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An Overview of *Entada phaseoloides*: Current Research and Future Prospects

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Abstract: In recent times, focus on plant research and herbal products has increased tremendously in the western world as well as in developed and developing countries. *Entada phaseoloides*, a well-known creeper widely used therapeutically in the orient and has become increasingly popular as an important medicinal plant. Many studies have been carried out on this medicinal plant and have generated immense data about the morphology, chemical composition, corresponding to biological activity of extracts and isolated secondary metabolites. Biological studies and traditional clinical practice demonstrated that *Entada phaseoloides* and its bioactive compounds possess various pharmacological properties. The plant has been traditionally used in Ayurvedic medicine for centuries as an anti-inflammatory, analgesic, antipyretic, antiarthritis, antidiabetic, antioxidant, cytotoxic, antimicrobial and molluscidal agent. The present review summarizes current knowledge on morphology, major bioactive(s) constituents and its chemistry, reported medicinal properties, pharmacological actions, folklore uses and the possibility of interactions of the herb with the conventional drugs. Despite this, further investigations are required to explore *Entada phaseoloides* and to evaluate the different biological activities of either its extracts or the isolated compounds with probable modes of action.

Key words: *Entada phaseoloides*, morphology, bioactive constituents, folklore uses.

1. Introduction

Throughout the ages, humans have traditionally relied on plants, animals and minerals for their basic needs, such as food, protection against enemies, hunting, and healing of infections and health disorders. A number of traditional medicinal systems have evolved that have been used for centuries and today, are still a source of interesting drugs for phytotherapy [1]. Nature always stands as a gold mark to exemplify the outstanding phenomenon of symbiosis [2, 3]. Interest in the use of herbal products has grown dramatically in the western world [4] as well as in developed countries [5]. The herbal vendors are the mobile men seen on the busy streets of many Indian cities selling crude medicinal plants and its products. They prescribe herbal treatment for several diseases, a skill they inherited from their forefathers through several generations of experience [6]. One of the important medicinal plants, widely used therapeutically in the orient and becoming increasingly popular is *Entada phaseoloides*, a creeper, of genus *Entada* which consists of 30 species of trees, shrubs and tropical lianas. About 21 species are known from Africa, six from Asia, two from the American tropics and one with a pan tropical distribution [7]. *Entada phaseoloides* is a very large woody climber belonging to Order Fabales, Family Fabaceae or Leguminosae, Subfamily Mimosoideae and Tribe of Mimoseae. Botanical name is *Entada phaseoloides* (L.) Merril [8]. Synonyms of *Entada phaseoloides* is *Entada scadens* (L.) [9], *Lens phaseoloides* L. [10] and is commonly known as Matchbox Bean, Vine, Gogo, Elva Climber, etc. [11].

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In India, the species is widely distributed in the eastern Himalayas, East Bengal, Tirupati (Andhra Pradesh) etc. [12]. In the folklore of Indian medicine, the herb has been used traditionally in various diseases as analgesic, counter irritant, hair growth stimulant, emetic and remedy for cerebral haemorrhage. This comprehensive review summarizes our current knowledge of the major bioactivities and clinical efficacy of *Entada phaseoloides* as one of the currently used popular herbal plant. The popularity of *Entada phaseoloides* as a medicinal plant can be best determined by the number of papers published per year over a period of time which is presented in Fig. 1 [13-41]. We aim to derive an impressive and convenient review; scientifically beneficial for both investigators and readers who are interested in the pharmaceutical aspects of medicinally active herbs. However, it was not the intention of this review to go beyond the field of phytochemistry and ethnobotany.

2. Morphology

The woody creeper *Entada phaseoloides* with all its parts stem, leaves, leaves with flowers, flowers, fruits and fruit with seed are presented in Figs. 2a-2f, respectively [8].

Stem diameters measures up to 18 cm, laterally compressed or flattened and twisted like a corkscrew. Vessels are large, readily visible to the naked eye in transverse sections. Pith is located eccentrically much closer to one margin than the other in stem cross sections.

Leaves are bipinnate with about 8-16 leaflets, (two to four leaflets on each secondary axis) main rhachis projecting as a branched tendril beyond the leaf. Leaflet blades measure about (4-11) × 2.5-5.5 cm, while leaflet stalks are of about 0.1-0.7 cm long and are transversely wrinkled.

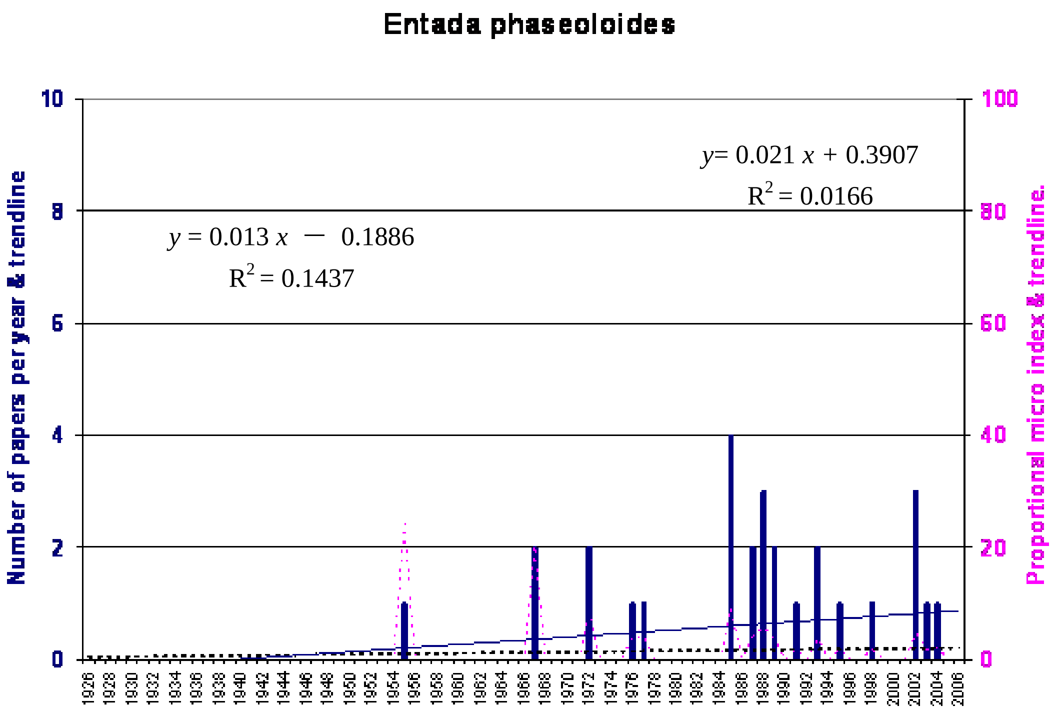


Fig. 1 Popularity of *Entada phaseoloides* over time.

Plots of numbers of papers mentioning *Entada phaseoloides* (filled column histogram and left hand axis scale) and line of best fit, 1926 to 2006 (complete line, with equation and % variation accounted for, in box on the left hand side); plots of a proportional micro index, derived from numbers of papers mentioning *Entada phaseoloides* as a proportion (scaled by multiplying by one million) of the total number of papers published for that year (broken line frequency polygon and right hand scale) and line of best fit, 1926 to 2006 (broken line, with equation and % variation accounted for, in broken line box on the right hand side).

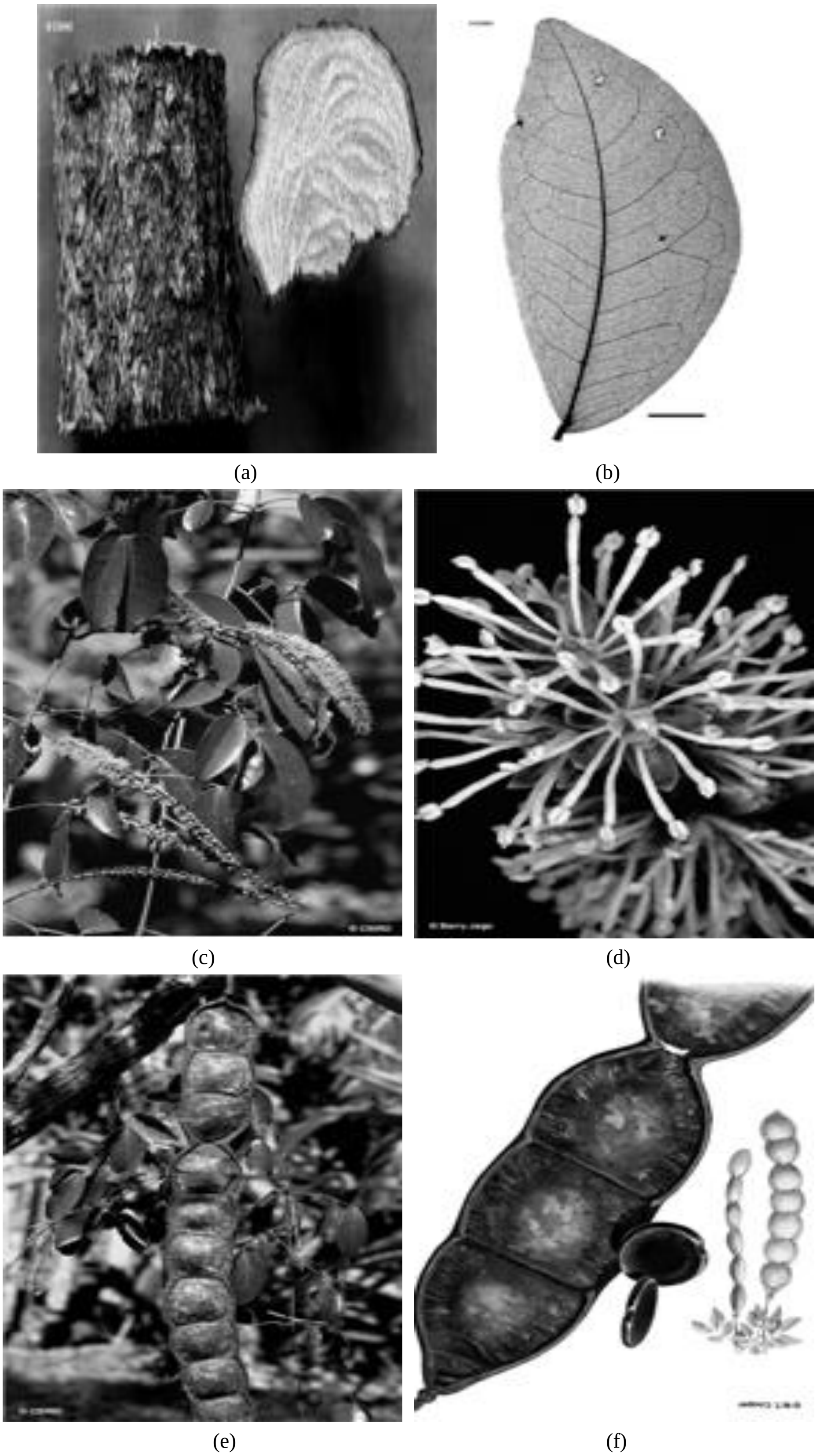


Fig. 2 (a) Stem bark & stem transverse section; (b) *Entada* leave (10 mm); (c) Entada leaves & flowers; (d) Entada fruit; (e) Entada seed; (f) Entada fruit & seeds.

Stipules are linear and falcate which measures 2-4 × 2 mm. Scattered large clear glands are visible to the naked eye in the leaflet blades, whereas numerous smaller glands can be visible with a lens.

Flowers are more or less cup-shaped, about 1.5 mm in diameter at the apex. Corolla is pink to red in colour and cream or translucent in colour on the inner surface. Petals are about 3 × (1-1.5) mm. Staminal filaments crumpled in the bud which are of about 6-7 mm long at anthesis. Style crumpled in the bud.

Fruits are flattened, about (88-100) × (9-12) cm, constricted at intervals and divided into about 12 segments, each segment measures about 7 × (9-10) cm, surrounded by endocarp and falling from the pod leaving only the sutures of the pod attached to the vine. Exocarp shed by rolling up into rolls of tissue. Endocarp is not hard but more or less leathery or like parchment.

Seeds are laterally compressed, about 5-6 cm in diameter and 1-1.5 cm thick. Testa is hard. Cotyledons are hard, about (4.5-5.5) × (4.5-5) cm in diameter which fused around the margin. Radicle measures about 4 mm long [11].

3. Distribution and Ecology

It is distributed in the altitudinal range from near sea-level to 100 m. The plant grows in beach forest, gallery forest, monsoon forest and lowland rain forest and also occurs in New Guinea and other parts of Malaysia, Asia and the Pacific islands [11]. The plant occurs throughout the sub-Himalayan tract, from Nepal eastwards ascending to 4,000 ft. in Sikkim, in Assam, Bihar and Orissa, and in the monsoon forest of western and eastern ghats; it is abundant in Andaman Islands [42]. Also found in forests at low and medium altitudes, from Northern Luzon (Cagayan) to Mindanao and Palawan [43].

4. Natural History

Entada phaseoloides is a food plant for the larval stages of the tailed green-banded blue butterfly [44]. This species may have medicinal properties and has been used as a fish poison. The species has been used medicinally in Malaysia, the Philippines and Java. The seed are considered as tonic, emetic and anthelmintic [42].

5. Properties

The seeds of *Entada phaseoloides* are slightly bitter-acrid in taste and mildly cooling in nature. It was reported as antirheumatic, relieving gastrointestinal disorders and aids circulation. The juice extracted from the bark was reportedly found to be irritating to the eyes, causing conjunctivitis. *Entada phaseoloides* was also found to exhibit detectable genotoxicity [11].

6. Utility and Edibility

Bark, seeds and vines were usually the utilized parts of *Entada phaseoloides*. The vines may be collected during any time of the year, rinse, section into slices, steamed and lastly sundried. The seeds may be collected from January to April. Seed coats are removed and roasted in a frying pan, sun-dried and pulverized. In the Dutch Indies, young leaves are eaten, raw or cooked. In Bali and Sumatra, the seeds are eaten while in South Africa, pod and seeds are used as coffee substitute [11]. The white kernels of the seeds are eaten by the poor, after soaking in water and roasting to remove toxic principles. Roasted pods are occasionally used as substitute for calabar bean. The seeds, stems and barks are poisonous. The leaves are reported to be free from the toxic saponins which are present in other parts of the plant. They are eaten by elephants [42].

7. Folkloric Uses

Dried vine materials of about 15 g to 30 g in decoction are reported to be effective in rheumatic lumbar, leg pains, sprains and contusions. Powdered seeds of about 3 g to 9 g when taken orally with water can cure jaundice and edema due to malnutrition. In abdominal pains and colic, the pound kernels of seeds after mixing with oil can be applied as poultice onto affected area. The paste of seed is used as counterirritant and applied to glandular swellings in the axilla, loins and joints, and swollen hands and feet. It is also used as hair growth stimulant. Seeds are used as emetic. It is used as febrifuge. In South Africa, seeds are used by infants to bite on during their teething period. Also, used as remedy for cerebral hemorrhage. As a treatment of skin itches, the affected part is washed with a decoction of the bark of *Entada phaseoloides*. Stem macerated in cold water used as cleansing soap and also used as an emetic [11].

8. Local Application

The seeds of *Entada phaseoloides* used extensively in the Philippines and other oriental countries for washing the hair. Also it is an ingredient of hair tonics. The bark is soaked in water until soft, the fibers are spread, the juice is expressed by rubbing the fibers against each other until it lathers, which is then used to cleanse the scalp. Bark is used as cordage. In Europe, it is used for tinder and for making match boxes. Large pods and seeds were used by children as playthings. In Sunda Islands, a fatty oil extracted from the seeds is used as an illuminant. In Europe, seeds were reportedly used for snuff [11]. The saponins have a strong haemolytic action on human red blood cells. A sharp fall in blood pressure was observed in experimental animals after doses of saponins varying from 0.0005-0.002 g/kg of body weight; the fall was associated with an increase in the volume of the intestines and, to a lesser extent, of the kidneys; there was no fall in blood pressure in animals which had received atropine [42, 45]. The saponins are reported to have a depressant effect on the respiratory system and inhibit the movements of unstriped muscles of the intestines and the uterus. Entagenic acid has antifungal activity against phytopathogenic fungi. A glycoside of entagenic acid possesses antineoplastic activity. The oil is used in lamps for illuminating purposes. A potable watery fluid exudes from the fresh stem when cut. The bark fibre, which is coarse but durable, is used for cordage and nets. The hard and smooth-shelled seeds are used for burnishing pottery, polishing hand-made paper and crimpling linen. The seeds are hollowed out and employed in making trinkets and small receptacles e.g., snuff and tinder boxes [42].

9. Constituents and Chemistry

9.1 Saponin

Entada phaseoloides yields saponin which is reported to be abundant in the bark, less so in the wood, plentiful in the seeds, and absent from the leave [43], a crystalline saponin isolated from seed kernels of *Entada phaseoloides*, which have the tentative empirical formula $C_{45}H_{82}O_{27}$. Acid hydrolysis yields a crystalline sapogenin $C_{30}H_{48}O_5$ which appears to be identical with entagenic acid, together with arabinose and xylose [33], the chemical formula of saponin [46], sapogenin [47], entagenic acid, arabinose and xylose are presented in Figs. 3a-3e, respectively [48].

9.2 Phaseoloidin

The structure of phaseoloidin isolated from the seeds of *Entada phaseoloides* has been determined as homogentisic acid 2-O-β-D-glucopyranoside by chemical and spectral means [34], whose chemical formula is presented in Fig. 4 [48].

9.3 Amides

Entadamide A [35] and Entadamide B [36], the two new sulfur-containing amides, isolated from the seeds of *Entada phaseoloides* which were synthesized by the addition reaction of methanethiol to propiolic acid followed by condensation with ethanolamine by the use of dicyclohexylcarbodiimide. These compounds inhibited the 5-lipoxygenase activity of RBL-1 cells at 10^{-4} g/mL. This finding suggests that entadamides A and B may be examples of a new type of anti-inflammatory drug [37]. Entadamide B was characterized by spectroscopic methods as N-(2-hydroxyethyl)-3,3-bis(methylthio) propaneamide

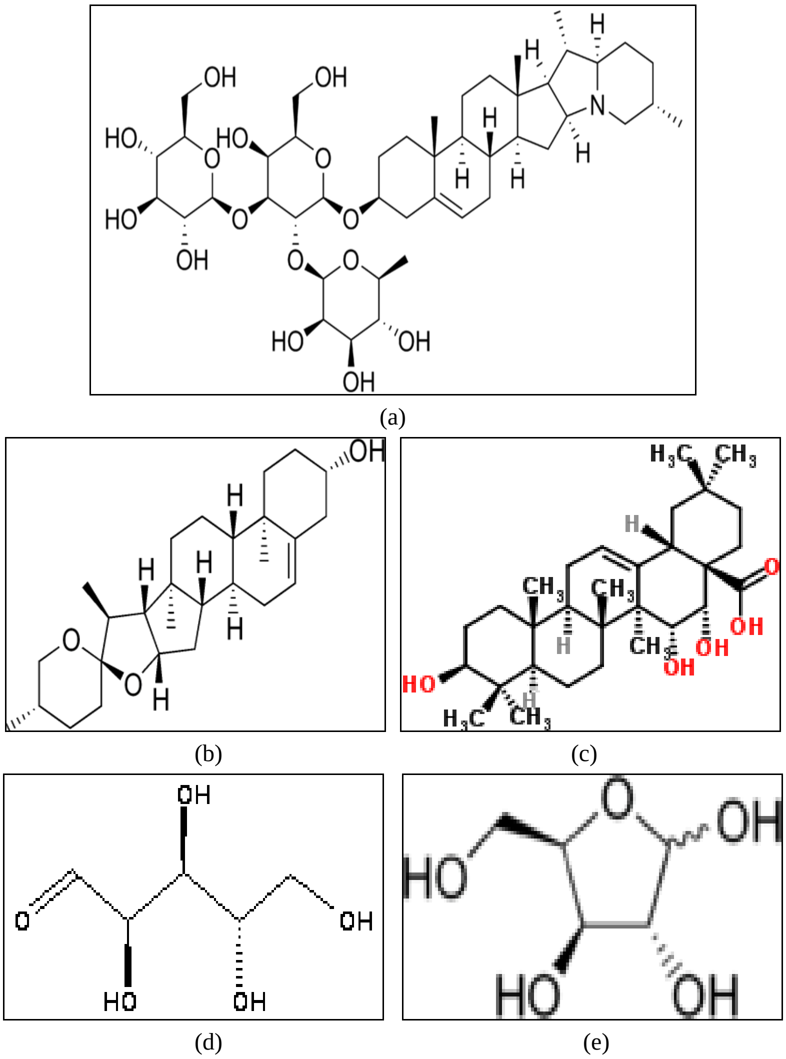


Fig. 3 (a) Chemical structure of the saponinl; (b) Chemical structure of the sapogenin; (c) Chemical structure of the entagenic acid; (d) Chemical structure of the arabinose; (e) Chemical structure of the xylose.

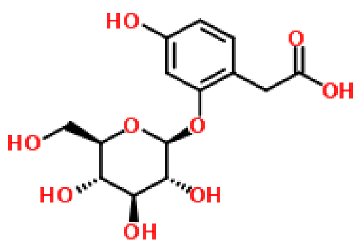
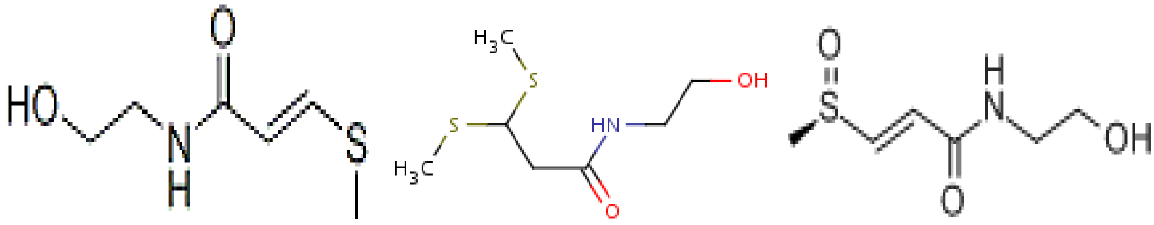


Fig. 4 Chemical structure of phaseoloidin.

and was synthesized in two steps from propiolic acid [37]. The chemical formula of Entadamide A [49] and Entadamide B [50] are presented in Figs. 5a and 5b, respectively.

Entadamide C, a third new sulphur-containing amide, has been isolated from the leaves of *Entada phaseoloides* together with entadamide A. Entadamide C, the sulphoxide form of entadamide A, is called as (*R*)-(+)-*trans*-*N*-(2-hydroxyethyl)-3-methylsulphinylpropenamide. Chemical synthesis of (±)-entadamide C was achieved in three steps from propiolic acid [21].

The chemical formula of Entadamide C is presented in Fig. 5c [51]. Again four sulfur-containing amide compounds were isolated from the n-BuOH-soluble fraction and identified as entadamide A-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (Compound 1), which is a new compound along with and entadamide A (Compound 2), entadamide A-β-D-glucopyranoside (Compound 3) and clinacoside



(a) (b) (c)

Fig. 5 (a) Chemical structure of entadamide A; (b) Chemical structure of entadamide B; (c) Chemical structure of the entadamide C.

C (Compound 4). Compound 4 is isolated from the genus *Entada* for the first time. The chemical formula of Compound 1, Compound 2, Compound 3 and Compound 4 are presented in Figs. 6a-6d, respectively [52].

9.4 Glycosides

Three new compounds, 2-hydroxy-5-butoxyphenylacetic acid, 2-β-D glucopyranosyloxy-5-butoxyphenylacetic acid, and entadamide A-β-D-glucopyranoside, in addition to the new natural product 2,5-dihydroxyphenylacetic acid methyl ester isolated and characterized from seeds of *Entada phaseoloides* collected in Indonesia. None of these compounds was found to demonstrate significant cytotoxicity for cultured human cancer cells, but 2-hydroxy-5-butoxyphenylacetic acid and 2,5-dihydroxyphenylacetic acid methyl ester gave ED_{50} values of 1.01.7 μg mL^{-1} and 1.7 μg mL^{-1}, respectively, with cultured P-388 cell [39].

9.5 Chalcone Glycosides

Two new chalcone glycosides4'-O-(6″-O-galloyl-β-D-glucopyranosyl)-2', 4 dihydroxychalcone (1) and 4'-O-(6″-O-galloyl-β-D-glucopyranosyl)-2'-hydroxy-4 methoxychalcone (2) together with one known chalcone glycoside 4'-O-β-d-glucopyranosyl-2'-hydroxy-4-methoxychalcone (3) isolated from the stems of *Entada phaseoloides*. The structures of the new compounds were elucidated on the basis of extensive spectroscopic analysis, including HSQC (heteronuclear single quantum correlation spectroscopy), HMBC (heteronuclear multiple bond correlation spectroscopy), ^{1}H-^{1}H COSY (^{1}H-^{1}H correlation spectroscopy), and chemical evidences. This was the first report of chalcone-type compounds isolated from the genus *Entada*. The chemical structure of three isolated compounds, i.e., Compound 1, Compound 2 and Compound 3 are presented in Fig. 7 [53].

9.6 Glucosides

The phytochemical investigation of the defatted seeds of *Entada phaseoloides* Merill. (Mimosaceae) led to the isolation of three new phenolic acid glucosides,

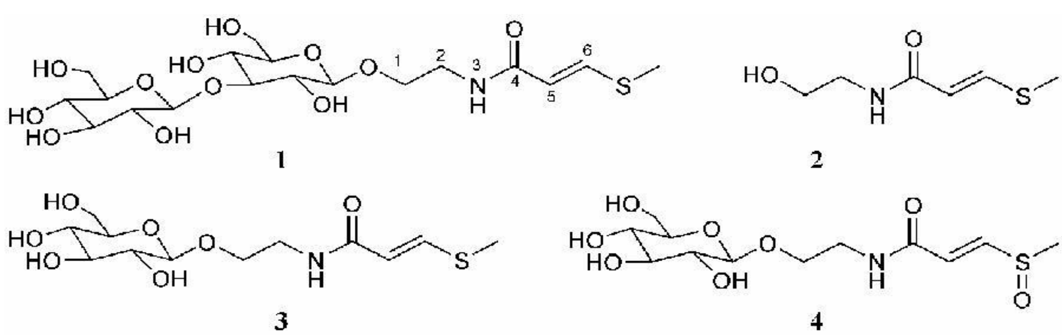


Fig. 6 The chemical structures of four sulphur containing amides, i.e., Compound 1, Compound 2, Compound 3 and Compound 4.

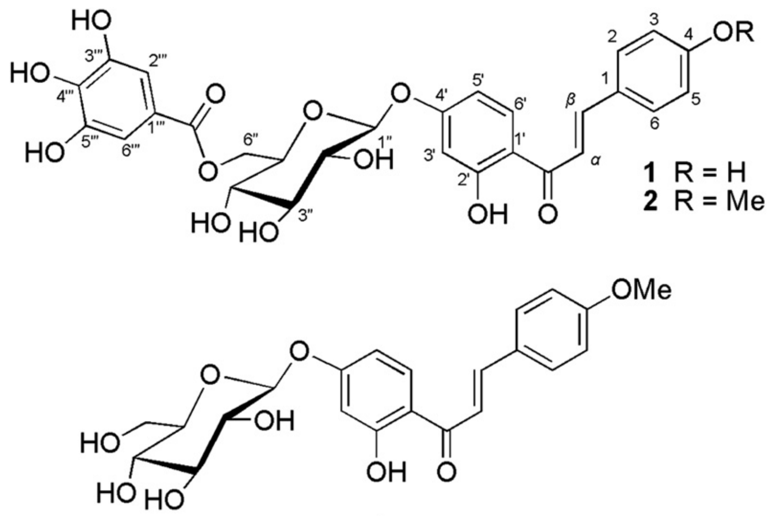


Fig. 7 The chemical structures of three chalcone glycosides, i.e., Compound 1, Compound 2 and Compound 3 .

which were characterized as 2-hydroxy-5-methylbenzoyl-β-L-glucopyranoside[p-cresotyl glucoside, 1(first phenolic acid glucosides)], 2-hydroxy-5-methylbenzoy l-β-L-glucopyranosyl (2→1)-β-glucopyranosyl(2→1)-β-L-glucopyranoside [p-cresotyltriglucoside, 2(second phenolic acid glucosides)], and 2-hydroxybenzoyl-β-Lglucopyranosyl(2→1)-β-L-glucopyranosyl(2→1)-β-L-glucopyranosyl(2→1)-β-L-glucopyranoside (salicylic acid tetraglucoside, 5(fifth phenolic acid glucosides)], along with sucrose and triglucoside. The structures of these phytoconstituents have been established on the basis of spectral data analysis and chemical reactions [54].

9.7 Sulphur-Containing Glucoside

One new and one known sulphur-containing glucoside from a MeOH extract, along with four new triterpene saponins containing *N*-acetylglucosamine in their sugar chains were isolated from the 1-BuOH-soluble fraction of a H_2O extract of kernel nuts of *Entada phaseoloides (L.) Merrill* [55].

9.8 Flavonoids

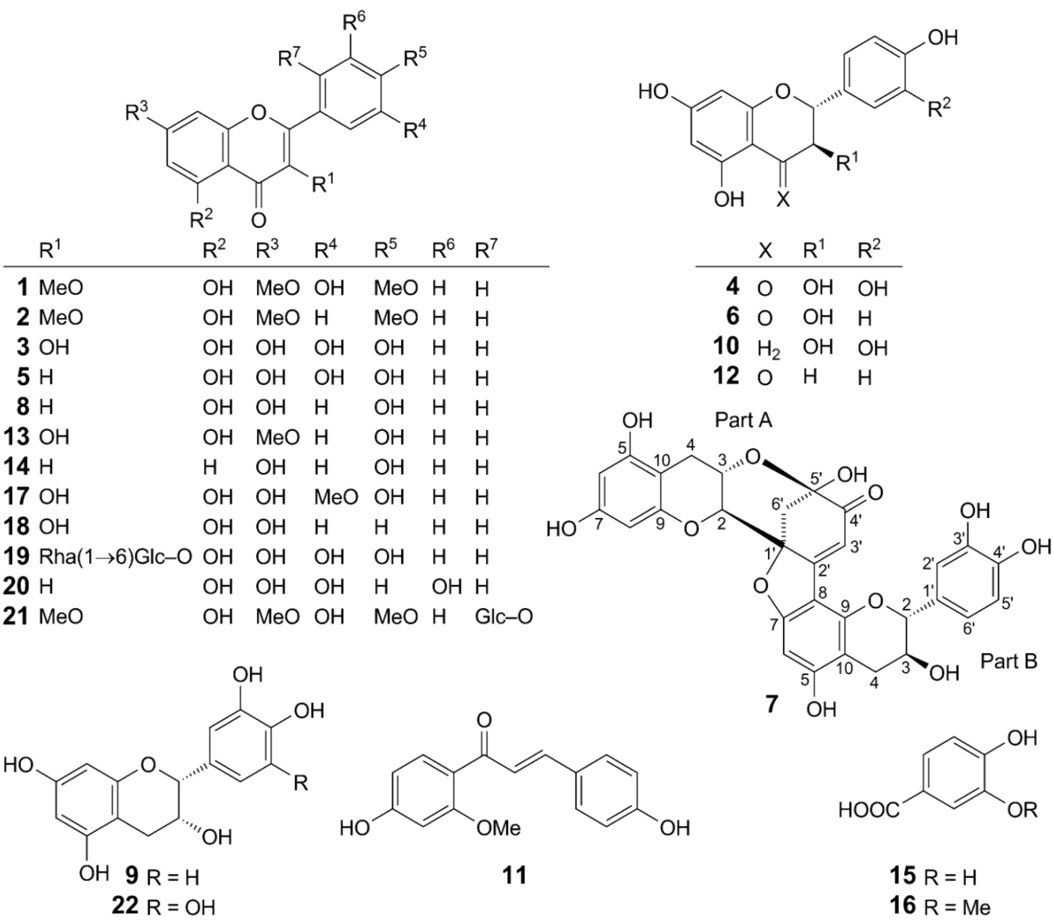
The compound 5,6,7,5'-Tetramethoxy-3', 4'-methylene dioxy flavones monohydrate (systematic name: 5,6,7-trimethoxy-2-(7-methoxy-1,3-dihydro-2-benzofuran-5-yl)-4H-chromen-4-onemonohydrate), was isolated from the popular Chinese medicinal plant *Entada phaseoloides*. In the crystal, inversion-related molecules are joined by pairs of weak C-H⋯O hydrogen bonds. The dimers are further interconnected by a bridging water molecule *via* weak C-H⋯O_{water} and pairs of $(O\text{-}H)_{water}$⋯O hydrogen bonds into a linear tape running parallel to the *b* axis [56].

9.9 Antioxidants

The EtOH extract of the stems of *Entada phaseoloides* displayed potent antioxidant activity when assessed by the 1,1-diphenyl-2-picrylhydrazyl(DPPH) and 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical-scavenging, reducing power, β-carotene-bleaching and superoxide radical-scavenging assays. Fractionation of the ethanol (EtOH) extracts showed that the ethyl acetate (AcOEt) fraction is the most active, which inhibited the linoleic acid oxidant to the greatest extent, had the strongest DPPH and ABTS radical-scavenging abilities, and possessed significant reducing power over other fractions followed by the H_2O fraction, while BuOH (butanol) fraction was least active. Further activity-guided fractionation studies on the active fractions resulted in the isolation of 22 compounds, i.e., 3,4’,7-trimethylquercetin (1), 5-hydroxy-3,4’,7-trimethoxyflavone (2) [57], quercetin (3), (þ)-3,3’,5’,5,7-pentahydroxyflavanone (4) [58], luteolin (5), (þ)-dihydrokaempferol (6) [58], dehydrodicatechin A (7) [59], apigenin (8), (_)-epicatechin (9), (þ)-catechin (10) [60], 3-deoxysappanchalcone (11) [61], naringenin (12), rhamnocitrin (13), 4’,7-dihydroxyflavone (14) [62], protocatechuic acid (15), vanillic acid (16), 4’,5,7-trihydroxy-3’-methoxyflavonol (17) [63], galangin (18), rutin (19), 3’,5,5’,7-tetrahydroxyflavanone (20) [64], 2’,5,5’-trihydroxy-3,4’,7-trimethoxyflavone-2’-O-b-d-glucoside (21) [65] and (_)-epigallocatechin (22) [60] were confirmed by comparing their HPLC, HPTLC, and characteristic spectroscopic data with those of the standards or with those reported in the literature. The chemical structures of the isolated compounds are presented in Fig. 8. The identities of these compounds were established based on extensive spectroscopic studies. Furthermore, the antioxidant activities of the isolated compounds were evaluated by using the above-mentioned five assays. The results demonstrated that the EtOH extract of *E. phaseoloides* stems exhibit an excellent antioxidant activity and thus presents a great potential as a source of natural antioxidants. The antioxidant activity of EtOH extract and three fractions from stem of *E. phaseoloides* are presented graphically in Fig. 9. This is claimed to be the first extensive study of all compounds from *E. phaseoloides* and genus *Entada* by the author [66].

9.10 Crude and Processed Products

The chemical constituents of the *Entada phaseoloides* (L.) Merrill were studied by extracting it



	R1	R2	R3	R4	R5	R6	R7
1	MeO	OH	MeO	OH	MeO	H	H
2	MeO	OH	MeO	H	MeO	H	H
3	OH	OH	OH	OH	OH	H	H
5	H	OH	OH	OH	OH	H	H
8	H	OH	OH	H	OH	H	H
13	OH	OH	MeO	H	OH	H	H
14	H	H	OH	H	OH	H	H
17	OH	OH	OH	MeO	OH	H	H
18	OH	OH	OH	H	H	H	H
19	Rha(1→6)Glc–O	OH	OH	OH	OH	H	H
20	H	OH	OH	OH	H	OH	H
21	MeO	OH	MeO	OH	MeO	H	Glc–O

	X	R1	R2
4	O	OH	OH
6	O	OH	H
10	H_2	OH	OH
12	O	H	H

Fig. 8 Chemical structures of isolated compounds 1-22 from the stems of *Entada phaseoloides.*

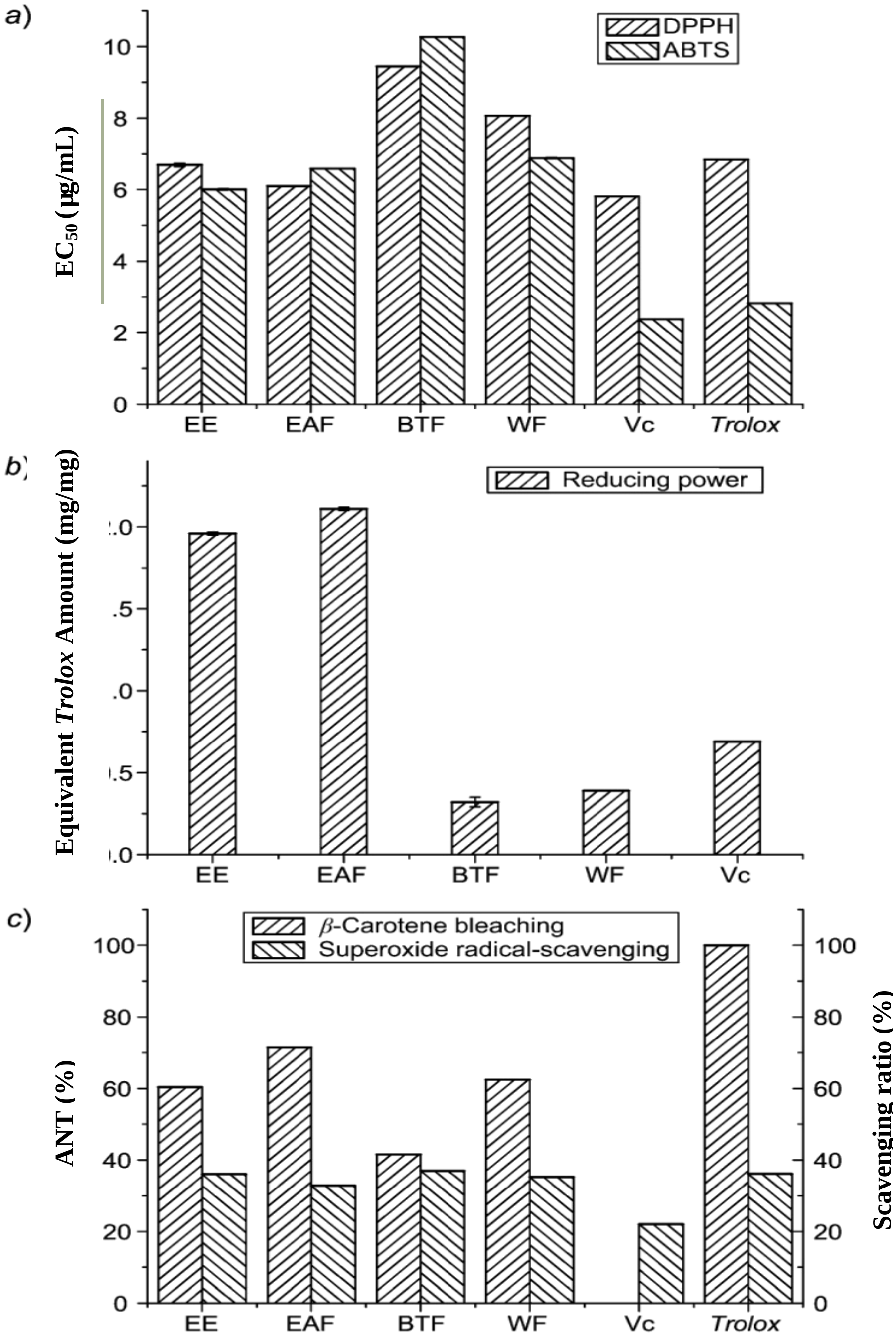


Fig. 9 The antioxidant activity of EtOH extract and three fractions from the stems of *Entada phaseoloides*. (a) DPPH and ABTS radical-scavenging assays; (b) Reducing power; (c) β-carotene-linoleate and superoxide radical-scavenging assays.

with 70% ethanol at room temperature. Isolation and purification were performed by silica gel, reversed-phase silica gel column chromatography and semi-preparative HPLC. Structures of the pure compounds were established on the basis of spectral analysis [46]. A novel method established and the results were compared for HPLC fingerprint determination of crude and processed products of *E. phaseoloides (L.) Merrill.* HPLC-ESI-MS was introduced to analyze the common peaks in each batch of crude *E. phaseoloides (L.) Merrill.* Sixteen characteristic peaks were found in crude *E.*

phaseoloides samples and twenty-one common peaks existed in processed *E.phaseoloides* samples. Nine characteristic peaks of which were identified by comparison of the retention time and their molecular weights of chemical standards, most of which were identified belong to triterpenoid saponins and glucosides. After processing, the chemical composition of the extraction with solution of 60% methanol from crude *E. phaseoloides* are found to be less or more similar to that of processed *E. phaseoloides*, and the changes in the main peaks of fingerprint chromatography suggest that HPLC can be used to reflect the difference of chemical composition of *E. phaseoloides* and their processed products. As per their report, it would be an efficient way for qualitative control of *E. phaseoloides* [67].

9.11 Nutrients

The physical characteristics of pods and seeds, proximate composition, different protein fractionation, SDS-PAGE analysis of proteins, amino acid composition, starch content, fatty acid profiles and various anti metabolic substances of *Entada phaseoloides* Merrill were also studied. The pod length and the number of seeds per pod ranged from 55 cm to 90 cm and from 5 to 11 respectively. The kernel was found to be comprised of 66.1% of the seed weight (18.41 ± 1.14 g). The seed kernels contained 256.7 g kg^{-1} crude protein, 108.1 g kg^{-1} lipid, 27.3 g kg^{-1} ash and a high content of carbohydrate (585.7 g kg^{-1}). The levels of potassium, phosphorus, zinc and iron were similar to those in conventional pulses. Among the different protein fractions of seed kernels, albumins constituted the major storage proteins (69.7%). The kernel proteins were rich in essential amino acids, particularly sulphur-containing amino acids, and their values appeared to be higher than the FAO/WHO (1990) reference protein for a 2-5-year-old growing child and soybean, and comparable to hen egg. Seed kernel lipids contained high levels of unsaturated fatty acids, oleic and linoleic acids, which accounted for 83% of the total fatty acid recovered. The kernel exhibited high trypsin and chymotrypsin inhibitor activities (96.65 mg TI g^{-1} and 30.02 CIU mg^{-1} sample respectively) in addition to containing phenolics, phytic acid, lectins and oligosaccharides. Another major toxic constituent was identified as a group of triterpenoid saponins (3.21%), which had high HeU (haemolytic activity) against cattle erythrocytes and caused high mortality in fish. The *in vitro* digestibility of the kernel protein was low (67%) [40].

10. Pharmacological Activity

10.1 Anti-inflammatory and Analgesic Activities

On the basis of various previous study models, saponins obtained from *Entada phaseoloides*, was reported to have significant anti-inflammatory activity and specifically the saponin from seed kernels of *Entada phaseoloides*, was reported to have significant activity against Walker 256 carcinosarcoma in rats [33].

Anti-inflammatory activity of saponin was explained in the study of methanolic extract of *Entada phaseoloides* seeds in animal models of inflammation where the LD_{50} was found to be more than 5,000 mg/kg in acute oral toxicity testing. Pre-treatment with the extract (400 mg/kg) reduced carrageenan induced rat paw edema at 3rd hour compared to control group of rats. Dose dependent (100, 200 and 400 mg/kg) reduction in inhibition of granuloma formation of cotton pellet granuloma, exudate volume, and total leukocyte count was observed with the extract. The extract inhibited acetic acid induced writhing dose dependently (40, 80 and 120 mg/kg) but was found inactive in reducing the pain produced by thermal injury. C-reactive proteins were absent in extract treated group. The results indicated that extract possesses weaker acute but strong sub-acute anti-inflammatory activity and strong peripheral analgesic activity. The results also suggested that the extract may act on the “proliferative phases of inflammation” [68].

In another study of anti-inflammatory effect of topical application of different formulations of seed pulp of EP (*Entada phaseoloides*), localized inflammatory reaction were developed in all the rats in 24 h. In control group, there was no resolution of swelling even in 21 days. Both EP formulations showed significant ($P < 0.001$) anti-inflammatory activity as compared to that of control. *Entada phaseoloides* ointment was equi-effective to that of diclofenac sodium on 12th day. Its paste was significantly ($P < 0.05$) found to be more effective than diclofenac sodium on 21st day. Both the formulations of *Entada phaseoloides* were found to have anti-inflammatory activity, but the paste was significantly more effective than Diclofenac sodium [69].

10.2 Anti Arthritic Activity

The effect of two formulations of *Entada phaseoloides* seeds after topical application in “monoiodoacetate-induced osteoarthritis” in rats was studied since arthritis is a very common clinical condition affecting both sexes and all ages. Most common forms of arthritis are osteoarthritis and rheumatoid arthritis. In all types of arthritis pain, inflammation and functional restriction are the presenting manifestation. Anti-inflammatory drugs like NSAIDs, corticosteroids and disease-modifying antirheumatic drugs, etc. are used for symptomatic relief, but many times they are associated with adverse effects that can often be as difficult to manage as the disease itself. Therefore, a need exists for new ways to treat these patients. The effect of topical application of two formulations of EP (*Entada phaseoloides*) seeds was studied in the MIA (monoiodoacetate-induced osteoarthritis) model in rats. Both the paste and ointment formulations of EP were tested on 32 Wistar rats weighing 150-200 g, divided into four groups as (I) vehicle, (II) EP paste, (III) EP ointment and (IV) diclofenac ointment. Osteoarthritis was induced by intra articular injection of 50 μL of MIA solution. Drug treatment was given topically according to groups for 14 days. Animals were observed for joint inflammation and gait. Joint histopathology was studied and scored. Swelling and redness of left knee was seen in all rats within 24 h which subsided gradually. Lame to gait and thickening of the joint capsule was seen only in control rats. Histopathologically, osteoarthritic changes were significantly less in drug-treated groups compared to control. As a result, both the formulations of EP were found be effective in preventing the damage to the joint [70].

10.3 Antidiabetic and Hypolipidemic Activities

On the basis of previous study, the TSEP (Total Saponin from *Entada phaseoloides*) was reported to dramatically reduce the fasting blood glucose and serum insulin levels and alleviated hyperglycemia associated oxidative stress in T2DM (type 2 Diabetes mellitus) rats. Moreover, a significantly hypolipidemic effect and an improvement in tissue steatosis were observed after TSEP administration. Further investigations revealed a possible anti-inflammation effect of TSEP by examining serum levels of IL-6 (interleukin-6), TNF-α (tumor necrosis factor-alpha) and CRP (C-reactive protein). The effects of TSEP exhibited a dose-dependent manner and were comparable to metformin. Both hypoglycemic and hypolipidemic activities of TSEP in T2DM rats supported its anti-diabetic property. TSEP exerted its therapeutic effect through repressing chronic inflammation responses [71].

In another experimental model, the anti-diabetic effects of AcOEt (Ethyl acetate), Pet ether (Petroleum-ether) and Chloroform fractions were investigated from the methanolic extract of seeds of *Entada phaseoloides* in AIDM (alloxan induced diabetic mice). The effect of these fractions (200 mg/kg body weight i.p) was observed on FBG (fasting blood glucose) level and active fraction was further investigated for its dose dependent activity (250 mg/kg and 350 mg/kg body weight) on fasting blood glucose level and also on TC (total cholesterol), TG (triglyceride), SGOT (serum glutamate oxaloacetate transaminases) and SGPT (serum glutamate pyruvate transaminases) level in AIDM which showed significant effects. The most significant reduction of FBG level of around 72.02% was observed for Et-Ac fraction in AIDM. A significant reduction (*$p < 0.05$) in serum TC and TG level of 53.00% and 57.25% respectively was also found for Et-Ac fraction of *E. Phaseoloides*. The hypoglycemic and hypolipidemic activities were comparable to metformin HCl (150 mg/kg). In diabetic mice, SGOT and SGPT levels were significantly elevated that were further reduced after intraperitoneal administration of this fraction. These results indicated AcOEt fraction of *E. Phaseoloides* have favourable effects in bringing down the severity of diabetes together with hepatoprotectivity [72].

In another study, to observe the effect of TSEP (total saponins from *Entada phaseoloides*) on islet morphology and skeletal muscle PI3K pathway-related protein expression of type 2 diabetic rats, the type 2 diabetic rats were induced by high-fat diet and low-dose streptozotocin and then randomly divided into 5 groups, i.e., the normal control, the model group, the positive control drug (200 mg kg^{-1} metformin), the low-dose TSEP (25 mg kg^{-1}) group and the high-dose TSEP (50 mg kg^{-1}. Three weeks later, the islet morphology of rat pancreas were observed by HE (Hematoxylin and Eosin) staining, and protein expressions of IRS-1 (insulin receptor substrate-1), PI3K (phosphatidyl inositol 3-kinase), PTP-1 B (protein tyrosine phosphatase-1B) and GLUT4 (glucose transporter 4) in rat skeletal muscle were detected by Western blot. When compared with the model group, TSEP administered groups showed relatively normal structures, clear pancreatic cells and intact capsula structures in pancreatic tissue pathological sections, with the number of pancreatic islets close to the normal control group. Meanwhile, above TSEP administered groups showed increased IRS-1, PI3K and GLUT4 protein expressions in their skeletal muscle tissues and decreased PTP-1B protein expression compared with the model group. TSEP has an effect on protecting pancreatic tissues of type 2 diabetic rats and intervening in abnormal expression of proteins in skeletal muscle tissues [73].

10.4 Anti-Toxicity Activities

Entada africana, a widely used African medicinal plant of the same genus *Entada*, has been reported for various medicinal properties. When the acute toxicity of the methanolic stem bark and leaf extracts of *Entada africana* Guill. and Perr., (Mimosaceae) was assessed on mice, it revealed an average toxicity with a LD_{50} of 146.7 mg kg^{-1} and 249.9 mg kg^{-1} body weight for stem barks and leaves, respectively. The extracts showed no cytotoxicity against Human epidermoid carcinoma (KB) and African green monkey (Vero) cells. Sub-chronic toxicity was assessed in rabbits, which received orally, daily for a month, a dose corresponding to 10% of the LD_{50}. Compared to the control group, this dose caused no significant ($p > 0.05$) modification of haematological and biochemical parameters, total cholesterol, urea, creatinine and AST (aspartate amino-transferase). The extracts lowered serum glucose significantly ($p < 0.05$) by 52% at first two weeks of treatment. The stem bark and leaf extracts showed temporary decrease ($p < 0.05$) of ALT (alanine amino transferase) by 26.1 % and 39.1%, respectively. The stem bark extracts increased triglycerides significantly ($p < 0.01$) by 108% at the end of last week of treatment. These investigations seemed to indicate the safety of sub-chronic oral administration (up to 14.67 mg kg^{-1} and 24.9 mg kg^{-1} body weight) of the methanolic extracts of *Entada africana* in rabbits [74].

The impact of the crude and processed products of *Entada phaseoloides* on gastrointestinal movement in mice was studied with the methods of charcoal propulsion of small intestine and methyl orange colorimetry of gastric emptying to observe acute-toxicity. The oral LD_{50} of crude *Entada phaseoloides*, and two processed products of *Entada phaseoloides* in mice were 27.17 g/kg, 35.13 g/kg and 42.18 g/kg body weight respectively. Crude and processed products of *Entada phaseoloides* can significantly promote the enteric propulsion of normal mice, and can significantly counteract the depressing status induced by atropine, but have no influence on the overactive status induced by neostigmine. The high, middle and low-dose of groups showed significant inhibition of the gastric emptying in normal mice. Processed *Entada phaseoloides* showed effects on the enteric propulsion of normal and depressing mice, can restrain the gastric emptying under normal mice, but its safety was better than crude *Entada phaseoloides* [75].

10.5 Antiulcer Activities

The ethanol extract of the seeds of *Entada phaseoloides* was assessed for its antiulcer activity against aspirin plus pylorus ligation induced gastric ulcers in rats, HCl- ethanol induced ulcer in mice and water immersion stress-induced ulcers in rats. A significant ($P < 0.001$) antiulcer activity was observed in all the models. The parameters taken to assess antiulcer activity were volume of gastric secretion, free acidity, total acidity and ulcer index. Preliminary phytochemical screening of the *Entada Phaseoloides* gave positive test for steroids, saponins and alkaloids. The results indicate that *Entada phaseoloides* possessed antiulcer activity [2].

10.6 Anticomplement and Antimicrobial Activities

Seventeen flavonoids isolated from the extracts of the stem of *Entada phaseoloides*, which were investigated for their anticomplement (both classic and alternative pathways) and antimicrobial activities against Gram-positive bacteria MSSA (Methicillin sensitive *Staphylococcus aureus*), MRSA (Methicillin resistant *Staphylococcus aureus*), Standard Enterococcus and *Bacillus subtilis*], Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeuroginosa*) and the yeast-like pathogenic fungus *Candida albicans*. The anti-complement studies revealed a dose-dependent activity among isolated quercetin, luteolin, apigenin, galangin, 5,2',5'-trihydroxy-3,7,4'-trimethoxyflavone-2'-O-β-D-glucoside(+)-3,3',5',5,7-pentahydroflavanone, (+)-dihydrokaempferol, (-)-epicatechin, (+)-catechin, naringenin, and 5,7,3',5'-tetrahydroxyflavanone, and the antimicrobial results indicated that quercetin, 5,7,4'-trihydroxy-3'-methoxyflavonol and galangin produced the inhibitory activities against MRSA, MSSA, and Standard Enterococcus, while luteolin and rhamnocitrin displayed inhibition against only MRSA and MSSA [76].

10.7 Antioxidant and Cytotoxic Activities

The methanolic crude extract of the bark and seed of *Entada phaseoloides* (L.) Merrill and its different organic soluble partitionates were screened for antioxidant, cytotoxic, membrane stabilizing and antimicrobial activities. The crude extract, carbon tetrachloride and aqueous soluble fractions of both bark and seed showed higher level of total phenolic content (TPC, 245.59, 240.22, 240.03 and 117.0 mg of Gallic acid equivalent (GAE)/gm of dried extract). In the DPPH (1,1-diphenyl-2-picrylhydrazyl) assay, the crude extract of bark and its chloroform and aqueous soluble fractions demonstrated strong antioxidant property with the IC_{50} of 3.24, 1.55 and 3.6 μg/mL, respectively, whereas, all the fractions of seed extract revealed mild antioxidant activity. The petroleum ether soluble fraction of both seed and bark exhibited significant cytotoxicity (LC_{50} = 1.54 mg/mL and 5.4 mg/mL) which confers the presence of bioactive metabolites in this plant. On the other hand, the crude extract of seed and petroleum ether soluble fraction of bark inhibited the hemolysis of RBC of rat's blood by 78.89% and 57.43%, respectively, as compared to 84.44% exerted by acetyl salicylic acid (0.10 mg/mL). In antimicrobial screening, the carbon tetrachloride soluble fraction of bark showed significant antimicrobial activity against *Staphylococcus aureus* (zone of inhibition = 17.0 mm) with MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) values of 7.81 mg/mL and 125 mg/mL, respectively [77].

Apart from the above, the bark of *Entada phaseoloides* exhibits potent molluscidal activity against *Oncomelenia quadrasi*, the snail intermediate host of *Schistosoma japonicum* with LC_{50} of 3.6-5.8 ppm since *Entada phaseoloides* remained stable over a wide range of pH values, in the presence of minerals and yeast cells and after ultraviolet irradiation of solutions. Under field conditions, the Gogo bark at a dose rate of $\geq$ 40 g/m^2 was sufficient to produce a satisfactory molluscicidal effect [41] or commercial gogo bark at a dose rate of 2 g/L of water with *Oncomelenia quadrasi* can kill 100% of snail within 24 h. Thus the molluscidal effect of *Entada phaseoloides* is very much effective in controlling Schistosomiasis, a snail transmitting debilitating and fatal endemic disease which is of major public health concern [78].

11. Current Finding and Future Prospects

Natural products are promising candidates for drug discovery and they still continue to play an important role in future small organic compound drug development programs [79]. Reports on pharmacological effects of medicinal plants are growing almost exponentially. However, it was found to be very difficult to attribute the pharmacological activity in a multi-component mixture to only a single compound of an extract, as plant extracts consist of a diversity of secondary metabolites [80]. From the above review of literature, it is evident that *Entada phaseoloides* has been one of the most thoroughly studied interesting plants as reported during the last 2 decades. The body of knowledge about plants, herbs and spices, and their respective and collective roles in promoting health is modest [81, 82]. Though modern synthetic drugs are very effective in curing diseases but also cause a number of side effects; although crude drugs are less efficient in curing diseases but are relatively free from side effects [83]. Herbs have been used as food and for medicinal purpose for centuries [82]. In recent times, the use of herbal products has increased enormously in the western world as well as in developed countries [84]. But the traditional herbal medicine has simple solution which is both easier and economical. Nature keeps ready in her vast green reservoir some of those herbal remedies which can cure all human ailments and diseases that take place on this earth. The need is only to locate those miraculous herbs through trained eyes which could alleviate the pains and sufferings of mankind.

12. Prospects

Since the use of medicinal plants is a widely accepted therapeutic strategy for millions of people, further attention should be focused on the discovery of the exact modes of action of their extracts as well as the isolated pure compounds and potential combinations, so as to exploit them commercially. However, because of the diverse molecular pharmacological data, the spectrum of interpretation and speculations seem to be endless. Therefore, in future studies there is a need for thorough phytochemical, clinical and possible studies on molecular mechanism of action along with preclinical trials that are required for an integration and acceptance of many *Entada phaseoloides* extracts in conventional medicine. At the same time efforts should be made to standardise the plant extracts and formulate best alternative herbal preparations to replace or complement the synthetic drugs which are currently in use.

13. Conclusions

Entada phaseoloides offers a wide range of ethnobotanical utilizations, which are based on the diverse patterns of secondary metabolites of which most abundant are saponins, diterpenes, triterpenes and phenolics compounds. Phenolic compounds, saponins, diterpenes as well as triterpenes were reported to contribute the pharmacological properties of *Entada phaseoloides* such as anti-inflammatory, antidiabetic, antitumour and analgesic activity (saponin); anticomplement, antimicrobial and antioxidants (phenolics); as antiulcer, anti toxic in addition to molluscicidal activities (crude and processed product of *Entada phaseoloides).*

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