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Phytochemical constituents and biological activities of *Erythrina indica*

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ABSTRACT

Erythrina indica commonly known as Coral tree has been widely used in Indian traditional medicine for treating common ailments such as asthma, arthritis, diarrhoea, fever, inflammation and leprosy. Certain phytochemical constituents such as: alkaloids, aliphatic fatty acids, alkaloids have also been reported. A wide range of medicinal formulations have been developed from *E. indica* that exhibit analgesic, antiarthritic, anti-hypertriglyceridemia, anti-inflammatory and muscle relaxing effects. This review summarizes the phytochemical investigations and pharmacological activities of *E. indica*.

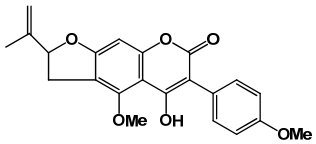
1. Introduction

The genus *Erythrina* (Leguminosae) which is distributed in the tropical and subtropical regions comprises of approximately 110 species [1,2]. Some of the species of this genus are a rich source of alkaloids and flavonoids, and certain species are used in traditional medicine for the treatment of several diseases [3-6].

Erythrina indica (Coral tree) which is found in the wild tropics and deciduous forests of India, grows to a height of 18 m, possess a thin, smooth and grey bark with small conical dark coloured prickles. *E. indica* bark is used medicinally as febrifuge, anti-bilious, antidiarrhoeal and antirheumatic, the bark has also been used in the treatment of asthma, burning sensation, itching, fever and leprosy. Its leaves are 15-30 cm long and are used to improve appetite and urinary discharge inflammation. Traditionally, the leaves are known to possess analgesic, anthelmintic, antiulcer and sedative properties. Extracts of the leaves have been employd to treat liver, diuretic, dysentery and joint pain [7-13].

2. Phytochemical investigations with bio-activity

There have been very few phytochemical investigations with bioactivity on *E. indica*, and most of the studies have been done on the bark. Examinations of the root bark of *E. indica* indicated the presence of a new 3-phenylcoumarin, indicanine A (**1**) (Scheme 1), along with three known compounds robustic acid, daidzein, and 8-prenyldaidzein. The isolated constituents were examined for *in vitro* antibacterial activity, however, no potent activity was observed for any of the compounds [14]. Waffo *et al.*, reported from the root bark of *E. indica* two new componds a 3-phenylcoumarin metabolite, indicanine B (**2**) and an isoflavone derivative indicanine C (**3**). The isolated compounds indicated potent antimicrobial activities [15].



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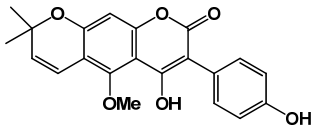

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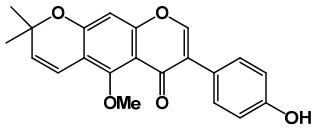

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Scheme 1

Bio-guided isolations of the CH_2Cl_2-MeOH (1:1) extract of the stem bark of *E. indica*, yielded two new compounds indicanines D (**4**) (Scheme 2) and E (**5**) along with 11 known compounds genistein, wighteone, alpinumisoflavone, dimethyl-alpinumisoflavone, 8-prenylerythrinin C, erysenegalensein E, erythrinassinate B, oleanolic acid, erythrodiol, stigmasterol and stigmasterol 3-*O*-β-D-glucopyranoside). Potent *in vitro* cyto-toxic activity against KB cells was observed for the isolated compounds [2].

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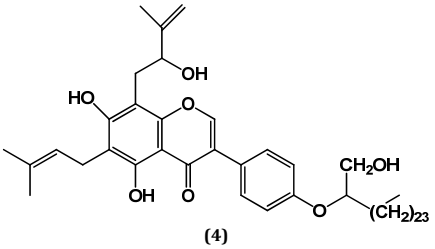

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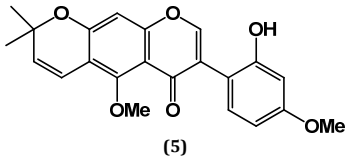
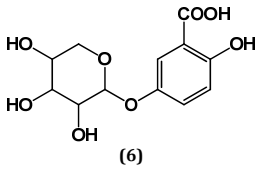


(5)

Scheme 2

Nassar *et al.*, isolated from the ethanol extract of the leaves of *E. indica* a new gentisic acid glycoside, 5-O-β-D-xylopyranoside (**6**) (Scheme 3), along with seven known flavone C-glycosides isovitexin, vitexin, vicenin 2, apigenin 6-C-α-L-rhamnopyranoside, orientin, isoorientin and luteolin 6,8-di-C-α-L-rhamnopyranoside. The ethanol extract of *E. indica* leaves also exhibited strong antioxidant activity [16].



(6)

Scheme 3

3. Phytochemical investigations

Phytochemical investigations of *E. indica* are mostly based on the compositions of the particular components and a limited number of phytochemicals have been reported.

Examinations of the seeds of *E. indica* indicated the presence of an oil (11.9%, yield) exhibiting unsaponifiable matter 0.49%. The oil contained behenic, arachidic, palmitic and lignoceric, oleic and linoleic acids [17]. Extraction of the seeds of *E. indica* with petroleum ether produced a yellow fatty oil (11.3%) yield. The saponification of the oil gave a mixture of 36.7% saturated and 63.3% unsaturated acids. The saturated acids were found to contain oleic 84.4% and linoleic acids 15.6%. Further investigations of the ethanol extract of the seeds produced a compound hypaphorine [18].

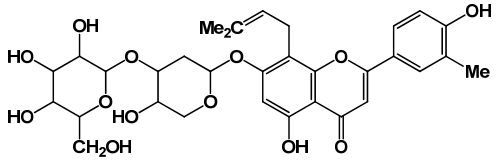
A comparative study of the seeds of the two white and red varieties of *E. indica* was conducted by extracting the seeds with petroleum ether to obtain the oils. The white variety yielded 12% of a reddish fixed oil having a specific gravity 0.8603 at 30ºC and the oil extracted from the red variety of *E. indica*, had a specific gravity 0.8821 at 30 °C the alcoholic extract of the oil-free seeds of the white variety yielded a white crystalline alkaloid nitrate, identical to hypaphorine nitrate isolated from the seeds of the red variety [19].

The examination of the acid components of the seeds of *E. indica* revelaed the presence of palmitic 8.2%, stearic 8.0%, arachidic 4.3%, behenic 13.3%, hexadecenoic 3.1%, oleic, 45.6%, linoleic 7.1%, eicosenoic 9.8%, and lignoceric 0.6% [20]. Investigations of the seeds of *E. indica*, suggested the presence of hypaphorine [11].

Kartha and Narayanan, examined the glyceride structure of *E. indica* seed fat by azelao-glyceride analysis techniques. The amount of saturated acids was found to be 34 mole % and trisaturated glycerides were not detected. The triglycerides were observed to be composed of disaturated 27.1, monosaturated 48.3 and triunsaturated glycerides 24.6 mole % [21].

Pant and Tulsiani, reported the total soluble carbohydrates in seeds of five plants including *E. indica* to be 12.02-22.98 grams of glucose/100 grams of seed. Total reducing substances were 2.35-5.32 grams of glucose/100 grams of seed. All the edible seed species including *E. indica* appeared to be adequately nutritious sources of proteins, carbohydrates, and minerals [22]. Studies of the physicochemical composition of certain seed plants including *E. indica*, revealed the following compositions: mineral elements (2.1-8.0%), protein (9.1-26.5%), cellulose (5.8-28.4%), and lipid (0.4-29.7%) [23].

Yadava and Reddy, isoalted a novel prenylated flavone glycoside 5,7,4'-trihydroxy-3'-methoxy-8-C-prenylflavone 7-*O*-β-D-glucopyranosyl-(1→3)-α-L-arabinopyranoside (**7**) (Scheme 4) was isolated from the seeds of *E. indica* [24].

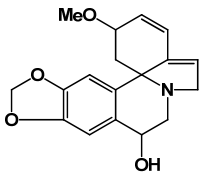


(7)

Scheme 4

Singh *et al.*, isolated from the water soluble sugar extracts of *E. indica* seeds, D-galactose and D-mannose in 2:3 molar ratio. The methyl sugars afforded 2, 3, 4, 6-tetra-O-methyl-D-galactose; 2, 3, 4-tri-O-methyl-D-galactose; 2, 3, 6-tri-O-methyl-D-mannose and 2, 3-di-O-methyl-D-mannose in 1: 1: 2: 1 molar ratios, respectively. Furthermore, the water soluble sugar solutions (D-galactose and D-mannose in 2: 3 molar ratio) were isolated from *E. Indica* seeds by graded hydrolytic studies. It yielded three disaccharides α-D-galactopyranosyl-(1→6)-O-α-D-galactopyranose, α-D-galactopyranosyl-(1→6)-O-α-D-mannopyranose and β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranose and two trisaccharides α-D-galactopyranosyl-(1→6)-O-α-galactopyranosyl-(1→6)-O-α-mannopyranose and β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranosyl-(1→4)-O-β-D-mannopyranose by graded hydrolytic studies [25,26].

Chakravarti *et al.*. examined the leaves of *E. indica* and indicated the presence of a white solid which was not a phytosterol or glucoside and an alkaloid. Further investigations of the leaves of *E. indica* indicated the presence of a new compound erythrinine (**8**) (Scheme 5) along with erysodine and de-*N*-methylorientaline [27,28].



(8)

Scheme 5

Investigations of the bark of *E. indica* indicated the presence of fixed oils and an inert alkaloid which decomposes at 97 °C [29]. Further investigations of the alcoholic extract of *E. indica* bark indicated the presence of docosyl alcohol, β-sitosterol, γ-sitosterol, δ-sitosterol, and 2,4-dinitrophenyl-hydrazone [30].

4. Lectin based studies

A large number of studies have been conducted on the lectins isolated from *E. indica*, most of which that describe the

phytochemical and biological significance of *E. indica* have been described.

Horejsi *et al.*, isolated lectins from the seeds of *B. frondosa, E. indica* and *M. charantia* using affinity chromatography. The lectin from *E. indica* seeds were reported to have a sedimentation coefficient s20, w = 4.0 S, its molecular weight was 66,200, and it was found to consist of two subunits having molecular weights 30,000 and 34,000, respectively. The lectin is devoid of cysteine, has a neutral sugar content of 5.6%, and glucosamine content of 0.46%. the lectin probably contains one Mn atom per subunit, and the N-terminal amino acid sequence is Val-Glu-Val-Leu-(Phe)-Phe-(Ala)-Phe- [31].

Bhattacharyya *et al.*, isolated lectins from the seeds of four species of the genus *Erythrina* by affinity chromatography. The SDS-gel electrophoresis showed that *E. indica* produced two bands with subunit having molecular weights 26,000 and 28,000. The lectins exhibited a neutral sugar contents between 4-9%. *E. indica* lectins indicated higher hemagglutinating activity toward the erythrocytes of O group [32].

In a comparitive study of certain physicochemical and structural properties of the lectins from the seeds of the genus *Erythrina*, it was noted that *E. indica* possess higher quantities of acidic and hydroxy amino acids and low quantities of sulphur containing amino acids, and possess valine as the only N-terminal amino acid. *E. indica* lectins are glycoproteins containing higher quantities of mannose type complex oligosaccharide chains, and also contain arabinose, xylose, fucose, glucose, and galactose. *E. indica* lectins bind to Con-A-Sepharose but not with lentil or pea lectin-Sepharose, thus indicating the presence of terminal non-reducing α-D-mannose and/or internal 2-*O*-α-linked mannose residues in these lectins, and the absence of α(1→6) linked L-fucose residues in the core regions of the oligosaccharide units [33].

Bhattacharyya and Brewer, investigated the interactions of the oligosaccharide with *E. indica* leaf by quantitative precipitation analysis. The equivalence point of the precipition curve indicated that the glycopeptide is trivalent for *E. indica* leaf binding. Thus it was suggested that each arm of the oligosaccharide could independently be bound to separate lectin molecules and lead to precipitation of the complex [34].

Sudakevitz *et al.*, purified lectins from certain *Erythrina* species and detected their capacity for H/HI blood groups. The reactions of *E. indica* lectins with erythrocytes of different ABO(H) and Ii blood groups showed the following order of activity: O(H)I > A2I > O(H)i adult > A2BI > BI > O(H)i cord >A1I > A1i adult > Bi cord > A1BI > Ai cord > ABi cord > OhI. Furthermore the lectin of *E. indica* indicated a lower differentiation between the agglutination of O(H) and Oh erythrocytes [35].

Mandal and Brewer, examined the capacities of the 14-kDa β-galactoside-specific lectin from calf spleen, a dimeric S-type animal lectin, and certain galactose-specific plant lectins from three plants including *E. indica*, to produce specific cross-linked complexes with asialofetuin, the formation was compared using quantitative precipitation analyses. The two dimeric lectins from *E. indica* formed 1:9 and 1:3 stoichiometric asialofetuin - lectin cross-linked complexes [36].

Bhattacharyya and Brewer, showed that Gal-specific lectins from *E. indica* and *Ricinus communis* produce homogeneous crosslinked complexes with individual carbohydrates in binary mixtures of triantennary and tetraantennary complex-type oligosaccharides with terminal Gal residues. Binary mixtures of Gal/GalNAc-specific lectins from *E. indica*, in the presence branched-chain oligosaccharide with terminal GalNAc or Gal residues indicate the production of separate crosslinked lattices between each lectin and the carbohydrate [37].

Gupta *et al.*, studied the thermodynamics of carbohydrate binding to the 14-kDa dimeric β-galactoside-binding lectin galectin-1 (Gal-1) from Chinese hamster ovary cells and four galactose-specific plant lectins (including *E. indica*). The *E. indica* lectins indicated greater affinities and -ΔH values for lactose and N-acetyllactosamine [38].

Konozy *et al.*, isolated lectin from the leaves of *E. indica* by affinity chromatography. In SDS-gel electrophoresis under reducing and non-reducing conditions the isolated lectin split into two bands with subunit having a molecular weight of 30 and 33 kDa, and the weight of the intact lectin obtained by gel filtration was found to be 58 kDa. *E. indica* leaf lectin agglutinated all human RBC types, with a slight preference for the O blood group. Lectin was found to be a glycoprotein having a neutral sugar content of 9.5%. *E. indica* leaf lectin exhibited optimum pH 7.0; above and below this pH lectin lost sugar-binding capacity. Lectin exhibited broad temperature optima from 25 to 50 °C; but, at 55 °C the lectin lost more than 90% of its activity and at 60 °C it became completely inactive. The lectin was found to be abundant in acidic as well as hydrophobic amino acids and completely lacked cysteine and methionine [39].

Kestwal *et al.*, isolated a glycoprotien α-mannosidase from the seeds of *E. indica* and purified it (26-times) to homogeneity by gel filtration by Bio-Gel P-100 and affinity chromatography. The molecular weight of α-mannosidase was found to be 124 and 127 kDa by gel filtration and SDS-PAGE, respectively. The optimum pH and temperature for enzyme activity were found to be 4.6 and 50 °C, respectively. The Km of the enzyme for p-nitrophenyl-β-D-mannopyranoside was 2.1 mM, and its activity was found to depend on the presence of Zn^{2+} [40].

Kestwal *et al.*, isolated the enzyme α-mannosidase from *Erythrina indica* seeds and tested it for certain properties. This enzyme is reported to be Zn^{2+} dependent glycoprotein with 8.6% carbohydrate; it has a temperature optimum of 50 °C and energy of activation 23 kJ/mol. The chemical modification studies showed that the treatment of the enzyme with N-bromosuccinimide (NBS) led to total loss of enzyme activity, while the modification of a single tryptophan residue led to the inactivation of the enzyme. Fluorescence studies with in a pH range of 3–8 have indicated tryptophan residue to be in a highly hydrophobic environment and pH change was not able to alter the environment. An α-helical structure was observed by Far-UV CD spectrum and α-mannosidase from *E indica* was found to be immunological identitical to the α-mannosidase from *Canavalia ensiformis* but not with those from *Glycine max* and *Cicer arietinum*. A 35% increase in enzyme activity was observed by incubating the *E. indica* lectin with α-mannosidase, but no such activation was observed for acid phosphatase from *E. indica*. The Lectin induced activation of α-mannosidase could be lost in presence of lactose [41].

Kestwal *et al.*, isolated an enzyme β-galactosidase from the seeds of *E. indica*, and prepared a homogeneous solution of the enzyme by ion-exchange chromatography followed by gel filtration, the enzyme was also tested for certain properties. The enzyme appeared to be a dimmer, and its molecular weights by gel filtration and SDS-PAGE, were found to be 74 kDa and 78 kDa, respectively. The optimum pH and temperature for enzyme activity were 4.4 and 50 oC, respectively. The enzyme indicated a Km value of 2.6 mM and Vmax of 3.86 U/mg for p-nitrophenyl-β-D-galactopyranoside as substrate and was inhibited by Zn^{2+} and Hg^{2+}. Enzyme activity was regulated by feedback inhibition, since it was found to be inhibited by β-D-galactose. Chemical modification studies showed a role of tryptophan and histidine for enzyme activity, the role of tryptophan was confirmed by fluorescence studies and one tryptophan was indicated to be present in the active site of β-galactosidase. Circular dichroism examinations indicated 37% α-helix, 27% β-sheet and 38% random coil in the secondary structure of the purified enzyme [42].

5. Biological activities and formulations

5.1. Antibacterial and antifungal

Bhale *et al.*, examined activity of the seed oil of *E. indica* against ten bacterial and ten fungal strains. The oil was found to be more active than penicillin and streptomycin, and potent activity was observed against the other tested bacterial and fungal strains [43].

Singh *et al*., studied the effects of D-galactose-binding lectin isolated from *E. indica* on the eggs and larvae *Bactrocera cucurbitae*. The various concentrations of lectin (0, 125, 250, 500, and 1000 µg/mL) did not show any significant reduction in percent hatching of eggs. However, percent pupation was significantly reduced [44].

5.2. Adenosinetriphosphatase inhibitory activity

Nguyen *et al.*, reported the aqueous alkaloid extracts of *Ziziphus jujuba*, *Nelumbo nucifera*, and *E. indica* to exhibit adenosinetriphosphatase inhibitory activity in rat brain membranes [45].

5.3. Antioxidant activity

Moon *et al.*, examined the methanolic extracts *E. indica* bark for DPPH free radical scavenging activity, reducing power and nitric oxide scavenging activity, as well as the total phenolic content. *E. indica* was found to exhibit potent antioxidant activity [7].

Sakat and Juvekar, examined the aqueous and methanolic extracts of the leaves of *E. indica*, using in vitro methods such as: 1,1-Diphenyl-2-Picrylhydrazyl, nitric oxide radical scavenging activity, and inhibition of lipid peroxidation by thiobarbituric acid reactive substances (TBARS) method on isolated rat liver tissues. The study also quantified the antioxidative constituents such as: total phenolics, flavonoids, and flavonols using spectrophotometric method. The IC_{50} values for the aqueous and methanolic extracts for the various tests were as follows: DPPH radicals scavenging activity (342.59 ± 19.59 and 283.24 ± 12.28 µg/mL), nitric oxide radical scavenging activity (250.12 ± 10.66 and 328.29 ± 3.74 µg/mL), lipid peroxidation induced by the Fe^{2+} (283.74 ± 5.70 and 97.29 ± 2.05 µg/mL). The total flavonoids and flavonols were found to be higher in the aqueous extract, while the total phenolics content was equal in both the extracts. According to the study the presence of flavonoids and polyphenolics, may be responsible for the good antioxidant activity of *E. indica* [10].

5.4. Fat lowering formulation

A fat absorption formulation was prepared from a group of medicinal plants including the cortex of *E. indica*. The formulation is claimed to possess fat, lipase and obesity inhibitory properties, it is also suggested to reduce hypertriglyceridemia [46].

5.5. Health care/enhancing formulations

A suppository was prepared from a group of plants including *E. indica*, the suppositories were mixed with various oils such as cocoa butter, olive oil, soybean oil, vegetable oil, other hydrogenate fatty acids, petrolatum, various forms of paraffin, stearic acid and oleic acid to produce oil-based suppositories. The suppositories were also mixed with polymers glycerinated gelatine and polysorbate to produce aqueous based suppositories. The suppositories are claimed to treat infections of upper the respiratory tract, and undesired symptoms from allergic rhinitis, sinusitis, nasal congestion, nasal dripping, nasal polyps, infections, fevers, coughs, spasms, dizziness and convulsions [47].

Two formulations were prepared from a group of plants including *E. indica*; one formulation was found to be effective against sarafotoxins present in snake venom. The other formulation is claimed to induce apoptosis [48,49].

A composition for a liniment was prepared by mixing sodium hyaluronate, polyvinyl alcohol, ethanol, p-hydroxybenzoate, and the liquid extracts of certain traditional Chinese medicinal plants including *E. indica*. The liniment produced is claimed to be effective in foot care of patients suffering from diabetes [50].

Cotton product was formulated by mixing a group of plants including *E. indica* and certain other constituents such as: impregnant liquid, orpiment, sulphur and burkeite. The mixture is decocted with water, filtered and soaked in cotton and dried in a dark place. The product can be used for making health-care pillows and cushions [51].

A medicated bag was produced from a group of plants in including *E. indica*, by decocting the plant materials in water followed by drying in sunlight, pulverizing and filling in a cotton bag. The medicated bag after steam heating can be used hot compress therapy. It is suggested to possess effects such as relaxing muscles and tendons, reliving cold and removing toxins. It is also suggested to treat rheumatic arthritis, cervical spondylosis, lumbar spondylosis, scapulohumeral periarthritis, sciatica, lumbar strain, sprain and contusion [52].

A composition for a foot bath powder was developed by grinding Chinese medicinal plant materials including *E. indica* and mixing with sodium polyacrylate. The use of the composition is suggested to prevent diseases by stimulating acupoints, balancing yin and yang, tranquilizing mind, reducing blood viscosity, blood lipid and blood cholesterol levels, increasing immunity, relaxing tendons, activating collateral flow and relieving fatigue [53].

An oral solution for a Chinese medicine composition was developed from a group of plants in including *E. indica* bark, by decocting the plant material in water followed by vacuum packing to produce an oral solution. The solution is suggested to possess heat clearing, dampness and channel blockage reducing properties. It can also be used for treating warm numbness, joint pain, chlorosis in face and eyes and scanty dark urine [54].

5.6. Pain relieving formulations

Boddupalli *et al.*, developed a composition from a plant selected from a group of plants including *E. indica*. The composition is suggested to treat or regulated bone and joint conditions such as joint inflammation, joint swelling, joint pain, gout, childhood arthritis, lupus arthritis, rheumatoid arthritis, and osteoarthritis [55].

A preparation for a Chinese medicine composition was developed from a group of plants in including *Erythrina indica*. The composition is suggested to be used for eliminating hemorrhage and diarrhea as well as treating pains caused by periarthritis humeroscapularis, arthritis, convulsion, fatigue and wounds [56].

A preparation for a tincture and a plaster was developed from a group of in including *Erythrina indica*, the tincture is claimed to treat scapulohumeral periarthritis, arthralgia, rheumatalgia, hyperosteogeny, soft tissue injury and traumatic injury. The plaster is suggested to treat traumatic injury and rheumatic diseases [57,58].

Han, developed a method for the preparation of Chinese medicinal spray from a group of plants including *Erythrina indica*. The solution was prepared by soaking the plants material for 24-hours followed by decocting the mixture fir half an hour to yield a concentrated solution, finally borneol was added to the solution. The spray is suggested to be absorbed by transdermal osmosis and possess anti-inflammatory and analgesic effects [59].

5.7. Skin whitening formulation

Kimura and Takayama, developed a skin preparation from a plant selected from a group of plants including *E. indica*. The

formulation is suggested to possess Maillard reaction inhibitory, collagen bridging, skin whitening, wrinkle reduction and anti-aging properties [60].

6. Conclusion

The present review describes the significance of *E. indica* as an important medicinal plant exhibiting diverse biological activities. Since the number of phytochemical constituents identified from the *E. indica* is limited it would be a rich opportunity to isolate more bioactive chemical constituents. For this plant, furthermore, it would also be valuable to determine the structure activity relationship of the identified compounds.

Acknowledgements

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