



A review on Biochemical studies of *Elephantopus scaber* L. growing in India.

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Abstract

The little Indian plant, known as *Elephantopus scaber* Linn., is from the Asteraceae family. Although "Elephant's Foot" is the most frequent English name for *Elephantopus scaber*, the scientific term "*Elephantopus scaber*" is more Elephant's Foot, also known as Prickly-leaves or Rough-leaves. Traditional medicine has long relied on this plant's components to cure a wide range of illnesses. The principal chemical classes found by biochemical analysis include phenolic acids, terpenoids, flavonoids, coumarines, essential oils, and quinones. Deoxyelephantopin, which is found in high concentrations in this plant, has been the focus of rigorous screening and confirmation of its anticancer potential. Various study publications have documented a broad range of other biological properties, like antibacterial, antidiarrheal, diuretic, wound healing ability, antioxidant, antidiabetic, anti-inflammatory, analgesic, anti-asthmatic, antiplatelet, and so on. The main purpose of the review is to assess the traditional uses, biochemical constituents, biochemical and physiological effects and bioactivities of *Elephantopus scaber* L. growing in India.

Keywords: *Elephantopus scaber* L., India, biochemical compounds, bioactivities

1. Introduction

Elephantopus is a genus of at least twelve perennial species belonging to the asteraceae family. *Elephantopus scaber* L. is indigenous to India and the Himalayas (Bai et al., 2023; Masih et al., 2014) [1,2]. *Elephantopus mollis*, *Elephantopus carolinianus*, *Elephantopus scaber*, and *Elephantopus tomentosus* are only a few of the plants in this family (Chan et al., 2018) [3]. The plant's name is derived from the Greek words "elephas," meaning elephant, and "pous," meaning foot. Also, in New England, it is called the "devil's grandmother," in the USA as the "woolly elephant foot," and in Puerto Rico as the "cow's tongue". Only 1/32 species, *E. scaber*, flourishes in India. The plant has been extensively dispersed in the Achanakmar forest, Chhattisgarh, and is abundantly found across other parts of India, including in the Western Ghats (Hiradeve and Rangari, 2015; Misra et al., 2023) [4, 5]. It is referred to in India by a number of regional names, including Gobhi (Hindi) and Gojivha or Hastipadi (Sanskrit) (Masih et al., 2014) [2].

The plant that has been claimed to be utilised in the treatment of various ailments (Kabiru and Por, 2013) [6]. The studies involve an investigation at the kinds of secondary metabolites that the plant has (photochemistry/phytochemistry) (Junairiah et al., 2021; Widyaningrum et al., 2020; Zuo et al., 2016) [7, 8, 9]. The traditional claims of a plant's effectiveness in treating a disease condition are examined using in vitro and/or in vivo disease condition models (Pharmacology) (Hiremath et al., 2016) [10]. To determine the chemicals contained in the plant material and its physicochemical characteristics, isolation and characterisation of the plant are also conducted. *Elephantopus scaber* L. is the species of this genus that has been the subject of the most research. It has been studied for their potential as medicines, and several chemicals were isolated from the plant (Hiremath et al., 2016; Iqbal et al., 2017; Rachmadiarti et al., 2019; Mandal et al., 2018) [10, 11, 12, 13]. Solvent fractionation, a term used to describe the solubility of certain chemicals in particular solvents, has been used to inform these research (Hiremath et al., 2016) [10]. There have been several reports on the traditional applications, pharmacologic characteristics, biochemical makeup, and the different substances extracted from the plants (Chan, 2018; Widyaningrum et al., 2020; Iqbal et al., 2017) [3, 8, 11]. This article aims to provide an overview and examine the isolated chemicals, pharmacological characteristics, phytochemical compositions, traditional applications, and bioactivities of *Elephantopus scaber* L.

1.1 Traditional uses of *Elephantopus scaber*

According to Kumar (2014) [14], the complete *E. scaber* plant is used as a toothbrush in India to heal toothaches. Leukaemia, insomnia, bronchitis, diabetes, viral or even bacterial infection, snake bite, rheumatism, diuresis, along with antipyresis, the removal of bladder stones, and filariasis have also been claimed to be treated with the entire plant (Mandal et al., 2018; Kumar, 2014; Bhatta, 2015) [13, 15, 16]. According to Jasmine et al. (2021) [16], the leaves are crushed and combined with salt to cure dysentery, whereas Jamal and Jose (2017) [17] applied a water extract of the leaves to the skin to treat dermatitis and ulcers.

1.2 Biochemical constituents of *Elephantopus scaber* L.

For the Asteraceae, flavonoids have shown to be useful taxonomic markers. With some implications for flavonols, along with flavones, and also other kinds of the Asteraceae family, more than 800 compounds, totalling 4700 flavonoids, were discovered. Besides that, *Elephantopus scaber* has been extensively researched for minerals, including calcium, magnesium, iron, and zinc, as well as huge amounts of salt, such as potassium chloride (Hiradeve and Rangari, 2015) [4]. It has been claimed that the air-dried powdered seed extract in organic solvents like acetone contains terpenoids, flavonoids (fig 1) steroids, glycosides, alkaloids, quinones, terpenoids, coumarines, essential oils and phenols which are the most prevalent (Narwade et al., 2023; Suresh et al., 2023) [18, 19].

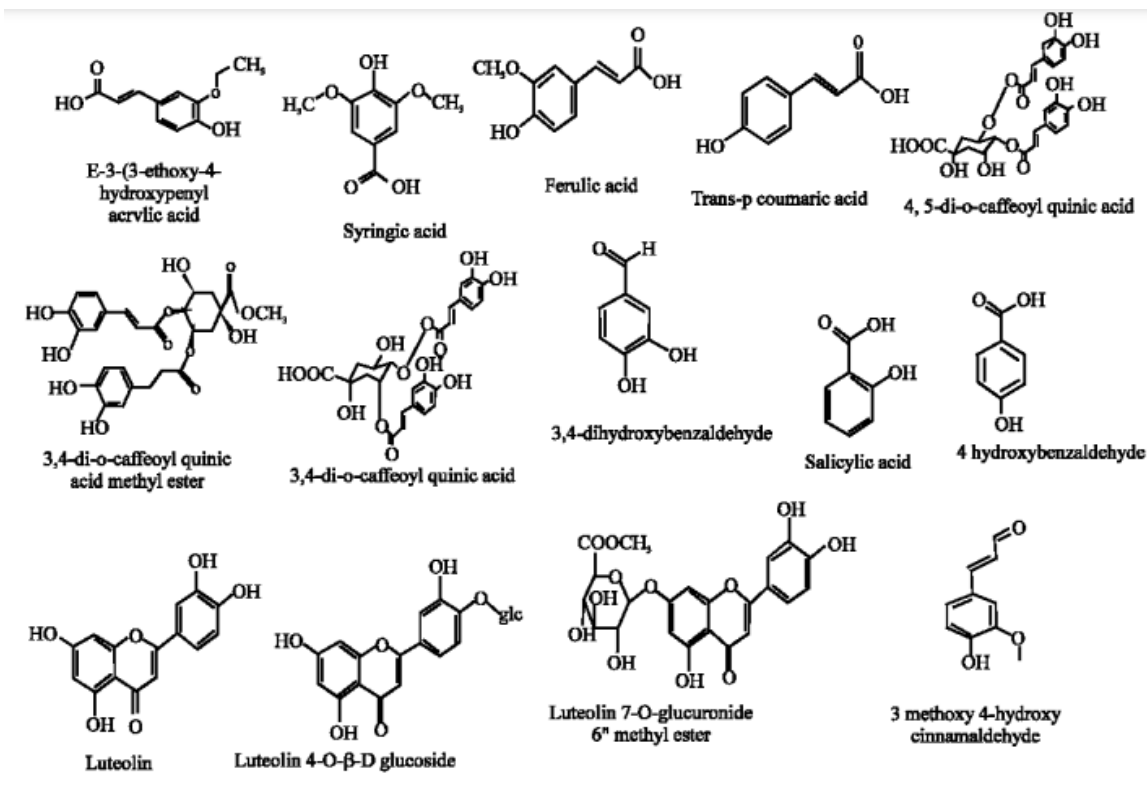


Fig.1: Essential flavanoids of Elephantopus scaber (Kabeer and Prathapan, 2014) [20]

1.3 Chemical Compounds isolated from Elephantopus scaber

In research by Kabiru and Por (2013) [6], three separate plant parts—the roots, leaves, and stem—along with two solvents—n-hexane (polar) and methanol (non-polar) solvent—were used to isolate six chemicals from *E. scaber*. The identified substances included stigmasterol, lupeol, the deoxyelephantopin isomers of stearic acid, as well as its analogues 1 and 2. According to Ali et al., (2020)[21], the plant's main phytochemical components include elephantopin, triterpenes, stigmasterol epifriedelinol, and lupeol [21].

In the dichloromethane-soluble region of the dried leaves of *E. mollis*, the following substances were discovered: stigmasterol, 2-deethoxy-2-hydroxyphantomolin, amyryn fatty acid ester, and also lupeol fatty acid ester. Their ^{13}C NMR was compared to those in the literature to corroborate their structures (Rashed, 2021) [22]. In their report on the chemical composition of *E. scaber*'s essential oils, listed the following compounds: Cyclosativene, Copaene, Isopropyl dimethyl hexahydronaphthalene, Zingiberene, Trimethyl dimethylene decahydronaphthalene, Caryophyllene, Dimethyl-6-(4-methyl-3-pentenyl), norpinene, -βSesquiphellandrene, β Caryophyllene, Isocaryophyllene, α-SantalolLedol, α-Bisabolol, Caryophyllene oxide, Cadinol, Bisabolol, Isopropyl dimethyl- tetrahydronaphthalenol, Hexahydrofarnesyl acetone, Hexadecanoic acid, Phytol and Octadecadienoic acid (Rashed, 2021) [22].

1.4 Biochemical and physiological effect of Elephantopus scaber

1.4.1 Antimicrobial activity:

The antibacterial activity of *E. scaber* has been shown by Suresh et al., (2021)[19]. By using several strains of harmful bacteria and fungi, Al-Shaheen et al. (2019) [23] conducted more investigation into the antibacterial activity. Also, the DPPH free-radical scavenging assay was utilised to test the antioxidant action of *E. scaber*, and the methanol fraction had the highest hydroxyl while the ethyl acetate fractions had the highest phenol content (Anugraha et al., 2019) [24]. Synthetic antioxidants have many adverse effects. So, we need natural antioxidants to prevent many diseases and promotion of health. In a similar manner, *E. scaber* was tested for its ability to combat *Salmonella typhimurium*, *Salmonella paratyphi A*, *Shigella sonnei*, *S. aureus*, *E. coli*, *K. pneumonia*, *P. aeruginosa* and demonstrated excellent antibacterial action against *Escherichia coli* (Hiradeve and Rangari, 2015) [4].

1.4.2 Antidiarrheal activity:

E. scaber's antidiarrheal and cardiotoxic properties were studied [Jamal and Jose, 2017 (17), Kabeer and Prathapan, 2014 (20)]. In comparison to other extracts of *Elephantopus Scaber*, the ethyl acetate extract exhibited a significant antidiarrheal effect. On the heart of the hypodynamic frog, the petroleum ether extract demonstrated significant cardiotoxic activity (Jamal and Jose, 2017; Sukho et al., 2022; Zailani and Ahmad, 2016) [17, 25, 26].

1.4.3 Antidiabetic activity:

Blood sugar may be lowered through the use of the ethnomedicinal herb *elephantopus scaber* (Narwade et al., 2023) [18]. The antihyperglycaemic effects of *E. scaber* fractions were examined in streptozotocine-induced diabetic rats. The methanol extract, acetone extract, and aqueous fractions had good hypoglycaemic effects in rats. Additionally, the extracts were shown to exhibit anticholesterolemic action. These extracts also decreased triglyceride levels. These exercises resulted in lower blood glucose levels and higher insulin concentrations.

1.4.4 Antitumor activity:

The anticancer effects of 44 sesquiterpenelactones (Fig. 2) isolated from the Asteraceae plant *Elephantopus scaber* Linn. were examined using the MTT assay. On HepG2 and Hep3B cells, deoxyelephantopin (DET) was discovered to have strong cytotoxic effects (Chen et al., 2023) [27]. The herb has undergone thorough anti-cancer studies. Deoxyelephantopin, isodeoxyelephantopin, scabertopin, and isoscabertopin are only a few examples of the sesquiterpene lactones that have been shown to be potent anticancer agents (Hiradeve and Rangari, 2015)[4]. *Elephantopus* extracts induce apoptosis and antiproliferation in human lung cancer and myeloid leukaemia cells (Nguyen, 2023)[28].

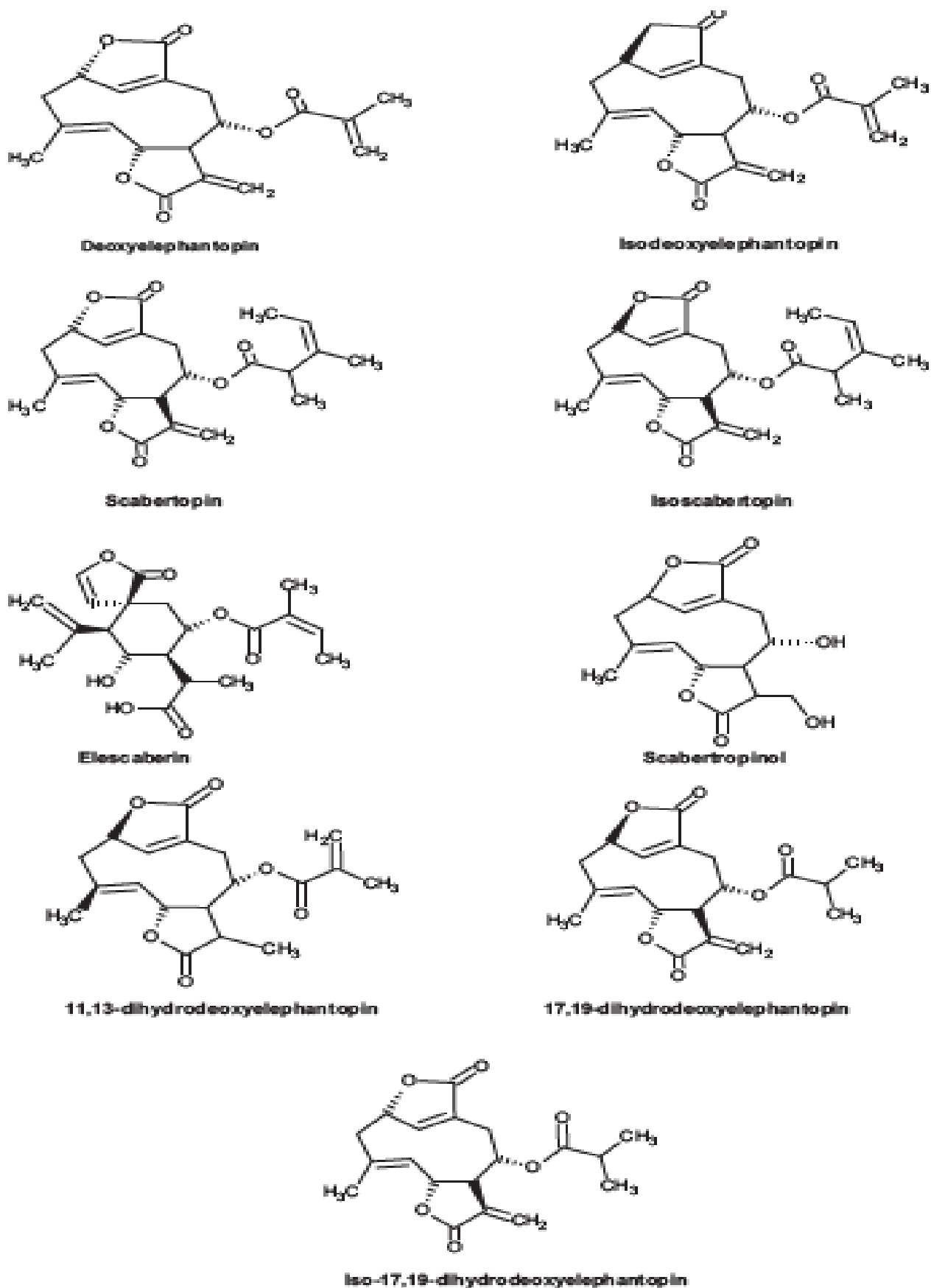


Fig 2: Sesquiterpene showing potential antitumor activity

Leukaemia, Ehrlich ascites carcinoma, and Phantomolin, two compounds derived from *Elephantopus*, all showed significant anticancer action and Molephantin also showed strong cytotoxic properties (Nguyen, 2022) [28]. Human nasopharyngeal cancer CNE cells are exposed to deoxyelephantopin, an ingredient in *Elephantopus scaber* L., which causes cell-cycle arrest and death. Deoxyelephantopin's tumor-suppressing action was studied in relation to mammary adenocarcinoma (Chen et al., 2023) [27]. In addition to acting as a selective partial agonist against PPAR γ , deoxyelephantopin was discovered to decrease the growth of cancer cells (Mehmood and Muanprasat, 2022) [29]. The potential of apoptosis to potentiate, to decrease invasion, and to eliminate osteoclastogenesis. Isodeoxyelephantopin derived from *Elephantopus scaber* (Didanco) triggers an arrest in the cell cycle and caspase-3-mediated apoptosis in T47D breast cancer cells (Kabeer et al., 2014) [30].

1.4.5 Analgesic and anti-inflammatory activity

Chan, 2018 [3] studied the analgesic impact of *Elephantopus scaber*. *Elephantopus scaber* L. exhibits anti-neuroinflammatory activity via activation of Nrf2/HO-1 signalling and inhibition of p38 MAPK pathway in LPS-Induced Microglia BV-2 Cells. Neuroinflammation plays a vital function in the pathogenesis of neurodegenerative diseases, as supported by substantial scientific evidence. Unfortunately, the currently available clinical medications evaluated for anti-neuroinflammatory therapy offer only symptomatic relief and are frequently associated with significant and intolerable side effects. The leaves of the plant inhibited the induction of iNOS, COX-2, IL-1, and TNF- by LPS via inhibition of p38 and NF-B. In addition, it is noteworthy that plant leaves suppress the inflammatory response in BV-2 cells via NF-B signalling. By modulating a myriad of genes, including HO-1, SOD, and catalase, Nrf2 signalling by plant-derived therapeutic agents induces an antioxidative response against inflammation-related chronic diseases and reduces oxidative stress. It was found that the herb had strong analgesic and anti-inflammatory properties.

1.4.6 Hepatoprotective and Antioxidant Effect

E. scaber's hepatoprotective potential was shown, where the plant extract could repair liver damage brought on by ethanol treatment. The plant's historical usage as a liver tonic was supported by this activity (Ho et al., 2012) [31]. The protective mechanism of *E. scaber* in LPS-stressed acute hepatic damage in SD rats includes an antioxidant effect as well as suppression of p38 MAP kinase and also COX-2 expressions (Ho et al., 2012) [31]. *E. scaber*'s methanolic extract was used to assess its hepatoprotective and antioxidant properties. Additionally, the damage was reversed when damaged by carbon tetrachloride on rat liver proved the extract's capacity to scavenge free radicals (Rashed, 2021) [22].

1.4.7 WOUND HEALING PROPERTIES

By employing the incision, excision, and dead space wound models in rats, it was possible to study *E. scaber*'s potential to speed up wound healing. According to research by Mandal et al., (2018) [13], the plant's deoxyelephantopin and ethanol extract both seem to hasten the healing of rat wounds.

1.4.8 Diuretic effect

Healthy volunteers were used to study the diuretic impact of *E. scaber*, which was found to have a weak effect (Narwade et al., 2023) [18]. The ability to combat histamine-induced constriction on an isolated guinea pig tracheal chain, asthma mast cell degranulation, and histamine-induced bronchospasm were used to test the antiasthmatic activity of *E. scaber* at various dosage levels. Bronchospasm brought on by acetylcholine, histamine, and protected mast cell degranulation was shown to be considerably reduced by the plant's ethanolic extract has an impact on bone regrowth. Experimental rats were used to test the efficacy of an ethanol extract of *E. mollis* in regenerating a broken bone (Hiradeve and Rangari, 2015) [4].

1.4.9 Other bioactivities:

Some chemicals obtained from *E. scaber* were discovered to have leishmanicidal action. Elephantopin, Melantophin, Isoelephantopin, and 2-deethoxy-2-methoxyphantomolin are some of the substances (Kabiru and Por, 2013) [6]. According to reports of Kabiru and Por (2013), water extracts from the *E. scaber* plants have a liver-protective effect against acute liver damage caused by carbon tetrachloride (CCl₄) (Kabiru and Por, 2013) [6].

1.5 CONCLUSION

Given the wealth of research that has previously been conducted on the plant, the current review attempted to take a wide picture of the *Elephantopus* family. This review attempted to highlight the several traditional applications of the *Elephantopus* species, including its usage as a liver tonic, pain reliever, skin tonic, and cure for skin infections. Additionally, the presence of several phytochemicals such terpenoids, tannins, and saponins was discovered in the plant. Given that they were associated with the majority of the activities that were looked at, flavonoids and phenols seem to be the most significant phytochemicals. The main substances that were identified from the plants were sesquiterpene lactones such elephantopin, triterpenes, stigmasterol, epifriedelinol, and lupeol. The plant has been studied for its many biological properties, including its antibacterial, antitumor, hepatoprotective, and anti-inflammatory properties. Analgesic, antihyperglycemic, and anticholesterolemic action were among the other identified activities. *Elephantopus* species is a potential source of cash generating for the areas where it is located, as indicated by the deluge of publications describing its biological activity and chemical make-up. In addition, more chemical constituents' study is needed to make medications from the isolated molecule in enormous quantities; this will lessen reliance on the natural supply and, as a result, lessen deforestation.

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