

## Review Article



## The Review: Phytochemical and Bioactive Screening of “Karanja” belonging to family Leguminosae.

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### ABSTRACT

Traditional medicine consists of huge number of plants with different pharmacological and medicinal values. The bioactive molecules have been identified. *Pongamia pinnata* (Linn.) Pierre is one of the oldest plants with numerous properties, which is found all over the globe. It is commonly known as “Indian beech tree” and has been identified in Ayurvedic and Siddha system of medicines for the healing effect of human beings. Different parts of whole plant are used for treatment of various diseases including rheumatism, diarrhoea, gonorrhoea, whooping cough, leprosy and bronchitis. Extracts of the whole plant show significant anti-plasmodial, anti-ulcerogenic, anti-diarrhoeal, anti-inflammatory, anti-fungal, and analgesic activities. Its oil is used as a source of biodiesel. The present review paper was aimed to update the information of *Pongamia pinnata* with reference to its pharmacological properties, chemical constituents and its use as anti-urolithiatic agent for the treatment of Urolithiasis.

**Keywords:** *Pongamia pinata*, Indian beech tree, Healing effect, Anti-urolithiatic agent, urolithiasis.

### INTRODUCTION

Plants contain a large source of phytochemicals that provides maximum healing effect with less or no adverse effects. Many traditional therapeutic applications have been dependent on plants for treatment of numerous diseases. Earlier, plants were being used as extracts or plant mixtures for treatment of the disease without the knowledge of the actual bioactive compound responsible for the healing effect. But recently, a lot of focus has been done for the identification of the active principle from the plant source. So as to extend their application as biomedicine in drug discovery. It has been widely reported for several activities, including secondary metabolites have been isolated reported for various activities. This review attempts to give an updated comprehensive description of the phytochemicals isolated from plant and the pharmacological activities reported so far.

*Pongamia pinnata* (L.) Pierre is commonly referred to as Pongam Tree (Tamil), Karanja (Marathi, Hindi, Bengali) Maktamala or Gaura (Sanskrit), Honge, Hulugala or Kanigemara (Kannada), Indian Beech Nut Tree/Pongam oil tree/malva nut/Hongay oil tree (English), Ki pahang laut (Indonesian), and Kacang kayu laut (Malay)<sup>1</sup>. It belongs to the family Fabaceae (*Leguminosae*) and subfamily *Pipilionaceae*. This plant is also well known as *Millettia pinnata* (L.)<sup>2,3</sup>.

### Botanical Description

*Pongamia pinnata* is a glabrous, medium-sized and evergreen tree containing five to seven leaflets that are alternate, odd-pinnate, opposite and ovate; flowers are pinkish white, in axillary racemes. The calyx is cup-shaped,

four- to five-toothed, with a papilionaceous corolla. Stamens are Monadelphous, 9-10 in number. The ovary is subsessile, two-ovuled, incurved, glabrous ending in a capitate stigma. The seed pod is woody, compressed, indehiscent, and yellowish-gray during the ripened, it alters in size and shape, 4.2–7.7 cm long and 1.8–3.4 cm wide, with a short-curved beak. It usually contains two elliptical or uniform seeds, 1.7–2.0 cm long and 1.3–1.9 cm wide, which are having reddish-brown leathery Testa<sup>4</sup>.

### Geographical Distribution (Species Distribution)

*Pongamia pinnata* is indigenous to the India and distributed eastwards, which includes regions of south-eastern Asia. It is characteristic to distant countries like Australia, China, Egypt, Fiji, Indonesia, Japan, Malaysia, Mauritius, New Zealand, Pakistan, Philippines, Seychelles, Solomon Islands, Sri Lanka, Sudan and United States of America (Florida, Hawaii). In India, it is found in tropical dry region to subtropical dry forest regions and in Western Ghats of tidal forests, in the river banks and near sea coast<sup>4</sup>.

### Ethnobotanical Uses

In Ayurveda and Siddha system of Indian medicine in the initial days *Pongamia pinnata* was being used in the treatment of various diseases. For the treatment of wounds, ulcers, painful rheumatic joints, tumours, piles, skin diseases, itches, diarrhoea and other diseases. The leaves of plant are used for wound healing, relieving rheumatic pains, anti-helminthic, cleaning ulcers, gonorrhea, digestive, laxative, genitalia, cold, cough, gonorrhoea, diarrhoea, dyspepsia, and leprosy. Flowers were used in the treatment of diabetes. Bark portion were used as antimicrobial agent, for treating bleeding piles,



beriberi, diabetes. Febrifuge was treated using seed powder, tonic for whooping cough and bronchitis, scabies using seed oil, ulcers, leprosy, piles and chronic fever. Roots are used for cleaning gums, teeth and ulcers. The extract of leaves, seeds and roots are used to treat infection in diseases such as leukoderma, leprosy, lumbago, muscular and articular rheumatism<sup>5</sup>.

Other applications of *Pongamia pinnata* includes its use as animal fodder, timber and fish poison. It has also been used for variety of other application in agriculture as green manure, as insecticide and nematicide and in environmental management<sup>6</sup>. Karanjin and furanoflavonol presence is used in agricultural practices for its pesticidal, insecticidal and acaricidal activities. It is commercially available as a bio-pesticide targeting the pests<sup>7</sup>. *Pongamia pinnata* when inoculated with *Bradyrhizobium liaoningense* PZHK1 has shown to be effective in the phytoremediation process and to produce biofuel feedstock on the marginal land<sup>8</sup>.

## Phytochemistry

### Whole Plant

*Pongamia pinnata* contains numerous secondary metabolites/phytochemicals. Phytochemical examinations of different parts of plant have shown the plant is rich in flavonoids, isoflavonoids, chalcones, flavanones, triterpenes and alkaloid<sup>9,10</sup>. As an evidence to this, several flavonoids and its derivatives such as furanodiketones, furanoflavones, coumarins, terpenes and modified phenylalanine dipeptides have been isolated from this plant<sup>11</sup>. Presence of other compounds like protocathechuic, ellagic, ferulic, gallic, gentisic acid, 4-hydroxybenzoic and 4-hydroxycinnamic acids in bark; sorbic, ferulic, gallic, salicylic and p-coumaric acids in leaves; vanillic, gallic and tannic acids in seeds as the main phenolic acids have also been noticed<sup>12</sup>.

### Seeds

*Pongamia pinnata* seeds are rich in oil and are reported it contains 28-34% oil with high percentage of polyunsaturated fatty acids. The seed oil is rich in sterols, fatty acids and their derivatives<sup>13</sup>. Totally six sterols, their derivatives and eight fatty acids (three saturated and five unsaturated fatty acids) have been isolated from the seeds. Fatty acids reported from the plant are two monoenoic acids i.e., Oleic (44.24%) and stearic acid (29.64%), one dienoic acid i.e., palmitic acids (18.58%) and two trienoic that includes octadecatrienoic acids in trace amounts (0.88%). Also, compounds such as karangin, pongamol, pongagalabrone, pongapin, pinnatin, kanjone, glabrin (complex amino acid) furanoflavone and pyranoflavonoid (Karanjachromene) have been isolated and characterized from seeds of the plant [9]. Other metabolites such as beta-sitosteryl acetate and its galactoside, stigma sterol, and sucrose are also reported from this plant. Flavonoids like the Glabrachalcone isopongachromene and flavone derivative pongol have also been reported from the seeds of this plant<sup>13,14</sup>.

## Roots

Altogether, 52 flavonoids have been reported from the roots of *Pongamia pinnata* play an important role as phytoalexins. Almost 11 pterocarpanoids were identified for phytochemical analysis of the roots *Pongamia pinnata*, out of which four new unreported flavone and four new chalcone derivatives have been reported by Wen *et al.*, (2018a). Resulted in the identification of various types of compounds including flavones, chalcones, isoflavones, flavanones, and pterocarpanoids<sup>15,16</sup>.

Wen *et al.*, (2018c) have isolated 29 flavanones and flavanols including 7 previously undescribed compounds from roots of *Pongamia pinnata*. They are as follows (2S)-7-hydroxy-6,8-di-(3-methylbut-2-enyl)-3',4'-dimethoxy flavanone; (2S)-7-(2-methylbut-3-enyloxy)-8-(3-methylbut-2-enyl)-3',4'-dimethoxyflavanone; ponganone III; isoglabrachromene; pongachin; 6-methoxy-6'',6''-dimethyl chromeno-[2'',3'':7,8]-flavanone; isolonchocarpin; maxima flavanone A; 6-(γ,γ-dimethylallyl)-3',4'-dimethoxy-6'',6''-dimethylpyran[2'',3'':7,8]flavanone; pongamone C; 3',4',7-trimethoxyflavanone; pinostrobin; liquiritigenin; griffinone C; griffinone A and pongaflavanol<sup>17</sup>.

Ghosh *et al.*, (2009) Pterocarpanoids constitute the second largest group of natural isoflavonoids from root extracts. Other compounds reported from the roots of plant includes flavanols such as methyl ether-tetra-O-methyl fisetin, kanugin, desmethoxykanugin, karanjapin (chalcone) and two flavonoids namely a pyranoflavonoid (karanjachromene) and a furanoflavonoid (karanjin)<sup>18</sup>.

Tanaka *et al.*, (1992) have reported the presence of nine new flavonoid compounds referred as pongamones III-XI, from its root bark along with 18 flavanoids already reported<sup>19</sup>.

### Leaves and Stem

The leaves and stem of *Pongamia pinnata* are also rich in several flavone and chalcone derivatives such as pongone, galbone, pongalabol, pongagallone A and B. Li *et al.*, (2006) have reported isolation and characterization of five flavonoids referred as pongamones A-E, along with 16 known flavonoid metabolites<sup>20</sup>. Yin *et al.*, (2004) and Yin *et al.*, (2006) have reported seven flavonoids such as pongaflavone, karanjin, pongapin, pongachrome, 3,7-dimethoxy-3',4,7-tetramethoxyflavone, two prenylated flavonoid derivatives (pongaflavanol and tunicatachalcone) from the bark<sup>21,22</sup>. Also, two hydroxy chalcones (onganones I and II), cycloart-23-ene-3β, 25-diol, and phenylpropanoids (pongapinone A and B) have been isolated and characterized from the bark<sup>23-25</sup>.

Li *et al.*, (2015) has isolated chlorinated flavonoid: 2',6'-dichloro-3',5'-dimethoxy-[2'',300:7,8]-furanoflavone, along with 29 known compounds from the stem extracts. The isolated compounds are pongaglabol methyl ether; pongapin; lanceolatin B; karanjin; pongaglabrone; 3'-methoxy-[2'',3'':7,8]-furanoflavone; 3',5'-dimethoxy-[2'',3'':7,8]-furanoflavone; millettocalyxins; pongapinnols

A; pinnatin; gamatin; kanugin; desmethoxykanugin; 3,7,3',4'-tetramethoxyflavone; apigenin-6-C-galactosyl-8-C-arabinoside; pongachromene; maxima isoflavone J; formononetin; pseudobaptigenin; 3',7,8-trihydroxy-4'-methoxyisoflavone; 8-O-methylretusin; 8-hydroxy-7,4'-dimethoxyisoflavone; lonchocarpin; glabrachromene II; isolonchocarpin; ovalichromene B; betulonic acid; machaeroceric acid; (2S,4R) ovalin<sup>10</sup>.

The leaves contain kanugin, desmethoxykanugin, and pinnatin triterpenoids, glabrachromenes I and II, 3'-methoxypongapin, and 4'-methoxyfurano [2''3'':7,8]-flavone<sup>4</sup>. Marzouk *et al.*, (2008) isolated two isoflavonoid diglycosides (4'-O-methyl-genistein 7-O-beta-D-rutinoside and 2',5'-dimethoxy-genistein 7-O-beta-D-apiofuranosyl-(1'''-->6'')-O-beta-D-glucopyranoside) and a rotenoid (12a-hydroxy-alpha-toxicarol ) together with nine known metabolites vecinin-2, kaempferol 3-O-beta-D-rutinoside, rutin, vitexin, isoquercitrin, kaempferol 3-O-beta-D-glucopyranoside, 11,12a-dihydroxy-munduserone, kaempferol, and quercetin<sup>26</sup>.

### Flowers

*Pongamia pinnata* flowers have been reported containing phytochemicals like flavones, hydroxyfuranoflavones (Pongaglabol), furanoflavones (karanjin, lanceolatin B, kanjone and pinnatin), a chromenoflavone, triterpenes, beta sitosterol glucosides, phenyl alanine dipeptide and aurantiamide acetate<sup>11</sup>.

### Fruits

The Furanoflavonoid glucosides (pongamosides A-C), flavanol glucoside pongamoside D and furanoflavonoid aglycones have been reported from the fruits of *pongamia pinnata*<sup>27</sup>. Recently, Saraphon *et al.*, (2017) have reported the presence of furanoflavonoid derivative (4'-hydroxypinnatin), along with compounds from the fruit extracts of *Pongamia pinnata*. The isolated compounds are 4'-hydroxypinnatin; pinnatin; pongaglabol methyl ether; kanjone; 3,7,3',4'-tetramethoxyflavone and 5,7-dimethoxy-8-(2''-hydroxy-3''-methyl-3''-butenyl) flavanone<sup>28</sup>.

## PHARMACOLOGICAL PROFILE

*Pongamia pinnata* have been investigated for its biological activity based on the traditional therapeutic knowledge.

### Antimicrobial activity

Extracts and compounds of *Pongamia pinnata* leaves, bark, seeds and seed oil have been widely reported for its antibacterial, antifungal and antiviral activities. The alcoholic extracts of the seed have been reported having antibacterial property against several gram positive, gram negative bacteria and anti-fungal property<sup>29</sup>. Wagh *et al.*, (2007) have reported that the fatty oil of *Pongamia pinnata* can be used for developing antimicrobial drugs, have potential antifungal and antibacterial activity against *Aspergillus niger*, *A. fumigatus*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*<sup>30</sup>.

Bajpai *et al.*, (2009) has reported the use of leaves extract in food industry and pharmaceutical industries as an antimicrobial effect against several strains *Bacillus subtilis*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Listeria monocytogenes*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*<sup>31</sup>. Dahikar *et al.*, (2017) reported antifungal activity against set of bacterial and fungal strains<sup>32,12</sup>.

Several isolated compounds such as cycloart-23-ene-3β-25-diol, a terpenoid isolated from stem bark, Pongarotene, a new rotenoid and karanjin, a flavanol from seeds have shown broad spectrum of antimicrobial activity for bacteria like *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and fungi such as *Candida albicans*, *Aspergillus niger*, *Aspergillus fumigatus*. *Penicillium notatum* doesnot showing any effect<sup>29,24</sup>. Flavonoids isolated from the stems and roots of *Pongamia pinnata* (*Derris indica*) exhibited anti-mycobacterial activity<sup>33</sup>. Lanceolatin B, a furanoflavone present in whole plant possesses moderate antibacterial activity against *Shigella dysenteriae*, *Salmonella typhi*, *Streptococcus-β-haemolyticus* and *Staphylococcus aureus*<sup>34</sup>.

### Antiviral activity

*Pongamia pinnata* has been used widely in the Ayurveda and Siddha traditional medicine systems for the treatment of clinical lesions of skin and genitalia<sup>5</sup>. Elanchezhiyan *et al.*, (1993) reported the antiviral properties of aqueous extract of the seeds of *Pongamia pinnata* against herpes simplex virus type-1 and type 2 (HSV-1 & 2) using Vero cells as an *in vitro* model<sup>35</sup>. Rameshthangam and Ramasamy (2007) have reported the antiviral activity of the ethanol extract from the leaves and the isolated compound bis (2-methylheptyl) phthalate against White Spot Syndrome Virus (WSSV) belonging to *Penaeus monodon* Fabricius, which causes White spot syndrome in shrimps<sup>36</sup>. Mathaiyan *et al.*, (2018) also reported the HIV-1 p24 inhibition (66.9 ± 4.4 %) and Reverse Transcriptase (RT) inhibition (36.8%) activity of aqueous seed extracts of *Pongamia pinnata*. The study also revealed the binding efficiency of the active chalcone derivatives namely Glabarachalcone and Karanijin with binding on to p24 protein and RT enzymes<sup>37</sup>.

### Anti-diabetic activity

*Pongamia pinnata* extracts have shown potential as phytomedicine for diabetes due to its anti-hyperglycemic potential against several diabetes induced animal models. Oral administration of ethanol extract of *Pongamia pinnata* flower showed significant anti-hyperglycemic effects oral administered in alloxan-induced diabetic rats<sup>38</sup>. Sikarwar *et al.*, (2010) suggested potential hypoglycemic and hypolipidemic effect of aqueous extract of leaves<sup>39</sup>. Also, Sweetey *et al.*, (2011) have inferred that ethanol extract of *Pongamia pinnata* showed potential hypoglycemic activity in OGTT and normoglycemic rats and anti-diabetic activity in alloxanized rats comparable to the reference drug glibenclamide<sup>40</sup>. Anti-hyperglycaemic activity of the stem bark aqueous extract of *Pongamia*

*pinnata* has also been reported reduced serum glucose level by Badole *et al.*, (2009) using alloxan induced diabetic mice models<sup>41</sup>. Vadivelu *et al.*, (2011) also reported methanol extract of seeds of *Pongamia pinnata* with inhibitory effect against  $\alpha$ -amylase and  $\alpha$ -glucosidase enzyme Type II diabetes<sup>42</sup>.

Likewise, isolated the compound Cycloart-23-ene-3,25-diol from the stems and reduced administration promoted reduction in serum glucose levels by increasing serum and pancreatic insulin level in diabetic mice. Bandole *et al.*, (2009, 2010) other biochemical parameters such as, glycosylated haemoglobin, serum cholesterol, triglycerides, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, globulin, bilirubin, lactate dehydrogenase, urea and uric acid were reduced and increased serum and pancreatic insulin levels in diabetic mice<sup>41,43</sup>. The compound (Cycloart-23-ene-3,25-diol) also had protective effect on the vital organs against induced toxicity of STZ-nicotinamide induced diabetic mice<sup>24</sup>. It decreases plasma glucose level by increasing plasma and pancreatic insulin level through increased plasma and colonic active glucagon-like peptide (GLP-1) amide secretion as well as decreased oxidative stress in STZ-nicotinamide induced diabetic rats<sup>44</sup>. Tamrakar *et al.*, (2008) reported the anti hyperglycemic activity of pongamol and karangin from the fruits of *Pongamia pinnata* in Streptozotocin-induced diabetic rats and type 2 diabetic db/db mice. They have also hypothesised protein tyrosine phosphatase-1B (PTP1B) as the target responsible for their activity<sup>45</sup>. Pongamiaflavonol (Difuranoflavonone) isolated from *Pongamia pinnata* pods, pod and flower extracts exhibited promising hypoglycemic activity in streptozotocin-induced diabetic rats<sup>46</sup>.

#### Anti-lipidemic activity

*Pongamia pinnata* pod and flower extracts showed potential hypolipidemic activity in streptozotocin-induced diabetic rats<sup>46</sup>. *Pongamia pinnata* leaves extract possessed significant anti-hyperlipidemic activity by exhibiting reduced serum lipid parameters like total cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein (VLDL) and increase in high density lipoprotein (HDL) in atherogenic diet induced hyperlipidemic rats<sup>47</sup>.

#### Antioxidant activity

Methanolic extract of seed possess antioxidant activity by enhancing ferric reducing/antioxidant power (FRAP activity) and inhibiting  $\beta$ -carotene degradation, DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity and superoxide levels. The antioxidant activity may be due to the presence of total free phenolic content. In addition, sprouted seeds and oil fried seeds exhibited increased phenolic content, enhanced antioxidant and free radical scavenging activity. This confirmed antioxidant potential involvement of phenolic compounds<sup>42</sup>. *Pongamia pinnata* flower extract on oral administration showed significant anti-lipid peroxidative effect and enhancement in

antioxidant defence system in alloxan-induced diabetic rats<sup>38</sup>. Significant free radical scavenging potential of biosynthetic silver nanoparticles (AgNPs) prepared using *Pongamia pinnata* was observed in vitro assays for free radicals (DPPH, ABT<sup>+</sup>, Hydroxyl, Superoxide anion and Nitric oxide). The study has further inferred that capping of silver nanoparticles by various polyphenolic compounds present in *Pongamia pinnata* leaf extract lowers the toxicity of silver nanoparticles suggesting their therapeutic usage against oxidative stress related degenerative diseases<sup>48</sup>. Sajid *et al.*, (2012) demonstrated the presence of higher phenolic and flavonoid content in the bark extract with significant antioxidant property<sup>12</sup>. Essa *et al.*, (2006) showed that anti-oxidant property of leaf extract was due to modulation of lipid peroxidation by reversing the oxidant-antioxidant imbalance in ammonium chloride-induced hyperammonemic rats<sup>49</sup>.

Karanjapin (chalcone) and karanjachromene (pyranoflavonoid) were found to possessed enhanced total antioxidant status through inhibition of the radical cation ABTS<sup>50</sup>. Cycloart-23-ene-3 $\beta$ , 25-diol isolated from stem bark of *Pongamia pinnata*. Dose dependent antioxidant activity exhibited enhanced potential in scavenging a variety of free radicals including DPPH, superoxide, hydroxyl, hydrogen peroxide, nitric oxide radical and metal chelates<sup>24</sup>. Karanjin and Pongapin, two important furanoflavone of *Pongamia pinnata* to possess nitric oxide scavenging potential of about 95.60% 68.05% respectively as reported by Ghosh *et al.*, (2018)<sup>51</sup>.

#### Anti-cancer activity

Pongapin and Karanjin, two furanoflavonoid derivatives exhibited anti-tumour activity in a differential manner proving their potential as natural anticancer agents. Pongapin inhibited the growth of cervical cancer cells (HeLa) by significantly increasing the intracellular reactive oxygen species (ROS) while stabilization the expression of I- $\kappa$ B (nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor) and reducing the expression of NF- $\kappa$ B (nuclear factor kappa-light-chain-enhancer of activated B cells). It also significantly increased DNA damage-induced p53 and p21 expression. Whereas, Karanjin decreased ROS level by inhibition of I- $\kappa$ B degradation restricting NF- $\kappa$ B nuclear translocation. Further, it induced low DNA damage with increased p53 expression, induced G2/M arrest and increased SubG1 population, indicating induction of apoptosis. Pongapin induced caspase-dependent apoptosis through induction of Bax/Bcl-2 ratio through increased expression of Bax whereas Karanjin induced caspase-dependent apoptosis through low expression of Bcl-2<sup>52</sup>.

Sharma *et al.*, (2018) have investigated the chemo preventive potential of a flavonoid-rich *Pongamia pinnata* seed extract due to cytochrome P1A1 (CYP1A1) in CYP1A1-overexpressing normal human HEK293 cells at an IC<sub>50</sub> of 0.6  $\mu$ g/mL. The secondary metabolites pongapin/lanceolatin B (furanoflavonoids), inhibited CYP1A1 at IC<sub>50</sub> of 20 nM. Furthermore,





pongapin/lanceolatin B inhibited cell cycle at G<sub>0</sub>-G<sub>1</sub> phase, repressed cyclin D1 levels and induced cellular-senescence in CYP1A1-overexpressing MCF-7 breast cancer cells. The study supported molecular modelling of pongapin/lanceolatin B with CYP1A1<sup>53</sup>.

Pinnatin isolated from *Pongamia pinnata* showed strong cytotoxicity against cholangiocarcinoma (KKU-100) (IC<sub>50</sub> 6.0 ± 2.7 µg/ml) and human hepatoma (HepG2) cell lines (IC<sub>50</sub> 9.0 ± 4.1 µg/ml) with a maximal cell killing efficiency of about 88-90%. The flavone, 3,7,3',4'-tetramethoxyflavone 5 isolated from ethanol extract exhibited the cytotoxicity against KKU-100 with a moderate efficacy<sup>28</sup>.

### Anti-inflammatory activity

*Pongamia pinnata* leaves and seed extracts have been reported to show potent anti-inflammatory activity against acute, subacute and chronic inflammation induced rat models<sup>54</sup>. Likewise, the seed extracts (ethanol) exhibited anti-inflammatory effect in chemically induced paw inflammation in rats. However, the anti-inflammatory effect was best seen against bradykinin and PGE1-induced inflammation and minimal against histamine and 5-HT-induced inflammation. Also, significant antipyretic action against Brewer's yeast induced pyrexia was seen in the extract<sup>55</sup>. Seeds and seed oil have been used for treating various inflammatory conditions like leukoderma, lumbago and rheumatism. Seeds and root extracts of *Pongamia pinnata* have been reported to have ulcer protective and healing effects in experimental rats<sup>56,57</sup>.

Patel and Trivedi (2017) have shown that Karanjin has the potential to cure colitis in 2,4,6-trinitrobenzenesulfonic acid (TNBS) induced colitis mice models. Karanjin ameliorated the macroscopic damage and histological changes includes cellular infiltration, tissue necrosis, mucosal and submucosal damage) as compared to the TNBS control group significantly in a dose dependant manner. It also reduced the myeloperoxidase (MPO) activity, malondialdehyde (MDA), and nitric oxide (NO) levels and restored the catalase (CAT), superoxide dismutase (SOD), and reduced glutathione (GSH) levels to normal when compared to the TNBS induced colitis group<sup>58</sup>.

In the management of Psoriasis an inflammatory disease, nitric oxide free radical quenching property of Karanjin and Pongapin had significant activities on par with ascorbic acid. Furthermore, molecular docking scores for the flavones (Karanjin and Pongapin) with the receptors responsible for psoriasis (IL-17A, IL-17F, IL-23, ROR $\gamma$ t, and TLR-7) in composition to standard methotrexate<sup>51</sup>. Karanjachromene, a flavonoid derivative isolated from the Seeds of *Pongamia pinnata* had potent against paw edema during all phases of inhibition of different inflammatory mediators. further Karanjachromene inhibited both mechanisms of pain and inflammation mechanism. Hence with significant anti-inflammatory and analgesic activities<sup>59</sup>.

Twelve flavonoid derivatives isolated from the roots had different levels of inhibitory effects against nitric oxide production in lipopolysaccharide (LPS) stimulated BV-2 microglial cells. Phenyl isoflavone possessed an 1,2-dioxetane ring with the maximum nitric oxide inhibitory activity at an IC<sub>50</sub> of 9.0 Mm<sup>16</sup>. Similarly, Wen *et al.*, (2019) evaluated the inhibitory effects of 11 pterocarpanoids isolated from the roots of *Pongamia pinnata* on LPS stimulated nitric oxide production using BV-2 microglial cells. Six compounds out of eleven pterocarpanoids possess potent inhibitory effects against nitric oxide production. Pterocarpanoid maackiain, a showed the best inhibitory activity against nitric oxide production with an IC<sub>50</sub> value at 12.0 µM. Wen *et al.*, (2018a), isolated 29 flavanones and flavanols from the roots showing inhibitory effects against nitric oxide production was exhibited by all the compounds at an IC<sub>50</sub> < 20 µM. However, dehydroisoderricin was the most active compound with an IC<sub>50</sub> of 9.6 µM<sup>17</sup>. Similarly, in a study by the same group out of 52 flavonoids from the roots of *Pongamia pinnata*, ten compounds showed significant inhibitory effects against nitric oxide production, comparable to the positive control (dexamethasone) in LPS-stimulated BV-2 microglial cells<sup>15</sup>.

### Anti-urolithiatic activity

Traditionally the seed powder was prescribed for treating the kidney disease. Ahmed *et al.*, (2016) have reported the anti-urolithiatic activity *Pongamia pinnata* seeds<sup>61</sup>.

### Other pharmacological activities

**A) Skin protection:** *Pongamia pinnata* leaf extracts have shown extremely good photo-absorbance property throughout the UV region. Hence it has been proposed to be used in sunscreen preparations as it has UV protection ability and also has the advantage of avoiding the adverse and undesired effects of synthetic sunscreen compounds<sup>62</sup>. The seeds of *Pongamia pinnata* extracts were found to be extremely good absorbents of the UV rays in the UVA and B regions as they contain photo absorptive compounds and hence have been proposed to be used in a single herbal formulation like ointments, lotions or creams as they have been reported to show protective action throughout the broad ultraviolet region<sup>63</sup>.

**B) Anti-plasmodial activity:** The methanol extract of the bark of *Pongamia pinnata* had shown potent *in vitro* antimalarial activity (IC<sub>50</sub> value of 11.67 µg/mL) against chloroquine-sensitive *Plasmodium falciparum* (3D7 strain) and exhibited significant activity against *Plasmodium berghei* malaria parasite *in vivo*<sup>64</sup>.

**C) Neuroprotective activity:** Neurodegenerative diseases are associated with neuroinflammation, manifested by over-production of nitric oxide (NO) by microglial cells. Three compounds from *Pongamia pinnata* namely Pongaglabol methyl ether (flavonoid), and lonchocarpin (chalcone) and glabrachromene II (chalcone) were shown to be potential therapeutic agents for neurodegenerative

diseases due to their significant inhibitory potential on LPS-induced nitric oxide production in microglial BV-2 cells<sup>10</sup>.

**D) Anti-mutagenic activity:** Significant anti-mutagenicity was exhibited by monofloral honey from *Pongamia pinnata*. The monofloral honey on solid phase extraction followed by HPLC guided testing for mutagenicity identified the fraction displaying maximum anti-mutagenicity and characterized it to contain abscisic acid (ABA). Moreover, ABA isolated from the honey also displayed strong anti-mutagenicity<sup>65</sup>. Significant anti-convulsant activity was shown by ethanol extract of leaves *Pongamia pinnata* in maximal electroshock-induced seizure (MES) model of wistar albino mice and pentylenetetrazole-induced convulsion (PTZ) in rat models<sup>66,67</sup>.

## CONCLUSION

*Pongamia pinnata* an indigenous plant of Indian subcontinent has been widely used in the traditional folklore as medicine for numerous diseases due to their non-toxic nature with no/minimal side effects. This review provides comprehensive information about the phytochemicals isolated from different parts of *Pongamia pinnata* and the biological activities reported from the plant extracts and its compounds. Based on the traditional knowledge available for the plant, research effort to identify components responsible for the healing effect was initiated which led to the extraction, isolation and characterization of the plant. *Pongamia pinnata* on screening for biological activities through *in vitro* and *in vivo* models for different diseases exhibited significant properties that includes anti-microbial, anti-diabetic, anti-inflammatory, anti-cancer and so on. The phytochemicals responsible for these effects have also been identified, characterised and reported by many authors. With this basic and advanced studies of *Pongamia pinnata*, the next focus must be emphasised on mechanism of action of bioactive compounds or extracts have to be understood to report the complex pharmacological effects.

Further, the clinical studies ensure the safety of therapeutic regimens using *Pongamia pinnata* in modern medicinal formulations.

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