Exploring the therapeutic landscape of *Baccharoides anthelmintica*: from traditional use to modern applications

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Review

Abstract

Background: *Baccharoides anthelmintica* (also known as *Vernonia anthelmintica*), a medicinal plant from the Asteraceae family, is widely recognized in Ayurveda, Unani, Siddha, and traditional Chinese medicine. It has been traditionally utilized to address inflammatory issues, gastrointestinal disorders, skin ailments, and reproductive health problems. Its seeds are particularly esteemed for their capability to eliminate parasitic worms, which is reflected in its species name "*anthelmintica*." Beyond its ethnomedicinal importance, the plant has piqued the interest of modern science for its potential pharmacological benefits and industrial applications.

Methods: This review involved the examination of 25-30 original research studies, 10-15 review articles, classical literature, ethnobotanical surveys, and electronic databases (PubMed, Scopus, Web of Science, Google Scholar). Local traditional knowledge was also gathered from healers in Uttarakhand. Information on phytochemical components, pharmacological effects, and therapeutic uses was systematically compiled, with a focus on its anthelmintic properties.

Results: Phytochemical investigations uncovered a variety of bioactive compounds, including sesquiterpene lactones, fatty acids, flavonoids and triterpenoids. These compounds exhibit antihelmintic, antimicrobial, antioxidant, anticancer, and anti-inflammatory effects. Their mechanisms include disruption of the parasite, inhibition of larval development, modulation of oxidative stress and induction of apoptosis in cancer cells.

Conclusions: *B. anthelmintica* stands out as a valuable natural resource for the development of innovative anthelmintic and multi-target therapeutic agents. Its diverse phytochemical profile provides a scientific foundation for traditional claims; however, additional in vivo studies, clinical trials, and safety assessments are necessary for sustainable pharmacological and industrial use**.**

Keywords: *Baccharoides anthelmintica*; Anthelmintic; Phytochemistry; Traditional Medicine; Asteraceae

Background

Since the dawn of civilization, the utilization of plants has been fundamental to traditional medicinal systems around the world, providing comprehensive strategies for health maintenance and disease treatment. *Baccharoides anthelmintica* (Syn *Vernonia anthelmintica*), commonly referred to as kalijiri, stands as a prominent example of a medicinal plant deeply entrenched in the Ayurvedic, Unani, and Siddha medical frameworks (Sahoo *et al.* 2013). Historically, *B. anthelmintica* has been employed to manage a diverse spectrum of health issues, ranging from helminthic infestations, asthma, and inflammation to kidney ailments, stomachache, convulsions, leucoderma, ringworms, herpes and various dermatoses. In the Siddha healing practices, the seeds of this plant are particularly emphasized, featuring in formulations such as Iraca, Kanthi, Mezuku and Karappān Tailam (Shalini & Ilango, 2021). Within Ayurveda, these seeds are integral to the formulation of Madhusnuhi Rasayana, a polyherbal remedy aimed at addressing diabetic carbuncles, lymphadenitis, neoplastic growths, haemorrhoids, and skin-related disorders (Prakash *et al.* 2023).

Recent scientific inquiries have begun to substantiate the therapeutic efficacy of *B. anthelmintica*, especially focusing on its potential as an antihelminthic agent. Phytochemical analyzes have identified various bioactive constituents, including vernodalin, vernodalol, and vernolic acid, which are believed to play critical roles in the plant's medicinal properties (Ngeh *et al.* 2013). These compounds, characterized by their bitter taste, are not only central to the plant's traditional use in deworming practices but also contribute to its anti-inflammatory, antidiabetic, antioxidant, antibacterial, and anticancer properties (Kothari & Chachad, 2024). The presence of a vast array of phytochemicals, including flavonoids, sesquiterpene lactones, and essential oils, highlights the extensive pharmacological activities of *B. anthelmintica*, positioning it as a promising candidate for future pharmacological developments (Lambertini *et al.* 2004).

Besides its medicinal applications, *B. anthelmintica* is increasingly recognized for its economic potential. Its capacity to yield epoxy oil, a compound of significant industrial value, has garnered attention in agricultural sectors (Chinnadurai *et al.* 2016). This versatility, which merges health benefits with economic viability, has prompted the cultivation of *B. anthelmintica* in non-native areas, such as the United States, where there is a burgeoning interest in natural therapeutics and bio-based industrial materials (Ghosh *et al.* 2022).

Helminthiasis stands out as a major concern in animal & human health, leading to significant production losses, especially in developing countries. The primary approach to managing helminth infections globally has been through chemical treatments paired with improved management practices (Mashelkar *et al.* 2008). However, the increasing resistance of gastrointestinal trichostrongylids in domestic small ruminants to standard anthelmintics, along with the economic consequences, highlights the urgent need for alternative strategies to reduce worm burdens (Kirtikar & Basu, 2003). Traditionally, plants have been harnessed to treat various ailments in both humans and animals. This herbal treatment approach is commonly referred to as Unani, folk, Eastern, or indigenous medicine in the Indo-Pakistan context. Numerous studies have documented the antihelminthic effects of various plant species from regions across Asia, Africa, America, and Europe, suggesting that these plants could serve as a valuable alternative for tackling helminthiasis (Chinnadurai *et al.* 2016).

In this review, we aim to explore the therapeutic potential of *Baccharoides anthelmintica* with a primary focus on its anthelmintic potential. By integrating traditional knowledge with modern scientific evidence, we try to assess its phytochemical composition, mechanisms of action, and efficacy against parasitic worm infections, providing a comprehensive understanding of its value as a natural antiparasitic agent.

Materials and Methods

The present review was conducted using a comprehensive and integrative approach to explore the therapeutic potential of *B. anthelmintica*, combining both scientific and traditional knowledge sources. A total of 25-30 original research papers and 10-15 review articles were analyzed, along with books, thesis, ancient Ayurvedic texts, and ethnobotanical records. Information was gathered from various databases such as PubMed, Scopus, Web of Science, SpringerLink, and Google Scholar, as well as from libraries and herbariums. Additionally, traditional knowledge was collected through informal interactions with local healers and villagers in Uttarakhand, focusing on the plant's cultural uses, especially for deworming. Data on plant parts used, preparation methods, phytochemical constituents, pharmacological effects, and therapeutic applications were extracted, verified, and organized thematically.

Results

Scientific Classification

Kingdom: Plantae **Division:** Angiosperms **Class:** Eudicots **Subclass:** Asterids **Order:** Asterales **Family:** Asteraceae **Subfamily:** Cichorioideae **Tribe:** Vernonieae **Genus:** *Baccharoides* **Species:** *Baccharoides anthelmintica*

Botanical Description

Baccharoides anthelmintica is a tall, upright annual plant that can grow up to 1.5 meters. (Figure 1a) The stems are branched, rough, and hairy, giving them a sturdy feel. The leaves grow alternately on the stem and are connected by short stalks that are about 1-2 cm long (Ghosh *et al.* 2022)**.** They come in different lance shaped, measuring between 5-13 cm long and 2.5-5 cm wide. The leaves have jagged edges, pointed tips, and a fuzzy (hairy) surface on both sides, with a soft and rough feel. Each leaf typically has 10-11 pairs of noticeable veins, which help support the structure (Mashelkar 2008, Kirtikar & Basu 2003).

The flowers of this plant are also unique. It forms flower heads (around 15 × 12 mm) on stalks that can be solitary or grouped together in a flat-topped arrangement (Muthee *et al.* 2011)**.** Each flower head is surrounded by several layers of bracts. The outer bracts are shorter, hairy, and thin; the middle bracts are sharp-tipped and leafy; while the innermost bracts are the longest, often purple, and have a dry, papery texture (Hussain *et al.* 2008).

Inside each head, there are about 30-40 individual flowers with smooth, tubular purple petals (Figure 1b) that are around 10 mm long, each ending in five pointed tips. The stamens have rounded anthers (~2 mm), while the styles are thin, slightly hairy, and designed to catch pollen (Iqbal *et al.* 2006).

Once fertilized, the plant produces oblong, cylindrical seeds (4-6 mm long) that have 8-10 gland-like ribs covered in fine hairs. The pappus, which helps with seed dispersal, has two parts: an outer layer that looks like scales and stays attached, and an inner ring of crimson bristles that are a bit flattened and help the seeds (Fig. 1c, Fig. 1d). to float away with the wind (Higgins *et al.* 1968).

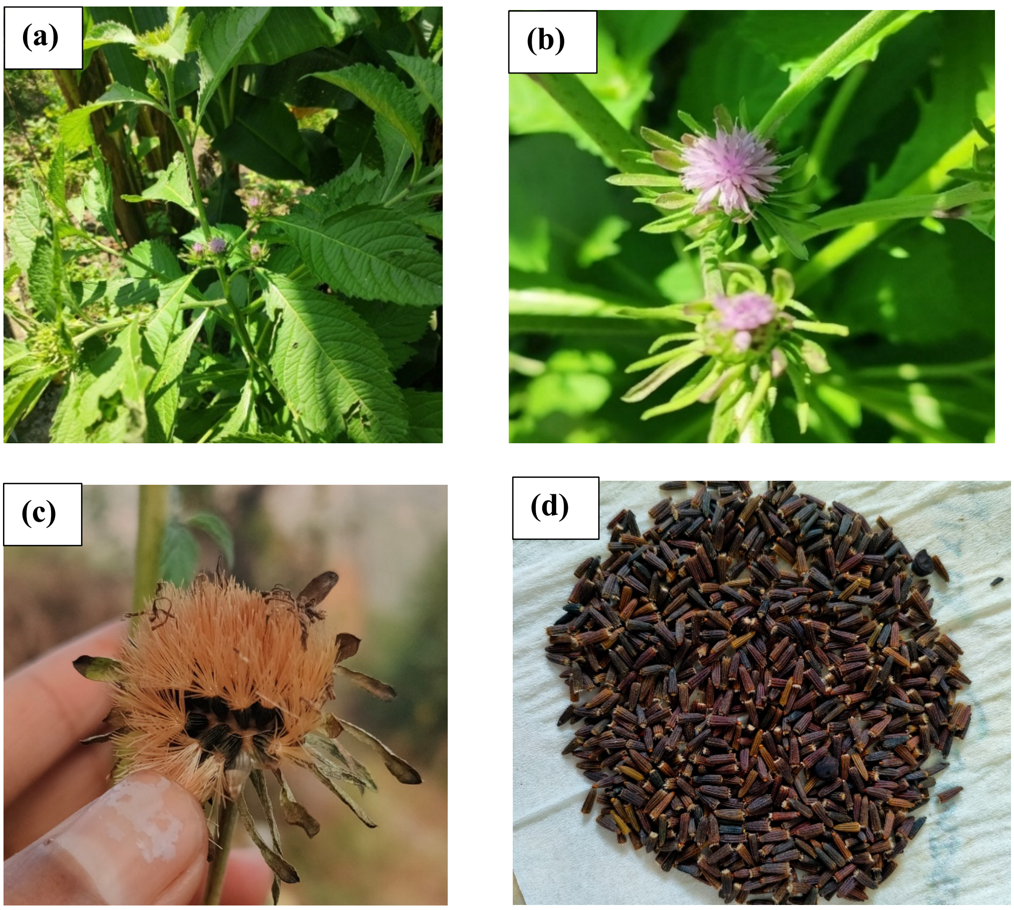


Figure 1. Different parts of *Baccharoides anthelmintica* (a). Whole plant, (b). Flower, (c). Fruit, and (d). Seeds.

Economic Importance

B. anthelmintica is emerging as a noteworthy species in both medicinal and industrial sectors, demonstrating substantial economic prospects. This herb is readily available in the market under various trade names, with prices ranging from ₹1000 to ₹1800 per kilogram, indicative of its robust market demand (Nisha *et al.* 2007). Research indicates a potential yield of approximately 500 to 600 kilograms of seeds per hectare. At prevailing market prices, this yield has the potential to generate annual revenue between ₹5 to ₹10 lakh per hectare, highlighting its profitability relative to traditional cereal and pulse crops (Singhal *et al.* 1992).

In addition to its medicinal applications, the oil extracted from its seeds, rich in vernolic acid, presents significant utility for industries such as paints, adhesives, polymers, lubricants, cosmetics, and pharmaceuticals. This oil serves as an environmentally friendly alternative to petroleum-based products (Ani *et al.* 2008). Furthermore, the seeds of *B. anthelmintica* are recognized in culinary contexts; they have historically been employed as a spice, digestif, and ingredient in herbal preparations targeting gastrointestinal ailments, enhancing metabolic processes, and enriching functional food formulations. With the integration of advanced agronomic techniques, micropropagation methods, and refined post-harvest practices, the large-scale cultivation of *B. anthelmintica* can transform it into a commercially viable dual-purpose crop (https://www.gbif.org/species/5385185). This transition not only promises elevated incomes for farmers but also fosters the availability of sustainable raw materials for a variety of industries, thereby promoting ecological balance and economic stability (Nisha *et al.* 2007).

It is interesting to note that the plant has received little attention from government programs that promote Non-Timber Forest Produce (NTFP) due to its low protein content (albumins, globulins, and glutelins) and low free amino acid composition (Mondo *et al.* 2024). During India's 10th and 11th plan periods, the Ministry of Environment and Forests (MoEF) and the National Afforestation and Eco-Development Board (NAEB) made efforts to increase the populations of herbaceous and shrubby Non-Timber Forest Produce (NTFP) species, but they did not give *B. anthelmintica* much attention (Ani *et al.* 2008).

<u>Traditional Uses</u>

(Regional Variations)

Ethnobotanical surveys reveal diverse regional applications:

India: In addition to the applications discussed previously, specific communities use leaf juice for tonsillitis or root decoctions for urinary problems (Chopra *et al.* 1956). In some areas, it's used against lice.

Pakistan: Similar uses for worms, skin diseases, and fever are documented (Prakash *et al.* 2023).

Africa (e.g., Ethiopia, Nigeria): Used for parasitic infections, fever, skin diseases, stomach ache, and sometimes as an ingredient in remedies for schistosomiasis or malaria (Maroyi, 2020). Leaves are sometimes used as a vegetable or in soups (Rajpoot, 2024).

China: Employed in traditional Chinese medicine for similar indications, including parasitic infections and skin ailments (Nadkarni, 1954).

Sri-Lanka: Used in Ayurveda for skin ailments, helminthic infections and digestive problems (Chopra *et al.* 1956).

Myanmar: Traditional medicine employs seeds for worm infestations, skin diseases and as a bitter tonic.

Uganda: Folk medicine applies seeds for expelling worms, managing malaria-like fever and improving skin health.

Zambia: Employed in ethnomedicine as a vermifuge, for fevers and to treat skin discoloration (Javed *et al.* 1990).

Zimbabwe: Seeds used in herbal remedies for intestinal parasites, skin issues and as a tonic for general health.

Tanzania: Traditional healers use it for intestinal worms, malaria-related symptoms and skin diseases (Mukherji, 1953).

The different parts of *B. anthelmintica* have several traditional applications, that are listed as in Table 1 (Baig *et al.* 2022, Hu *et al.* 2022).

Table 1. Traditional uses of various plant parts of *B. anthelmintica*.

Plant part	Usage	Reference
Seeds	• Anthelmintic: Expels intestinal worms. • Skin Disorders: Treats vitiligo (promotes repigmentation), psoriasis, and eczema. • Blood Sugar Regulation: Used for managing diabetes. • Reproductive Health: Manages menstrual disorders and gynaecological issues. • Ayurveda: Treats ulcers, balances vata and kapha doshas, manages skin diseases, leukoderma, and fever. • Unani: Treats asthma, kidney troubles, hiccough, inflammatory swellings, liver-related issues, sores, and eye itching.	Ghosh *et al.* 2022

Leaves	• Phlegm: Juice is used to cure phlegmatic discharges from the nostrils. • Jaundice: A decoction of seeds and leaves is given to cure jaundice. • Wound Healing: Crushed leaves are applied to cuts, wounds, and ulcers. • Anti-inflammatory: Used as a poultice to reduce swelling and pain. • Fever/Infections: Leaf decoctions are consumed to manage fevers and infections.	Mashelkar, 2008
Roots	• Digestive Aid: Provides relief from constipation, indigestion, and stomach pain. • Diuretic: Assists in treating urinary issues and kidney disorders. • Neurological Conditions: Used for treating epilepsy and convulsions.	Kirtikar & Basu, 2003
Stem	• Antimicrobial: Used to combat bacterial and fungal infections. • Bone Health: Believed to strengthen bones and joints.	Ghosh *et al.* 2022

Traditional Knowledge

Charak Samhita (The Siddha pharmacopoeia of India 2008)

The Charaka Samhita, a pivotal text in the field of Ayurveda originating from the 1st millennium BCE, discusses *B. anthelmintica* (Kaala Jeera), commonly referred to as Krishna Jiraka. This classical work systematically categorizes herbs according to their therapeutic properties and places *B. anthelmintica* in the classifications of Deepaniya, which are known to function as appetizers, and Pachaniya, which are crucial for digestive enhancement. The action of these herbs is understood to invigorate Agni, or the digestive fire, thereby facilitating optimal digestive performance.

B. anthelmintica is notably incorporated in formulations aimed at alleviating Ama, the toxic accumulation resulting from improper digestion of food, which is viewed as a fundamental contributor to various health issues within the Ayurvedic paradigm. Its relevance extends to postnatal care, where it is utilized to aid maternal recovery, restore physiological balance, and enhance lactation processes.

The Charaka Samhita highlights the herb's warming properties and its carminative effects, underscoring its efficacy in regulating the Vata and Kapha doshas. The balancing of these doshas is essential for maintaining health and preventing disease, illustrating the multifaceted role of *B. anthelmintica* in holistic health and wellness according to Ayurvedic principles.

Sushruta Samhita

The Sushruta Samhita, a foundational text in Ayurvedic medicine with a particular emphasis on surgical procedures and therapeutic treatments, meticulously documents the medicinal applications of *B. anthelmintica* (commonly referred to as Krishna Jiraka or, in a broader context, simply Jiraka). This ancient text references the inclusion of *B. anthelmintica* in various medicinal formulations aimed at the management of gastrointestinal disorders, including but not limited to indigestion, colic, and diarrhoea.

Sushruta elaborates on the application of *B. anthelmintica* in wound care, highlighting its use in poultices and medicated oils due to its established antiseptic and anti-inflammatory properties. The text also extends its scope to discuss the role of *B. anthelmintica* in herbal preparations that are beneficial for women's health. Notably, it is cited for its efficacy in postpartum recovery and in the regulation of menstrual irregularities.

Furthermore, *B. anthelmintica* is regarded as a valuable natural agent for purifying the digestive tract and enhancing the body's intrinsic detoxification mechanisms.

Bhavaprakasha Nighantu

The Bhavaprakasha Nighantu, a significant Ayurvedic text compiled by Bhavamisra in the 16th century CE, serves as an extensive resource that catalogs various herbs and medicinal substances utilized in Ayurvedic medicine. Among the entries, *B. anthelmintica* (Kaala Jeera/ Krishna Jiraka) is distinctly classified apart from its counterpart, Shweta Jiraka, or white cumin.

In terms of its pharmacological profile, *B. anthelmintica* is characterized by a taste profile that is predominantly pungent (Katu) and bitter (Tikta). It possesses a hot (Ushna) potency, which is crucial for its therapeutic applications, further complemented by a pungent post-digestive effect (Katu Vipaka). These qualities render *B. anthelmintica* particularly effective in enhancing digestive function, alleviating intestinal gas, and mitigating abdominal discomfort.

Clinical application of *B. anthelmintica* reveals its efficacy in treating several conditions, including Arshas, commonly known as haemorrhoids, as well as Krimi, which refers to intestinal parasites. Moreover, its role in managing Shoola (abdominal pain) has been documented due to its ability to stimulate digestive processes and promote overall gastrointestinal health.

Beyond gastrointestinal applications, *B. anthelmintica* also contributes to respiratory health. Its properties are beneficial in managing conditions such as asthma and coughing, attributable to its Kapha-vata hara characteristics, which help regulate the excess doshas of Kapha and Vata.

Phytochemical Constituents of *B. anthelmintica*

B. anthelmintica is a rich source of diverse phytochemicals, which are responsible for its observed medicinal properties and industrial potential (https://en.wikipedia.org/wiki/Baccharoides_anthelmintica). Various classes of compounds have been isolated and identified from different parts of the plant, particularly the seeds (Patel & Bhalerao, 2017).

Major Chemical Constituents

Fatty Acids and Lipids:

The seeds are renowned for their high oil content (typically 18-42%), which is exceptionally rich in vernolic acid (cis-12,13-epoxy-cis-9-octadecenoic acid (Dogra *et al.* 2020). Vernolic acid often constitutes 65-80% of the total fatty acids in the seed oil. This epoxy fatty acid is the primary reason for the industrial interest in the plant as a source of natural epoxy oil for manufacturing polymers, plastics, coatings, and adhesives (Kalimuthu *et al.* 2016). Other fatty acids present in significant amounts include linoleic acid, oleic acid, palmitic acid, and stearic acid (Ashok *et al.* 2009). Minor amounts of cyclopropane fatty acids like sterculic acid and malvalic acid have also been reported. Additionally, triacylglycerols containing vernolic acid (e.g., trivernolin) are major components of the oil (Panda *et al.* 2018).

Sesquiterpene Lactones

This class of compounds is characteristic of the Asteraceae family and contributes significantly to the biological activity, often including bitterness and cytotoxicity (Zhang *et al.* 2019). Several sesquiterpene lactones have been isolated from *B. anthelmintica*, primarily of the guaianolide and germacranolide types (Arya *et al.* 2012).

Examples include: Baccharolide, Baccharin, Vernodalol, Vernolide, Vernodalin, Hydroxyvernolide**,** Centratherin (isolated from *Centratherum anthelminticum*)**,** and Vernomenin.

Associated phytochemicals: Various derivatives and related compounds have been reported across studies using different synonyms (Dogra *et al.* 2020). These compounds are often implicated in the plant's anthelmintic, cytotoxic, and anti-inflammatory effects.

Steroids and Triterpenoids: Phytosterols and triterpenes are common plant metabolites.

Sterols: β-Sitosterol, stigmasterol, stigmasterol acetate, and their glucosides (e.g., β-sitosterol-3-O-β-D-glucopyranoside) have been isolated (Dogra *et al.* 2020).

Triterpenoids: Lupeol, lupeol acetate, α-amyrin, β-amyrin, β-amyrin acetate, oleanolic acid, and ursolic acid have been reported (Panda *et al.* 2018).

Flavonoids: Flavonoids are known for their antioxidant and anti-inflammatory properties. Compounds isolated from *B. anthelmintica* include: Apigenin, Luteolin, Quercetin, Kaempferol, Isorhamnetin, Myricetin, Rutin, Chrysoeriol, and Various glycosides of these aglycones (e.g., luteolin-7-O-glucoside, apigenin-7-O-glucoside) (Arya *et al.* 2012, Abulikemu *et al.* 2018).

Phenolic Acids: Simple phenolic acids contribute to the plant's antioxidant activity.
Examples include: Caffeic acid**,** Ferulic acid**,** Chlorogenic acid**,** Gallic acid**,** Protocatechuic acid**,** Vanillic acid (Arya *et al.* 2012).

Other Compounds
Alkaloids: Presence of alkaloids has been suggested in some preliminary screenings, but specific structures are not well characterized (Dogra *et al.* 2020). Trace amounts might be present e.g., vernonine, vernovan.

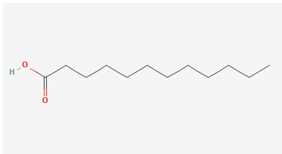
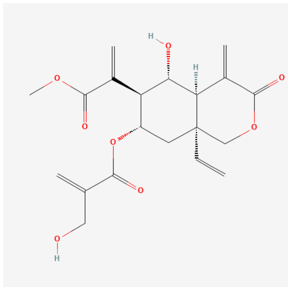
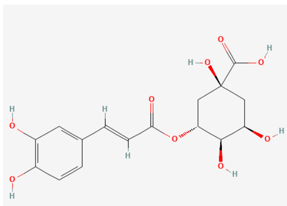
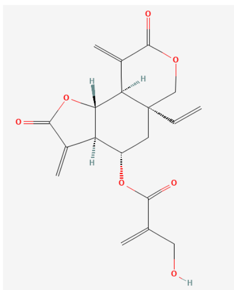
Saponins: Detected in phytochemical screenings, potentially contributing to detergent and anthelmintic properties e.g., stigmastane-type saponins.

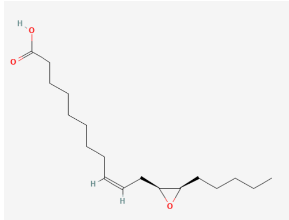
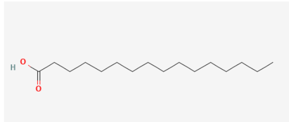
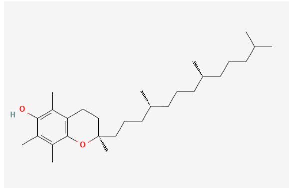
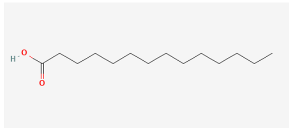
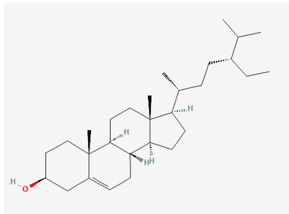
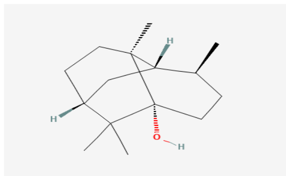
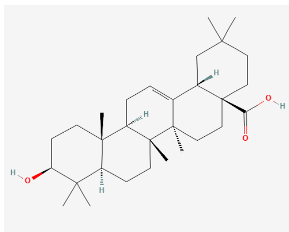
Amino Acids: Free amino acids have been identified in the seeds (Panda *et al.* 2018, Dogra *et al.* 2020).

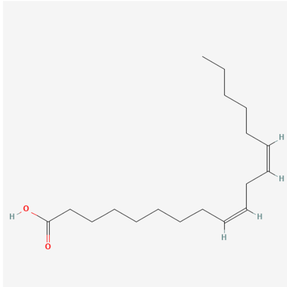
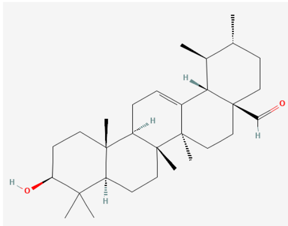
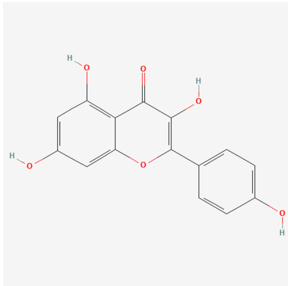
Volatile Oils: The plant possesses an aroma, suggesting the presence of volatile components, although these are less studied compared to the fixed oil. Limonene, α-pinene, and β-caryophyllene are examples sometimes found in related species or mentioned anecdotally (Panda *et al.* 2018, Gopalkrishna *et al.* 2016).

There are different bioactive compounds or phytochemicals present in the seed extract of *B. anthelmintica*, which can be identified through GC-MS analysis. Some of the important compounds are listed in Table 2. The structures of these compounds were retrieved from the PubChem database of the National Center for Biotechnology Information (NCBI).

Table 2. List of important phytochemicals of *B. anthelmintica* with their structure and formula (PubChem, NCBI database).

IUPAC Name	Common Name	Chemical Formula	Structure
Dodecanoic acid	Lauric acid	$C_{12}H_{24}O_2$	
[(4aR,5R,6S,7S,8aR)-8a-ethenyl-5-hydroxy-6-(3-methoxy-3-oxoprop-1-en-2-yl)-4-methylidene-3-oxo-1,4a,5,6,7,8-hexahydroisochromen-7-yl] 2-(hydroxymethyl)prop-2-enoate	Vernodalol	$C_{20}H_{24}O_8$	
(1S,3R,4R,5R)-3-[(E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-1,4,5-trihydroxycyclohexane-1-carboxylic acid	Chlorogenic acid	$C_{16}H_{18}O_9$	
[(3aR,4S,5aR,9aR,9bR)-5a-ethenyl-3,9-dimethylidene-2,8-dioxo-3a,4,5,6,9a,9b-hexahydrofuro[2,3-f]isochromen-4-yl] 2-(hydroxymethyl)prop-2-enoate	Vernodalin	$C_{19}H_{20}O_7$	

(Z)-11-[(2S,3R)-3-pentyloxiran-2-yl]undec-9-enoic acid	Vernolic acid	$C_{18}H_{32}O_3$	
Hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	
(2R)-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-3,4-dihydro-2H-1-benzopyran-6-ol	Tocopherol	$C_{29}H_{50}O_2$	
Tetradecanoic acid	Myristic acid	$C_{14}H_{28}O_2$	
(3S,8S,9S,10R,13R,14S,17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	β-Sitosterol	$C_{29}H_{50}O$	
(1R,3R,6S,7S,8S)-2,2,6,8-tetramethyltricyclo[5.3.1.03,8]undecan-3-ol	Patchouli alcohol	$C_{15}H_{26}O$	
(4aS,6aR,6aS,6bR,8aR,10S,12aR,14bS)-10-hydroxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid	Oleanolic acid	$C_{30}H_{48}O_3$	

(9Z,12Z)-octadeca-9,12-dienoic acid	Linoleic acid	$C_{18}H_{32}O_2$	
10-hydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydro-1H-picene-4a-carbaldehyde	Ursolic aldehyde	$C_{30}H_{48}O_2$	
3,5,7-trihydroxy-2-(4-hydroxyphenyl)chromen-4-one	Kaempferol	$C_{15}H_{10}O_6$	

Potential of Phytochemicals

Several compounds have demonstrated promising anthelmintic and anticancer activities in recent research. Regarding anthelmintic properties, studies have explored the effects of fatty acids on nematode control. While the specific fatty acids mentioned (lauric acid, vernolic acid, palmitic acid, linoleic acid, and myristic acid) aren't individually highlighted in the provided references, some sources allude to the anthelmintic potential of fatty acids in general. For example, *Nigella sativa* seeds possess anthelmintic activity against gastrointestinal nematodes in sheep (Shaibani *et al.* 2008, Dwivedi *et al.* 2011). *Myristica fragrans* (Nutmeg) extract exhibited anthelmintic activity, which implies some effect on fatty acids, although the active components were not confirmed. Several studies support anthelmintic effects of pumpkin seed extract against *Aspiculuris tetraptera* according to Ayaz *et al.* (2015) *Carica papaya* seeds against gastro-intestinal helminths in Red Sokoto goats according Ameen *et al.* (2005), however these are not fatty acids, so they do not fit the above-mentioned compounds. Furthermore, Adak & Kumar (2022) offer a narrative review of herbal anthelmintic agents, providing a broader perspective on plant-derived anthelmintics.

Terpenoids vernodalol and vernodalin show antitumor potential; Wu *et al.* (2022) found that vernodalol mediates antitumor effects in acute promyelocytic leukaemia cells, while Looi *et al.* (2013) demonstrated that vernodalin, isolated from *Centratherum anthelminticum* seeds, induces apoptosis in human breast cancer cells via the caspase pathway.

Alkaloids are recognized for their anthelmintic properties, with the ability to paralyze the central nervous system of parasites and exhibit antioxidant activity, as noted by Adak & Kumar (2022) although the exact mechanism remains unexplained, supporting the need for exploration. Saponins, such as sitosterol and oleanolic acid, have been reported to inhibit larval metamorphosis and damage parasitic cuticles, ultimately causing paralysis or death. Patchouli alcohol has been studied for its anticancer and anti-inflammatory properties. Cai *et al.* (2022) demonstrated its ability to suppress castration-resistant prostate cancer progression via inhibition of the NF-κB signalling pathway, while Liao *et al.* (2013) reported its immunomodulatory activity in mice. Ursolic aldehyde is suggested to exert anthelmintic effects through protein denaturation and ROS-mediated damage, and kaempferol is considered promising due to its reported ability to induce worm paralysis and reduce egg per gram (EPG) counts; however, further research is required. Instead, Pang *et al.* (2021) highlighted kaempferol's therapeutic potential for vitiligo, noting that it activates the Nrf2/HO-1 pathway and protects melanocytes.

As stated earlier, *B. anthelmintica* is capable of various activities, such as anticancerous, antihelmintic, antidiabetic, etc., owing to several bioactive compounds present in it. Table 3 depicts some of those important chemical compounds with their activity and mechanism of action, among which most of them are known for their anthelmintic properties.

Table 3. Tabulated data of bioactive compounds of *B. anthelmintica* with their potential mechanism of action.

Name	**Activity**	**Class**	**Mechanism of action**	**References**
Lauric acid	Anthelmintic, Antimicrobial	Fatty acid	• Disrupting the parasite's cell membrane, leading to leakage and inhibiting larval development and motility.	https://www.rxlist.com/supplements/lauric_acid.htm
Vernodalol	Antitumor	Terpene lactone	• Induction of apoptosis in acute promyelocytic leukaemia (APL) cells	Wu *et al.* 2018
Chlorogenic acid	Anthelmintic	Phenolic compound	• Directly interfere with egg development, preventing the larvae from hatching.	Ayaz *et al.* 2015
Vernodalin	Anticancerous	Terpenoid	• Activates caspase-9, -3, and -7, leading to PARP cleavage and the execution of the apoptotic program. • Alters the balance of Bcl-2 family proteins (increased Bax, decreased Bcl-2) to favor mitochondrial-mediated apoptosis.	Bhinge *et al.* 2010
Vernolic acid	Anthelmintic	Fatty acid	• Its ability to destabilize bacterial membranes and interfere with bacterial metabolic processes	Looi *et al.* 2013
Palmitic acid	Anthelmintic	Fatty acid	• By blocking the antioxidant enzymes, a defensive system against the oxidants produced by the parasitic worm is developed. • It either binds to the host's free GIT protein or prevents helminths from producing energy, which kills the parasites. stops larvae from developing from eggs and lowers EPG.	Herndon *et al.* 2020, Ayaz *et al*. 2015
Tocopherol	Anthelmintic	Phenolic compounds	• Eosinophils kill parasitic worms by attacking nematode structural proteins. • Disrupt the cell surface glycoprotein and uncouple the oxidative phosphorylation process, which will kill the parasite.	Looi *et al.* 2013, Bhinge *et al.* 2010
Myristic acid	Anthelmintic	Fatty acid	• Its ability to disrupt cell membranes and interfere with protein function in parasites.	Haye *et al.* 2016
Sitosterol	Anthelmintic	Saponins	• Reduces EPG by inhibiting the metamorphosis of larvae from eggs. • Infected parasitic worms become paralyzed or die. • Targets the permeability of the	Adak *et al.* 2022

			parasitic cuticle.	
Patchouli alcohol	Anticancerous Anti-inflammatory	Terpenoid	• Upregulating miR-497-5p expression. • Downregulating SFN (Stratifin) expression • Blocks the NF-κB inflammatory pathway by inhibiting RK activation.	Herndon *et al.* 2010 Ayaz *et al.* 2015, Looi *et al.* 2013
Oleanolic acid	Anthelmintic	Saponins	• It inhibited the development of L3 Heligmosmoides polygyrus larvae, the infective stage of this intestinal parasite nematode.	Hayes *et al.* 2016
Linoleic acid	Anthelmintic	Fatty acid	• Inhibiting antioxidant enzymes results in a defensive mechanism against oxidants produced by the parasitic worm. • It attaches to free proteins in the host's GIT or interferes with helminth energy synthesis, causing parasite death. • Reduces EPG by inhibiting the metamorphosis of larvae from eggs. • Reduce the worm's faecal egg count while simultaneously inhibiting egg hatching.	Adak *et al.* 2022
Ursolic aldehyde	Anthelmintic	Triterpenoids	• Infected parasitic worms become paralyzed or die. • Protein denaturation produces a defensive mechanism and damages the characteristics of reactive oxygen species (ROS).	Hayes *et al.* 2016, Wu *et al.* 2018
Kaempferol	Anthelmintic Anti-vitiligo	Flavonoids	• Worm paralysis and a decrease in EPG. • Activating the Nrf2/HO-1 signalling pathway. • Reducing oxidative stress in melanocytes. • Protecting melanocytes from apoptosis.	Herndon *et al.* 2020

Precautions and Contraindications

Dosage: Traditional systems emphasize using the plant, especially the seeds, in specific, often low doses. Overdosing is generally advised (Ayaz *et al.* 2015, Pang *et al.* 2021)**.** High doses of the seeds are considered potentially toxic or emetic (causing vomiting).

Pregnancy and Lactation: Use during pregnancy and lactation is often contraindicated or recommended only with extreme caution in traditional texts due to potential adverse effects on the foetus or infant (Mali *et al.* 2007).

Specific Conditions: Some sources advise caution in individuals with high 'Pitta' (a concept in Ayurveda related to heat and metabolism) due to the plant's perceived heating nature.

Formal toxicological studies, primarily in rodent models, provide more quantitative data
Acute Toxicity (LD_{50}): Studies evaluating the acute toxicity (LD_{50} - the dose lethal to 50% of test animals) of various extracts have generally indicated low acute toxicity for oral administration.

For example, LD_{50} values for aqueous and ethanolic seed extracts in rats or mice have often been reported to be greater than 2000 mg/kg or even 5000 mg/kg body weight, classifying them as relatively non-toxic according to standard guidelines (Shaibani *et al.*, 2008, Wu *et al.* 2018). One study reported a higher LD_{50} (>16 g/kg) for aqueous extract in rats. Another found no mortality up to 2 g/kg for an ethanolic extract (Karumari *et al.* 2014).

However, some variability exists, and intraperitoneal administration typically shows higher toxicity (lower LD_{50}) than oral administration.

Sub-chronic Toxicity: Studies involving repeated administration over several weeks (e.g., 28 or 90 days) are crucial for assessing potential target organ toxicity.

Some sub-chronic studies (e.g., 28 days) with ethanolic or aqueous seed extracts at doses relevant to potential therapeutic use (e.g., up to 500 mg/kg or 1000 mg/kg/day in rats) have reported no significant adverse effects on body weight, food/water consumption, haematological parameters (RBC, WBC, platelets, haemoglobin), or serum biochemical markers of liver function (ALT, AST, ALP, bilirubin) and kidney function (urea, creatinine). Histopathological examination of major organs (liver, kidney, heart, spleen, lungs) in these studies often revealed no significant treatment-related abnormalities (Cai *et al.* 2022, Mali *et al.* 2007).

However, other studies or higher doses might reveal subtle changes, emphasizing the need for dose-dependent evaluations.

Cytotoxicity of Isolated Compounds
While extracts may show low overall toxicity, certain isolated compounds, particularly the sesquiterpene lactones (vernodalin, vernolide, etc.), exhibit significant cytotoxicity *in vitro* (Looi *et al.* 2013, Adak *et al.* 2005).
Therapeutic Window: This cytotoxicity is the basis for their potential anticancer activity but also raises concerns about their potential toxicity to normal cells. The therapeutic index (ratio of toxic dose to therapeutic dose) for these compounds needs careful determination.

Selective Toxicity: Ideally, anticancer compounds should exhibit selective toxicity towards cancer cells over normal cells. While some sesquiterpene lactones show promise, their general alkylating ability suggests potential for non-specific toxicity if concentrations become too high systemically (Roeber *et al.* 2013, Mali *et al.* 2007).

Potential Adverse Effects and Concerns
Gastrointestinal Irritation: The bitter taste and potential irritant nature of some constituents (e.g., saponins, terpenes) could cause nausea, vomiting, or abdominal discomfort, especially at higher doses. This aligns with traditional cautions about high doses being emetic (Cai *et al.* 2022, Ayaz *et al.* 2015, Tangpu *et al.* 2005).

Allergenic Potential: Like many plants in the Asteraceae family, *B. anthelmintica* contains sesquiterpene lactones, which are known contact allergens in sensitive individuals, potentially causing allergic contact dermatitis upon handling the plant or topical application (Tangpu *et al.* 2005).

Drug Interactions**:** The potential for pharmacokinetic or pharmacodynamic interactions with conventional drugs exists. For example, components inhibiting cytochrome P450 enzymes (CYPs) could alter the metabolism of co-administered drugs. Its antidiabetic or anti-inflammatory effects could potentially interact with corresponding medications. Research in this area is lacking.

Hepatotoxicity/Nephrotoxicity**:** While most sub-chronic studies at tested doses showed no significant liver or kidney toxicity (Karumari *et al.* 2014, Pang *et al.* 2021), the potential cannot be entirely ruled out, especially with long-term use, high doses, or in individuals with pre-existing conditions. Continuous monitoring in longer-term studies is advisable.

Discussion

The present study explores the potential of *B. anthelmintica,* encapsulating its traditional applications, phytochemical composition, and pharmacological properties, with particular emphasis on its anthelmintic capabilities. The plant's extensive distribution and the various uses of its different parts in traditional medicinal practices, especially in regions like India and China, underscore its historical and cultural importance.

The diverse array of phytochemicals present in *B. anthelmintica* is integral to its medicinal efficacy. Noteworthy among these are fatty acids, with vernolic acid being particularly significant, alongside sesquiterpene lactones, steroids, triterpenoids, flavonoids, and phenolic acids. This rich composition endows the plant with an extensive spectrum of pharmacological properties. Vernolic acid, a predominant constituent of the seed oil, serves not only industrial purposes but may also enhance the plant's therapeutic capabilities.

Sesquiterpene lactones deserve special attention due to their demonstrated cytotoxic and anti-inflammatory properties. These compounds offer potential avenues for cancer therapy; however, their safety profile requires meticulous scrutiny due to concerns regarding toxicity. The utilization of GC-MS in compound identification facilitates a more detailed comprehension of the correlation between specific phytochemicals and their bioactive effects. For reference, Table 2 presents a comprehensive compilation of these identified compounds, serving as a valuable resource for further investigation into their therapeutic roles.

Various chemical compounds present in the plant work in different ways to fight parasites. These compounds damage the structure of parasitic worms, hurting their cells and leading to their death. They also disrupt important processes that the parasites need to create energy and survive. Moreover, these chemical compounds can stop the development of parasite larvae, which helps control the spread and reproduction of infections.

Such multifaceted therapeutic potential indicates that *B. anthelmintica* may be beneficial in addressing a variety of health concerns, thus warranting further investigation into its comprehensive pharmacological applications. In consolidating existing research, the review identifies several avenues for future inquiry. There is a pressing need for detailed studies aimed at delineating the precise mechanisms of action of the identified phytochemicals, particularly through rigorous in vivo experimental models. Additionally, well-structured clinical trials are needed to validate the safety and efficacy of *B. anthelmintica* and its constituents across various therapeutic contexts. This highlights the importance of refining extraction methods, implementing quality control measures, and pursuing sustainable agricultural practices to enhance the therapeutic effectiveness and economic viability of this significant medicinal plant.

Hence, in-depth studies are required to clarify the potential mechanisms of action of the identified phytochemicals, particularly through *in vivo* models. Also, well-structured clinical trials are essential to validate the efficacy and safety of *B. anthelmintica* and its isolated constituents for diverse therapeutic applications.

Conclusion

B. anthelmintica serves as a significant resource within both the realm of traditional medicinal practices and the contemporary landscape of pharmaceutical development. To fully realize its pharmacological potential and therapeutic efficacy, it is imperative that we engage in continued, rigorous scientific inquiry and adopt responsible methodologies for its utilization. Such efforts are crucial not only for enhancing our understanding of its bioactive compounds but also for ensuring the sustainable preservation and accessibility of this valuable organism for future generations who may benefit from its medicinal potential.

Bridging the gap between traditional knowledge and modern scientific validation through continued, rigorous research holds immense promise for developing novel therapeutics for parasitic diseases, inflammatory conditions, metabolic disorders, skin ailments, and potentially cancer, as well as providing sustainable industrial materials. Furthermore, research on optimizing extraction methods, ensuring quality control, and investigating sustainable cultivation practices is imperative to maximize the therapeutic advantages and economic viability of this valuable medicinal plant.

Declarations

List of abbreviations: *B. anthelmintica - Baccharoides anthelmintica*

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