A review on phytochemical, ethnomedicinal and pharmacological studies of genus *Pittosporum* (Pittosporaceae), in India

Riyas CT, Arun R Pillai, Kamarudeenkunju M and TS Swapna

**Abstract**

*Pittosporum* is a genus of family Pittosporaceae, which includes approximately 200 species having world wide distribution and the richest concentration is in Australia and China. In India only 11 species were reported till date. Among these, 7 species have been explored for its phytochemical compounds. In this review phytochemical, pharmacological and ethnomedicinal properties of the genus *Pittosporum*, in India has been evaluated and documented with maximum available data from journals, thesis, and various books. So far 26 principle compounds were isolated from the four species of the genus *Pittosporum*. Most of them belongs to the class of essential oils followed by glycosides and diterpenes. A highly promising compound Isosteviol isolated from the *P. tetraspermum* has anti-microbial as well as anti-biofilm activity. Methanolic extract of different species of *Pittosporum* bark showed promising antimicrobial, anti-inflammatory, antioxidant and hepatoprotective activity. The different species have been used traditionally for ethnomedicinal purpose especially for eczema, arthritis, diabetes, diuretic, ester pain and antidote of snake bite etc. Hence, in this review an attempt was made to analyse and review the information generated through pharmacological studies of phytocomponents from the genus *Pittosporum* distributed in different parts of India.

**Keywords:** phytochemistry, essential oils, pharmacology, isosteviol, *Pittosporum*

**Introduction**

*Pittosporum* is the genus of the family Pittosporaceae which consists of approximately 200 species in the world [1]. The family Pittosporaceae includes trees, shrubs, and lianas with nearly about 200 species that included in 9 genera. In India, the family is represented only by one genera, *Pittosporum* which contains eleven species such as *Pittosporum anamallayense*, *P. ceylanicum*, *P. dasycaulon*, *P. eriocarpum*, *P. ferrugineum*, *P. humile*, *P. neelgherrense*, *P. podocarpum*, *P. tetraspermum*, *P. viridulum* and *P. wightii* [2].

The history of the genus *Pittosporum* began from the specimen collected and defined by Joseph Banks from New Zealand. The generic name derived from the Greek word “Pitta”, pitch, and “sporos” defining the ‘seeds’ which are enveloped by resinous pulp. During his expedition to Japan, Kaempfer collected the first member of this genus which was scientifically studied by European botanists for the first time. The genus is mainly concentrated in Australia, but China has the richest concentrations of species in Asiatic continent. In India most of the species were known by the mid-19th century and a Scottish botanist William Roxburg recorded the species in Flora of India [3] as the genus *Celastrus*, for first time where the botanist Wight observed *Celastrus* as the genus *Pittosporum* [4]. It is commonly known as ‘cheese woods’. Gondwana is probably considered as the origin of the genus *Pittosporum*. Now it is distributed in parts of Australia, Eastern Asia and some parts of Africa [5].

Different species of *Pittosporum* were widely used for medicinal purposes. Flower, root, bark and leaves were used traditionally against inflammations, arthritis, snake poison, rheumatic swelling, chronic bronchitis etc [6]. Phytochemical screening of several *Pittosporum* species had been started from the last decades. From this investigations, several physiologically potent chemical constituents such as triterpenoids, flavinoids, glycosides, sesquiterpenes, saponins, carotinoids and essential oils were reported [7–8]. The different parts of the plants such as root, bark, leaves and flowers of the genus *Pittosporum* were used as anti-inflammatory as well as anti-septic drug and also used for rheumatic disorders as reported by Wetson [9, 10]. Several phytochemical studies emphasized the genus *Pittosporum* having wide range of pharmacological actions such as anti-oxidant, anti-inflammatory, anti-cancer, anti-microbial, etc. [11]. The different species of *Pittosporum*. (*P. dasycaulon* and *P. floribundum*) were used against inflammation and an anti-dote for snake poison etc [12, 13]. (Table; 1).
Among the eleven Species reported in India phytochemical investigations are confined to seven species. In the present review an effort is being made to retrieve maximum available data based on the phytochemical works of the seven species in genus *Pittosporum* from the available literature and assess its important potential phytochemical constituents with respect to their pharmacological actions.

Table 1: Ethnomedicinal values of selected species of the genus Pittosporum

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Binomial nomenclature</th>
<th>Local name</th>
<th>IUCN status</th>
<th>Ethnomedicinal Uses</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>P. floribundum</em></td>
<td>Rakamuki</td>
<td>Not evaluated</td>
<td>Antidote of snake poison, arthritis and chest pain</td>
<td>[14, 15]</td>
</tr>
<tr>
<td>2.</td>
<td><em>P. eriocarpum</em></td>
<td>Agni</td>
<td>Endangered</td>
<td>Diabetes and bronchitis etc.</td>
<td>[16, 14]</td>
</tr>
<tr>
<td>3.</td>
<td><em>P. tetraspermum</em></td>
<td>Analivelagam</td>
<td>Endangered</td>
<td>Chronic bronchitis, rheumatism, leprosy, snake poison, secondary syphilis, chest infections</td>
<td>[17, 18]</td>
</tr>
<tr>
<td>4.</td>
<td><em>P. dasycaulon</em></td>
<td>Kasumaram</td>
<td>Not evaluated</td>
<td>Anti-dote of snake poison, chronic bronchitis, Intestinal diseases etc.</td>
<td>[19]</td>
</tr>
<tr>
<td>5.</td>
<td><em>P. neelgherrense</em></td>
<td>Analivelagam</td>
<td>Not evaluated</td>
<td>Anti dot of snake poison and bowel complaints</td>
<td>[20, 11]</td>
</tr>
<tr>
<td>6.</td>
<td><em>P. ferrugineum</em></td>
<td>Un known</td>
<td>Not evaluated</td>
<td>Leaves and fruits used against fish poison</td>
<td>[11]</td>
</tr>
</tbody>
</table>

1.1 Distribution pattern in India

The members of *Pittosporum* are mainly found in rain forest, usually at altitudes between 500-2800 m which covers Western Ghats and Himalayan regions. *P. anamallayense*, *P. ceylanicum*, *P. dasycaulon*, *P. neelgherrense*, *P. tetraspermum*, *P. viridulum* and *P. wightii* were are commonly found in peninsular India and *P. anamallayense*, *P. dasycaulon*, *P. neelgherrense*, *P. viridulum* are endemic to the Western Ghats [21]. *P. eriocarpum* and *P. humile* were recorded as endemic to Himalaya [4].

1.2 Systematic position of the genus Pittosporum

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Apiales
Family : Pittosporaceae R. Br.
Genus : *Pittosporum* Banks ex Soland

1.3 List Pittosporum species in India

1. *P. anamallayense* M. P. Nayar & G. S. Giri
2. *P. ceylanicum* Wight
4. *P. eriocarpum* Royle
5. *P. ferrugineum* W. T. Aiton
7. *P. humile* Hook. F. & Thomson
9. *P. podocarpum* Gagnep
11. *P. viridulum* M. P. Nayar, G. S. Giri & V. Chandradas

1.4 Discription

The members of the genus are tree or large shrub or climbers, growing 2-30 m tall, commonly with lenticels or resin canals. Leaves are simple, entire, rarely lobed and spirally arranged around the stem. Flowers are hermaphrodite, complete, actinomorphic, and solitary and found in racemose as corymb or umbel inflorescence. Sepals and petals are five each, and flowers are sweetly scented. Fruit is a capsule with many seeds which are enveloped by resinous pulp. Several species of the genus is aromatic with fragrant flowers and hence are cultivated in gardens.

2. Materials and Methods

The information regarding the pharmacological, ethnomedicinal and isolated phytoconstituents of selected plants are retrieved from the reported online data, thesis, websites, and other accessible journals. A comprehensive investigation was taken under for this work during the time period 2018. The work reported from time period 1951-2018 were collected for the review.

3. Phytochemical constituents

Phytoconstituents like terpenoids, flavonoids, lignans, coumarins, saponins, and carotenoids from traditional herbs are sources of many therapeutic drugs for different kinds of diseases [22, 23, 24].

The preliminary phytochemical screening of different species of *Pittosporum* were reported by many authors. Different types of phytoconstituents like flavonoids, phenols, alkaloids, lignins, antroquinones, steroids, tannins, saponins, fixed oils and glycosides were reported from *Pittosporum* [14, 19].

Phenolic compounds are principal plant compounds with potential biological activities due to its redox potential, hence it exhibit diverse biological activities including anticancerous, anti-inflammatory properties. Anticancerous potential of the plant could be due to its phenolic compounds having ability to neutralize the free radicals [26, 27]. In most of the selected species, it is observed that only preliminary phytochemical analysis were reported, whereas in *P. neelgherrense* and *P. viridulum* detailed investigations on essential oil from leaves and fruits has been studied. Only in *P. dasycaulon* detailed studies on phytochemical constituent’s hves been reported [4].

By analyzing the available data of the selected *Pittosporum* species, details regarding the name of phytochemical constituents and it source of accumulation is represented in Table 2.

Table 2: phytochemical constituents of investigated species in Pittosporum

<table>
<thead>
<tr>
<th>Sl no</th>
<th>Phytoconstituents</th>
<th>Class</th>
<th>Plant species</th>
<th>Source</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cis-3- nonene -1-ol</td>
<td>Alkenes</td>
<td><em>P. dasycaulon</em></td>
<td>Stem bark</td>
<td>[28]</td>
</tr>
<tr>
<td>2.</td>
<td>Beta-citronellol</td>
<td>Monoterpenes</td>
<td><em>P. dasycaulon</em></td>
<td>Stem bark</td>
<td>[28]</td>
</tr>
<tr>
<td>3.</td>
<td>Phytol</td>
<td>Diterpene alcohol</td>
<td><em>P. dasycaulon</em></td>
<td>Stem bark</td>
<td>[28]</td>
</tr>
<tr>
<td>4.</td>
<td>β- 1 arabinopyranoside</td>
<td>Glycosides</td>
<td><em>P. dasycaulon</em></td>
<td>Stem bark</td>
<td>[28]</td>
</tr>
<tr>
<td>5.</td>
<td>1,2 bis benzene</td>
<td>Hydrocarbons</td>
<td><em>P. dasycaulon</em></td>
<td>Stem bark</td>
<td>[28]</td>
</tr>
<tr>
<td>6.</td>
<td>Isosteviol</td>
<td>Diterpene</td>
<td><em>P. tetraspermum</em></td>
<td>Stem bark</td>
<td>[18]</td>
</tr>
</tbody>
</table>
### 4. Pharmacology of Isolated compounds

The reported pharmacological uses and structure of the phytoconstituents were shown below in Figure 1

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound</th>
<th>Source</th>
<th>Part</th>
<th>Species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Carophyllene oxide</td>
<td>Essential oils</td>
<td>P. neelgherrense</td>
<td>Leaves and fruits</td>
<td>[11]</td>
</tr>
<tr>
<td>8</td>
<td>Undecane</td>
<td>Essential oils</td>
<td>P. neelgherrense</td>
<td>Leaves and fruits</td>
<td>[11]</td>
</tr>
<tr>
<td>9</td>
<td>Nonanal</td>
<td>Essential oils</td>
<td>P. neelgherrense</td>
<td>Fruit</td>
<td>[11]</td>
</tr>
<tr>
<td>14</td>
<td>α-cardinal</td>
<td>Essential oils</td>
<td>P. neelgherrense</td>
<td>Fruit and leaves</td>
<td>[11]</td>
</tr>
<tr>
<td>16</td>
<td>Caryophyllene oxide</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>17</td>
<td>Spathulenol</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit and leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>18</td>
<td>Epi α muurolol</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>19</td>
<td>Undecane</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>20</td>
<td>α-copaene</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit and leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>21</td>
<td>germacrene D</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit</td>
<td>[29]</td>
</tr>
<tr>
<td>22</td>
<td>α-cadinol</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit and leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>23</td>
<td>trans-calamene-10-ol</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit</td>
<td>[29]</td>
</tr>
<tr>
<td>24</td>
<td>δ-cadinene</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit</td>
<td>[29]</td>
</tr>
<tr>
<td>25</td>
<td>β-elemene</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Leaves</td>
<td>[29]</td>
</tr>
<tr>
<td>26</td>
<td>Cyclocolorenone</td>
<td>Essential oils</td>
<td>P. viridulum</td>
<td>Fruit</td>
<td>[29]</td>
</tr>
</tbody>
</table>
4.1 Isosteviol
Acid hydroxylation of steviosides forms isosteviol [51]. It is keto sugar 200 times sweeter than the sugar naturally obtained from the leaves of Stevia rebaudiana [41]. Hence it is used as natural sweetener in Japan and Brazil [52]. Several studies reported that it inhibit Human DNA polymerase and topoisomerase 1 [41], hence can be used as anti tumour agents and anti-inflammatory agent [53]. Anti-inflammatory effect of Isosteviol can reduce ischaemia/ reperfusion injury in rat brains and heart by inhibiting calcium uptake in membranes of heart cells [54]. Isosteviole showed anti hyperglycemic activity because it helps to reduces plasma glucose level in fatty liver cells of rat [55].

4.2 Caryophyllene oxide
Beta caryophyllene and its oxide obtained from the leaves of Laurus novo canariensis showed significant repellent activities against Anopheles gambier [56]. It induces glutathione S transferase enzyme activity which helps for the detoxification in liver and intestine of mouse [57]. Caryophyllene oxide has been reported with anti-inflammatory activity by decreasing the level of nitric oxide suppression along with its analgesic activity [58].

4.3 α-copaene
It is the general name of oily liquid hydrocarbons with tricyclic sesquiterpenes. α-copaene was first isolated from the resin producing tropical tree Copaiba. The studies about alflacopaene revealed anti-genotoxicity (prevent damages of genes for protecting genetic information) effect and it significantly exhibited anti-oxidant capacity in human lymphocytes in vitro [59].

4.4 Germacrene D
It is a class of volatile sesquiterpenes which showed anti-fungal and insecticidal property [49] and play an important role as insect pheromones [60]. Antioxidant property of germacrene D by scavenging super oxide ions was established well by Dickson which may be due to the action of its cyclic moiety [61].

4.5 βelemene
Belemene is one of the predominant essential oil constituent found in Curcumz zedoaria with anti-microbial property [62]. It induces cell cycle arrest by inhibiting G2/ M phase and apoptosis hence, studies revealed that beta elemene showed anti tumour effect [63, 64]. Development of scar tissues in an organ or tissues in response to injury or repair is known as fibrosis [11]. In liver it mainly occur due to impairment in the repair system of hepatic tissue. Investigation revealed that beta elemene has been reported anti-fibrotic effect by interacting with Angiotensinogen 2 enzymes [65].

5. Pharmacogical Property of Pittosporum
5.1 Antioxidant activity (Free radical scavenging property)
Metabolic reaction in animal system usually end up with a highly reactive molecules such as super oxide anion, hydroxyl radicals and hydrogen peroxide which are called as free radicals or reactive oxygen species (ROS) [28]. They have several detrimental effects on other biomolecules which alters the normal physiological process. Anti-oxidants are compounds that are involved in scavenging these free radicals and thereby protecting other vital molecules of the living system [19]. The antioxidant molecules can helps directly or indirectly to scavenging free radicals by inducing the activity of scavenging enzymes or induce non-enzymatic compounds like vitamin E, and C [61]. Anti-oxidant property were reported in Pittosporum species like P. eriocarpum [16], P. dasycaulon and P. floribundum [15]. Free radical scavenging property was determined in the methanolic and ethanolic leaf extract of P. eriocarpum by using DPPH assay, using ascorbic acid as standard by Semwal [8, 10]. In the assay maximum radicle scavenging property was observed in methanolic extract followed by ethanolic extract [8]. Antioxidant activity of methanolic and aqueous extract of stem bark of P. dasycaulon were assessed and was proportionally effective with its concentration. Nitric oxide scavenging property was also reported in P. dasycaulon, which indicated higher nitric acid scavenging potential of aqueous extract than methanolic extract [19].

5.2 Anti-inflammatory activity
Inflammation is the series of tissue responses of living body against pathogens, injuries or diseased conditions. These mechanisms consisting of extravagations of fluids, plasma and affected inflammatory cells in to the affected tissues. During the inflammation different types of chemicals are produced primarily by phagocytic cells, such as histamine, free radicals, prostaglandins and serotonin. Dilation of blood vessels is another sign of inflammatory responses. Some chemical compound (Aspirin) used against these kind of inflammations are said to be antiinflammatory drugs [15]. Different plant species having potential anti-inflammatory activity were investigated and reported. Phyto constituent can be considered as valid drugs only after passing through rigorous evaluation processes for its efficacy and safety. For this purpose methanolic extracts of plant parts such as bark of stem, root and leaf of Pittosporum tetraspernum were evaluated using, Phenylbutazone as standard. Plant extract exhibited high suppressant activity against carrageenan induced edema in albino rat. The methanolic extract of bark of P. teraspermum induced significant reduction in the edema level with increasing dosage [17]. The methanolic bark extract of P. floribundum showed significant dose dependent antiinflammatory action against carrageenan induced edema in rat. In these investigations methanolic bark extracts showed
57% of inhibition compared to standard drug diclofenac sodium which showed 53% of inhibition against carrageenan induced in vitro inflammation.[15]

5.3 Anti-microbial activity
According to World Health Organization, current classes of antibiotics are insufficient to resist growing threats of microbial resistance. Number of newly discovered antibiotics are modified versions of existing class of antibiotics. Due to this reason some kind of pathogens can withstand those kinds of antibiotics. Hence, scientific world focus on urgent need of identification of new anti-microbial products especially against gram negative bacteria, multi drug resistant strains and many antibiotic resistant infections including Tuberculosis[66]. In everyday life, plants have been used worldwide to treat several diseases due to its viable options[67]. The use of natural compounds as anti-biotic was started at the time of 2nd World War. Microbial derived Penicillin and Streptomycin were commonly used in those days. Now a day’s plant derived compounds were also used as anti-microbial agents. Many scientific studies pointed out therapeutic potential of secondary metabolites in plants[68]. Among the Pittosporum spp. in India 7 species such as P. floribundum, P. dasycaulon, P. neelgherrense, P. ferrugeneum, P. tetraspernum, P. eriocarpum and P. viridulum were reported to have anti-microbial compounds. Methanolic extracts of all parts of P. floribundum exhibited better effect against the bacterial strains such as Bacillus subtilis and E. coli compared to Ampicillin which was used as control. The methanolic extract of leaf and bark extract of P. floribudum showed effective inhibition against two fungal strains such as Candida albicus and Aspergillus niger [14]. The leaf methanolic and ethanolic extracts of P. eriocarpum was also effective against the fungal strains C. glabrata, C. tropicalis and C. albicus. The aqueous extract of leafs of this species also showed anti-bacterial activity against the strains Pseudomonas aureus and P. Aeruginosa[16]. By using the disc diffusion methods the anti-bacterial property of P. neelgherrense and P. viridulum leaves and fruit oils were analyzed against strains of gram positive bacteria namely Staphylococcus aureus, Bacillus subtilis, B. Cereus, Salmonella typhi, and gram negative bacteria like Pseudomonas fluorescense, P. aerugenosa, Klebsiella pneumonia and E. coli. From these above investigations on antibacterial activity, leaf oil showed high potential due to the chemical constituents such as 3,4 undecane and carophyllene oxide [29]. The antibacterial property of P. ferrugineum was repeated with Ampicillin as reference drug using Disc diffusion method. The chloroform extract from the plants effectively inhibit the bacterial strains such as Salmonella typhi, Pseudomonas aeruginosa and E. coli[68]. The GC/MS evaluation of P. dasycaulon showed the presence of effective phytoconstituents as cis- 3 Nonene-1-ol; beta-citronellol, methyl: phyto; urolitic acid; 1,4,2,5, Cyclohexanetetrol and beta-1- Arabinoppyranoside having action against both gram positive and gram negative bacteria namely, Bacillus cereus and Pseudomonas aeruginosa respectively[28]. Hence, the species can be considered as a good source antibacterial compounds [5]. Isosteviol obtained from the Pittosporum tetraspernum showed anti-bacterial activity along with antibiofilm activity[69].

5.4 Ant biofilm activity
Some strains of bacteria is now recognized to have ability to withstand and survive the stress from various sources as including antibiotics, nutrient limitation, heat shock and immune responses of host body. Biofilms forming capacity is one of the main reason behind resistance which, refers to structural aggregation of microbial mass which enveloped in an extra cellular matrix of host cell. Osteomyelitis and Endocarditis are some of the important life threatening infections caused by Staphylococcus aureus because of the biofilm formation. So many studies emphasized the significance and repeated the development of therapeutic drugs against biofilm formations[69]. Isosteviol isolated from the plant Pittosporum tetraspernum showed in vitro anti-biofilm activity against the strains of bacteria such as E. coli, Salmonella. typhi, Pseudomonas aeruginosa etc. which was concentration dependent. In this investigation maximum reductions of cell attachment were observed in P. aeruginosa at 100 mg/ml concentration[18].

5.5 Hepato protective activity
Liver is the major organ in human body which execute diverse functions including storage of glycogen, fats etc, synthesis, detoxification and secretion, hence its protection must be prioritized[70]. The quest of scientific community for an effective and nontoxic hepatoprotective drug has been mainly focused on plant derived products[71]. Silymarin is a previously investigated phyto constituent obtained from Silybum marianum (Asteraceae) which was used to treat acute and chronic hepatic diseases[72, 73]. Sylimarin is the combination of lignin and flavanoids[74]. Stem bark of Pittosporum neelgherrense showed significant hepato protective effect against the liver damage induced by toxins such as CCI4, D- GalN, and APAP in rat cells which was confirmed by SGOT and SGPT assay. Histopathological studies indicated that the toxin induced liver damage seems to be reverted in rat group treated with the stem bark extracts and was comparable to group treated with the standard hepato protective compound Silymarin[20].

6. Conclusion
The genus Pittosporum includes 300 species which are distributed all over the world. India is reported to have 11 species of the genus with traditional ethanomedicinal values. Among these only 7 species were subjected to preliminary phytochemical and pharmacological analysis by the scientific community. By keeping the available literature from the few species of the genus Pittosporum, the investigated studies emphasized that, the so far discovered phytoconstituents have potent biological activities. About 26 predominant compounds were reported in different species of Pittosporum in India which includes essential oils, glycosides, alkaloids, flavanoids, alcohols, and phenols. From these compounds essential oils were mostly reported in fruits and leaves of the genus Pittosporum which has high potent values. The crude methanolic extract of stem bark showed more biological potent activities. There for, the remaining species of the genus Pittosporum should be given more attention for research studies especially focusing on the analysis of phytochemicals along with its pharmacological properties. So far in vivo and in vitro studies have been conducted using the phytochemical compounds derived from different species of this highly potential genus. Clinical trials should be done ahead which can pave the way to drug development from the bioactive compounds discovered so far.
References


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