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Review Article

Therapeutic Potential of *Phyllanthus amarus Schumach. & Thonn*: Integrating Ethnopharmacology, Bioactive Compounds, and Preclinical Evidence

Utekar V. S.*, Mohazzib Husain, Wadulkar R. D., Satpute K. L.

DES' Dayanand College of Pharmacy, Latur. Maharashtra, India

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ABSTRACT

The objective of this study is to analyze a medicinal plant species widely distributed in tropical and subtropical regions of India and extensively used in traditional systems of medicine for the management of liver disorders, inflammation, diabetes, infections, and other ailments. Phyllanthus amarus Schumach. & Thonn. (Bhuiamla or Stonebreaker) is commonly found across India, including Maharashtra, Madhya Pradesh, Tamil Nadu, and Kerala. It has a long history of ethnomedicinal use for hepatic disorders, jaundice, kidney stones, diabetes, gastrointestinal disturbances, and infectious diseases. The plant is rich in bioactive phytoconstituents such as lignans (phyllanthin, hypophyllanthin), flavonoids, tannins, alkaloids, glycosides, saponins, and polyphenolic compounds, which are responsible for its antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, antiviral, anti-diabetic, and nephroprotective properties. Common pharmacological activities reported for this plant include hepatoprotective and antiviral effects. Hydroalcoholic and aqueous extracts of the whole plant have shown significant pharmacological evidence in various in vivo and in vitro studies. The extract demonstrated notable hepatoprotective activity against chemically induced liver damage in experimental models and showed a significant reduction in blood glucose levels at doses ranging from 200 to 400 mg/kg. Traditionally, the whole plant is used as a decoction for liver ailments and urinary disorders. Experimental studies have also reported modulation of inflammatory mediators, inhibition of viral replication, and enhancement of antioxidant defense mechanisms. Despite encouraging preclinical findings, comprehensive toxicological evaluations and well-designed clinical trials remain limited. Therefore, while further studies focusing on mechanisms of action, safety profiling, and formulation standardization are required, P. amarus holds strong potential as a phytopharmaceutical candidate for the management of chronic liver, metabolic, inflammatory, and infectious diseases.

***Corresponding Author:** Utekar V. S.
Address: *DES' Dayanand College of Pharmacy, Latur. Maharashtra, India*
Email : uvijay569@gmail.com

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INTRODUCTION

The field of science is receiving increasing global attention due to a growing interest in evidence-based herbal medicine and safer therapeutic alternatives derived from natural sources. Phytopharmaceuticals and traditional herbal remedies are widely used in the management of chronic metabolic, inflammatory, infectious, and hepatic disorders owing to their multi-component nature, synergistic effects, and relatively favourable safety profiles. [1]

Phyllanthus amarus Schumach. & Thonn., belonging to the family Phyllanthaceae, is an annual herb widely distributed throughout tropical and subtropical regions of India, Africa, Southeast Asia, and South America. In India, it is commonly found in states such as Maharashtra, Madhya Pradesh, Tamil Nadu, Kerala, and Andhra Pradesh. The plant is popularly known as Bhuiamla, Bhumyamalaki, or Stonebreaker, and holds a significant place in Ayurvedic, Siddha, and folk medicinal systems. [2,3]

Ethnomedicinal records document the extensive use of *Phyllanthus amarus* in the treatment of liver disorders such as jaundice and hepatitis, along with diabetes, kidney stones, gastrointestinal disturbances, urinary tract infections, and inflammatory conditions. Traditionally, the whole plant is administered as a decoction or infusion for hepatoprotection, detoxification, and management of metabolic disorders. Its widespread use across different cultures highlights its therapeutic relevance and long-standing safety in traditional medicine. [4]

Phytochemical investigations of *Phyllanthus amarus* have revealed the presence of a wide range of bioactive compounds, including lignans (notably phyllanthin and hypophyllanthin), flavonoids, tannins, alkaloids, saponins, glycosides, and polyphenolic compounds. These constituents are recognized for their potent antioxidant, anti-inflammatory, antiviral, antimicrobial, and enzyme-modulatory activities, which contribute significantly to the plant's pharmacological potential.[5]

Pharmacological studies have demonstrated that *Phyllanthus amarus* exhibits hepatoprotective, antiviral (particularly against hepatitis B virus), anti-diabetic, nephroprotective, antioxidant, and immunomodulatory properties in various in vivo and in vitro experimental models. The plant has also been reported to modulate inflammatory mediators, enhance endogenous antioxidant defence systems, and protect against chemically induced organ damage. Despite these promising findings, comprehensive toxicological evaluations, standardization of extracts, and mechanistic studies remain limited. [6]

The existing literature on *Phyllanthus amarus* is dispersed across ethnobotanical surveys, phytochemical investigations, and pharmacological reports, with relatively few studies addressing its safety profile, molecular mechanisms of action, and clinical validation. This gap underscores the need for systematic compilation and critical evaluation of available data. [4,5]

Therefore, the aims of this review are the systematic collection and organization of updated phytochemical information, evaluation of toxicological and safety data, assessment of biological and pharmacological activities, identification of gaps in current knowledge, and outlining future research directions to support the development of *Phyllanthus amarus* as an evidence-based phytopharmaceutical. [7]



Fig 1: *Phyllanthus Amarus*

1. Botanical aspects

Phyllanthus amarus Schumach. & Thonn. is an annual, erect, small herb belonging to the Phyllanthaceae family. It is widely distributed throughout tropical and subtropical regions, particularly in north, south, and central India, as well as in Africa, Southeast Asia, South America, and the Caribbean. The plant commonly grows as a weed in cultivated fields, roadsides, gardens, and wastelands, especially during the monsoon season. [4,13]

1.1 Taxonomy

Table 1: Scientific Classification [10, 11]

Kingdom	**Plantae**
Phylum	Tracheophyta
Sub-phylum	Angiospermae
Class	Magnoliopsida (Dicotyledons)
Sub-class	Rosidae
Order	Malpighiales
Family	Malpighiales
Genus	Phyllanthus
Species	*Phyllanthus amarus S*chumach. & Thonn.

1.2 Vernacular name

Table 2: Vernacular Names [14]

Sr.no	Language	Plant name
1.	Hindi	Jangli, Amla, Bhui Amla
2.	English	Gulf leaf flower, Black catnip, Stonebreaker, Weed
3.	Sanskrit	Raajaadan, Phalaadhyakhsa, Khsirikoo
4.	Tamil	Keelanelli (Keezhanelli)
5.	Telugu	Nela uirika, Nelavusari
6.	Ayurvedic	Bhumyamalaki
7.	Gujarati	Bhonya ammali
8.	America	Hurricane weed, Chanca piedra
9.	Kanada	Kirunelli, Nela-nelli
10.	Netherland	Fini bita

1.3 Morphology

Phyllanthus amarus Schumach. & Thonn. is a small, erect, annual herb that typically grows to a height of 30–60 cm. The plant is commonly found in tropical and subtropical regions, growing as a weed in cultivated fields, roadsides, gardens, and wastelands, especially during the rainy season.

The root system consists of a slender taproot with few lateral branches. The stem is smooth, green to light brown, cylindrical, and often profusely branched, giving the plant a delicate appearance. The leaves are simple, small, alternate, distichous, and arranged in a characteristic manner resembling a pinnate leaf. They are elliptic to oblong, glabrous, with an entire margin, obtuse to acute apex, and a symmetrical base, measuring approximately 7–15 mm in length and 3–6 mm in width.

The flowers are minute, greenish-white, and unisexual, occurring singly or in small clusters in the axils of the leaves. Male flowers are borne on slender pedicels with 3–5 stamens, while female flowers are usually solitary with a tricarpellary, superior ovary. The flowering period generally occurs during the monsoon season.

The fruit is a small, smooth, depressed-globose capsule, about 2–3 mm in diameter, which splits into three segments upon maturity. Each segment

contains a small, triangular, light brown seed with a hard seed coat. The overall morphological features of Phyllanthus amarus are distinctive and play an important role in its botanical identification and authentication.

1.4 Habitat, Ecology, Distribution

Phyllanthus amarus Schumach. & Thonn. is an annual herbaceous plant that thrives in tropical and subtropical climates, particularly in areas with warm temperatures and moderate to heavy rainfall. It prefers well-drained, sandy-loam to clay-loam soils and can often be found in cultivated fields, gardens, roadsides, wastelands, and riverbanks, demonstrating its ability to grow as a ruderal or colonizing species.

The plant contributes to the local ecosystem by providing green cover and soil protection, and its presence in cultivated and uncultivated areas supports biodiversity by offering microhabitats for small insects and microorganisms. *P. amarus* exhibits remarkable adaptability to a range of ecological conditions, from partially shaded areas to full sun exposure, indicating its resilience and widespread occurrence.

It is native to India (states such as Maharashtra, Madhya Pradesh, Tamil Nadu, Kerala, Andhra Pradesh), Africa, Southeast Asia, South America, and the Caribbean, and is widely naturalized in tropical and subtropical regions worldwide. The plant is cultivated locally for its medicinal properties and is often used in traditional systems of medicine, including Ayurveda and Siddha, for liver disorders, urinary ailments, and other therapeutic applications. [8,10, 14]

2.Phytochemical constituent

Phyllanthus amarus is a medicinal herb in the family Phyllanthaceae widely studied for its rich secondary metabolite profile. Phytochemical investigations of *P. amarus* across various solvent extracts (ethanol, methanol, aqueous, etc.) have identified a large spectrum of bioactive constituents, including tannins, flavonoids, saponins, alkaloids, glycosides, terpenoids, lignans, sterols, and phenolic compounds. [10,28,29,30]

Table 3: Phytochemical Comparison [10,12, 14]

Major classes	Representative compounds (examples)
Lignans	Phyllanthin, hypophyllanthin, niranthin, phyltetralin, nirtetralin, isonirtetralin, hinokinin, Lintetralin, isolintetralin, demethylenedioxy-niranthin, 5-demethoxy-niranthin.
flavonoids	Rutin, astragalin, kaempferol, quercetin, quercitrin, quercetin-3-O-glucoside
Ellagitannins (Hydrolysable tannin) Tannin precursors	Gallic acid, ellagic acid, gallocatechin
Alkaloids	Securinine, dihydrosecurinine, tetrahydrosecurinine, securinol, phyllanthine, allo-securine, nor-securinine, epibubbialine, isobubbialine, 4-methoxy-nor-securinine4-methoxy dihydrosecurinine,
Triterpenes	Phenazine and phenazine derivatives 2Z, 6Z, 10Z, 14E, 18E, 22E-farnesylfarnesol Lupeol, phyllanthenol, phyllanthenone, phyllantheol, Oleanolic acid, ursolic acid.
Sterols	Amarosterol A, Amarosterol B
Triterpenes	Phenazine and phenazine derivatives 2Z, 6Z, 10Z, 14E, 18E, 22E-farnesylfarnesol Lupeol, phyllanthenol, phyllanthenone, phyllantheol, Oleanolic acid, ursolic acid
Volatile oil	Linalool, phytol

Complex tannins	Geraniin, amariin, furosin, geraniinic acid B, amariinic acid, amarulone, repandusinic acid A,

Table 4: Quantitative estimation of Secondary Metabolites in the plant part studied [8,5, 25]

Phytochemicals	Leaves (%)	Roots (%)
Saponins	0.73±0.01	0.91 ± 0.01
Tannins	1.85±0.03	1.53 ± 0.03
Phenolics	1.12±0.01	0.70 ± 0.01
Flavonoids	-	2.47 ± 0.03
Alkaloids	1.59 ± 0.50	-
Steroids	-	2.97 ± 0.10
Anthocyanin	1.80 ± 0.01	0.62 ± 0.01
Triterpenoids	0.13 ± 0.10	-
Glycosides	0.86 ± 0.01	0.90 ± 0.01
Coumarins	-	2.02 ± 0.10

3. Ethnopharmacology [21,22,23]

Phyllanthus amarus (Family: Phyllanthaceae), commonly known as Bhumi Amla in Ayurveda and Chanca piedra in South America, has an extensive history of ethnomedicinal use in Ayurveda, Siddha, Unani, and various folk medicinal systems across tropical regions.

Traditionally used as Kaasahara (antitussive), Shwaasahara (relieves dyspnea), Kaphapittahara, Pipaasaaghna (relieves excessive thirst), Raktapittahara (anti-hemorrhagic), Paanduhara (antianemic), Kaamalaahara (anti-jaundice), Kushthaghna (useful in skin diseases), Daahaghna (refrigerant), Kshatakshayaghna (useful in trauma), and Mootrarogahara (urinary disorders).

- Whole plant decoction is traditionally administered for liver disorders, jaundice, hepatitis, diabetes, dysentery, and intestinal parasitic infections.
- Known as “chanca piedra” (stone breaker), it is widely used by Amazonian tribes for the treatment and prevention of kidney stones and gall bladder stones.
- Decoctions of the plant are used as a diuretic, antilithic, antispasmodic, and antipyretic, and are also employed in urinary tract infections and renal colic.
- Leaf and whole plant extracts are used externally for skin diseases, itching, wounds, and inflammatory conditions.
- Herbal baths prepared from *P. amarus* are traditionally used after labor for uterine complaints, cramps, asthma, and stomachache.
- In South America, the plant is also used for bronchial infections, cardiovascular disorders, influenza, malaria, and digestive ailments.
- Tribal communities across Asia, Africa, and South America use *P. amarus* as a blood purifier, vermifuge, and remedy for fever, anemia, and metabolic disorders.
- America, has been used to eliminate gall bladder and kidney stones, and also to treat gall bladder and bronchial infections.
- *P. amarus* are even used in herbal baths and after labor, cramps, asthma, uterus complaints and to treat stomachache. [34]
- Some other studies have also shown that the plant *P. amarus*, when boiled with the leaves, is considered to be a diuretic and is used in the treatment of menstrual disorders and skin disorders.[35]

4. Pharmacological Activities of *Manilkara hexandra*

4.1 Hepatoprotective activity

Phyllanthus amarus is widely recognized for its hepatoprotective activity. Experimental studies using carbon tetrachloride-, paracetamol-, and alcohol-induced liver toxicity models show significant reductions in serum liver enzymes such as AST, ALT, ALP, and bilirubin following extract administration. Histopathological

examination reveals restoration of normal liver architecture and reduced necrosis and fatty degeneration. Lignans such as phyllanthin and hypophyllanthin play a key role by enhancing antioxidant defenses and stabilizing hepatocellular membranes, validating its traditional use in jaundice and hepatitis. [4,34]

4.2 Antidiabetic activity

Has antidiabetic potential of *Phyllanthus amarus* has been validated by numerous experimental studies in various diabetic animal models. Methanolic and aqueous extracts of the plant significantly reduce fasting blood glucose levels and enhance glucose tolerance in alloxan-induced diabetic rats, demonstrating clear hypoglycemic effects comparable to standard antidiabetic drugs like glibenclamide. In one study, alloxan-induced diabetic rats treated with methanol leaf extract at 200–400 mg/kg exhibited marked reductions in fasting glucose and improved oral glucose tolerance tests without observable pancreatic, liver, or kidney lesions, supporting its safety profile.

Further work indicates that the antihyperglycemic activity of *P. amarus* involves modulation of key carbohydrate-metabolizing enzymes. In vitro analyses of polyphenolic fractions from aqueous extracts showed significant inhibition of glucose-6-phosphatase and enhanced glucose uptake, aligning with improved glycemic control mechanisms. Moreover, aqueous leaf and seed extracts produced dose-dependent reductions in fasting glucose and dyslipidemia, likely enhancing peripheral glucose utilization. Antioxidant properties of the extracts also contribute to protection of pancreatic β-cells from oxidative damage, a major contributor to diabetic pathology. Collectively, flavonoids, tannins, lignans, and other phenolic compounds in *P. amarus* underpin its antidiabetic effects, scientifically validating its ethnomedicinal use in diabetes management. [3, 20, 25]

4.3 Antimalarial activity

Phyllanthus amarus has demonstrated promising antimalarial activity in several experimental studies. Extracts of the whole plant and leaves exhibit significant antiplasmodial effects by inhibiting β-hematin (hemozoin) formation, thereby disrupting the detoxification of free heme essential for the survival of Plasmodium species within erythrocytes. In vivo studies using Plasmodium berghei-infected mice have shown marked suppression of parasitemia and improvement in survival rates following extract administration. Additionally, P. amarus modulates malaria-associated inflammatory responses by reducing pro-inflammatory cytokines and oxidative stress, which contribute to disease severity. The antimalarial activity is largely attributed to the presence of flavonoids, phenolic compounds, and lignans that exert both antiparasitic and immunomodulatory effects. These findings provide pharmacological support for the traditional use of P. amarus in febrile illnesses and malaria-like conditions and suggest its potential role as a complementary or alternative antimalarial phytotherapeutic agent. [23]

4.4 Antimicrobial activity

Phyllanthus amarus has shown broad-spectrum antimicrobial activity against a wide range of Gram-positive and Gram-negative bacteria as well as pathogenic fungi. Methanolic, ethanolic, and aqueous extracts of the whole plant and leaves exhibit concentration-dependent inhibition against microorganisms such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella* spp., and fungal strains including *Candida albicans*. The antimicrobial activity is mainly attributed to the presence of bioactive

phytoconstituents such as flavonoids, tannins, alkaloids, and phenolic compounds. These compounds exert antimicrobial effects by disrupting microbial cell wall integrity, inhibiting key enzymatic systems, interfering with nucleic acid synthesis, and suppressing microbial replication. Studies have reported that polar extracts, particularly methanolic extracts, show higher antimicrobial efficacy due to better extraction of active constituents. These findings scientifically validate the traditional use of *P. amarus* in the treatment of infectious diseases, gastrointestinal infections, and microbial-associated inflammatory conditions.

4.5 Anti-inflammatory activity

Phyllanthus amarus exhibits significant anti-inflammatory activity in both in vitro and in vivo models. Extracts of the whole plant inhibit protein denaturation, membrane destabilization, and cyclooxygenase-mediated inflammatory pathways. In animal models such as carrageenan- and formalin-induced paw edema, the extracts significantly reduce inflammation and edema. These effects are linked to the suppression of pro-inflammatory mediators, cytokines, and reactive oxygen species. Bioactive compounds such as flavonoids, lignans, and phenolic acids contribute to the anti-inflammatory response through antioxidant, enzyme-inhibitory, and membrane-stabilizing mechanisms. [23,24]

4.6 Antianxiety activity

The anxiolytic activity of *Phyllanthus amarus* has been evaluated using animal behavioural models such as the elevated plus maze and open-field tests. Oral administration of plant extracts results in reduced anxiety-related behaviours without causing sedation. These effects are believed to occur through modulation of neurotransmitter pathways, particularly the GABAergic system. Bioactive constituents including flavonoids and alkaloids may cross the blood–brain barrier and regulate neuronal excitability, supporting the plant's traditional use in stress-related and neurological disorders. [16]

4.7 Antioxidant activity

Phyllanthus amarus has been widely recognized for its potent antioxidant activity, demonstrated through multiple in vitro assays including DPPH, ABTS, FRAP, nitric oxide, and hydroxyl radical scavenging tests. Methanolic, ethanolic, and aqueous extracts of the whole plant, leaves, and stems exhibit strong dose-dependent free radical scavenging activity. These effects are primarily attributed to the presence of bioactive phytoconstituents such as polyphenols, flavonoids, lignans (phyllanthin, hypophyllanthin), and tannins.

The extracts efficiently neutralize reactive oxygen species (ROS), inhibit lipid peroxidation, and protect cellular macromolecules from oxidative damage. Such antioxidant properties also contribute to the modulation of inflammatory responses, enhancement of endogenous antioxidant enzyme activity (e.g., superoxide dismutase, catalase, glutathione peroxidase), and protection of vital organs such as liver and pancreas. By mitigating oxidative stress, *P. amarus* helps prevent the progression of chronic metabolic and inflammatory disorders, including diabetes, liver injury, cardiovascular dysfunction, and neurodegenerative diseases. These pharmacological findings provide scientific validation for the traditional use of P. amarus in herbal medicine and suggest its potential as a natural antioxidant supplement. [6,12,24,25]

4.8 Antiarthritic activity

The antiarthritic potential of *Phyllanthus amarus* has been extensively investigated in experimental models of arthritis, including Freund's complete adjuvant- and formaldehyde-induced arthritis in rodents. Administration of aqueous, methanolic, and ethanolic extracts of the whole plant or leaves significantly reduces paw edema, joint inflammation, and arthritic scores, indicating robust antiarthritic efficacy. The mechanism of action is attributed to suppression of pro-inflammatory mediators such as cytokines, inhibition of cyclooxygenase and lipoxygenase pathways, stabilization of lysosomal membranes, and reduction of oxidative stress in joint tissues. Bioactive constituents, including flavonoids, tannins, and lignans (phyllanthin, hypophyllanthin), play a central role in these pharmacological effects. These findings provide pharmacological validation for the traditional use of *P. amarus* in the management of rheumatism, chronic inflammatory joint disorders, and related musculoskeletal conditions, highlighting its potential as a natural antiarthritic agent. [8,12,17]

4.9 Anti-Tumor Activity

Phyllanthus amarus exhibits significant antitumor and anticancer potential in both in vitro and in vivo studies. Methanolic, ethanolic, and aqueous extracts of the whole plant have demonstrated cytotoxic activity against various cancer cell lines, including breast (MCF-7), liver (HepG2), colon (HCT116), and leukemia (HL-60) cells, primarily through induction of apoptosis, cell cycle arrest, and generation of reactive oxygen species. In vivo studies using Ehrlich ascites carcinoma and Dalton's lymphoma models have shown that oral or intraperitoneal administration of *P. amarus* extracts significantly reduces tumor volume, improves survival rates, and mitigates tumor-induced hematological abnormalities. The anticancer effects are largely attributed to bioactive compounds such as lignans (phyllanthin, hypophyllanthin), flavonoids, and polyphenols, which inhibit cell proliferation, angiogenesis, and oxidative DNA damage, while modulating apoptosis-related pathways. These findings validate the traditional use of *P. amarus* and highlight its potential as a complementary or alternative antitumor phytotherapeutic agent.[9]

4.10 Antihyperlipidemic Activity

The antihyperlipidemic potential of *Phyllanthus amarus* has been demonstrated in several experimental models of diet- and sucrose-induced dyslipidemia. Oral administration of aqueous leaf and seed extracts significantly lowers serum total cholesterol, triglycerides, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels while increasing high-density lipoprotein (HDL) cholesterol in treated animals compared with controls. These lipid-lowering effects are attributed to enhanced peripheral lipid metabolism, inhibition of cholesterol absorption, and antioxidant-mediated prevention of lipid peroxidation, which collectively improve cardiovascular risk profiles. In a 10% sucrose-induced insulin resistance model, *P. amarus* attenuated diet-induced hyperlipidemia by significantly reducing plasma triglycerides, total cholesterol, and LDL-cholesterol, and improving HDL-cholesterol and atherogenic indices. The presence of flavonoids, saponins, lignans, and phenolic compounds in the plant is believed to underlie these effects through modulation of lipid enzymes and enhancement of antioxidant defenses. These pharmacological findings support the traditional use of *P. amarus* in metabolic and cardiovascular disorders including hyperlipidemia and corroborate its potential as a natural therapeutic agent for lipid regulation. [25,32]s

CONCLUSION

Phyllanthus amarus is a well-researched and widely utilized medicinal plant, valued for its rich phytochemical profile and broad spectrum of biological activities, including anti-inflammatory, antioxidant, antidiabetic, antimicrobial, hepatoprotective, antimalarial, anticancer, and neuroprotective effects. The plant has demonstrated considerable therapeutic potential in numerous preclinical studies, supporting its long-standing use in traditional systems of medicine across tropical regions.

Despite promising pharmacological evidence, the translation of *P. amarus* into modern clinical applications faces challenges such as lack of standardization, limited pharmacokinetic and pharmacodynamic data, and insufficient comprehensive safety evaluations. Variability in plant extracts and dosage forms further complicates its clinical development.

Future research should emphasize standardized extraction procedures, bioactive compound isolation, and advanced formulation strategies to convert traditional knowledge into scientifically validated therapeutics. The integration of modern biotechnological approaches such as nanotechnology, metabolomics, and systems biology may enhance the efficacy, safety, and reproducibility of *Phyllanthus amarus*–based herbal formulations. These efforts could facilitate the development of safe, effective, and affordable natural therapies to address global health challenges.

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