Journal of Pharmaceutical and Biological Sciences 2022;10(2):57–67

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Journal of Pharmaceutical and Biological Sciences

Journal homepage: https://www.jpbs.in/

Review Article

Review on phytochemical composition and pharmacological activities of *Bixa orellana* L.

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ARTICLE INFO

Article history:
Received 01-10-2022
Accepted 28-12-2022
Available online 27-01-2023

Keywords:
Bixa orellana
Annatto
Bixin
Carotenoids
Pharmacological Activity

ABSTRACT

Bixa orellana commonly known as Annatto is a lipstick tree belonging to the family *Bixaceae.* Indigenous populations in Brazil and other tropical nations have employed *B. orellana L.* for a variety of therapeutic purposes which is also known as "*sappiravirai*". The essential natural apocarotenoid obtained from *B. orellana* seeds namely bixin is broadly applied as a cosmetic and textile colorant. The carotenoids, which contribute to more than 80% of the annatto seed coat are responsible for the color orange-red. It is well known for its medicinal value and as a coloring agent. Annatto is used in food dye, body paint and the treatment of heartburn and it also reduces inflammation and blood sugar. The various parts of this plant has been reported to show many therapeutic indications like anti-bacterial, anti-hyperglycaemic, anti-histaminic, anti-diarrheal, anti-cancer, anti-inflammatory and anti-oxidant activities. Carotenoids, apocarotenoids, terpenes, terpenoids, sterols and aliphatic compounds are the main compounds found in all parts of this plant. The various annatto plant parts have been utilized in traditional medicine for both the prevention and treatment of a variety of health issues. This review aimed to report the primary evidence found in the literature, concerning the pharmacological activities and phytochemical studies related to *B. orellana*. Regarding its application in food, cosmetics, leather, solar cells and other industries, significant research has already been done and is presently being conducted. This review demonstrates the well-studied pharmacological effect that might be relevant for the upcoming creation of a novel therapeutic medication.

1. Introduction

Bixa orellana Linn., known as annatto in English, achiote in Spanish, *yanzhimu* in Chinese or *urucum* in *Portuguese* (Brazil), is a member of the family *Bixaceae*. The Bixa plant is a shrub or tree that is spread throughout the tropics and is native to the Neotropics. Bixin is a dicarboxylic monomethyl ester apocarotenoid pigment that confers orange-red color in the *B. orellana* seed. Plant secondary metabolites have enormous potential for use in nutrition and medicine. Limited studies and genetic improvement have been done on many plant species used for the production of secondary metabolites that are essential parts of human food, animal feed, pharmaceuticals, biopesticides, and bioherbicides. Due to its high bixin content, this tropical perennial and ligneous plant is very interesting to the agroindustrial sector. South America is the origin of the *B. orellana,* also known as annatto. In pre-Colombian times, *B. orellana* was used as a cosmetic and traditional food ingredient. It is cultivated in Central America, Africa and South Asia.[1–5]

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https://doi.org/10.18231/j.jpbs.2022.012

The Annatto seeds stand second worldwide economically. The concentration of the color compounds affects the color of the pigment found in the outer coat of annatto seed, which ranges from yellow to red. *Bixin* (oil soluble) and nor-bixin (water soluble) which are derived from the seed's outer coating, are the primary color pigments of annatto seeds. The absorption coefficient (E^1 1cm) of 3090 at 487nm concentration was calculated in bixin. The absorption coefficient (E^1 1cm) of 2870 at 482nm concentration was calculated in nor-bixin. Annatto seed dye is significant commercially, various bioactive and beneficial chemicals from this plant's components would justify its usage as an extract in medicine. In ancient, people used leaves, roots, and seeds as medicines, including to heal wounds, cure diarrhea and treat asthma. The seeds of this plant have purgative, anti-pruritic and buccal tumor-treating properties. The decoction of leaves from the *B. orellana* is used for gastric ulcers and stomach discomforts and to treat colic as well as oral and throat inflammation. The plant is used for the treatment of indigestion and infectious diseases.[6,7]

Two pigments, bixin and norbixin have a variety of industrial applications as natural colorants in cosmetics and food. The basic extract includes Bixin, Norbixin and other carotenoids that were referred to be annatto as a whole. Because of its non-toxic characteristics and plant-derived origin, annatto is frequently used as a natural colorant. Because of its antioxidant, anticancer, analgesic, hypoglycemic, antibacterial, antidiarrheal and anti-inflammatory characteristics, the pigment bixin has been used in several therapeutic applications. Bixin has two different stereochemical configurations are cis- bixin and trans-bixin. Cis-bixin is soluble in the most polar organic solvent, which is orange in color and insoluble in vegetable oils. Trans-bixin is a stable isomer, which is soluble in vegetable oil. The decoction of leaves from the *B. orellana* is a remedy for gastric ulcers and stomach discomforts and to treat colic, oral and throat inflammation. The plant is used for the treatment of indigestion and other digestive disorders and also for the treatment of infectious diseases. *B. orellana* is a resource for future genetic studies on this and other related species, Phylogenetic position of *Bixa* within the order Malvales, chloroplast genome sequences of eight are Aquilaria Yunnanensis, Bombax ceiba, Daphne kiusiana, Firmiana major, Gossypium arboretum, Heritiera anagustata, Theobroma cacao, Tilia oliveri were download from NCBI database. The plant-derived product and essential oil are used for the antileishmanial activity of several marine microalgae that have been evaluated in mice. The fresh seeds and aerial parts of *B. orellana* (manually crushed) hydro distillation using Clevenger-type equipment and obtained essential oil were corroborated by gas chromatography coupled with mass spectrometry (GC-MS). The endophytic fungus residing is isolated from *B. orellana.* L are novel lactone pigment. The isolated lactone was identified as (E)-3,3-dimethyl — 4-(pent-1-en-1-yl)-4 propyl-dihydro furane-2(3H)-one. The pigment investigated acute oral toxicity study.[7–10] The standard literature was collected from Science Direct, Pub med, Google Scholar, Research Gate, Google Database, and springer.

2. Plant Profile

2.1. Taxonomical Classification

1. Kingdom: Plantae
2. Clas: Magnoliopsida
3. Order: Malvales
4. Family: Bixaceae
5. Genus: *Bixa*
6. Species: *Bixa orellana*

2.2. Morphological character

Evergreen shrub or small tree (6-8) m tall, diameter-10cm.

1. Leaves: Spirally, simple, blade ovate
2. Margin: Entire
3. Odor: Characteristics
4. Taste: Slightly bitter taste
5. Apex and Base: Acute
6. Flower: Bisexual, regular, fragrant
7. Fruit: Globose or broadly to elongated ovoid capsule
8. Seed: Bright orange-red fleshy seed coat

2.3. Microscopic character

Fig. 1: Different parts of the plant *B. orellana*

Phloem fibers, Starch grains, Calcium oxalate crystals, Lower epidermal layer: Presence of stomata; Upper epidermal layer: Devoid of stomata.[11,12] The different parts of the plant *B. orellana* is given in Figure 1.

2.4. Ethnobotanical use

Traditional medicine uses *B. orellana* extensively for the prevention and treatment of a wide range of illnesses, including jaundice, gonorrhea, blood problems, fever, epilepsy and dysentery. The leaves in Ngaoundere, Cameroon, *B. orellana* are abundantly accessible and have long been utilized by this community to relieve joint pain, jaundice, fever and gastrointestinal pain. They are also used for the treatment of asthma and also traditionally used as a gargle for sore throats. The bark and root are used for the fever. The leaves of *B. orellana* are used to cure snakebites, jaundice, diabetes, and hypertension. The leaves of *B. orellana* possess anti-microbial, anti-fungal, anti-leishmanial, anti-inflammatory, analgesic and anti-convulsion activity.[7,13]

3. Phytochemistry

B. orellana has undergone phytochemical screening which has resulted in the isolation and identification of several chemical compounds with various structural characteristics. Carotenoids, apocarotenoids, sterols, aliphatic compounds, monoterpenes, sesquiterpenes, triterpenoids and other chemical elements have all been found and isolated, primarily from the seeds, seed coat and leaves of *B. orellana.* The phytochemical screening of the crude aqueous extract of *B. orellana* indicates the presence of flavonoids, tannins, anthraquinones, saponins and terpenoids. Acetone extract indicates the presence of terpenoids and glycosides. Methanol extract indicates the presence of tannins and glycosides. Ethanolic extract indicates the presence of tannins, flavonoids, saponins, steroids and terpenoids. Hexane extract indicates the presence of glycosides. Terpenoids can be isolated in ether extract. Ethyl acetate extract indicates the presence of tannins, flavonoids, saponins, steroids and terpenoids. The Hydroethanolic extract of *B. orellana* (leaves) showed the presence of terpenes, flavonoids, tannins, coumarins and saponins and absence of alkaloids and anthraquinones.[4,14,15]

3.1. Carotenoids

Microorganisms and plants produce the yellow to red pigments known as carotenoids. They build up in the plastids (chromoplasts) of flowers and fruits in plants. In both plants and animals, abscisic acid (ABA) and vitamin A (retinol) are primarily derived from carotenoids. Isopentenyl diphosphate (IPP), which is produced through the plastidial methylerythritol phosphate (MEP) pathway, serves as the starting point for the production of all carotenoids through a series of condensation reactions. The seeds have a high carotenoid content, mainly bixin which makes up 80% of the total pigment in some seeds, was the first cis-carotenoid to be isolated from natural sources. However, there are numerous apocarotenoids, both linear and cyclic. The biological and medicinal qualities of this natural pigment have been the subject of several studies. This pro-vitamin inactive carotenoid is oil-soluble. Numerous research teams have also investigated the anticancer and apoptotic properties of *B. orellana.* These therapeutic and nutritive qualities demand more research. Bixin is a linear apocarotenoid of 25 carbon atoms with 9 double bonds and its scientific name is methyl hydrogen 9'-cis-6,6'-diapocarteno-6,6'-dioate ester. Apocarotenoids are terpenoid compounds derived from the oxidative cleavage of carotenoids. The seed contains a variety of apocarotenoids including both linear and cyclic molecules. Carotenoid have a different component like Lutein, methyl (9Z)-10'-oxo-6,10'-diapocaroten-6-oate from seed, and methyl(9'Z)-apo-6'-lycopenoate, methyl-(all-E)-apo-8'-lycopenoate from the seed coat.[3,4,16] The structures of some carotenoids are given in Figure 2.

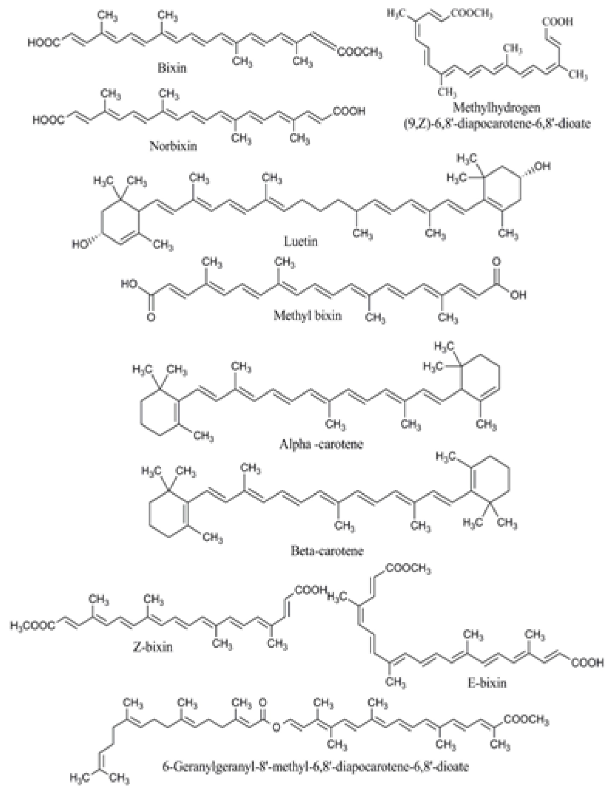

Fig. 2: Structures of Carotenoids from *B. orellana*

3.2. Terpenoids

B. orellana dry seeds were first extracted with hexane to yield an oleoresin, and then with methanolic-methylene dichloride to yield crystalline bixin and a filtrate containing a combination of various colors and terpenoids. Chromatographic analysis of the epi-phase indicated the formation of several components, including geranylgeranyl octadecanoate, geranylgeranyl formate, δ-tocoterienol, and the diapo 8-oxo ester, which have isolated after multiple elutions in HPLC. Quantitative study showed that all-E-geranylgeraniol was present in Bixa oleoresin to the extent of 57%, or estimated 1% of dry seeds. *B. orellana* is therefore the richest common source of this major terpene alcohol. Terpenoids may extract from seeds which are Farnesylacetone, Geranylgeranyl octadecenoate and Geranylgeranyl formate. Apocarotenoid is a terpenoid compound derived from the oxidative cleavage of carotenoids.[3,16] The structures of some terpenoids are given in Figure 3.

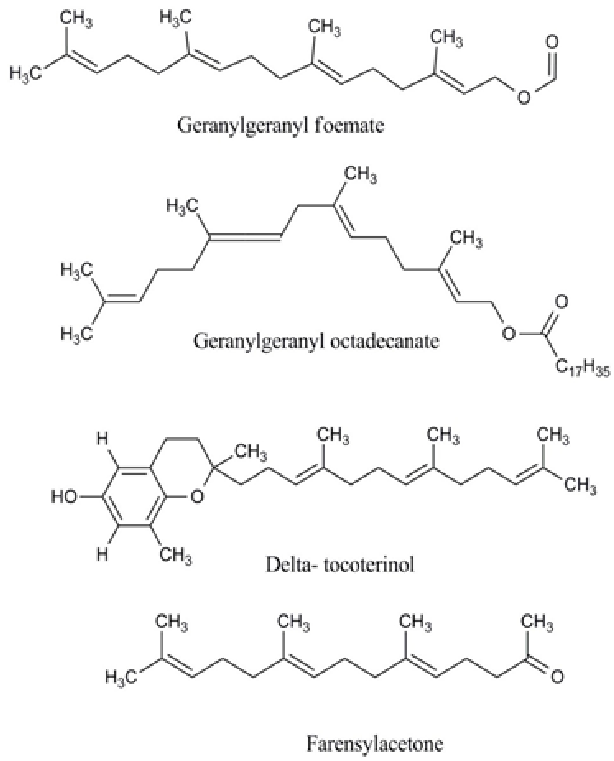

Fig. 3: Structures of terpenoids from *B. Orellana*

3.3. Tocotrienols

Tocotrienols are vitamin-E molecules that are found in nature. In nature, tocotrienols (TOC) can be found in four different chemical forms depending on how much of their chromanyl core has been methylated: alpha, beta, gamma, and delta tocotrienols. The annatto (*B. orellana*) bean, contains 90% delta tocotrienols, 10% gamma tocotrienols and no alpha tocotrienols. The addition of alpha tocotrienols decreased the biological activities of tocotrienols. As a result, alpha tocotrienols reduced the effects of inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase and their ability to lower cholesterol. The monomethylated congener delta-T3 of tocotrienols, a subclass of vitamin E mimics, appears to be the most active form.[13,17]

3.4. Other chemical constituents

By drying and mincing the root tissue, the *B. orellana* ethanolic extracts produced several substances that were classified as known compounds (ishwarane, ellagic acid, -tocotrienol, bixin, ursolic acid, maslinic acid, arjunolic acid, inositol, and stigmasterol). This unrefined combination also contained several amino acids (Trp, Phe, and Thr), but they were not separated. The hairy root line was cultured in a modified liquid Murashige and Skoog medium (MSV). The MEP, carotenoid and bixin pathways genes are all expressed in unison during the formation of bixin in immature seeds. The chemical constituents of the aqueous extract of B. orellana (AEBO) detected by GC-MS are 2-Butanamine (Amine), Acetic acid (Organic acid), Pentanoic acid (Fatty acid), Phenol (Carbolic acid), Pantolactone (Lactone) and Benzoic acid (Organic acid).[4,18] The structures of some other chemical constituents are given in Figure 4 and the phytoconstituents present in the various parts of B. orellana are summarized in Table 1.

4. Pharmacological Applications

As a consequence of the many ethnomedical benefits of *B. orellana* during the past few decades, numerous pharmacological studies have been started by researchers all over the world. Through scrutiny of its ethnomedical uses, a wide range of biological activities, including 'antibacterial, antifungal, antioxidant, anti-inflammatory, anti-carcinogenic, enhanced gastrointestinal motility, neuropharmacological, anticonvulsant and anti-hypercholesterolemic activities have been described in the literature.[19]

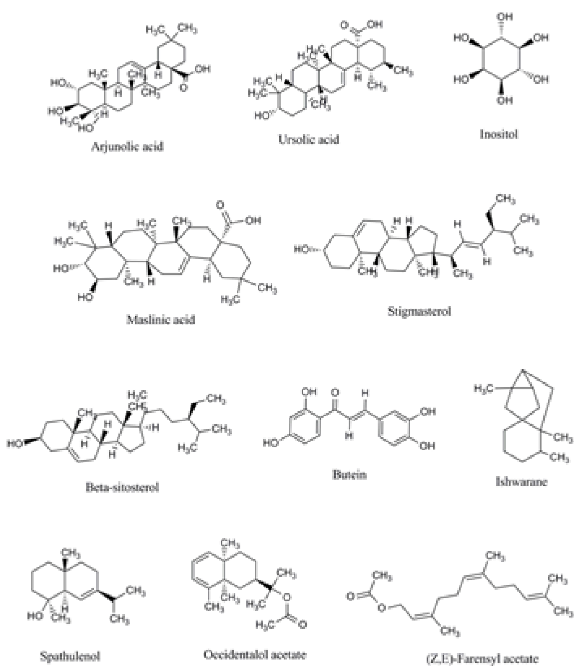

Fig. 4: Structures of other chemical constituents from *B. orellana*

Table 1: Phytoconstituents present in various parts of *B. orellana*

S.NO.	Plant parts	Extraction	Phytoconstituents	Reference
1.	Leaves	Ethanolic extraction	Saponins, alkaloids, and flavonoids	2
2.	Seeds	Ethanolic extraction	Saponins, alkaloids, and flavonoids	2
3.	Seeds	-	Bixin, Carotenoid content, Methyl-D-erythritol 4-phosphate MEP, Cis-carotenoid, Apocarotenoid, and Terpenoids, Methyl hydrogen 9'-cis-6,6'-diapocarotenoid-6,6'-dioate ester	3
4.	Seeds	Seed extract	Apocarotenoid, (linear) Methyl (9Z)-apo-8'-lycopenaote and cyclic molecules (all -E)-8'-apo-β-caroten-8'-oate.	3
5.	Seeds	-	Cis-bixin	3
6.	Seeds	-	Trans bixin	3
7.	Seeds	-	Cis-bixin	3
8.	Seeds	-	Trans-bixin	3
9.	Seeds	Aqueous extract	9'-cis-norbixin	3
10.	Seeds	Aqueous alkali (or) alkaline hydrolysis	Cis-bixin	3
11.	Immature seeds	-	Bixin, Carotenoid, lycopene	3
12.	Leaves and Seeds	Ethanol extract	Carotenoid derivatives, Archiote	3
13.	Leaves and Root	Alcoholic extract	Carotenoid derivatives	3
14.	Seeds extract	Hexane, Ethanol and Ethanol/water	Carotenoid derivatives, Archiote, and Bixin	3
15.	Seeds coat	-	Bixin and Nor-bixin	6
16.	Seed powder	-	Total phenolic compound	6
17.	Leaves	Aqueous extract	2-Butamine, Acetic acid, Pentanoic acid, Phenol, Pantolactone, Benzoic acid.	7
18.	Leaves	Dichloromethane extract	Ishwarane, Phytol, Polyprenol, Stigmasterol, Sitosterol.	7
19.	Leaves	Aqueous extract	L-arginine by Nitric oxide (NO)	7
20.	Seeds and aerial parts	-	Essential oil	10
21.	Leaves	Hydroethanolic extract	Terpenoids, sterol, flavonoids, tannis, saponins, hydroquinine, coumarins, triterpenes.	15
22.	Seeds	Lipid extract	Tocopherols (TOC), α-, β-, δ-,γ-Tocotrienol, carotenoid derivative bixin	17
23.	Root	Ethanolic extract	Ishwarane, ellagic acid, δ-tocotrienol, bixin, stigmasterol, β-sitosterol, inositol, ursolic acid, maslinic acid, and arjunolic acid	18
24.	Root	Inorganic extract	Ishwarane, Methyl jasmonate, Methyl cucurbate, Jasmonic acid, and inositol	18
25.	Seeds	Organic solvent extract	Volatile oil [(Z, E)-farnesyl acetate, Occidentalol acetate, and spathulenol	18
26.	Seeds	Ethanol extract	Polyphenol and Bixin, Gallic acid	20

Continued on next page

Table 1 continued

27.	Seeds	Solvent ectract	Polyphenol and Bixin, Gallic acid	20
28.	Seeds	Microwave-Assisted Extraction	Polyphenols, Hypolatin, Apigenin, Caffeic acid and Carotenoids, (Bixin or 6-methyl hydrogen (9Z)-6,6'-diapocarotene-6)	20
29.	Seeds	Lipophilic extract	Tocotrienols, Tocopherols, Terpenes, Flavonoids, cis-bixin	21
30.	Leaves	Lipophilic extract	α-Tocoferol and Tocotrienols (α, β, γ, δ)	21
31.	Seed powder	Lipophilic extract	Cis-bixin, Trans-bixin	21
32.	Seeds	Water soluble ectract	Nor-bixin (cis from)	21
33.	Seeds	-	Apocarotenes (Bixin, Iso-bixin, Nor-bixin). Carotenoids (β-Carotene, cryptoxanthin, Lutein, Zeaxanthin, Methylbixin, Apocarotenoids, and 8-diapocarotenoids). Terpenes (E-geranyl-geraniol). Isoprenoids (farnesylacetone, geranylgeranyl octadecenoate, and geranylgeranyl formate). Lipids (linoleic acid, α-linolenic, and oleic acid). Amino acid (glutamate, aspartate, leucine).	21
34.	Leaves	-	Bixaghanene, Bixein, Crocetin, Ellagic acid, Isobixin, Phenylalanine, Salicylic acid, Threonine, Tomentosic acid, Tryptophan, Flavonoid, bisulfates, Sterols, Tannis, Saponins.	21
35.	Root	-	Triterpene tomentosic acid	21
36.	Seeds and Leaves	-	Tocotrienols and Tocopherols (α, β, γ, δ)	21
37.	Seed coat	-	Bixin, Apocarotenoid (dicarboxylic monomethyl ester)	22
38.	Seeds	-	Cyclic apocarotenoids (methyl (all-E)-8-apo-β-caroten-8-oate). Linear apocarotenoids (methyl (9Z) -apo-8-lycopenoate), bixin	22
39.	Leaves	-	Carotenoids, Bixin	22
40.	Seeds	-	Chlorophyll a, b Total carotenoids, β-caroten, Bixin, abscisic acid (ABA)	22
41.	Seeds	-	Geranyl-geraniol and tocotrienols (90% δ and 10% γ)	23
42.	Seeds	(Encapsulated by Ionic gelation) Aqueous dispersion	Quinoa proteins (QP), Lentil proteins (LP), Soy proteins (SP), and Sodium caseinate proteins (SCP)	24
43.	Seeds	Ethanol extract	Bixin carotenoid (bixin or 6-methyl hydrogen (9Z) -6,6'-diapocarotene-6). Polyphenols (Catechin, Chlorogenic acid, Chrysin, Butein, Hypoaletin, and Xanthoangelol.	24

Continued on next page

Table 1 continued

44.	Vegetative parts	Ethanolic extraction	Mucilaginous polysaccharides (MPS), Starch, Reducing sugar content, Pentose, Uronic acid, Total phenolic content, and Total protein content	25
45.	Leaves and twig part	Mucilage extraction (Ethanolic precipitated)	Carbohydrates, Reducing sugar, Pentose sugars, Total proteins, Total phenolic content, and Uronic acid	25
46.	Leaves and twig part	Water soluble polysaccharides	Rhamnose, Arabinose, Xylose, Mannose, Galactose, and Glucose	25
47.	Seeds	Lipid soluble	Diapocarotenoid, Carotenoid, Bixin	26
48.	Leaves	Aqueous/ ethanolic/ methanol	Bixin and Carotenoids	26
49.	Defatted seeds	Chloroform with hexane	Bixin	26
50.	Leaves	Aqueous extract	Tannins, saponins, flavonoids, terpenoids, steroids, anthraquinone, and hydroquinone	27
51.	Leaves	Methanolic extract	Tannins and glycosides	27
52.	Leaves	Ether extract	Terpenoids	27
53.	Leaves	Acetone extract	Terpenoids and Glycosides	27
54.	Seeds	Organic solvent extract	Naringenin, 6,8’-diapocarotene-6,8’-dioic acid, E-norbixin, Eicosatrienoic acid, 6,7’-diapocarotene-6,7’-dioic acid, Z-norbixin, E-bixin, Z-bixin, Geranylgeraniol, Methyl-bixin, β-12’-apo-carotenoic acid, δ-tocotrienol and γ-tocotrienol	28

4.1. Antibacterial activity

The antibacterial effectiveness of deseeded and leaf extracts of *B. orellana* were analyzed against both Gram-positive and Gram-negative microorganisms. The disc diffusion method was used to investigate the antibacterial activity of the *B. orellana* extract against *Escherichia coli, Staphylococcus aureus, Bacillus cereus and Pseudomonas aeruginosa* using gentamycin sulphate as standard. The results revealed that the antibacterial activity of leaves was more prominent and fruit extracts displayed the same properties at significantly greater concentrations. In *Staphylococcus aureus, Bacillus cereus and Pseudomonas aeruginosa,* the growth of inhibition occurs only in the DMSO (Dimethyl sulphoxide) extract of seeds. The crude ethanolic leaves extract of *B. orellana* has shown antibacterial potential against *S. aureus* with a minimal inhibitory concentration of 62.5μg/ml. Similarly, the ethanolic extract of Bixa seeds also proved to be more active against *E. coli* and *B. cereus* than the standard.[2]

4.2. Antioxidant activity

The simplest way to control oxidation is to employ synthetic antioxidants. They increase the nutritional value and sensory quality of foods while extending their shelf life and reducing the production of undesirable oxidation products. One of the main factors contributing to food decomposition is the antioxidant of lipids and proteins. The antioxidant capacity of *B. orellana* leaf solvent extracts was evaluated. Significant antioxidant activity was seen in acetone, methanol, chloroform, and ether extracts. Thiobarbituric acid reactive substance (TBARS) and peroxide value (POV) were examined over 14-days of refrigeration to assess the antioxidant effects of annatto seeds on pork patties.[6]

4.3. Anticancer activity

Due to its high propensity to spread and substantial resistance to the standard therapeutic regimen, cutaneous melanoma is challenging to treat. *In vitro* anticancer potential of the apocarotenoid, bixin was demonstrated using HL60 (leukemia), B16 (melanoma), U20S (osteosarcoma), PC3 (prostate), HCT-116 (colon), MCF-& (breast), DRO (anaplastic thyroid) and BHP-16 (papillary thyroid) cell lines using dacarbazine as a standard. UPLC-DAD-MS/MS analyses of bioactive extracts from *B. orellana* seeds leds to identification of two apocarotenoids. Bixin was evaluated on A2058 cells expressing the oncogenic BRFA VE600 mutation and resistant to dacarbazine treatment. Bixin have anticancer activity in cultured Hep3B human liver cancer cells via., a combination multiple actions including arrest of cell cycle and inhibition of cell growth and induction of apoptotic cells death through extrinisic and intrinsic pathway and also inhibit COX-1 and COX-2 enzymes, growth inhibition against breast, colon stomach, CNS, and lungs tumour cells.[28,29]

4.4. Anti-inflammatory activity

The anti-inflammatory effect of bixin was caused by the activation of the antioxidant Nrf2 transcription factor, which is effective in accelerating wound healing and minimizing the amount of scar tissue. In the first and second hours following the administration of carrageenan, oral therapy with bixin encourages a considerable decrease in paw edema, because bixin can stop neutrophils from migrating to an inflamed location. Orally administered aqueous extract of *B. orellana* exhibits significant anti-inflammatory properties. It was demonstrated that the aqueous extract prevented the paw edema in rats at oral doses of 50 and 150 mg/kg 30 min after induction. The aqueous extract of the plant has considerable anti-inflammatory activity against the acute phase of inflammation, which may be brought on by anti-bradykinin activity. These findings confirm the historical application of *B. orellana* leaves to inflammation. One of the key factors contributing to CNS dysfunction in multiple sclerosis is oxidative stress. Additionally, ROS are the primary oxidative stress mediators and TXNIP/NLRP3 inflammasome initiators. In experimental autoimmune encephalomyelitis mice, bixin suppresses the TXNIP/NLRP3 inflammasome and promotes the NRF2 signaling pathway.[14,26,30]

4.5. Positive inotropic activity

Positive inotropic drugs were found to be clinically effective for treating cardiovascular disorders like congestive heart failure resulting in the improvement of cardiac contractility throughout the history of medicine and many other plant components that are thought to have beneficial inotropic effects like *B. orellana.* They are appropriately used as diuretics, antispasmodics, antitussives, cardiotonic and anxiolytics, which suggests that they could have important favorable inotropic characteristics. The aqueous extract of *B. orellana* appears to have beneficial inotropic qualities that could enhance cardiac function in ischemia-reperfusion injury without harming the myocytes.[15]

4.6. Antihyperglycemic activity

Foods from plants that have anti-diabetic qualities may offer a more valuable alternative in the prevalence of type 2 diabetes mellitus (T2DM). The antihyperglycemic and hypoglycaemic effects of *B. orellana* were investigated in this study. The healthy Wistar rats (group HSD) were tested for antihyperglycemic activities. In healthy CD1 mice, hypoglycaemic activity was measured. Antihyperglycemic medications, such as insulin and α-glucosidase inhibitors, as well as other substances, such as insulin sensitizers are used therapeutically to treat hyperglycemia. The presence of high-bioactive compounds namely phenolic compounds and flavonoids of *B. orellana* have significant anti-diabetic potential due to their inhibitory effect on α-amylase and α-glucosidase.

The presence of bioactive substances in plant products has been correlated to the antidiabetic effects, which include the inhibition of enzymes involved in carbohydrate metabolism (α*-amylase* and α*- glucosidase*), maintenance of α-cell function and effective control of glucose uptake in peripheral tissues. These substances affect biochemical functions in the body, which can cause negative outcomes (side effects) like hypoglycemia, gastrointestinal, kidney, cardiovascular and liver diseases. Rapid glucose absorption in the intestinal lumen occurs by α-amylase and α-glucosidase enzymes by hydrolysing the polysaccharides into oligosaccharides and monosaccharides resulting in postprandial hyperglycemia. Acarbose is a substance utilized in the treatment of T2DM. It is well known that this complex oligosaccharide inhibits the enzymes α-amylase and α-glucosidase, so reducing and delaying the intestinal absorption of glucose and, as a result, preventing the postprandial rise in blood glucose levels.[31]

4.7. Antiosteoporosis activity

Annatto tocotrienol can halt the degenerative changes to the bones in rats receiving buserelin. Three features of healthy bones bone microstructure, calcium content and biological strength have been shown in annatto tocotrienol. On the markers of bone microstructure, bone calcium content and bone biomechanical properties in a male osteoporosis model brought on by the GnRH agonist buserelin. An orchiectomy is conducted, which results in reduced testosterone production, to artificially induce osteoporosis in rate. After orchiectomy, rats lose their androgens and develop a state resembling the illness.[13,23]

4.8. Antidiarrhoeal activity

Urinary incontinence and faecal urgency are symptoms of diarrhoea, which are caused by an imbalance between the mechanisms of intestinal production and absorption. The imbalance frequently occurs with intestinal hypermotility which results in an excessive loss of bodily fluid and electrolytes in the stool. It is associated with viral diseases, food poisoning, and other gastrointestinal disorders that are marked by an increase in bowel frequency. The methanolic extract of *B. orellana* causes maximal antidiarrhoeal activity (85% at 500mg/kg). Hydroethanolic extract of antidiarrheal compounds such as flavonoids, tannins, terpenes, saponins and sterols which are known for their antidiarrhoeal activity.[15]

4.9. Antimalarial activity

The Potential chemical constituents of *B. orellana* which is present in the hairy root line was used for the treatment of malaria. The anti-malarial activity of *B. orellana* against malaria strains 3D7 and K1. The root line was cultured in a modified liquid Murashige and Skoog medium (MSV). The results revealed that the root line of *B. orellana* showed significant anti-malarial activity against the malarial strains. The hairy roots shows that anti-malarial property in the 15-20 mm range and no cytotoxicity was observed in mammalian cell line.[3,18]

4.10. Antihistamine activity

The antihistaminic activity of the aqueous extract of *B. orellana* was evaluated using the rat models of acute inflammation. One of the most prevalent inflammatory mediators, histamine induces allergic reaction symptoms, which are largely caused by acute inflammation mediated by the H1 histamine receptor. The histamine H1 receptor is found primarily in endothelial cells, smooth muscle cells and the brain which aids in vasodilation. The results revealed that increased vascular permeability and pain occur at the cellular level while increasing intracellular calcium (Ca2+) and nitric oxide (NO) production occurs at the molecular level. Histamine-induced paw edema, intraperitoneal vascular permeability, nitric oxide (NO) production and Vascular endothelial growth factor (VEGF) production in rats.[7]

5. Conclusion

Consequently, *B. orellana* is used to cure diseases like microbial infections, cancer, diabetes and malaria. Recent studies on the phytochemistry and pharmacology of the *B. orellana* plant are summarized in this review. Various biological and ethnopharmacological uses have been reviewed. The extensive scope of biological activities of annatto has been proven by review. However, more detailed research is required to investigate each chemical component and its mode of action in displaying certain biological and pharmacological activity to make this plant available to the pharmaceutical and other fields. The final section of this review has shown that annatto seeds, which have yellow colouring qualities, contain carotenoid pigments, primarily bixin and nor-bixin. The FDA has approved the commercial use of seed extract as a natural colorant in foods and beverages in the United States.

6. Authors Contribution

All the authors have contributed equally.

7. Source of Funding

None.

8. Disclosure of Conflict of Interest

The authors hereby disclose no conflicts of interest regarding the publication of this paper.

Acknowledgment

We thank the Management and Dr. G. Murugananthan, Principal of our college for giving constant support and encouragement for writing this review.

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Cite this article: Raju SK, Chandrasekar S, Vengadhajalapathy P, Sundaram R, Periyasamy S, Chinnaraj T, Sekar P, Kumar S. Review on phytochemical composition and pharmacological activities of *Bixa orellana* L.. *J Pharm Biol Sci* 2022;10(2):57-67.