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The Botanical, Ethnopharmacological, Phytochemical, and Pharmacological Significance of *Plectranthus barbatus*: An Updated Review

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Plectranthus barbatus Andrews is one of the most significant species in the genus *Plectranthus* of the *Lamiaceae* (Labiatae) family. The leaves and roots of this plant are considered to be economically valuable. *P. barbatus* has been used for centuries in traditional Ayurvedic medicine as well as traditional medicine in Africa, South America, and the Far East, due to its medicinal benefits. Clinical studies of *P. barbatus* and its significant constituents support its ethno-pharmacological uses, ascribing pharmacological properties to the most important bioactive constituent in the roots, forskolin. It works alongside the enzyme adenylyl cyclase to improve the production of cyclic adenosine monophosphate (cAMP), which increases intracellular cAMP levels and decreases signal transmitters in several chronic diseases. Regardless of forskolin, various phytochemicals and essential oils (EOs) have been isolated from *P. barbatus*; they have been employed as potential agents to treat several diseases and might be promising agents that can be developed in the future for numerous pharmacological purposes. This work aimed to provide an updated review of the botanical, ethnopharmacological, phytochemical, and pharmacological significance as well as the safety of *P. barbatus*.

Keywords: ***Plectranthus barbatus*****, Ethnopharmacological uses, Pharmacological activities, EOs, Forskolin, cAMP**

INTRODUCTION

Throughout ancient times, almost all civilizations have used plants as medicines (Ikram et al. 2023). Furthermore, the world continues to see remarkable growth in the usage of medicinal herbs to treat a wide range of diseases (Chaughule and Barve, 2023). One of the most significant species in the genus *Plectranthus* of the *Lamiaceae* (Labiatae) family is *Plectranthus barbatus* Andrews (*P. barbatus*) (Obiero et al. 2023). Notably, due to its nutritional and medicinal values, *P. barbatus* possesses an important economic effect worldwide (Ibrahim et al. 2018). The most important bioactive substance in the roots is labdane diterpenoid, often known as forskolin (Badhepuri et al. 2023), which has demonstrated efficacy for cardiovascular diseases, hypertension, asthma, diabetes, and overweight, among other diseases (Amezcua et al. 2022). Despite the abundance of recent literature and studies on *P. barbatus*, there remains a lack of consolidation and organization since the existing research and knowledge on this plant are scattered and have not yet been synthesized into a cohesive body of work. This fragmentation hampers the ability of readers to easily access and comprehend the collective knowledge available on *P. barbatus*. Therefore, this updated review aimed to fill the gaps in existing literature by gathering all the information on the botany, ethnopharmacological uses, and other various uses of *P. barbatus*, as well as including recent discoveries of its phytochemicals and essential oils (EOs). It also aimed to include the scattered reports on its pharmacological uses and its safety profile, providing a recent and comprehensive understanding of the medicinal plant *P. barbatus*.

BOTANY

Taxonomy and nomenclature

Plectranthus, a genus of about 350 species, belongs to the *Lamiaceae* family, *Nepetoideae* subfamily, *Ocimeae* tribe, and *Plectranthinae* subtribe, primarily found in subtropical Australia, Asia, and Africa (Antao et al. 2021). The taxonomy of *P. barbatus* species is unclear, with it being placed in either *Coleus* or *Plectranthus* due to overlapping generic characters. *Coleus* merged into *Plectranthus*, and accordingly, all species of *Coleus* were transferred to *Plectranthus* (Paton et al. 2018). *Plectranthus*, which originated from the Greek words plectron, meaning spur, and anthos, meaning flower, refers to spur-shaped flowers in plants. However, limited knowledge about external features causes taxonomic naming issues and improper placement of related genera like *Coleus*, *Solenostemon*, and *Englerastrum* (Prasad et al. 2020). It is known as Forskohlii in English, coléus à forskoline in French, cóleo in Spanish, falso-boldo in Portuguese (de Almeida et al. 2021), Mainmul, Makandiberu, Patharcheer, and Makandi in India (Joshi, 2021). *P. barbatus*, a species with various names in popular imaginary and systematic nomenclature, is also referred to by synonyms such as *Coleus forskohlii* (Willd.) Briq., *Coleus barbatus* (Andrews) Benth., and *Solenocarpus barbatus* (Andr.) Codd.(Kanyal et al. 2021).

Geographical distribution

Plectranthus barbatus is found in mountainous areas with warm subtropical climates, and it is grown all over the world in countries including Burma, Nepal, India, Thailand, and Sri Lanka. Additionally, it is reported to extend to other countries such as the Arabian Peninsula, tropical East Africa, Ethiopia, Egypt, and Brazil. It is thought to have come from the Indian subcontinent (Reddymalla et al. 2021), and it was brought to Europe and then America by botanists and traders (Nisar et al. 2020). Notably, *P. barbatus* has become popular in continental regions, especially in Africa, as a result of its adaptability to dry and tropical conditions (Amaral et al. 2023). However, recent concerns have emerged regarding its conservation status in India, as it is now listed as a vulnerable plant species due to the ongoing collection of roots from natural habitats (Kumaresan et al. 2023). The distribution of *P. barbatus* worldwide is shown in Figure 1.

Botanical description

Plectranthus barbatus has a leaf that is 7.5 cm in length and 5 cm in width, has a distinctive teardrop shape, and is greenish in color; a purplish color in the leaf's center is possible, and pubescence is also visible. Moreover, the stem is upright and has four branches, as well as pubescence in the nodal regions. Also, its height ranges between 30 and 60 cm (Figure 2 A, B). Furthermore, the flowers are cross-fertilized, light purple or violet in color, have a hairy calyx, and the flowering is a raceme that measures 2 to 2.5 cm in length. Also, two lobes are added to the stigma, and the ovary is divided into four locules (Figure 2 C). Additionally, the plant's root, which has a fasciculated form with a diameter that ranges between 0.5 and 2.5 cm and is fusiform or conical in form, is the most important part (Mitra et al. 2020). Equally important, only *P. barbatus* has thick, golden-brown, tuberous, and fibrous roots; on the contrary, other species of the *Plectranthus* genus do not. Besides, essential oil (EO) from *P. barbatus* roots possesses a highly attractive, delicate smell with a spicy taste (Figure 2 D) (Reddymalla et al. 2021).

Figure 1: Distribution of *P. barbatus* around the world, adopted by (Reddymalla et al. 2021).

Cultivation

Plectranthus barbatus can be propagated through terminal stem cuttings, which are easy, economical, and advantageous compared to seed propagation methods (Shukla et al. 2022). It is a tropical crop that thrives in well-drained, porous soil with a pH of 5.5–7, particularly red sand, on barren hills. It prefers a humid climate with 80–95% relative humidity and a temperature of 10–25 ºC, with annual rainfall mainly during June–September. Its roots and leaves are economically valuable (Joshi, 2021). Plant terminal cuttings in nursery beds, allowing rooting, and transfer to land for cultivation in June/July and September/October, planting at 60 cm intervals (Reddymalla et al. 2021). It requires regular irrigation for growth and yield, and controlling pests like caterpillars and nematodes involves spraying with 0.1% methyl parathion and drenching roots with carbofuran granules. *Alcaligenes faecalis*, a native bacterial endophyte, influences plant productivity and forskolin content (Kumari et al. 2018).

ETHNOPHARMACOLOGICAL USES

Due to its therapeutic benefits, *P. barbatus* has been utilized for ages in conventional Ayurvedic medicine along with traditional medicine in African countries, Brazil, and the Far East (Kulbat-Warycha et al. 2022). In India, its roots are utilized to cure a wide range of conditions, including skin infections, festering boils, eczema (Kumawat and Trivedi, 2019), and constipation (Joshi, 2021). In Kenya, it is utilized for the treatment of mouth, toothache, nausea, throat, indigestion illnesses, malaria (Musila et al. 2017), and female reproductive disorders (Kaingu et al. 2013). In Kenya and Gabon, it is employed as a pesticide (Obiero et al. 2023). In Tanzania, its roots are employed to treat human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), as well as herpes zoster, herpes simplex, and dermatitis (Marealle et al. 2021). In Uganda, its leaves are employed for the treatment of HIV/AIDS-related ailments such as fever, oral candidiasis, and persistent cough (Nakibuuka and Mugabi, 2022). In Central Africa, it has been documented that *P. barbatus* is utilized for the treatment of syphilis (Musila et al. 2017). In the Democratic Republic of the Congo, it is used for the treatment of cancer (Kadima et al. 2016). In Egypt and Northern Africa, its roots and leaves are utilized as diuretics, antidepressants, and expectorants (Joshi, 2021). In Brazil, its leaves are commonly utilized for gastrointestinal disorders, including intestinal spasms and gastritis, along with hepatic diseases (do Amparo and Pinheiro, 2022), renal diseases (Cerqueira et al. 2020), hangovers (Brito et al. 2018), and diabetes (Simão et al. 2020). Relating to ethnoveterinary uses, *P. barbatus* is utilized in Kenya to treat cattle's East Coast fever, also known as theileriosis (Farah et al. 2014). Moreover, the leaves and roots of this plant are employed in India to treat various infectious diseases of dairy animals, such as inflammation, thrombotic, and spasmodic diseases (Misra et al. 2023). The ethnopharmacological uses of various parts of *P. barbatus* worldwide are presented in Table 1.

VARIOUS USES

The various uses of *P. barbatus* are summarized as follows:

Food, condiments, and dietary supplements

Plectranthus barbatus leaves are consumed as vegetables in Kenya and Yemen, while in Brazil, they are used in herbal tea (Falé et al. 2009; Amina et al. 2018a). The plant's tubers are edible and can be eaten in pickles (Mitra et al. 2020). It is also used in food recipes in South America, Africa, and the Eastern region (do Amparo and Pinheiro, 2022). In Thailand and Southeast Asia, it is used as a spice (Shivaprasad et al. 2014). The essential oils of this plant are used in the food as flavoring agents (Reddymalla et al. 2021). Its extract is a popular ingredient in weight-loss dietary supplements in Japan (Suzuki et al. 2020).

Cosmeceutical uses

The demand for forskolin in the medicine market has significantly increased in recent years (He et al. 2019). Forskolin is used in drugs to prevent hair graying and restore its regular color (Kannan et al. 2020). In Saudi Arabia, *P. barbatus* leaves are utilized as a deodorant (El-Shabasy, 2016). The essential oil of roots is used in the production of cosmetics like perfumes and creams (Kumari et al. 2018). *P. barbatus* extract is used in mouthwash and skin care preparations because of its antimicrobial properties (Mehan et al. 2019; Kulbat-Warycha et al. 2022).

Leather tanning

A study found that *P. barbatus* leaves contain sufficient tannin content needed for tanning, and this plant can be used to produce leather with quality similar to conventionally tanned leather. It was proposed to use *P. barbatus* leaf extracts for the tanning of light leather and also for re-tanning (Obiero et al. 2020).

Sanitary tissue

In Kenya, *P. barbatus* leaves are used to clean milk guards and are considered sanitary tissue (Pullaiah, 2022). The EO of roots will be useful for the development of herbal-based packaging or sanitizers (Chatterjee and Vittal, 2021).

Soil improver

Plectranthus barbatus is used for manure production (Obiero et al. 2023); it is also cultured on hillsides to avoid soil erosion; it provides antifungal compounds; and it may aid in disease management through intercropping and crop rotation as green grams, maize, and cowpeas (Lukhoba et al. 2006; Nidiry et al. 2015).

Floral resource

In Kenya, *P. barbatus* is considered a floral resource because it produces both nectar and pollen throughout the year. Also, it was found that the bee-floral interaction was high in *P. barbatus* since it was forage for 15 bee species. As a result, this plant is important for the provision of floral resources and nesting sites for bees (Guantai et al. 2019).

Other uses

Plectranthus barbatus is a traditional plant used in Kenya as a garden herb, ornamental plant, and fence (Amina et al. 2018a). It is also used as dry-season fodder in Yemen and Kenya (Shivaprasad et al. 2014) and for spiritual cleansing on Santa Catarina Island in Brazil (Pagnocca et al. 2020).

PHYTOCHEMISTRY

Phytochemicals isolated from various parts of *P. barbatus*

Phytochemical studies on *P. barbatus* revealed the presence of various secondary plant metabolites, including terpenoids, flavonoids, alkaloids, phenolics, saponins, steroids, tannins, anthraquinonoids, coumarins, cardiac glycosides, and proteins (De Freitas et al. 2018; Shanmugam and Pradeep, 2019; Masalu et al. 2020; Jamwal et al. 2023), with diterpenes being the most common components (Chatterjee and Vittal, 2021). Taxodione, dehydroabietane, and 13-abietatriene were isolated for the first time from the aerial parts, along with 20-deoxocarnosol and 5, 6-didehydro-7-hydroxy-taxodone. Another compounds, including barbatusol, barbatusin, cyclobutatusine, 3β-hydroxy-3-deoxybarbatusin, 7β-acetyl-12-deacetoxy-cyclobutatusine, and 6β-hydroxycarnosol, were isolated from *P. barbatus*. The plant also has coleons A, B, E, F, O, T, and S, as well as plectrinone A and B, Plectranthone J, 14-deoxycoleon U, sugiol, 11-hydroxysugiol, ferruginol, 13-epi-sclareol, and cariocal (Garcia et al. 2018). New compounds, including barbatusterol, barbaterpene (Amina et al. 2018b), and plectrabarbene (Al-Musayeib et al. 2020), were also isolated for the first time from aerial parts. It is worth mentioning that changes in growing altitudes affect the antioxidant potential and secondary metabolites of *P. barbatus*, suggesting that wild populations from higher altitudes may be more suitable for cultivation and therapeutic use (Rana et al. 2020). The chemical structures of major phytochemicals present in various parts of *P. barbatus* are shown in Figure 3.

Essential oils isolated from various parts of *P. barbatus*

Only a few phytochemical investigations have explored the EO composition of *P. barbatus*, revealing significant variability across genotypes, different organs, altitudes, and plant origins. However, the presence of bornyl acetate, 3-decanone, sesquiterpene alcohols, and sesquiterpene hydrocarbons provides a distinctive spicy and long-lasting odor (Lunz and Stappen, 2021). The composition of EOs from *P. barbatus* varies based on harvesting period and terpene content, with sesquiterpenes and monoterpenes being predominant. Common compounds include α-cedrene, α-humulene, α-pinene, β-caryophyllene, β-cadinene, β-o-cymene, limonene, citronellal, and trans-caryophyllene (Kulbat-Warycha et al. 2022). The EOs from stems and roots in northern Italy were analyzed using steam distillation and revealed that stems contained α-copaene, α-terpineol, β-linalool, γ-elemene, δ-cadinene, bornyl acetate, caryophyllene, humulene, and gurjunene, while roots contained β-phellandrene, β-caryophyllene, humulene, gurjunene, and decanal (Gelmini et al. 2015). The chemical structures of major EOs present in various parts of *P. barbatus* are shown in Figure 4.

PHARMACOLOGICAL USES

There are several potential pharmacological activities that have been reported in *P. barbatus* (Al-Musayeib et al. 2020). Clinical investigations of *P. barbatus* and its key compounds support its ethnopharmacological uses, attributing most of the pharmacological properties to forskolin (Lunz and Stappen, 2021). Forskolin interacts with the enzyme adenylyl cyclase to enhance the production of cyclic adenosine monophosphate (cAMP), which raises intracellular cAMP levels and lowers signal transmitters in diabetes, cardiovascular diseases, asthma, and obesity, among other chronic diseases (Tiwari et al. 2023). Clinical investigations of *P. barbatus* organic extracts from various parts demonstrated several pharmacological properties, including hypotensive, antimicrobial, anti-inflammatory, cytotoxic, antioxidant, anti-insect, hepatoprotective, weight reduction, lipolysis induction, melanogenesis activation, hair loss prevention, antiallergic, anti-aging, anti-hypoglycemic, and antispasmodic activities, among others (Figure 5) (Amina et al. 2018a). The in vitro and in vivo pharmacological activities of *P. barbatus* studied for the treatment of different diseases and disorders are summarized as follows:

Antimicrobial activity

Plectranthus species are widely utilized in folk medicine, particularly *P. barbatus*, and their recorded high antimicrobial effects and low cytotoxicity confirm that this plant can be considered an important source of bioactive new compounds as a result of its capability to inhibit the growth of pathogenic microbes (Musila et al. 2017). Within the context of antimicrobial activity, *P. barbatus* extracts exhibited antimicrobial activity due to the presence of secondary plant metabolites like carbohydrates, alkaloids, proteins, glycosides, flavonoids, phenolics, tannins, and terpenoids, along with EOs. Antimicrobial activity is also attributed to their targets in bacterial cells, making *P. barbatus* a potential inhibitor of quorum sensing (QS) in bacteria (Baskaran et al. 2011; Chatterjee and Vittal, 2021). Forskolin, isoforskolin, ferruginol, 5,6-dehydrosugiol, and sugiol obtained from aerial parts showed broad antimicrobial activity towards tested fungal and bacterial strains, with minimum inhibitory concentration (MIC) values between 15.6 and 129 mg/mL (Mothana et al. 2019). The ethyl acetate fraction (EAF) of the leaf demonstrated moderate activity against *Helicobacter pylori* (*H. pylori*), with a MIC value of 256 µg/mL (Borges et al. 2020). In an in vitro investigation, researchers examined the antiviral activity of ethanol leaf extract against human immunodeficiency virus type 1 (HIV-1), as well as HIV-1 protease (HIV-1 PR) and HIV-1 reverse transcriptase (HIV-1 RT). The ethanol leaf extract demonstrated inhibition of HIV-1 PR, which could be attributed to diterpenoid compounds (Kapewangolo et al. 2013). Several diterpenes, including forskolin, sugiol, ferruginol, and α-cadinol, among other compounds, exhibited antiviral activity against the severe acute respiratory syndrome coronavirus (SARS-CoV) (Wardana et al. 2021). With regard to antibiofilm activity, an in vitro study found that EO of roots, at a concentration (conc.) of 6.25%, inhibited violacein production in *Chromobacterium violaceum* (*C. violaceum*) and disrupted QS-regulated biofilm formation with 27.87%; it also inhibited biofilm formation with 63.6% at a double-MIC of 25% v/v in *Pseudomonas aeruginosa* (*P. aeruginosa*) PA01, along with prevented twitching motility and swarming at a conc. of 2.5% v/v (Chatterjee and Vittal, 2021). Another in vitro investigation was conducted to assess the inhibitory activity of biofilm formation by aqueous leaf extract presented half maximal inhibitory concentration (IC_{50}) values of 1.4 and 0.6 mg/mL for *Streptococcus mutans* (*S. mutans*) and *Streptococcus sobrinus* (*S. sobrinus*), respectively. Regarding anti-glucosyltransferase activity, rosmarinic acid isolated from aqueous leaf extract significantly inhibited glucosyltransferase activity, causing the cariogenic bacteria *S. mutans* and *S. sobrinus* to adhere to tooth surfaces, contributing to dental plaque formation (Figueiredo et al. 2010). Relating to anti-urease activity, a study that investigated the anti-urease activity of the EAF of leaves against *H. pylori* did not indicate important urease inhibition activity (Borges et al. 2020). The published scientific investigations that evaluated the antibacterial, antifungal, and antiviral activities of various parts' extracts and EOs of *P. barbatus* are summarized in Table 2.

Antioxidant activity

Several assays, such as 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP), and 2,2-azinobis-3-ethylbenzothiazoline-6-sulphonic acid (ABTS), are commonly used to estimate the potential antioxidant activities (Pohanka, 2023). In an in vitro study, the methanol plant extract exhibited DPPH radical scavenging activity by 92% at the maximum conc. of 10 mg/mL, while the DPPH radical scavenging activity with hexane extracts was recorded with the invitro plant by 64% at a conc. of 10 mg/mL (Ibrahim et al. 2018). The published scientific investigations that evaluated the antioxidant activity of various parts' extracts of *P. barbatus* are summarized in Table 3.

Anti-cancer activity

The 3-(4,5-dimethylthiazole-2-yl) -2,5- diphenyl tetra zolium bromide (MTT) assay is broadly used to investigate cell viability after treatment with potential anticancer agents (Constante et al. 2022). An in vitro study indicated that forskolin effectively weakens non-small-cell lung cancer cell growth, including A549 and H1299 cells, and affects their migration ability, regardless of mesenchymal-to-epithelial transition impact (Salzillo et al. 2023). Another in vitro study revealed that barbatusterol and barbaterpene have cytotoxic activity against neoplastic cells (Kulbat-Warycha et al. 2022). Moreover, ferruginol displayed anti-cancer properties by inhibiting cancer cell migration, inducing apoptosis, and G2/M phase cell cycle arrest, with IC_{50} values of 175.2 and 84.6 µM for treatment durations of 24 and 48 hours, respectively (Xiong et al. 2017). Furthermore, forskolin treatment restored protein phosphatase 2A activity in acute myeloid leukemia cells, affected protein kinase B, and extracellular signal-regulated kinase 1/2 activity, inhibited apoptosis and proliferation, and enhanced standard induction therapy (Cristobal et al. 2011). Forskolin also inhibited the proliferation of thyroid cancer cells at a conc. of 100 µM (Yano et al. 2007). The published scientific investigations that evaluated the anti-cancer activity of various parts' extracts and isolated chemical compounds from *P. barbatus* are summarized in Table 4.

Anti-inflammatory activity

The capability of *P. barbatus* extract to reduce inflammatory cytokines can be related to its traditional usage in treating different diseases (Kapewangolo et al. 2013). An in vivo study on chronic obstructive pulmonary disease (COPD) rats found that isoforskolin treatment reduced the number of inflammatory cells in peripheral blood and pro-inflammatory cytokines in bronchoalveolar lavage fluid and serum (Xiao et al. 2021). An in vitro study indicated that EOs of aerial and root parts have dose-dependent anti-inflammatory activity, with aerial parts EO showing 64.7% inhibition of protein denaturation and root parts EO showing 76.9% inhibition at 50 µg/mL (Kanyal et al. 2021). Another in vitro study has shown that forskolin and isoforskolin reduce inflammation in mononuclear leukocytes induced by lipopolysaccharide through down-regulating protein levels of TNF-α and IL-1β (Du et al. 2019). Likewise, ethanol leaf extract can reduce pro-inflammatory cytokine production, demonstrating its anti-inflammatory activity (Kapewangolo et al. 2013).

Anti-insect activity

A study investigated the impact of *P. barbatus* saline leaf extract in vitro on the survival of *Aedes aegypti* third instar larvae and revealed no mortality after 24 hours, but survival was not affected, and the half-lethal concentration (LC_{50}) value for saline extracts was 0.48% (de Almeida et al. 2021). Moreover, a study evaluated the antifeedant activity of EOs of aerial and root parts in vitro on *Spilosoma obliqua* larvae at different concentrations (100–500 ppm) and indicated that aerial parts EO had more mean leaf area consumed (3.1 cm^2) than root parts EO (2.5 cm^2) at a conc. of 500 ppm (Kanyal et al. 2021). Besides, a study showed that ethanol extracts of leaf, root, and twig were effective against *Anopheles gambiae* larvae, with leaf extract having the highest LC_{50} value at 55.65 µg/mL, followed by root and twig extracts at 636 and 465 µg/mL, respectively (Lawi et al. 2018). Forskolin treatment has been reported to affect *Tribolium confusum* ovarian development, causing ovarian variations, oocyte degeneration, resorption, and mature oocytes' inability to oviposit (El-Minshawy et al. 2018). Forskolin treatment has also been documented to affect *Papilio demoleus* fourth instar larvae, focusing on leaf area consumption, with maximum antifeedant activity of 66.01% at 200 ppm conc. for 24 hours and undamaged leaf areas observed after 48 hours (Vattikonda et al. 2014). Eugenol, a key component of *P. barbatus* leaves, demonstrated significant larvicidal activity against dengue vector *Aedes albopictus*, Japanese encephalitis vector *Culex tritaeniorhynchus*, and malaria vector *Anopheles subpictus*, with LC_{50} values of 87.25, 94.34, and 84.20 µg/mL, respectively (Govindarajan et al. 2016).

Anthelmintic activity

A study conducted to investigate the anthelmintic activity of the aqueous crude extract of *P. barbatus* leaf in vitro against *Haemonchus contortus* showed anthelmintic activity with a mean mortality of 0–16.7% at 6.25 mg/mL within a period of 24 hours (Sirama et al. 2019).

Figure 2: Growth of *P. barbatus* in its native environment: (A) *P. barbatus* cultivated in the field; (B) Leaves exhibiting a greenish teardrop shape; (C) Light purple flowers with hairy calyxes; (D) Thick, golden-brown, tuberous, and fibrous roots, adopted by (Chakraborty et al. 2022a, b; Pullaiah, 2022).

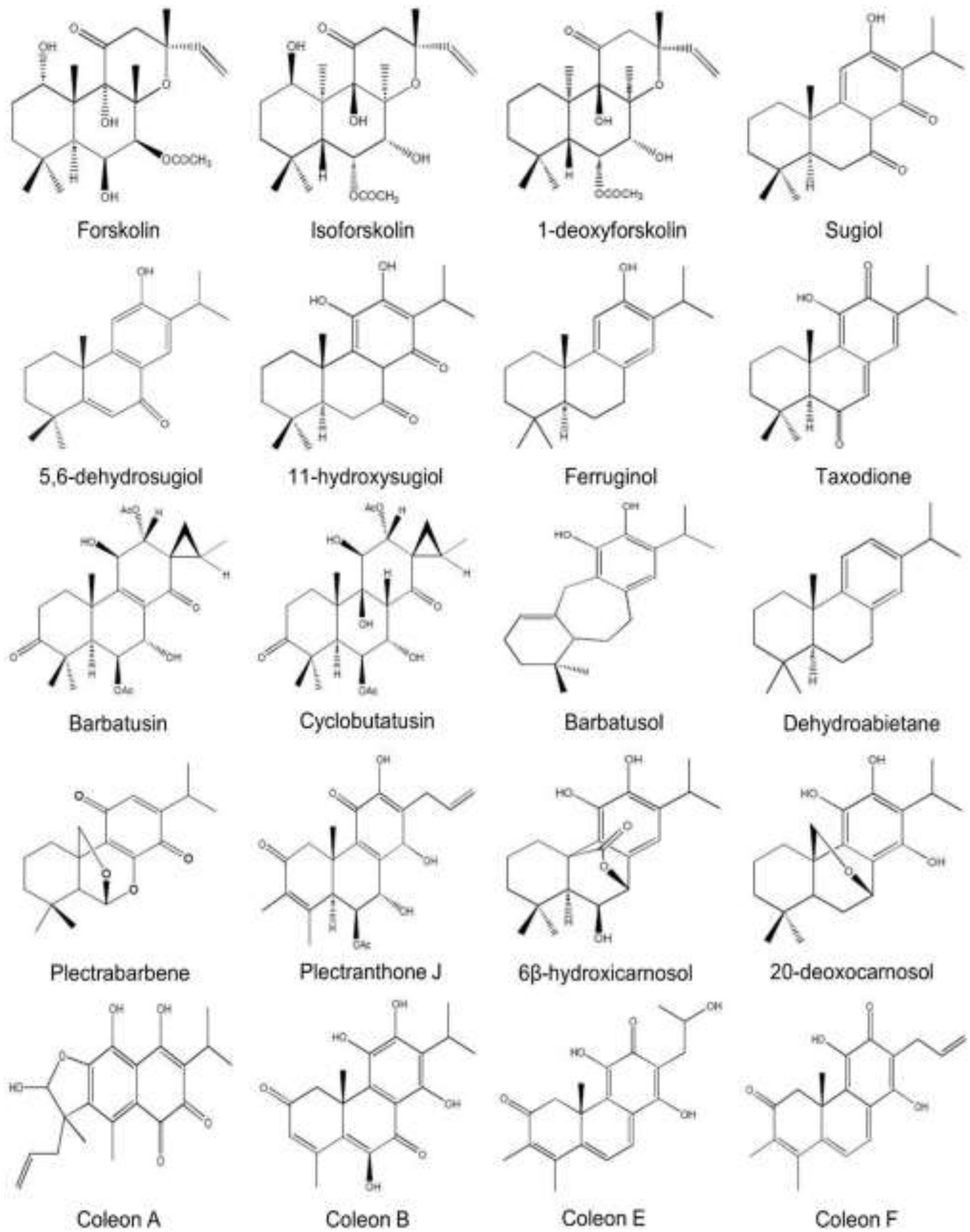

Figure 3: Chemical structures of major chemical constituents isolated from various parts of *P. barbatus*, adopted by (Garcia et al. 2018; Mothana et al. 2019; Al-Musayeib et al. 2020; Borges et al. 2020; Rathod et al. 2023).

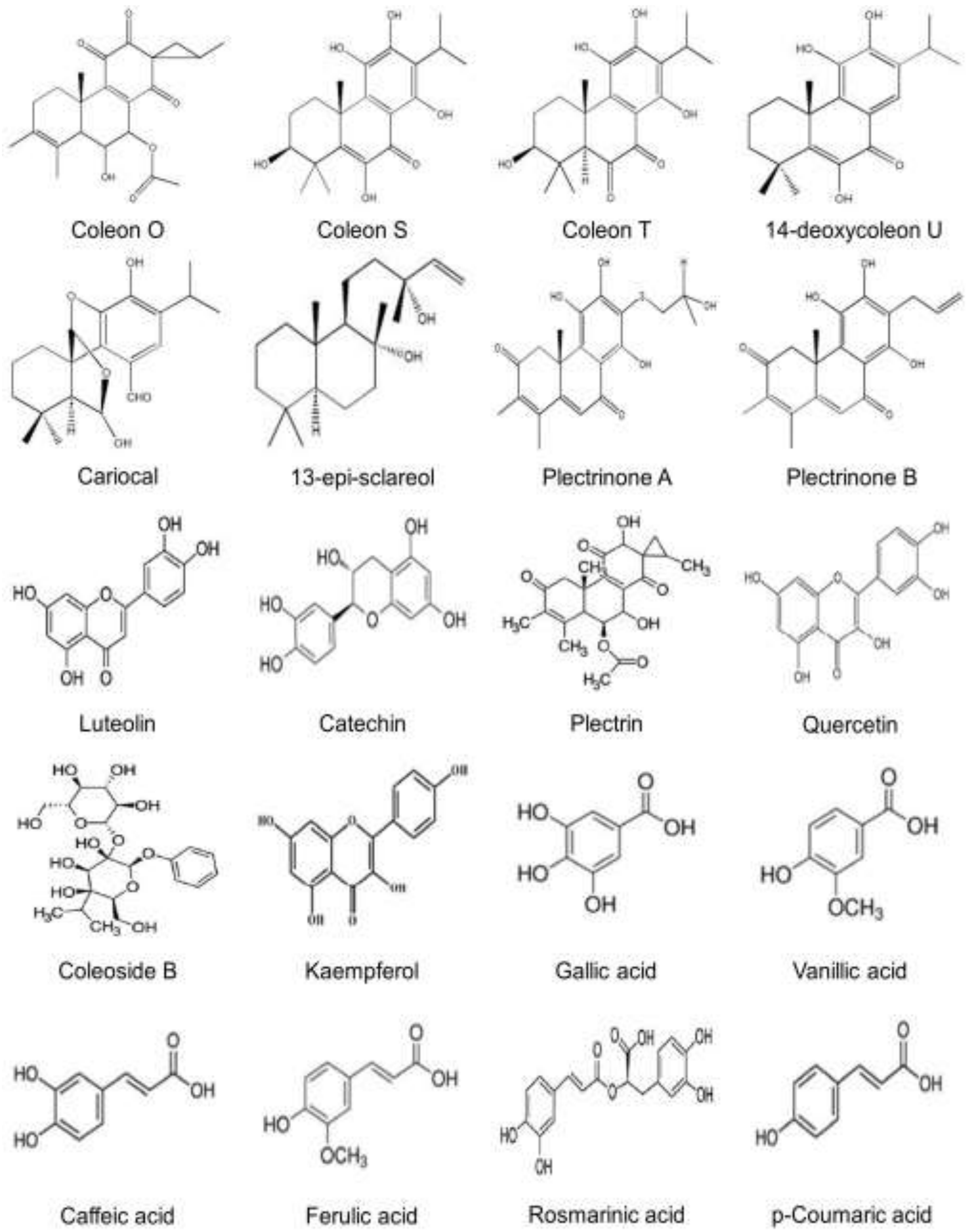

Figure 3: (continued)

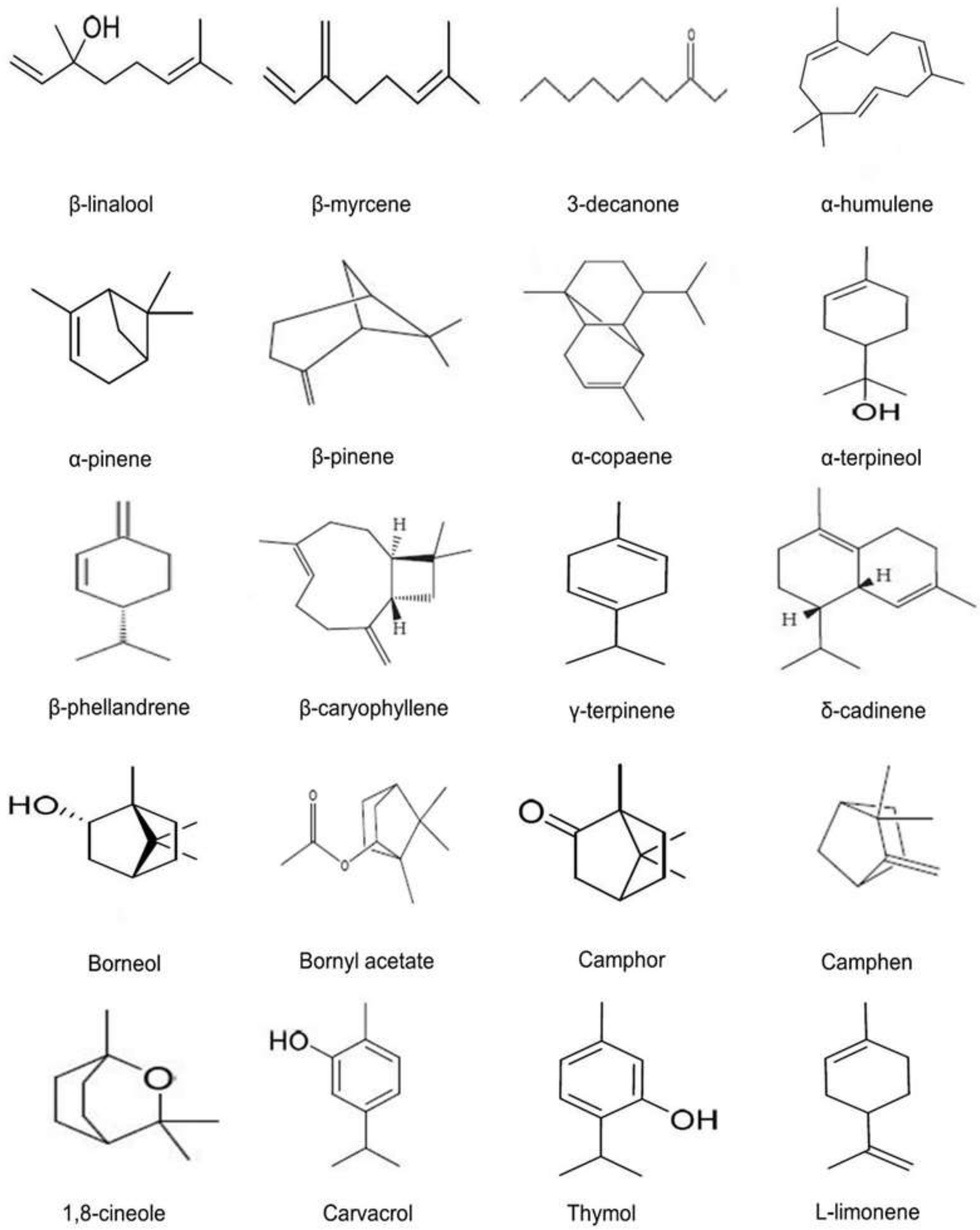

Figure 4: Chemical structures of major EOs isolated from various parts of *P. barbatus*, adopted by (Lunz and Stappen, 2021; Ramos da Silva et al. 2021; Elshafie et al. 2023; Wiart et al. 2023).

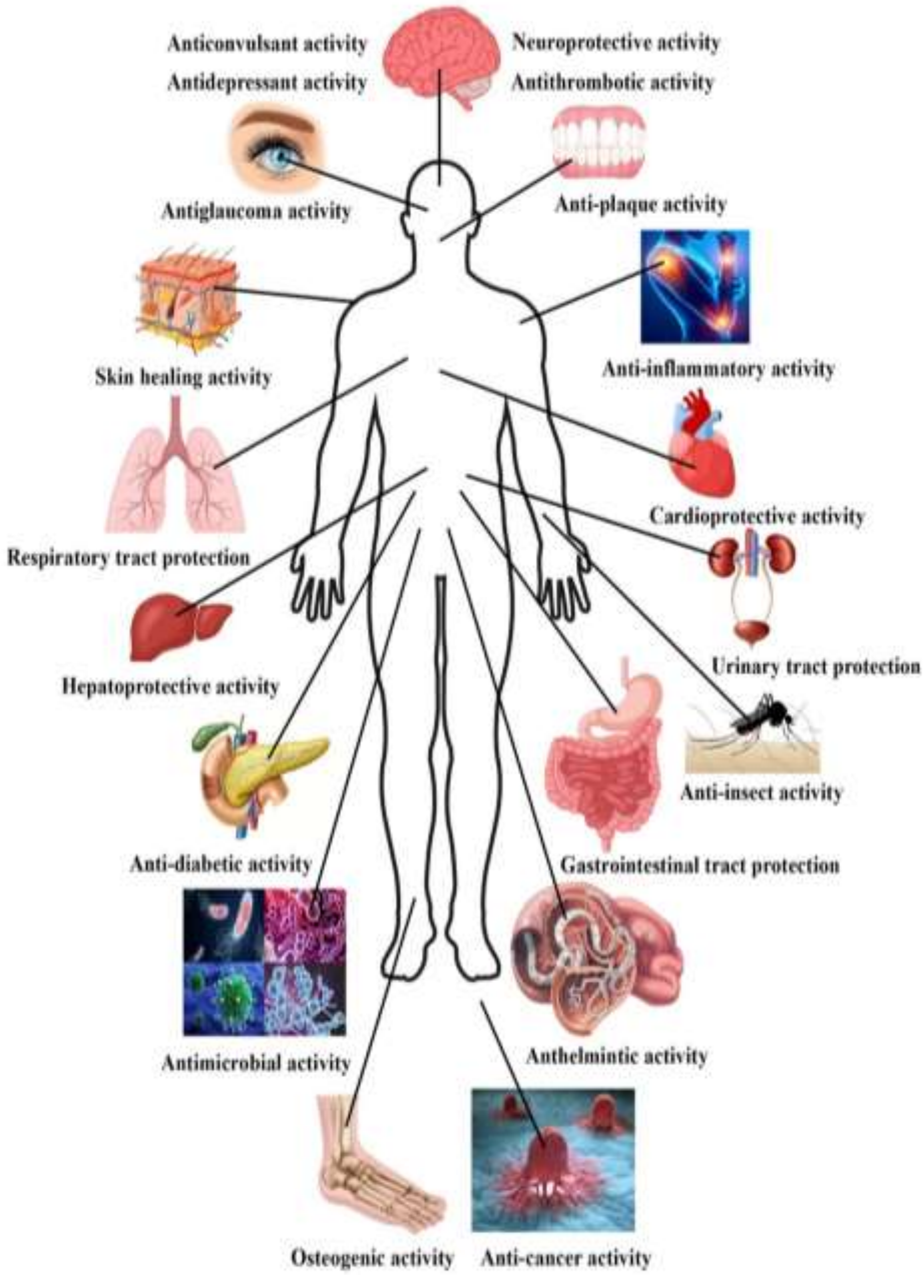

Figure 5: In vitro and in vivo pharmacological activities of *P. barbatus*, designed by the author.

Table 1: Ethnopharmacological uses of various parts of *P. barbatus* worldwide.

Country	Diseases treated	Parts used	Preparation and administration	References
Brazil	Nonspecific pain, fever, and toothache	Leaves	Leaves' infusion is taken orally	(Barbosa et al. 2023)
Brazil	Epigastric pain, dyspepsia, liver conditions, and headache	Leaves	Leaves' infusion is taken orally	(Inacio et al. 2023)
Kenya	Sexual disorders such as erectile dysfunction	Roots	Roots' decoction is taken orally by a half glass daily for 30 days	(Kyarimpa et al. 2023)
Brazil	Labyrinthitis and digestive diseases	Leaves	Leaves' maceration or infusion is taken orally; they are also used in the form of compressed powder	(Guimarães et al. 2022)
Uganda	HIV/AIDS	Leaves	Leaves' aqueous and steam extracts are taken by drinking 2 teaspoons	(Nakibuuka and Mugabi, 2022)
Tanzania	Genital warts	Roots	Roots' dry powder is administered to the affected regions	(Marealle et al. 2021)
Brazil	Indigestion, abdominal bloating, and abdominal pain	Leaves	Leaves' infusion and decoction are taken orally	(da Costa Ferreira et al. 2021)
Brazil	Digestive diseases, intestinal pains, and hepatic and renal diseases	Leaves	Leaves' infusion and decoction are taken orally	(Cerqueira et al. 2020)
India	Wounds, intestinal ulcer, cancer, and tumors	Leaves	NR	(Rolta et al. 2020)
Uganda	Heart diseases, colds and coughs, convulsions, pain, bronchitis, asthma, and tonsillitis	Leaves	Leaves' decoction is taken orally	(Ezeonwumelu et al. 2019)
Kenya	Skin diseases, chest diseases, stomachache, malaria, fever, sores, and wounds	Leaves and roots	Leaves and roots decoctions are taken orally	(Odongo et al. 2018)

NR: Not reported.

Table 2: Antibacterial, antifungal, and antiviral activities of extracts and essential oils obtained from various parts of *P. barbatus*.

Parts used	Extracts	Methods	Microorganisms tested	Standards	Effects	References
Antibacterial activity						
Fresh leaves	Ethanol	Agar cup	*Staphylococcus aureus* (*S. aureus*), *Staphylococcus saprophyticus* (*S. saprophyticus*), and *Klebsiella* spp.	15 antibiotics	Ethanol extract was only effective against *S. saprophyticus*, with a zone of inhibition (ZOI) value of 13.33 mm at 6.0 mg conc.	(Chakraborty et al. 2022b)
Fresh aerial and root parts	EOs	Agar well diffusion	*Bacillus cereus* (*B. cereus*) and *Escherichia coli* (*E. coli*)	Rifamycin	Root's EO was more effective against *B. cereus* and *E. coli*, with ZOI values of 21.7 and 22.0 mm, respectively, at 500 ppm conc.	(Kanyal et al. 2021)
Dried leaves	Acetone (70%) and aqueous	Broth microdilution	*Staphylococcus* spp., *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *E. coli*, and *P. aeruginosa*	Ciprofloxacin and Vancomycin	Acetone extract was more effective against tested bacteria, with MIC values ranging from 250 to 500 µg/mL	(Cordeiro et al. 2021)
Fresh leaves	EO	Disc diffusion	*S. aureus*, *Bacillus subtilis*, *P. aeruginosa*, and *E. coli*	NR	EO was effective against tested bacteria, with ZOI values between 16.33 and 19.67 mm at 100 mg/mL conc.	(Al-Ghamdi et al. 2021)
Fresh leaves	Ethanol (95%)	Broth microdilution	*P. aeruginosa*, *Proteus vulgaris*, *E. coli*, *B. cereus*, *S. aureus*, and multidrug-resistant *Staphylococcus aureus* (MRSA)	Kanamycin, gentamicin, and amikacin	Ethanol extract was effective against tested bacteria, with MIC values ranging from 16 to 256 µg/mL	(Rodrigues et al. 2021)

Table 2: (continued)

Parts used	Extracts	Methods	Microorganisms tested	Standards	Effects	References
Antifungal activity						
Fresh aerial and root parts	EOs	Poisoned food technique	*Curvularia lunata* (*C. lunata*) and *Alternaria alternata* (*A. alternata*)	Carbendazim	EO of the aerial part was more effective against *A. alternata* with 85%, while EO of the root part was more effective against *C. lunata* with 73.5% at 500 ppm conc.	(Kanyal et al. 2021)
Dried leaves	Acetone (70%) and aqueous	Disc diffusion and broth microdilution	*Trichophyton rubrum*	NR	Only aqueous extract was effective, with a MIC value of 800 µg/mL	(Cordeiro et al. 2021)
Fresh leaves	EO	Disc diffusion	*Candida albicans*	NR	EO was effective, with a ZOI value of 20.33 mm at 100 mg/mL	(Al-Ghamdi et al. 2021)
Antiviral activity						
Dried leaves and stems	Ethyl acetate	Reverse Transcriptase (RT) activity assay	HIV-1	Lamivudine (1 mg/mL)	Ethyl acetate extract was active against HIV-1 RT with an IC_{50} value of 1.82 mg/mL	(Masalu et al. 2020)
Fresh leaves	Ethanol	Protease fluorogenic assay	HIV-1	Acetyl-pepstatin	Ethanol extract was active against HIV-1 PR with an IC_{50} value of 62.02 µg/mL	(Kapewangolo et al. 2013)
Dried leaves	Aqueous	Virus titer reduction assay	Suid herpesvirus type 1 (SuHV-1) and bovine herpesvirus type 1 (BoHV-1)	NR	Aqueous extract was inactive in both tested SuHV-1 and BoHV-1	(Fernandes et al. 2012b)

NR: Not reported.

Table 3: Antioxidant activity of extracts obtained from various parts of *P. barbatus*.

Parts used	Extracts	Methods	Standards	Effects	References
Fresh leaves	Ethanol (70%) and aqueous	Ferrous ion chelation assay, liposome peroxidation assay, antioxidant capacity assay, DPPH assay, and ABTS assay	Trolox, butylated hydroxytoluene (BHT), and ethylene diamine tetra-acetic acid (EDTA)	Aqueous extract exhibited DPPH and ABTS radical scavenging with IC_{50} values of 2.07 and 3.74 mg/mL, respectively, while ethanol extract exhibited chelating power with an IC_{50} value of 3.04 mg/mL and antioxidant capacity with 2.96 mg AA/g	(Mendonça et al. 2023)
Fresh leaves	Ethanol (95%)	DPPH assay	Ascorbic acid	Ethanol extract exhibited antioxidant activity, with an IC_{50} value of 37.20 µg/mL	(Rodrigues et al. 2021)
Dried roots	Chloroform, petroleum ether, acetone, methanol, and aqueous	DPPH assay, FRAP assay, superoxide assay, and ABTS assay	Ascorbic acid	Methanol extract exhibited the strongest antioxidant activity, both DPPH and superoxide, with an IC_{50} value of 164.06 and 135.69 µg/mL, respectively, FRAP with 322.68, and ABTS inhibition of 81.80%	(Rana et al. 2020)
Fresh plant material	Ethanol	DPPH assay	Ascorbic acid and BHT	Ethanol extract exhibited antioxidant activity with an IC_{50} value of 6.92 µg/mL compared to BHT with an IC_{50} value of 16.36 µg/mL	(Araújo et al. 2019)
Dried leaves and roots	Hexane and Methanol (85%)	DPPH assay	Ascorbic acid	Methanol extract exhibited antioxidant activity, with inhibition of 92% at 10 mg/mL conc.	(Ibrahim et al. 2018)

Table 4: Anti-cancer activity of extracts and chemical compounds obtained from various parts of *P. barbatus*.

Parts used	Extracts/ compounds	Methods	Cancer cell lines	Standards	Effects	References
Dried leaves	Acetone (70%) and aqueous	Trypan blue assay and MTT	Human chronic myeloid leukemia (K562), human pancreatic cancer (PANC-1), human prostate cancer (DU-145), and Non-Hodgkin B Cell Lymphoma (TOLEDO)	NR	Only acetone extract was cytotoxic to four neoplastic cell lines at 100 µg/mL conc.	(Cordeiro et al. 2021)
Dried leaves	Ethanol (70%) and its EAF	MTT	Human gastric Adenocarcinoma (AGS)	Cisplatin	EAF showed significant cytotoxic activity, with an IC_{50} value of 33.89 µg/mL at 12.5 µg/mL conc.	(Borges et al. 2020)
Dried aerial parts	Ethanol/forskolin, isoforskolin, ferruginol, sugiol, and 5,6-dehydrosugiol	MTT	Human cervical cancer (HeLa), human hepatocellular liver carcinoma (HepG2), and human colon cancer (HT-29)	Dasatinib	Ethanol extract was cytotoxic against Hela, HepG2, and HT-29 cell lines, with IC_{50} values of 10.16, 10.72, and 32.06 µg/mL, respectively, while ferruginol was most cytotoxic, with IC_{50} values of 15.10, 26.58, and 25.98 µg/mL, respectively	(Mothana et al. 2019)
All dried plant parts	Ethyl acetate, dichloromethane, and methanol	Resazurin assay	Human leukemic Lymphoblasts (CCRF-CEM cells)	Doxorubicin	Only methanol extract was cytotoxic, with weak cytotoxicity (<70% cell viability)	(Adam et al. 2018)
Dried stems and leaves	Aqueous	MTT	Human lung carcinoma (A549)	NR	Aqueous extract was non-cytotoxic (>80% cell viability)	(De Freitas et al. 2018)

NR: Not reported.

Antiprotozoal activity

An in vivo study assessed the antimalarial activity of *P. barbatus* root bark extracts on mice and found that root extracts induce chemo-suppression, with aqueous extract causing 55.23% and chloroform/methanol extract 78.69%, and treated mice survived for 9 days (Kiraithe et al. 2016). 5,6-didehydro-7-hydroxy-taxodone, an isolated compound from the aerial parts, was assessed in vitro for its antiprotozoal activity against *Leishmania infantum* (*L. infantum*), *Plasmodium falciparum* (*P. falciparum*), *Trypanosoma brucei* (*T. brucei*), and *Trypanosoma cruzi* (*T. cruzi*), and showed interesting activity against *P. falciparum* (IC_{50} = 9.2 μM) and *T. brucei* (IC_{50} = 1.9 μM) (Mothana et al. 2014). Another in vitro study evaluated the antimalarial activity of the methanol extract of *P. barbatus* against *P. falciparum* showed antimalarial activity with an IC_{50} value of 6.5 μg/mL. Also, a very marginal antileishmanial activity was observed for the methanol extract against *L. infantum*, with an IC_{50} value of 24.1 μg/mL. On the other hand, the methanol extract demonstrated antitrypanosomal activity against *T. brucei* (IC_{50} = 2.6 μg/mL) (Al-Musayeib et al. 2012).

Herbicidal activity

An in vitro investigation reported that EOs extracted from the aerial and root parts of *P. barbatus* exhibited potent herbicidal activity against *Raphanus raphanistrum subsp. sativus*, with inhibition of seed germination by 60.0% and 56.7% and root growth by 92.9% and 80.4%, respectively, at a conc. of 25 μg/mL. More interestingly, EOs showed 100% shoot growth inhibition between 15 and 25 μg/mL concentrations (Kanyal et al. 2021). Another study investigated in vitro the herbicidal activity of the aqueous extract of *P. barbatus* leaf against lettuce seeds (*Lactuca sativa* L.) and indicated that the aqueous extract reduced the germination of seeds at a concentration of 250 g/L (Rizzi et al. 2016).

Immunomodulatory activity

In a study that evaluated the immunomodulatory properties of aqueous and acetone extracts of *P. barbatus* leaf in vitro against IL-17A and IFN-γ cytokines, it was revealed that the aqueous extract did not inhibit IL-17A production, but the acetone extract significantly decreased IL-17A levels, especially at 100 μg/mL (p = 0.03). Moreover, the aqueous extract only decreased IFN-γ levels at 100 μg/mL; on the other hand, the acetone extract significantly decreased IFN-γ levels at both evaluated concentrations (10 and 100 μg/mL) with significant values (p = 0.03) (Cordeiro et al. 2021). Another study investigated in vitro the immunomodulatory activity of the EAF of leaves against TNF-α and IL-6 cytokines and showed no significant decrease in TNF-α production but a 28% decrease in IL-6 at 25 μg/mL, suggesting immunomodulatory activity (Borges et al. 2020).

Anti-alcohol dehydrogenase activity

An in vitro study that evaluated decoctions from *P. barbatus* leaves and stems for their alcohol dehydrogenase inhibition related to alcohol metabolism revealed that decoctions have important activities that can be associated with their use to alleviate hangover symptoms (Brito et al. 2018).

Cardioprotective activity

Treatment with *P. barbatus* root extract showed anti-atherogenic and cardioprotective properties in rats' post-myocardial infarction, with forskolin responsible for these effects (Patrignani et al. 2021). An in vivo study on rats suggested that *P. barbatus* root extract could be a promising protective and curative agent against myocardial necrosis-associated ischemic heart disease (Ahsan et al. 2014). Forskolin is a common drug used to decrease cholesterol levels in the blood (Sharma and Vasundhara, 2015), it was also found to improve diastolic and systolic function in 30 patients with congestive heart failure (Shivaprasad et al. 2014). Equally important, it has been documented that forskolin can stimulate the histamine H_1 receptor to raise cAMP levels further in cardiomyocytes (Neumann et al. 2023).

Antithrombotic activity

It has been reported that the crude extract of *P. barbatus* has a potential phytotherapeutic antithrombotic effect due to its forskolin content, which reduces platelet aggregation via adenylate cyclase (AC) stimulation. This effect, which was observed in rabbits, can be enhanced by cerebral vasodilation (Patel and Saraf, 2016), resulting in increased blood flow, aiding in cerebral vascular insufficiency, and recovery from post-stroke complications (Lakshmanan and Manikandan, 2015).

Respiratory tract protection

Isoforskolin, one of the key components of *P. barbatus*, has been found to improve lung function and alleviate lung damage in COPD rats (Xiao et al. 2021). Equally important, forskolin is known to be an effective bronchodilator drug to treat asthma. An in vivo study has been performed to investigate the forskolin effects on asthmatic patients and showed that forskolin's powder formulations contributed to bronchodilation in asthma patients. Hence, both isoforskolin and forskolin are considered to be potential agents to treat respiratory tract diseases (Nisar et al. 2020).

Hepatoprotective activity

Plectranthus barbatus has been used to treat hepatic and gastrointestinal diseases since ancient times (do Amparo and Pinheiro, 2022). *P. barbatus* root extract can improve non-alcoholic steatohepatitis (NASH) treatment by affecting cytochrome P450 subtype mRNA expression and suppressing diet-induced improvements (Suzuki et al. 2020). The hexane extract of *P. barbatus* was observed to significantly decrease serum enzyme levels and prevent an increase in liver weight, demonstrating considerable hepatoprotective activity when compared to standard silymarin and preventing liver damage stimulated by paracetamol, thioacetamide, or carbon tetrachloride (Shivaprasad et al. 2014).

Antihypertensive activity

Plectranthus barbatus has been confirmed to work against hypertension by improving the body's ability to uptake calcium. This is because a diet high in calcium (> 1000 mg calcium per day) can reduce blood pressure by promoting the secretion of parathyroid hormone (PTH) along with the renin-angiotensin-aldosterone system, which in turn increases water absorption and sodium concentration in the plasma. Cardiac output and blood pressure increase as extracellular fluid levels rise. Forskolin, which is regarded as a beneficial supplement, helps to reduce blood pressure in those with low calcium levels in their bodies (Fatima et al. 2023).

Gastrointestinal tract protection

The infusion of *P. barbatus* is utilized to treat digestive system disorders by stimulating the secretion of pepsinogen and hydrochloric acid in the stomach (Kulbat-Warycha et al. 2022). An in vitro study concluded that *P. barbatus* stem and leaf decoctions significantly inhibit acetylcholinesterase (AChE), a key enzyme in intestinal motility, which aids digestion after a large meal (Brito et al. 2018). Another in vivo study proved that aqueous leaf extract injected into the duodenal lumen reduced gastric acid secretion volume and total acidity in pylorus-ligated mice (Schultz et al. 2007).

Anti-diabetic and associated diseases activities

Plectranthus barbatus leaves have been documented to have anti-diabetic properties, with forskolin being an active antidiabetic agent that stimulates insulin secretion from β-cells and decreases blood sugar levels, which makes it similar to oral hypoglycemic drugs (Naghibi et al. 2023). *P. barbatus* alcoholic turbo-extract has the highest inhibition percentage on the α-amylase enzyme, making it a potential candidate for managing type 2 diabetes complications (Mendonça et al. 2023). Forskolin has been reported to enhance testosterone levels and sperm conc. in type 2 diabetic male rats (Naghibi et al. 2023). In a glucose-induced cataract model, lenses treated with *P. barbatus* methanol extract and forskolin showed lower galactitol content, indicating their potential as anticataract agents (Sujatha et al. 2019). In fact, forskolin raises the cAMP level in β-cells, which stimulates two major signaling pathways in β-cells. Although several investigations have been conducted to check the effect of forskolin in diabetic rats, more studies are necessary to comprehend the entire effect of forskolin in diabetic patients and locate the exact dose for humans (Nisar et al. 2020).

Antiglaucoma activity

Forskolin aids in retinal ganglion cell survival by promoting neurotrophin-like activity and decreasing intraocular pressure (IOP) by reducing aqueous humor production (Satriano et al. 2023). Forskolin-containing supplements have been shown to reduce IOP beyond the reduction achieved by antiglaucoma medications alone (Mohan et al. 2022). In a double-blind, randomized controlled trial, primary open-angle glaucoma patients administrated with eye drops of aqueous solution standardized with 1% forskolin by two drops thrice a day for 4 weeks exhibited a considerable decrease in IOP (Sim et al. 2022).

Central nervous system-related activities

Plectranthus barbatus leaves have been documented to have anticonvulsant properties, with a hydroalcoholic extract reducing seizures in mice (Fernandes et al. 2012a). It has been reported that forskolin acts as a psychostimulant, improving mental alertness (Singh et al. 2023). Forskolin is also believed to have antidepressant properties by increasing cAMP and inhibiting phosphodiesterase, but its effects are limited to animal models (Patel and Saraf, 2016). Scutellarein, (16S)-coleon E, and rosmarinic acid are crucial in inhibiting AChE, an enzyme aiding in Alzheimer's disease treatment (do Amparo and Pinheiro, 2022). Additionally, *P. barbatus* extracts, including luteolin, rosmarinic acid, and apigenin, interact with the AChE enzyme without altering its structure. Flavonoids like apigenin and luteolin are better inhibitors due to hydrophobic interactions and hydrogen bonds (Falé et al. 2012). Moreover, *P. barbatus* aqueous leaf extract and rosmarinic acid can cross intestinal and blood-brain barriers, inhibiting AChE activity in rats (Falé et al. 2011). Besides, forskolin's neurorestorative and neuroprotective effects improve cognitive and motor functions as well as energy levels. Equally important, forskolin has been shown to play several roles in autism, including activating the cAMP response element-binding protein (CREB) and AC/cAMP-mediated protein kinase A (PKA), as well as acting as a co-activator in the brain by stimulating the dopamine D1 receptor, which in turn activates the Gs protein pathway (Mehan et al. 2019).

Urinary tract protection

Plectranthus barbatus has been documented as a natural remedy for urinary tract infections, enhancing antibiotics' ability to kill 90% of bladder infection bacteria (Patel and Saraf, 2016). A study evaluated the protective effects of *P. barbatus* in vivo against Gentamicin-induced nephrotoxicity in male albino Wistar rats. Nephrotoxicity was induced in rats by gentamicin (80 mg/kg) and treated with aqueous and ethanolic extracts of *P. barbatus* (500 mg/kg), respectively, for 15 days. Both extracts protected the kidney tissues from gentamicin's toxic effects, normalizing biochemical parameters, and improving histopathological changes (Fatima and Sultana, 2018).

Skin diseases

The capacity of forskolin to increase cAMP levels in epidermal cells has been found to be medicinally helpful to patients with psoriasis (Joshi, 2021). Forskolin also enhances the natural resistance of skin to ultraviolet light and promotes a tanning response when employed topically (Patel, 2010). Furthermore, *P. barbatus* oil efficiently inhibits skin pathogens such as *S. aureus* and *Propionibacterium acnes*, causing acne and other skin diseases; bornyl acetate is responsible for this activity (Kumari et al. 2018). Similarly, the skin-healing properties of this plant may be related to the existence of anthraquinones, which may be responsible for its inhibitory activities against *S. aureus* (Kisangau et al. 2007).

Anti-obesity activity

Forskolin is known as a popular weight loss supplement that has been demonstrated to significantly reduce fat mass in overweight and obese individuals (Nilsson et al. 2023). An in vivo study that assessed the anti-obesity effects of toluene extract from *P. barbatus* root on high-fat diet-stimulated obese mice concluded that the toluene extract reduced body weight and adipocyte size by enhancing fatty acid β-oxidation and modifying gut microbiota (Tung et al. 2021). Another in vivo study indicated that *P. barbatus* extract can inhibit pancreatic lipase activity and significantly reduce total body fat, with participants demonstrating decreased abdominal and total body fat after a daily intake of 1000 mg standardized with 10% forskolin (Badmaev et al. 2015).

Anti-ageing activity

In relation to skin aging, a study indicated that application of forskolin on skin enhances melanin secretion through a direct activation of adenylate cyclase that promotes cAMP production, resulting in melanin accumulation. This action is melanocortin-1 receptor-dependent, which is a protein that exists in the extracellular membranes of epidermal melanocytes (Mesa-Arango et al. 2017).

Analgesic activity

An in vivo study concluded that the aqueous leaf extract of *P. barbatus* demonstrated significant pain inhibition in thermal and formalin-induced pain models in rats. The thermal model presented significant inhibition at 100 mg/kg within 30 and 60 minutes, while the formalin-induced pain model presented significant inhibition at 200 and 400 mg/kg concentrations (Ezeonwumelu et al. 2019).

Osteogenic activity

An in vivo study confirmed that the acetonitrile extract of *P. barbatus* increases osteoblast differentiation, cAMP, and cyclic guanosine monophosphate (cGMP) levels in rat calvarial osteoblasts. It also significantly enhances calcein deposition at osteotomy sites at 25 mg/kg, as well as stimulating modeling-directed bone formation in growing rats (Kulkarni et al. 2023). Another study indicated that forskolin improves osteogenic differentiation of stem cells of human dental pulp in vitro and promotes bone formation in vivo (Jin et al. 2023).

Anti-hypothyroidism activity

It has been documented that forskolin promotes thyroid hormone formation and release by increasing the quantity of guanine nucleotide-binding proteins, potentially increasing normal body weight (Nisar et al. 2020; Vitiello et al. 2023).

Reproductive system-related activity

Plectranthus barbatus extract reduced IL-2 and IL-G levels in rats with androgen-induced polycystic ovarian syndrome and restored both immune and opioid functions. It also reduces calcium levels, resulting in increased vaginal secretion. Additionally, the highest dose of *P. barbatus* extract (880 mg/kg per day) had an anti-implantation effect, justifying its use for abortive purposes (Kumari et al. 2018).

SAFETY

Plectranthus barbatus extract is known for its low cytotoxicity, making it extensively used for treating various ailments without any reported side effects (De Freitas et al. 2018). A study was conducted in vivo to assess the cytotoxicity of organic and aqueous root bark extracts of *P. barbatus* in mice and presented no weight fluctuations, toxicity, or mortality in the tested mice (Kiraithe et al. 2016). Another in vivo study has indicated that repeated oral exposure to 2000 mg/kg daily did not show any toxic effects on Wistar rats, suggesting it can be treated with no observable adverse effects (Yadav et al. 2022). It must be taken into account that *P. barbatus* and forskolin are not fully evaluated for their safety. It should be avoided by people with ulcers for the reason that it may raise stomach acid secretion (Lokesh et al. 2018). Equally important, the intake of *P. barbatus* extract dietary supplements induced diarrhea at a dose of 1000 mg daily in humans (Yokotani et al. 2020).

CONCLUSIONS

The medicinal plant *P. barbatus* showed great potential to treat humans. However, there is a lack of research on the applications of forskolin and other active compounds for treating humans efficiently. Further in vitro and in vivo investigations are needed on other compounds, including isoforskolin, sugiol, taxodione, ferruginol, barbatusin, barbatusterol, barbaterpene, plectrabarbene, and 13-epi-sclareol. In vitro investigations should evaluate the activity of *P. barbatus* extract on parasites and worms, while in vivo investigations should explore its effects on NASH, brain hemorrhage, Parkinson's disease, Alzheimer's disease, Huntington's disease, senescence, diabetes, wounds, and bone formation. Due to its dearth and limited distribution, particularly in Saudi Arabia, this plant requires conservation attention and cultivation enhancement measures.

SUPPLEMENTARY MATERIALS

There are no supplementary materials for this work.

AUTHOR CONTRIBUTIONS

The author, Akram Abdullah Albaidhani (AAA), made contributions to the conceptualization, key literature identification, overall design of the manuscript, in-depth evaluation and combination of the material that was reviewed, manuscript's sections writing and organization, manuscript formatting, critical discussions, and reference management. The coauthor, Ehab Hussein Mattar (EHM), contributed to supervision, providing valuable feedback, and supervising the submission procedure. The final version of the manuscript was approved by all authors after it was read and reviewed.

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CONFLICT OF INTEREST

The authors declared that the present work was performed in the absence of any conflict of interest.

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