proteins such as HMGCR, NR3C1, CYP1A2, RXRA, CES1, HSD11B1, and CYP1A1, suggesting their potential mechanisms in modulating lipid metabolism and exerting antihyperlipidemic effects [30].

Antiarthritic activity

Total flavonoids from *B. bipinnata* (TFB) have been proven in trials to alleviate adjuvant-induced arthritis in rats by reducing synovial hyperplasia, inflammatory cell infiltration, and cartilage breakdown. TFB inhibits the synthesis of cytokines that trigger inflammation such as IL-1β, TNF-α, and IL-6. TFB also causes synovial apoptosis, as seen by an increase in TUNEL-positive cells, DNA fragmentation, and caspase-3 activity. These findings demonstrate that TFB from *B. bipinnata* may offer a therapeutic method for treating inflammatory illnesses like RA due to its dual anti-inflammatory and pro-apoptotic activity [53].

Hepatoprotective Effect

B. bipinnata's total flavonoids (TFB) showed substantial hepatoprotective benefits. According to experimental research, TFB has strong antioxidant capabilities that play an important role in preventing oxidative stress-induced liver damage. TFB treatment has been demonstrated to diminish high liver and spleen indices, serum transaminase levels, and liver fibrosis indicators including hyaluronic acid and type III procollagen. Lipid peroxidation is decreased because TFB increases levels of glutathione peroxidase and superoxide dismutase, two antioxidant enzymes. TFB protects against liver fibrosis by inhibiting the expression of NF-κB, α-SMA, and TGF-β1 genes, all of which play important roles in the fibrogenic process. These findings indicate that TFB might be a viable therapeutic drug in the treatment of liver fibrosis by reducing oxidative stress and regulating important fibrogenic pathways [54].

Neuropharmacological Activity

The pharmacological activity of *B. bipinnata*, often called Spanish needles or beggar's ticks, is substantial and includes neuroprotective properties. Research on rats has shown that total flavones from Bidens bipinnata L. (TFB) can prevent brain harm following experimental intracerebral hemorrhage. Reducing cerebral edema, improving microcirculation, and increasing antioxidant defenses are the primary determinants of this neuroprotective impact. Malondialdehyde (MDA) and Nitric Oxide (NO), two markers of oxidative stress and inflammation, are decreased by TFB treatment, while Superoxide Dismutase (SOD) activity is greatly increased. By reducing oxidative damage and enhancing neurological outcomes, these flavones forestall lipid peroxidation and NO production [55].

Conclusion

B. bipinnata is a tall annual plant that grows in low-temperature tropical locations all over the world. It has green leaves, yellow or white blooms, and brownish-blackish seeds. You may find it growing near roadside. *B. bipinnata* is a very nutritious food source that has an extensive record of usage in conventional healthcare. Research on *B. bipinnata* has been conducted in several disciplines, including botany, ethnomedicine, pharmacology, and phytochemistry. The wide variety of bioactive substances found in B. bipinnata, including tannins, terpenoids, vaginitis, candidiasis, stomachaches, dysentery, vaginitis, and bronchial illnesses, as well as many others, have long been utilized for medicinal purposes. Thanks to these phytoconstituents, it can effectively cure a variety of diseases and conditions, including as cancer, inflammation, diabetes, bacterial infections, gastrointestinal issues, and cardiovascular maladies. The therapeutic uses of *B. bipinnata* are highlighted, and its medicinal potential is examined in connection to its recognized phytochemicals. However, due to the possibility of hypoglycemia, hypotension, and allergic responses, it should be used with caution. Complete validation and exploitation of *B. bipinnata's* therapeutic value requires more study and clinical studies.

Future Perspectives

To enhance its use in contemporary medicine, future studies on *B. bipinnata* should concentrate on a few important areas. First things first: we need more comprehensive phytochemical research to identify and define the active ingredients that are therapeutically useful. Secondly, in order to have a better understanding of the medications' metabolism, excretion, distribution, and absorption, thorough pharmacokinetic and pharmacodynamic investigations should be carried out. To conclude, the effectiveness and safety of *B. bipinnata* in human populations can only be ascertained by conducting large-scale clinical studies. More research into its synergistic effects with other medicinal herbs or traditional pharmaceuticals could lead to exciting new possibilities in combination treatment. Last but not least, new treatments utilizing *B. bipinnata* can be developed by combining traditional knowledge with state-of-the-art scientific research.

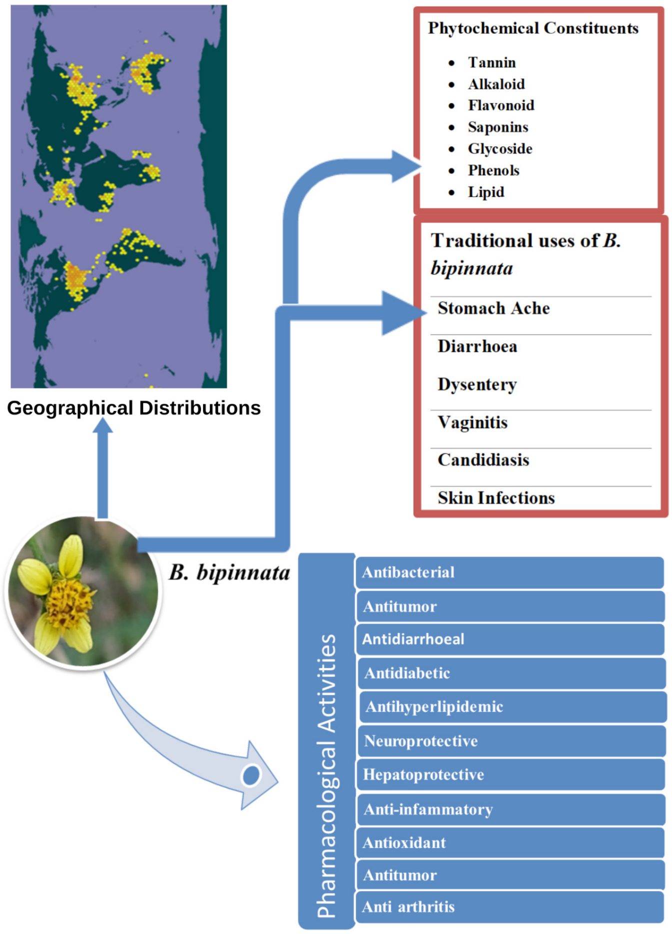


Figure 2: Phytochemical & pharmacological profile of *B.bipinnata*

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