

PHYTOPHARMACOLOGICAL PROPERTIES OF *ALBIZIA* SPECIES: A REVIEWKARUPPANNAN KOKILA, SUBRAMANIAN DEEPIKA PRIYADHARSHINI AND VENUGOPAL SUJATHA<sup>1\*</sup><sup>1</sup>Department of Chemistry, Periyar University, Salem, Tamil Nadu, India. Email: chemsujatha@gmail.com

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## ABSTRACT

The present investigation reviews *Albizia* species (Family- Mimosaceae) to tap out the shelf of bioactive constituents that possess pharmacological properties. These species are used in folk medicine for the treatment of rheumatism, stomach ache, cough, diarrhea, wounds, anthelmintic etc. In traditional Indian and Chinese medicine, *Albizia* plants are used therapeutically for insomnia, irritability, wounds, as antidiarrheal, antiseptic, antitubercular etc. Phytochemical studies on the genus *Albizia* have inferred them as a source of different group of natural product [triterpenoids, saponins, diterpenoids lignans and pyridine glycosides] active against cytotoxicity and many other diseases. The narrower approach to reveal phytochemical, pharmacological, antioxidant, antidiabetic, anthelmintic, antibacterial, hepatoprotective, anti-inflammatory, cytotoxic properties accompanied with possible number of bioactive constituents isolated from this species is discussed with a detailed description. This piece of report would promote these species for extensive research, to fetch the optimistic utility of phytoconstituents for its therapeutic applications.

**Keywords:** *Albizia*, Phenolics, Flavonoids, Terpenoids, Saponins, Cytotoxicity.

## INTRODUCTION

Scientists first started extracting and isolating chemicals from plants in the 18<sup>th</sup> century and since that time we have grown a custom of looking at herbs and their effects in terms of the active constituents they contain. Encyclopedia provides details of all the main active constituents of the medicinal herbs featured and explaining their actions. For the eternal health, longevity and remedy, to remove pain and discomfort, fragrance, flavor and food mankind all over the world dependent upon the plant kingdom to meet their all needs.

Among the vast diversity of plants, there are three subfamilies of the legume family which are Papilionoideae, Caesalpinioideae and Mimosoideae. Members of the subfamily Mimosoideae have flowers with radial symmetry, small, inconspicuous corollas and numerous, showy stamens. The flowers are typically in many-flowered heads or spikes. This subfamily includes *Acacia* (wattle), *Albizia* (silk tree), *Samanea* (monkey pod), *Prosopis* (mesquite) and *Calliandra* (powder puff). The genus *Albizia* comprises approximately 150 species, mostly trees and shrubs native to tropical and subtropical regions of Asia and Africa. Leaves are bipinnate with leaflets in numerous pairs or larger in fewer pairs. Petiolar glands are conspicuous. Flowers are in globose heads or spikes. Stamens elongate and are usually white. Corolla is funnel-shaped, connate beyond the middle. Fruit is broadly linear indehiscent or 2- valved, valves not twisted.

## Scientific classification

Kingdom	Plantae
(unranked)	Angiosperms
(unranked)	Eudicots
(unranked)	Rosids
Order	Fabales
Family	Fabaceae
Subfamily	Mimosoideae
Tribe	Ingae
Genus	<i>Albizia</i>

## Ethnomedicinal and ethnobotanical value

Many *Albizia* species are endemic to Indian subcontinent. The flowers are being commonly used to treat anxiety, depression and insomnia in traditional Chinese medicine. The Indian species *Albizia thomsonii* are classified as vulnerable. *Albizia* species are socially significant for producing high quality timber and as a valuable resource for gum yield. *Albizia julibrissin*, *Albizia lebeck*, *Albizia procera* and *Albizia amara* are some importantly considered species in Ayurvedic medicine. *A. lebeck* is an astringent, also used by some cultures to treat boils, cough, to treat the eye, flu, gingivitis, lung problems, pectoral problems, is used as a tonic, and is used to treat

abdominal tumors. This information was obtained via ethnobotanical records, which are a reference to how a plant is used by indigenous peoples, not verifiable, scientific or medical evaluation of the effectiveness of these claims. *A. lebeck* is also psychoactive. In ancient Tamil culture, the flowers of the *lebeck* decorated as a crown were used to welcome victorious soldiers. The leaves are boiled to make a drink, and the bark is cooked with food in Madagascar. Its sweet-smelling gum or resin is used in cosmetics in some African countries. The root bark and young shoots are widely used in traditional medicine. The bark is poisonous but is used medicinally by the Zulu of South Africa who also sometimes make a love charm from the plant. They also prepare an infusion (hot or cold) from the bark and roots to treat skin diseases such as scabies, inflamed eyes, bronchitis. Seeds of *Albizia amara* are regarded as astringent, and used in the treatment of piles, diarrhea and gonorrhoea. Some *Albizia* species are regarded as a potential fodder resource. They were also a plant of choice for silviculture and secondary plantation because of thick foliage and quick growing nature. Species like *A. lebeck* and *A. procera* have shown high potential in soil redevelopment process during early phase of mine spoil restoration in dry tropical environment.

## Phytochemical significance

Phytochemical investigation of different species belonging to genus *Albizia* afforded different classes of secondary metabolites such as saponins, terpenes, alkaloids and flavonoids. Some bioactive compounds isolated and identified from genus *Albizia* were e.g. triterpenoid saponins (julibroside J<sub>29</sub>, julibroside J<sub>30</sub>, julibroside J<sub>31</sub>), novel macrocyclic alkaloids (budmunchiamines A, B and C) and two flavonol glycosides (quercitrin and isoquercitrin) showed different biological activities such as antitumor, antiplatelets aggregation and bactericidal activities. The active constituents of *A. lebeck* bark extract were anthraquinone glycosides that cause the leakage of the cytoplasmic constituents [1]. Two active saponins, Albiziatriside A and B were isolated using bio-assay guided fractionation of a methanolic extract of *A. subdimidiata*, which showed significant cytotoxicity against the A2780 cell line [2]. Two new macrocyclic spermine alkaloids were isolated as a mixture from the leaves of *A. inopinata*. Preliminary studies on *A. inopinata* indicated that the compounds shown a possible pharmacological depression activity on the central nervous system [3].

Two new bioactive spermine alkaloids, budmunchiamines L<sub>4</sub> and L<sub>5</sub> were isolated from the crude methanol extract of the stem bark and leaves of *A. adinocephala*. Their extracts were found to inhibit the malarial enzyme plasmepsin II [4]. The methanolic extract of the stem bark of *Albizia lebeck*, a new cytotoxic saponin was isolated compound exhibited potent cytotoxic activity against human aqueous cell carcinoma (HSC-2 and HSC-3) [5]. 3-O-[ $\alpha$ -l-

arabinopyranosyl(1→6)]-2-acetamido-2-deoxy-β-D-glucopyranosyl echinocystic acid, 3-O-[α-L-arabinopyranosyl(1→2)-α-L-arabinopyranosyl(1→6)]-β-D-glucopyranosyl oleanolic acid, 3-O-[β-D-xylopyranosyl(1→2)-α-L-arabinopyranosyl(1→6)]-β-D-glucopyranosyloleanolic acid isolated from *Albizia inundata* showed cytotoxicity against human head and neck squamous cells (JMAR, MDA1986) and melanoma cells (B16F10, SKMEL28) [6].

### Pharmacological properties

*Albizia lebeck* is also used in Indian traditional system and folk medicine as well as to treat several inflammatory pathologies such as asthma, arthritis, antiseptic, burns, antidysentric, allergic rhinitis, learning of mice, bronchitis, leprosy, paralysis and helminth infections and anti-tubercular activities and burns. The bark and flowers of the *Albizia julibrissin* tree are used in China as medicine. Bark extract is applied to bruises, ulcers, abscesses, boils, hemorrhoids and fractures, and has displayed cytotoxic activity [7]. *Albizia saman* and *Albizia inundata* was found to have good anti-plasmodial and anti-candida activity [8]. *Albizia odoratissima* is used in the treatment of leprosy, ulcers and cough. *Albizia mollis* is well known for its sedative and sleeping pill properties [9].

The bark and leaves of *Albizia procera* were extensively used for the treatment of variety of wounds and considered useful in pregnancy and stomachache. Lipophilic extracts of *Albizia gummifera* revealed very promising anti-trypanosomal activity [10]. Also used in the indigenous medical system for various ailments, bacterial infections, skin diseases, malaria and stomach pains. The seeds of *Albizia amara* are used as an astringent, treating piles, diarrhoea, gonorrhoea, leprosy, leucoderma, erysipelas and abscesses. The leaves and flowers have been applied to boils, eruptions, and swellings, also regarded as an emetic and as a remedy for coughs, ulcer, dandruff and malaria [11]. *Albizia schimperiana* Oliv. is used as a traditional medicine for the treatment of bacterial and parasitic infections, notably pneumonia and malaria, respectively. The alcoholic extract of *A. lebeck* has antihistaminic property, by neutralizing the histamine directly or due to corticotrophic action as evidenced by raising cortisol levels in plasma [12]. *A. zygia* showed high anti-malarial activity [13]. Lipophilic extracts of *Albizia gummifera* revealed very promising anti-trypanosomal activity [14].

### Antioxidant properties

There are many reports on the antioxidant property for *Albizia* species. *A. julibrissin* foliage produced an unknown quercetin derivative, hyperoside (quercetin-3-O-galactoside) and quercitrin (quercetin-3-O-rhamnoside) that showed excellent antioxidant activity [15]. Two phenolic glycosides (albibrissinosides A and B) were isolated from the stem bark of *A. julibrissin*. The albibrissinoside B was found to be a radical scavenger on the 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical [16]. Khattoon et al. [17] studied the antioxidant activity of *Albizia procera* leaves through DPPH, reducing power and total antioxidant capacity. Their leaf extract exhibited an IC<sub>50</sub> value of about 90% among that of DPPH radicals. The aqueous ethanol extract of *Albizia anthelmintica* showed its significance for both analgesic and antioxidant activities. An attempt on isolation of this plant produced quercetin-3-O-β-D-glucopyranoside, kaempferol-3-O-β-D-glucopyranoside, kaempferol-3-O-(6β-O-galloyl-β-D-glucopyranoside) and quercetin-3-O-(6β-O-galloyl-β-D-glucopyranoside) exhibited potent antioxidant scavenging activity towards diphenyl-picrylhydrazine (DPPH). *Albizia myriophylla* [18] showed the highest antioxidant activity on DPPH radical assay (EC<sub>50</sub> value 14.45%), lipid peroxidation assay (IC<sub>50</sub> value 0.70%).

Aurantiamide acetate was the most active compound isolated from the stem bark of *A. adianthifolia* through antioxidant activity (DPPH) and trolox equivalent antioxidant capacity (TEAC) assays were used to detect the antioxidant activity EC<sub>50</sub> values 9.51 μg/ml and 78.81 μg/ml, respectively. The bark extracts of *Albizia lebeck* possess free radical scavenging activity against 1, 1-di diphenyl-2-picrylhydrazyl radical (DPPH) and reducing power assays. Their results on DPPH free radical scavenging at 1000 μg/ml indicated maximum antioxidant activity of 91.82% and 90.08% respectively. Ethanol extract of *Albizia procera* showed strong scavenging activity against

free radicals compared to various standards. These *in-vitro* assays indicate that these plant extracts are a better source of natural antioxidant, which might be helpful in preventing the progress of various oxidative stresses. Aliyu et al. [19] studied the antioxidant activity of *Albizia chevalieri* leaves through DPPH, by exhibiting an IC<sub>50</sub> value of about 94.7% against the standard ascorbic acid (94.81%). *Albizia amara* leaves extracts showed highest antioxidant activity, which were studied by three different methods, 2,2-diphenyl-1-picrylhydrazyl radical assay (IC<sub>50</sub> value 164%), nitric oxide free radical scavenging assay (IC<sub>50</sub> value 205%) and reducing power assay (EC<sub>50</sub> value 0.087 μg/ml), when compared to standard samples.

### Anticancer properties

Three triterpenoid saponins (julibroside J<sub>29</sub>, julibroside J<sub>30</sub> and julibroside J<sub>31</sub>) from *Albizia julibrissin* bark, served as anti-tumors by the induction of apoptosis in certain cell types (human acute leukemia junket T-cells) and butanol extract from the bark of *Albizia julibrissin* [20]. A new cytotoxic compound, Echinocystic acid 3, 16-O-bisglycosides from the bark of *Albizia procera* is worth mentioning. In contrast to other cytotoxic echinocystic acid glycosides with N-acetyl glucosamine unit, the new glycosides were found inactive when assayed by MTT method for their cytotoxicities against the HEPG2, A549, HT29 and MCF7 cell lines [21]. Three new oleanane-type triterpene saponins named grandibracteosides A-C were isolated from the methanolic extract of leaves of *A. grandibracteata* showed significant inhibitory activity against KB and MCF7 tumor cell lines *in vitro* [22]. Three new saponins from the bark of *A. procera*, characterized as 3-O-[β-D-xylopyranosyl-(1→2)-α-L-arabinopyranosyl-(1→6)]-2-acetamido-2-deoxy-β-D-glucopyranosyl] echinocystic acid exhibited cytotoxicity against HEPG2 cell line with IC<sub>50</sub> 9.13 μg/ml [23]. Three new oleanane type triterpene saponins, albizosides A-C were isolated from the stem bark of *A. chinensis*. These compounds showed cytotoxic activity against a small panel of human tumor cell lines as well as hemolytic activity against rabbit erythrocytes [24].

A new oleanane-type saponin coriariosides A, along with known saponin was isolated from the roots of *A. coriaria*. These compounds when tested for cytotoxicity against two colorectal human cancer cells, showed excellent activities viz. HCT 116 (IC<sub>50</sub> 4.2 μM) and HT-29 (IC<sub>50</sub> 6.7 μM) cell lines [25]. *Albizia harveyi* showed a significant cytotoxic activity on the RT-4 cell line (percentage survival 23%) at 10 μg/ml. It showed a weak cytotoxic activity on the HT-29 cell line. Two diastereomeric saponins, julibrosides J<sub>1</sub> (1) and J<sub>9</sub> (2), both of which show cytotoxic activity, were obtained from the stem bark of *Albizia julibrissin* Durazz. A new triterpenoidal saponin (Julibroside) with a xylopyranosyl moiety located at its C-21 side chain was isolated from *Albizia julibrissin* Durazz. (Leguminosae). This Julibroside showed marked inhibitory action against Bel-7402 cancer cell line at 10 micro/ml [26]. Two active cytotoxic saponins viz. Albiziatrisoside A and B from methanolic extract of *Albizia subdimidiata* showed significant effects against A2780 cell line [27]. *Albizia gummifera* led to the isolation of three new cytotoxic oleanane-type triterpenoid saponins, gummiferaosides, showing cytotoxicity against the A2780 human ovarian cancer cell line with IC<sub>50</sub> values of 0.8, 1.5 and 0.6 μg/ml respectively.

### Antidiabetic properties

Two flavonol glycosides, quercitrin and isoquercitrin from the flowers of *A. julibrissin* showed diabetic activity [28].

### Anti-inflammatory properties

A novel flavonol glycoside of *A. procera* stem showed moderate anti-inflammatory action on albino rats by using non-immunological carrageen an induced hind paw edema method. *Albizia lebeck* benth seed the ethanol extract showed highest anti-inflammatory activity was observed at 200 mg/kg dose. The aqueous ethanol extract of *Albizia anthelmintica* showed moderate anti-inflammatory activity.

### Antibacterial properties

The bark of *Albizia lebeck* has acrid taste and its extract showed antimicrobial activity. Novel macrocyclic alkaloids (budmunchiamines

A, B and C were isolated from *A. amara*. They were also found to have antiplatelets aggregation and bactericidal activity [29]. A new biologically active flavonol glycoside 3, 5, 4'-trihydroxy, 7, 3'-dimethoxy-3-O- $\beta$ -D-glucopyranosyl-(1 $\rightarrow$ 4)- $\alpha$ -L-xylopyranoside from the seeds of *A. julibrissin* was fairly active against gram positive and gram negative bacteria. The extracts of *Albizia ferruginea* were also reported to have significant anti-microbial activity on selected microorganisms. Three flavonoids such as 4', 7-dihydroxyflavanone, 3', 4', 7-trihydroxyflavone, 3-O-methylfisetin (3',4',7-trihydroxy-3-methoxyflavone, isolated for the first time from the Sudanese medicinal plant, *Albizia zygia*, when tested against *Plasmodium falciparum*.

#### Hepatoprotective effect

*Albizia procera*, *Albizia lebeck*, *Albizia inopinata* and *Albizia amara*, seem to exhibit potent hepatoprotective activity along with various pharmacological activities such as CNS activity, cardiotoxic activity, lipid-lowering activity, antioxidant activity, hypoglycemic activity etc. [30] [31].

#### Bioactive constituents

Genus *Albizia* has been known to contain substantial amounts of saponins. Lebbekanin E was isolated from *A. lebeck* [32]. Three saponins were also isolated from the seeds of *A. lucida* were established as 3-O-[ $\beta$ -D-xylopyranosyl (1 $\rightarrow$ 2)- $\alpha$ -L-arabinopyranosyl (1 $\rightarrow$ 6)] [ $\beta$ -D-glucopyranosyl (1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl echinocystic acid, 3-O-[ $\alpha$ -L-arabinopyranosyl (1 $\rightarrow$ 6)] [ $\beta$ -D-glucopyranosyl (1 $\rightarrow$ 2)]- $\beta$ -D-glucopyranosyl echinocystic acid and 3-O-[ $\beta$ -D-xylopyranosyl (1 $\rightarrow$ 2)- $\beta$ -D-fucopyranosyl (1 $\rightarrow$ 6)]-2-acetamido-2-deoxy- $\beta$ -D-glucopyranosyl echinocystic acid. In addition, three

main saponins were isolated from the bark of *A. lebeck* and named albiziasaponins A, B and C. The stem bark of *A. gummifera* yields oleanane saponins: vitalboside-A and vitalboside-A 2'-methylglucuronate. Moreover, albiziahexoside a new hexaglycosylated saponin, was isolated from the leaves of *A. lebeck*. Two new oleanane-type triterpene saponins, adianthifoliosides A and B were also isolated from an ethanolic extract of roots of *A. adianthifolia*.

A new monoterpene conjugated triterpene from the stem bark of *A. julibrissin* was isolated. The new terpene was identified as 21-[4-(ethylidene)-2-tetrahydrofuran methacryloyl] mechaerinic acid. Lupeol and acacic acid lactone were isolated from *A. versicolor*. Moreover, the stem bark of *A. gummifera* has yielded three triterpenes such as lupeol, lupenone and vitalboside-A. A novel macrocyclic spermidine alkaloid, albizzine-A was isolated from stem bark of *A. myriophylla*. Budmunchiamines L1-L3 was isolated from the methanol extract of seeds of *A. lebeck*. In addition, a new ceramide and its glycoside were isolated from the flower of *A. julibrissin* were established as (2S, 3S, 4R, 8E)-2-[(2'R)-hydroxyhexadecanoylamino-8-tetra-cosene-1, 3, 4-triol and 1-O- $\beta$ -D-glucopyranosyl- (2S, 3S, 4R, 8E)-2- [(2'R)-hydroxyhexadecanoylamino-8-tetracosene-1, 3, 4-triol on basis of chemical and spectroscopic studies [33] and also the four new glycosides and icariside E<sub>5</sub> were isolated from the dried stem bark of *A. julibrissin*. From *Albizia* bark powder (*A. myriophylla* and *A. kalkora*) 12 phenolic acids were qualitatively isolated viz. gallic acid, gentisic acid, p-hydroxybenzoic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, salicylic acid, quercetin, eugenol and kaempferol.

Table 1: Some isolated phytoconstituents

Species	Plant Parts	Phytoconstituents
<i>A. subdimidiata</i>	Whole plant	Albiziatriside A and B
<i>A. julibrissin</i>	Bark	Julibroside J29, J30 and J31
	Flowers	quercitrin and isoquercitrin 3, 5, 4'-trihydroxy, 7, 3- dimethoxy-3-O- $\beta$ -D-glucopyranosyl- $\alpha$ -L-xylopyranoside
<i>A. grandibracteata</i>	Leaves	Grandibracteosides A-C
<i>A. procera</i>	Bark	3-O-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 2)- $\alpha$ -L-arabinopyranosyl- (1 $\rightarrow$ 6)]-2 acetamido-2- deoxy- $\beta$ -Dglucopyranosyl] echinocystic acid, 5,2', 4'-trihydroxy-3,7,5'- trimethoxyflavonol-2'-O- $\beta$ -D-galactopyranosyl- (1 $\rightarrow$ 4)-O- $\beta$ D-glucopyranoside
<i>A. chinensis</i>	Bark	Albizosides A-C
	Leaves	Kaempferol-3-O- $\alpha$ -L-rhamnopyranoside, Quercetin-3-O- $\alpha$ -L-rhamnopyranoside, Luteolin, Kaempferol, Quercetin
<i>A. gummifera</i>	Bark	Vitalboside-A, vitalboside-A, 2'- methylglucuronate
	Stem bark	3-O-{ $\beta$ -D-glucopyranosyl(142)-[ $\alpha$ -L-arabinopyranosyl(146)]- $\beta$ -D-glucopyranosyl}-oleanolic acid
<i>A. lebeck</i>	Seeds	Budmunchiamines L1-L3.
	Leaves	Quercetin, kaempferol, 3-O- $\alpha$ -rhamnopyranosyl (1 $\rightarrow$ 6)- $\beta$ -glucopyranosyl(1 $\rightarrow$ 6)- $\beta$ -galactopyranosides.
<i>A. myriophylla</i>	Bark	Albiziasaponins A, B and C
	Stem	Albizzine A
<i>A. inopinata</i>	Leaves	Felipealbazine A, felipealbazine B
<i>A. versicolor</i>	Whole plant	Lupeol, acacic acid, lactone
<i>A. mollis</i>	Bark	Molliside A-B, Concinnoside A, Albiziasaponin A
<i>A. odoratissima</i>	Root bark	7,8-Dimethoxy-39,49 methylenedioxyflavone, 7,29,49-Trimethoxyflavone
<i>A. falcataria</i>	Bark	Syringaresinol

#### DISCUSSION

The traditional medicine all over the world is nowadays revalued by an extensive activity of research on different plant species and their therapeutic principles. Herbal drugs are rapidly becoming popular in recent years as an alternative therapy. Numerous polyherbal formulations, which are combinations of different herbal extracts/fractions, are used for the treatment of liver diseases. The small fraction of flowering plants that have so far been investigated have yielded about 120 therapeutic agents of known structure from about 90 species of plants. Some of the useful plant drugs include vinblastine, vincristine, taxol, podophyllotoxin, camptothecin, digitoxigenin, gitoxigenin, digoxigenin, tubocurarine, morphine, codeine, aspirin, atropine, pilocarpine, capscicine, allicin, curcumin, artemisinin and ephedrine among others. In some cases, the crude extract of medicinal plants may be used as medicaments. For

developing a satisfactory antioxidant herbal formulation, there is a need to evaluate the formulation for desired properties such as antioxidant activity [34]. On the other hand, the isolation and identification of the active principles and elucidation of the mechanism of action of a drug is of paramount importance. Hence, works in both mixture of traditional medicine and single active compounds are very important.

It has been estimated that in developed countries such as United States, plant drugs constitute as much as 25% of the total drugs, while in fast developing countries such as China and India, the contribution is as much as 80%. Thus, the economic importance of medicinal plants is much more to countries such as India than to rest of the world. Today this system of medicine is being practised in countries like Nepal, Bhutan, Sri Lanka, Bangladesh and Pakistan, while the traditional system of medicine in the other countries like

Tibet, Mongolia and Thailand appear to be derived from Ayurveda. A great deal of information is now available showing that several natural products are endowed with potent anticancer activity [35]. Among the plant species, *Albizia* seem to possess numerous pharmacological properties. Bioactive compounds such as saponins, alkaloids, flavonoids and phenolic compounds highly active against cytotoxicity, tumor cancer cells. They are widely used as anti-asthma, anti-septic, anti-dysentric, anti-tubercular, antioxidant activity, anti-microbial agents. It may be concluded that *Albizia* species shall be considered as a promising plant with various therapeutic properties and can be further explored pharmacologically against various ailments and for free-radical mediated diseases. And this review would open-up a refreshing study about the immense utility of *Albizia* and encourages the phytochemists to drive on the rest of the species. Apart from the huge number of research studies in the field of synthetic chemistry, the field of phytochemistry still needs more attention from scientists around the world for the evolution of preventive/ precautionary health care without any harmful toxic effects.

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