A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL ACTIVITY OF GENUS IXORA

AR. Kharat*, VV. Nambiar, YS. Tarkasband, RR. Pujari

PES Modern college of Pharmacy (For Ladies), Moshi, Pune, Maharashtra-412105, India.

ABSTRACT
Ixora is evergreen perennial shrub or tree belonging to family, Rubiaceae. Though native to the tropical and subtropical areas throughout the world, its centre of diversity is in Tropical Asia. This genus is known for its brightly colored flowers. The plant is traditionally found to be useful for many ailments like hepatic disorder, cancer, microbial infection, antioxidant, pain, inflammation etc and has been documented for various medicinal properties. The genus Ixora has been reported to posses different classes of compound mainly aromatic acrid oil, tannin, saponin, carbohydrate, fatty acid, flavonoids like β-sitosterol, and kaempferol. This review is an attempt to cover the available literature on Ixora genus with respect to pharmacognostic characters, traditional uses, chemical constituents and summary of its various pharmacological activities.

Keywords: Ixora, hepatic disorder, flavonoids, Rubiaceae.

INTRODUCTION
Ixora is a genus of flowering plants in the Rubiaceae family. It consists of tropical evergreen trees and shrubs and holds around 500 species. Ixora also grows commonly in subtropical climates in the United States, such as Florida. Although there are around 500 species in the genus Ixora, only a handful are commonly cultivated. There are numerous named cultivars differing in flower colour (yellow, pink, orange) and plant size. Several popular cultivars are dwarfs, usually staying under 3 ft (1 m) in height. Leaves are coriaceous, up to 10 cm long, sessile or subsessile, oblong, obtuse. Flowers are numerous and found to grow in clusters. They are bright scarlet, odorous, in sessile, corymbiform, dense-flowered cymes. Fruits are globose, fleshy, size of a pea and have 2-seeded berry seeds plano-convex. The plant flowers usually in April-May and fruits in May-June. 

Scientific classification
Kingdom: Plantae
Division: Angiosperms
Class: Eudicots
Subclass: Asterids
Order: Gentianales
Family: Rubiaceae
Subfamily: Ixoroideae
Tribe: Ixoreae
Genus: Ixora
Traditional uses
The genus Ixora is widely distributed in tropical and subtropical regions of Asia. The leaves, flowers, roots, stem and fruits are used for different purpose by ethnic groups of different region of Asia, Africa and Europe.

Leaves
The leaves of *I. coccinea* were found to have anti-inflammatory, anti-diarrheal, anti-asthmatic, anti-ulcer and antinociceptive activity. They are also used to pacify vitiated pitta, skin diseases, colic, flatulence, diarrhea, indigestion, ulcers, wounds, and used as antiseptic.

The leaves of *I. grandiflora* are used as poultice in fresh form for treatment of sprain, eczema, boils and concussions. The decoction of leaves was used in treatment of wounds and skin ulcer. *I. chinensis* leaves have been used to treat headache and stomachache and as a remedy for incipient tuberculosis. *I. finlaysoniana* leaves showed antigestagenic activity. The leaves of *I. javanica* are used in treatment of cancer. The leaf extract of *I. parviflora* showed antiviral, hypotensive and spasmyloytic activity.

Flowers
The flowers of *I. coccinea* were used for the treatment of cancer, leucorrhoea, dysentery, dysmenorrhoea, haemoptysis and hypertension. The flowers of *I. javanica* contains antitumor principal and are locally used as vegetable. In the Philippines, infusion of fresh flowers of *I. chinensis* is drunk ad libitum as it is said to be good for incipient tuberculosis and for hemorrhage and headache. Flower decoction used for amenorrhea and hypertension. *I. finlaysoniana* flowers has been scientifically documented to posses estrogenic, abortifacient and anti-implantation properties. *I. parviflora* flowers are used in treatment of whooping cough and in treatment of ulcers. The flowers of *I. macrothyrsa* are used to impart color to herbal preparation.
Roots
The roots of *I. coccinea* showed wound healing and anti microbial activity. It is also used as astringent and antiseptic against scabies and other skin diseases where as the roots of *I. parviflora* are used in treatment of menorrhagia. The roots of *I. chinensis* are used in urinary trouble. The decoction is also given after parturition. In Indonesia, decoction of roots is used for bronchial disorders. *I. macrothyrsus* pacifies vitiated kapha, pitta, burning sensations, eczema, ringworm other skin diseases menorrhagia, leucorrhea and general weakness. *I. grandiflora* is used in delivery and stomachache.

PHARMACOLOGICAL ACTIVITY
Antimicrobial activity was performed on 50% ethanolic extract of *I. Coccinea*. The effective inhibitory concentration of extract for both bacteria and fungus was found to be 125µg/ml beyond which the inhibitory activity declined and organism started reviving from antimicrobial principle. The aqueous extract of the plant was also evaluated for anti-diarrheal potential against several experimental models of diarrhea in albino rats. The result obtained substantiated the anti-diarrheal effect of the aqueous extract.

Antitumor activity of *I. coccinea* flowers was studied in comparison to intraperitoneal transplanted Daltons lymphoma and ehrlich ascites carcinoma tumors in mice and found that the flower extract showed considerable antitumor principle.

Antiasthmatic activity was investigated of hydro alcoholic extract of leaves of *I. coccinea* in an ovalbumin induced asthmatic rat. Results provided information that *I. coccinea* has antiasthmatic property.

The anti-inflammatory activity of methanolic leaf extract was also investigated and the result showed that anti-inflammatory activity of the plant is mediated via inhibition of nitric oxide production, phagocytic cell infiltration, antihistamine effect, scavenging of free radical membrane stabilizing activity and lipid peroxidation.

The antinociceptive potential of leaves of *Ixora coccinea* was studied and the results showed that the antinociceptive action was mediated centrally at supraspinal level via dopaminergic mechanism.

Hypoglycaemic and Hypolipidemic activity of the aqueous extract of leaves of *I.coccinea* and showed significant reduction in blood glucose level and serum lipid profile level.

*I. Parviflora* with high polyphenol content exhibited antioxidant activity and reducing UVB-induced intracellular reactive oxygen species production. The study, results of the photoaging screening experiments revealed that IPE at 1000µg/mL reduced the activity of bacterial collagenase by 92.7 ± 4.2% and reduced the activity of elastase by 32.6 ± 1.4%. The flowers of *I. pavetta* have been extracted by ethanol and evaluated for the antilucre activity by Aspirin induced and pylorus ligation of rats. The extract significantly decreased the gastric secretion, free acidity as well as gastric ulcers in the aspirin induced, pylorus ligated rats, and the effects were compared with omeprazole.

Topical application of 100 mg/kg body weight of *I. javanica* flower extract inhibited the growth, delayed the onset of papilloma formation in mice initiated with 7, 12-dimethylbenz [a] anthracene (DMBA), and promoted using croton oil. The extract at the same dose, when administered orally inhibited the growth of subcutaneously injected 20-methylcholanthrene (MCA)-induced soft tissue fibro sarcomas significantly. Oral administration of 200 mg/kg of the extract inhibited the growth of intraperitoneally transplanted sarcoma-180 and ehrlich ascites carcinoma tumours besides showing an increase in the life span of the treated mice.

Oral administration of crude ethanolic extract of the serial parts of *I. finlaysoniana* Wall. ex G. Don to adult female rats at 250 mg/kg dose on days 1–5 or 1–7 post-coitum prevented pregnancy in 100% rats. The extract was also effective when administered on days 1 or 1–3 post-coitum, but the minimum effective dose increased with decreased duration of administration and was 1000 mg/kg and 500 mg/kg, respectively.

PHYTOCHEMICAL ANALYSIS
The wide spread use of different parts of genus *Ixora* in traditional system of medicines has resulted in the chemical analysis of different species. The phytochemical investigation revealed that most of the plant belonging to the Rubiaceae family had flavonoids present in them. Other classes of chemical compound present are tannin, saponins, aromatic oil and fatty acid.

Phytochemical studies have shown that the major compounds present in *I. Coccinea* are lupeol, oleic acid, linolic acid, ursolic acid, oleanolic acid, stearic acid and sitosterol. Flowers are reported to contain rutin, leucocyanadin glycoside, cyanadin-3-rutinoside and delphinidin monoglucoside. The root bark contains Octadecadienoic acid while the root oil has been shown to posses methyl ester of palmitic, oleic, stearic and linolic acid.
Leaves are reported to contain ixoratannin A-2, epicatechin, procyanidin A2, cinnamotannin B-1 and the flavone-3-rhamnoside namely kaempferol-7-o-α-1-rhamnoside, kaempferol-3-o-α-1-rhamnoside, quercetin-3-o-α-1-rhamnopyanoside and kaempferol-3,7-o-α-1-dirhamnoside. Fractionation of the n-hexane fraction of I. finlaysoniana by repeated column chromatography using silica gel yielded compounds identified from its mass fragmentation pattern, 1H- and 13C-NMR as n-nonacosanol, α-amyrin, β-sitosterol. The chloroform fraction of the plant was fractionated using a combination of silica gel column chromatography and MPLC to yield compounds like 3-hydroxyhexan-5-olide, sitosterol-3-O-β-D-glucoside, protocatechuic acid and Gallic acid. Other compounds isolated were (3R, 5R)-3-(β-glucopyranosyloxy)-5-hexanolide (parasorbose), D-1-O-methyl-myoinositol, galactitol. The chloroform extract of I. parviflora was column chromatographed over silica gel and the compounds eluted and identified as β-sitosterol, kaempferol, β-sitosterol-β-D-glycoside, kaempferol-7-O-methyl ether. The mature seeds of I. chinensis yield an oil having fatty composition like palmatic, stearic, oleic, linolic, crepenyinic and ixoric acid. The purified fraction of I. javanica has been identified to contain Ferulic acid, Pyrocatacheic acid and caffeic acid.

CONCLUSION
The present review describes the phytochemical screening of genus Ixora for different medicinal purpose. The different compounds isolated from different species with the structures have been studied along with their traditional uses and pharmacological activity. The evaluation needs to be carried out on Ixora in order to use the plant in formulation for their practical and clinical applications, which can be used for the welfare of the mankind.
Ursolic acid  lupeol  oleanolic acid

Octadecadieonic acid

Fig. 3: Structures of Triterpenes

Stearic acid  Palmitic acid

Oleic acid

Fig. 4: Structures of Fatty acid and its derivatives

Cystine  Glycine  Serine  Proline

Fig. 5: Structures of Amino acid and its derivatives
Table 1: List of compounds isolated from various species of Ixora

<table>
<thead>
<tr>
<th>S.No</th>
<th>Class of compound</th>
<th>Name of the compound</th>
<th>Biological source</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Flavonoids</td>
<td>Kaempferol-7-0-α-1-rhamnoside,</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.2</td>
<td></td>
<td>Kaempferol-3-0-α-1-rhamnoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.3</td>
<td></td>
<td>Quercetin-3-0-α-1-rhamnopyranoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.4</td>
<td></td>
<td>Kaempferol-3,7-0-α-1-dirhamnoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.5</td>
<td></td>
<td>Kaempferol</td>
<td><em>I. Coccinea, I. parviflora</em></td>
<td>10,12,14</td>
</tr>
<tr>
<td>1.6</td>
<td></td>
<td>Rutin</td>
<td><em>I. Coccinea, I. parviflora</em></td>
<td>10,12,14</td>
</tr>
<tr>
<td>1.7</td>
<td></td>
<td>Cyanadin-3-rutinoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.8</td>
<td></td>
<td>Kaempferol-7-O-methyl ether</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.9</td>
<td></td>
<td>Kaempferol-3-rutinoside</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>1.10</td>
<td></td>
<td>Catechin</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>1.11</td>
<td></td>
<td>Epicatechin</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>2.1</td>
<td>Triterpenes</td>
<td>Ursolic acid</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>2.2</td>
<td></td>
<td>Oleoanic acid</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>2.3</td>
<td></td>
<td>Octadecadienoic acid</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>2.4</td>
<td></td>
<td>β-sitosterol</td>
<td><em>I. coccinea, I. parviflora, I. Finlaysoniana</em></td>
<td>10,12,13,14</td>
</tr>
<tr>
<td>2.5</td>
<td></td>
<td>β-sitosterol- β-D-glycoside,</td>
<td><em>I. parviflora</em></td>
<td>10,12</td>
</tr>
<tr>
<td>2.6</td>
<td></td>
<td>Sitosterol-3-O- β-D-glycoside</td>
<td><em>I. finlaysoniana</em></td>
<td>13</td>
</tr>
<tr>
<td>2.7</td>
<td></td>
<td>Lupeol</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>3.1</td>
<td>Fatty acid and its derivative</td>
<td>Palmatic acid</td>
<td><em>I. coccinea, I. parviflora, I. Finlaysoniana, I. Chinensis</em></td>
<td>10,11,13,14</td>
</tr>
<tr>
<td>3.2</td>
<td></td>
<td>Oleic acid</td>
<td><em>I. coccinea, I. parviflora</em></td>
<td>10,11,13,14</td>
</tr>
<tr>
<td>3.3</td>
<td></td>
<td>Stearic acid</td>
<td><em>I. coccinea, I. parviflora</em></td>
<td>10,11,13,14</td>
</tr>
<tr>
<td>3.4</td>
<td></td>
<td>Linolic acid</td>
<td><em>I. coccinea, I. parviflora</em></td>
<td>10,11,13,14</td>
</tr>
<tr>
<td>4.1</td>
<td>Phenolic and phenyl propenoid</td>
<td>Protocatechuic acid</td>
<td><em>I. finlaysoniana</em></td>
<td>13</td>
</tr>
<tr>
<td>4.2</td>
<td></td>
<td>Ferulic acid</td>
<td><em>I. coccinea, I. parviflora</em></td>
<td>13</td>
</tr>
<tr>
<td>4.3</td>
<td></td>
<td>Gallic acid</td>
<td><em>I. coccinea, I. parviflora</em></td>
<td>13</td>
</tr>
<tr>
<td>5.1</td>
<td>Amino acid and its derivative</td>
<td>Cysteine</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>5.2</td>
<td></td>
<td>Proline</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>5.3</td>
<td></td>
<td>Glycine</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>5.4</td>
<td></td>
<td>Serine</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>6.1</td>
<td>Sugar and its derivative</td>
<td>D-glucose,</td>
<td><em>I. parviflora</em></td>
<td>10</td>
</tr>
<tr>
<td>6.2</td>
<td></td>
<td>D-mannitol</td>
<td><em>I. coccinea</em></td>
<td>10</td>
</tr>
<tr>
<td>6.3</td>
<td></td>
<td>Lecocyanadin glycoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>6.4</td>
<td></td>
<td>Delphinidin monoglycoside</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>7.1</td>
<td>Miscellaneous</td>
<td>Ixoratannin A-2</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>7.2</td>
<td></td>
<td>Procyanidin A2</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>7.3</td>
<td></td>
<td>Cinnamtannin B-1</td>
<td><em>I. coccinea</em></td>
<td>14</td>
</tr>
<tr>
<td>7.4</td>
<td></td>
<td>Crepenynic</td>
<td><em>I. chinensis</em></td>
<td>11</td>
</tr>
<tr>
<td>7.5</td>
<td></td>
<td>Ixoric acid</td>
<td><em>I. chinensis</em></td>
<td>11</td>
</tr>
</tbody>
</table>

REFERENCES

35. Matthew KM. The flora of the Tamilnadu Carnatic. (F TamilC), 1983;67.