Pharmacogn J. 2020; 12(4): 938-945
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Review Article

Molecules of Interest – Karanjin – A Review

Aina Akmal Mohd Noor[1,2], Siti Nurul Najiha Othman[1], Pei Teng Lum[1], Shankar Mani[3], Mohd. Farooq Shaikh[4], Mahendran Sekar[1,*]

ABSTRACT

Background: At the present time, several plants are largely contributing to the medical field due to its valuable use. Scientific evidence generated with their special inherent compounds gave more confidence to the scientific community. *Pongamia pinnata* (Linn.) is an Indian native plant and well exploited in Ayurvedic medicinal system. Concurrently, a few pieces of scientific research have been done to prove the therapeutic activity of this medicinal plant. The medicinal properties of this plant are most likely due to its principal active compound, karanjin. As a molecule of interest, karanjin is an antioxidant and also exerts other biological benefits. Karanjin has also been recognized to be used in agricultural and environmental management other than medicinal purposes. **Objectives:** This review aimed to provide a brief information on the chemical and biological properties of karanjin along with its traditional uses. It is also discusses the scientific evidences available for its various biological properties. **Methods:** Various databases such as Google, Google Scholar, Scopus, Web of Science, Pubmed had been searched and the data was obtained. **Results:** The chemistry and reported biological properties of karanjin were highlighted. Karanjin revealed antidiabetic, anticancer, antioxidant, gastroprotective, anti-inflammatory, antibacterial and anti-Alzheimer's activities, and thus has several possible applications in clinical research. **Conclusion:** Therefore, further research may help in exploiting its properties and emergent phytopharmaceuticals based on it.

Key words: *Pongamia pinnata*, Karanjin, Flavonoid, Karanja, Pongam oil tree, Chemistry, Pharmacology.

Aina Akmal Mohd Noor[1,2], Siti Nurul Najiha Othman[1], Pei Teng Lum[1], Shankar Mani[3], Mohd. Farooq Shaikh[4], Mahendran Sekar[1,*]

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Health Sciences, Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh - 30450, Perak, MALAYSIA.
[2]Department of Immunology, School of Medical Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian, MALAYSIA.
[3]Department of Pharmaceutical Chemistry, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, BG Nagara, Nagamangala, Mandya - 571418, Karnataka, INDIA.
[4]Neuropharmacology Research Strength, Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Bandar Sunway 47500, Selangor, MALAYSIA.

Correspondence

Assoc. Prof. Dr. Mahendran Sekar

Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Health Sciences, Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh - 30450, Perak, MALAYSIA.

Phone no: (6016) – 3346653;

Fax: (605) – 2536634;

E-mail: mahendransekar@unikl.edu.my

History

- Submission Date: 20-03-2020;
- Review completed: 06-04-2020;
- Accepted Date: 04-05-2020;

DOI : 10.5530/pj.2020.12.133

Article Available online

http://www.phcogj.com/v12/i4

INTRODUCTION

Pongamia pinnata (Linn.) belongs to the Fabaceae family which contribute to folklore medicine for such a long time to treat various types of human ailments. This plant is commonly known as *Karanja* in Hindi, Bengali, and Sanskit. It is known as malapari in Indonesia, mempari in Malaysia and Karum tree in English.[1] Karanjin is one of the major phytoconstituent of *P. pinnata* and categorized under a furanoflavonol group; a type of flavonoid that obtained extensively from the seeds of Karanja tree. Karanjin belongs to the class of Benzofuran flavonoids since they contain fused benzene and furan ring in their molecular structure.[2] Phytoconstituents of karanjin are mainly contained flavonoids and in fixed inedible oils. Successful biological activities explored are potentially due to the inherent karanjin content in *P. pinnata*.[3] The versatility of the usage of karanjin can also be seen in agriculture purposes such as in biodiesel.[4] Thousands of plants existing in nature are an enormous pool of bioactive molecules that can be established as new derivatives, analogs, chemical entities, and synthetic compounds with natural product derivative pharmacophores or as natural product mimics. The identification of the right chemical entity is the only requirement. This review deals with the chemistry and up-to-date information about the biological properties of karanjin.

METHODS

To complete this review, relevant literature was collected from several scientific databases including Google, Google Scholar, Scopus, Web of Science, and Pubmed. The categories of keywords used for searching are "Karanjin" or "Karanja" or "*Pongamia pinnata*" or "Pongam oil tree" or "Karanjin oil" and "*In-vitro*" or "*In-vivo*" or "Biological studies" or "Pharmacological studies" or "Chemistry" or "Toxicity studies". After the complete screening, the obtained information has been summarized and included in the present review.

CHEMISTRY

Isolation of Karanjin from *P. pinnata* seed oil

Vismaya *et al.*[5] demonstrated the experimental procedure for isolation and purification of karangin from *P. pinnata* seed oil. According to their study, *P. pinnata* seed oil was subjected to liquid-liquid extraction with methanol in the ratio of 1:2 (v/v). Then, the extraction was repeated thrice for a total of 96 h. The separated methanolic extracts were concentrated and subjected to chromatography using methanol as an eluent to obtain pure karanjin. Karanjin (Figure 1) has a molecular formula of $C_{18}H_{12}O_4$, with molecular weight 292.3g/mol.[2] The literature melting point is 161°C. It is soluble in benzene, ether, chloroform, acetone, and alcohol but practically insoluble in petroleum ether.[3]

Cite this article: Noor AAM, Othman SNN, Lum PT, Mani S, Shaikh MF, Sekar M, *et al.* Molecules of Interest – Karanjin – A Review. Pharmacogn J. 2020;12(4):938-45.

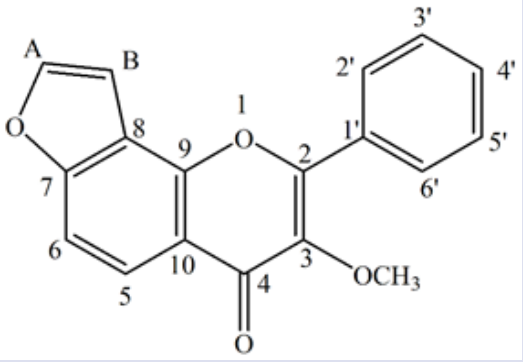


Figure 1: Structure of Karanjin.

IR spectrum (cm^{-1})

2930 (C-H stretching), 2851, 1635, 1625, 1605, 1570, 1525, 1409, 1340 (C-O), 1285, 1225, 1079, 1051, 956, 795.

UV spectrum (nm)

308 nm (ε = 9.7 x 10), 260 nm (ε = 1.61 x 10), 208 nm (ε = 2.21 x 10).

^{1}H NMR spectrum

δ 3.9 (3H, s, OCH_3), 7.14 (1H, d, J=2 Hz, H-A), 7.75 (1H, d, J=2Hz, H-B), 8.20 (1H, d, J=8.5 Hz, H-5), 8.10 (1H, d, J=8.5 Hz, H-6), 7.70 (1H, m, H-2′), 7.49 (1H, m H-3′), 7.1 (1H, m, H-4′), 7.45 (1H, m, H-5′), 7.50 (1H, m, H-6′).

^{13}C NMR spectrum

δ 60.9 (-OCH_3), 109.82 (C-A), 104.09 (C-B), 154.55 (C-2), 157.86 (C-3), 174.48 (C-4), 145.57 (C-5), 146.82 (C-6), 128.20 (C-7), 116.82 (C-8), 149.64 (C-9), 141.58 (C-10), 119.47 (C-1′), 130.73 (C-2′), 128.18 (C-3′), 121.64 (C-4′), 128.48 (C-5′), 130.52 (C-6′).

Mass spectrum

Karanjin does not elude under gas chromatographic conditions used by mass spectrometry. Thus, the spectrum is unable to be recorded.[6]

DISTRIBUTION AND GENERAL DEMEANOUR OF *P. PINNATA*

This mangrove plant (*P. pinnata*), which is the main source of karanjin molecule, is said to originate from India. However, it is known to be native of India, Myanmar, Malaysia, and Indonesia as well. Other tropical parts of the world such as Australia, Polynesia, Philippines, the United States of America, New Zealand and China are also well distributed of such plants. The most preferable area is in the drier part of a country; tidal and beach forest. Moreover, the hills with an elevation of about 1200 meters and the Himalayas up to 610 meters are also likely for this plant to grow.[5] This plant can stand wide ranges of surrounding temperatures up to 27-38 °C and also at a low temperature of 1-16 °C. It can withstand water logging and slight frost hence can be grown at various type of soil from stony to sandy to a clayey type of soils.[6]

MEDICINAL USES OF *P. PINNATA*

Since *P. pinnata* plant is the major known source of karanjin, this molecule may play an important role in terms of medicinal purposes. All parts of this plant have been used in treating different types of diseases and the commonly used parts were bark skin, leaves, flower, seeds, and roots. The bark of the plant is used in various preparations as a treatment for beriberi,[6] bleeding piles, reducing the swelling of the spleen, mental disorder, cough and cold.[7, 8] The leaves are utilized in treating flatulence, dyspepsia, leprosy and gonorrhea.[7, 8] If it is prepared as a medicinal juice, it is claimed to treat cold cough as well as diarrhoea. The flower can also be opted in treating diabetes, some skin ailments, renal diseases, and bleeding piles.[6, 7] Even the seeds of this plant which has a quite pungent smell and bitter taste are said to have carminative and anthelmintic properties.[6] Due to these properties, the prepared seeds of *P. pinnata* can treat inflammation, hemorrhoids and pectoral diseases.[7] The roots of the plant are usually good for teeth cleaning. However, by particular preparations, the roots are useful for cleansing foul ulcers as well as treating skin and vaginal health issues. It is claimed to have gastroprotective activity and antiparasitic property.[6, 8] Having the most significant content of karanjin in these various parts of *P. pinnata* plant is likely to be the factor of having these findings. Several biological properties of karanjin have been summarized in Figure 2.

BIOLOGICAL ACTIVITIES OF KARANJIN

Toxicity profile

Vismaya *et al.*[5] established the toxicity profile of karanjin (20 mg/kg b.w.) which was carried out in rats for 15 days. The results revealed that there is no lethal effect of up to 20 mg/kg b.w. when karanjin was orally fed for 14 days. There is no adverse effect on major organs are observed at the ingested concentrations. After the treatment schedule, the animals remained as healthy as normal control animals with normal food and water intake and body weight gain.

Antidiabetic activity

Mandal and Maity[9], investigated the hypoglycemic activity of karanjin against alloxan-induced diabetic albino rats. The results revealed that the oral administration of karanjin at 2 mg/kg/day for 7 days significantly reduced blood sugar level in alloxan-induced diabetic rats.[9] A study also suggested that the flower of *P. pinnata* containing karanjin is exceptional to alleviate diabetes. In the *in vivo* study of alloxan-induced diabetic rats provided results show that karanjin might help in the reduction of blood glucose level and glucose-6-phosphate activity.[5] On the contrary, increment readings in plasma insulin level and hexokinase activity showed after the end of the experiment were also reported. It was concluded that the antihyperglycemic effect of karanjin with the activity offered by glibenclamide, an antihyperglycemic drug.[10] It shows a successful reduction of blood glucose concentration similarly as compared to drug glibenclamide given to alloxan-induced diabetic rats.[11]

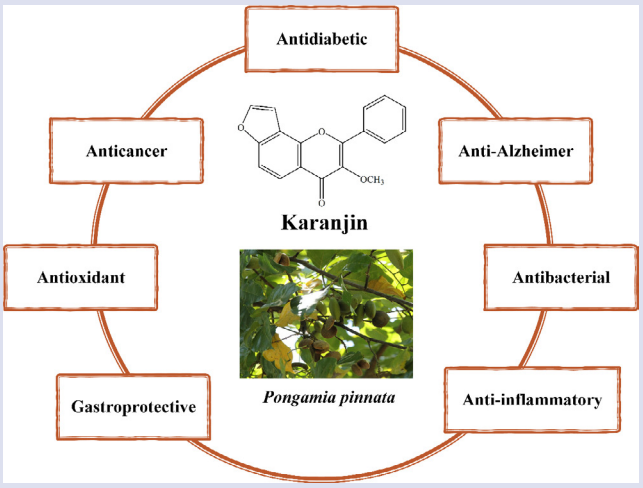


Figure 2: Biological properties of Karanjin.

Another study stated that the karanjin isolated from the fruits of *P. pinnata* portrayed a significant effect in lowering the blood sugar level in streptozotocin-induced-diabetic rats and type 2 diabetic db/db mice and protein tyrosine phosphatase-1B may be the possible target for their activity.[12] Karanjin also enhances the glucose uptake in skeletal muscle L6 myotubes. As a result, the translocation process of GLUT4 to the plasma membrane was delineated due to AMPK pathway activation.[13] The bark extract of *P. pinnata* that contained karanjin was tested on serum glucose levels in diabetic mice as well. It was found that petroleum ether extract of the bark helped in reducing serum glucose levels. However, no bodyweight reduction was observed at the end of the experiment.[14] *P. pinnata* leaves extract been used to test the effectiveness in reducing serum glucose level in alloxan-induced diabetic mice because it contains karanjin. This experiment succeeded as a hyperglycemic level reduced and concurrently with reduced mortality rate caused by the failure of β-cells of islets of Langerhans to function.[15] All the above studies were revealed that the karanjin has potential anti-diabetic properties.

Anticancer activity

Cancer is one of the most frightening diseases worldwide. Most healthcare companies are still trying to find versatile and potent cures to alleviate this burden. Joshi *et al.*[16] investigated the inhibitory effect of karanjin against CYP1A1 which is to facilitate carcinogenesis in oral, lung and epithelial cancers. According to their results, karanjin showed the most potent inhibition of CYP1A1 in human cells. Molecular docking and molecular dynamic simulations with CYP isoforms rationalize the observed trends in potency and selectivity of karanjin. Guo *et al.*[17] studied anticancer effects of karanjin against A549, HepG2 and HL-60 cancer cell lines using cytotoxic assay, cell cycle arrest and induction of apoptosis. According to their results, karanjin can induce cancer cell death through cell cycle arrest and enhance apoptosis. They also suggested that karanjin may be effective clinically for cancer pharmacotherapy.[17]

Moreover, karanjin can decrease reactive oxygen species (ROS) levels in cancer cells. It interferes with I-κB degradation causing inhibition of NF-κB nuclear translocation. Simultaneously, it also induces apoptosis to cancer cells[18], hence its anticancer potentiality. Chemoresistant cancer stem cells may express numbers of ATP binding cassette (ABC) transporters thus, interfering with one is inadequate to treat cancer. In a previous study, karanjin showed stronger effects on ABCB1, ABCC1, and ABCG2, more than one ABC, which were better than other flavonoids. Karanjin worked on ABC transporter-expressing tumor cells produced from three different types of tumor, neuroblastoma, glioblastoma and prostate carcinoma.[19] Thus, a combination of karanjin with anti-cancer drugs may have been useful to enhance the effectiveness of cancer treatment. Hence, it is possible to say that karanjin may play an important role in terms of anticancer activity.

Antioxidant activity

In an earlier study, the antioxidant activity of *P. pinnata* extracts has been done using ABTS and DPPH methods. Among the tested extracts, it was affirmed that the leaf extract showed potent antioxidant activity in both the methods due to the presence of the high amount of flavonoids and karanjin is among one of them.[20] The presence of the antioxidant activity of most of the traditionally used plants is confirmed due to their phenolic and flavonoids contents. After this study, in nitric oxide-scavenging activity, karanjin showed the highest value with 95.60% as compared to ascorbic acid standard with 11.60%.[21] To determine the nitric oxide scavenging ability, a decrease in absorbance induced by antioxidant were measured.[22] Thus, these previous experiments proved that karanjin portrayed a good antioxidant activity that might be beneficial to the human body. To further investigate the findings, the overall determination of antioxidant properties of karanjin using the DPPH method noted that radical scavenging activity was confirmed along with a decrease in absorption peak intensity, thus exhibited a considerable antioxidant activity.[23] In a previous experiment, it was stated that isolated karanjin with polyphenols had shown DPPH scavenging activity and metal ion chelating activity.[24] Furthermore, the ammonium chloride-induced hyperammonemic rats that were administered with *P. pinnata* leaf extract containing karanjin had shown an enhancement in antioxidant levels. The extract works by reverse oxidant-antioxidant imbalance that occurs in rats. However, the exact mechanism that shows this result still needs to be studied in the future.[25] In short, this molecule of interest from the flavonoid group is highly recommended to exploit its antioxidant activity.

Gastroprotective activity

Patel *et al.*[26] investigated the effect of karanjin on mice that were induced with colitis. Treatment with a low dose of karanjin (100 mg/kg) may help to fix tissue necrosis, edema, and inflammation. A high dose of karanjin of 200 mg/kg shows improvement in the histological injury of the mice with colitis and at the same time preserves the normal architecture of the organ. *P. pinnata* methanolic root extract can protect gastric lining against aspirin. As ethanol also might cause damage to gastric mucosa, this extract may help in reducing the value of the lesion index. Thus, the researcher concluded that it could prevent feasible gastric damages due to different inducing factors.[27] Karanjin might heal chronic gastric ulcer caused by various substances such as acetic acid and aspirin if it was given orally for 5 and 10 days. The ability to reduce acid secretion is likely simultaneous with improved mucin secretion and mucosal glycoprotein. At the same time, karanjin administration reduced mucosal cell shedding but did not cause any cell proliferation. Hence, in the former findings, the increment of gastric mucosal lipid peroxidation (LPO), nitric oxide (NO) and superoxide dismutase (SOD) levels were reversed. However, the levels of catalase (CAT) and glutathione (GSH) were significantly increased.[28] Karanjin was also claimed to show its significant ability to shield ulcers from aspirin and 4 hours pylorus ligation. According to the findings of the earlier investigation, the healing of acetic acid-induced gastric ulcers took about 10 days of treatment. The DNA concentration of gastric juice that was due to mucosal damage of gastric had decreased, concurrently exhibiting the gastroprotective ability of karanjin.[29]

Another study had found out that karanjin could alleviate DSS-induced gastric colitis in mice. They found out that consistent karanjin dose administration might change the macroscopic damage, tissue damage, mucosal and submucosal destruction, lower down myeloperoxidase activity and cellular infiltration. The CAT, GSH and SOD levels of tested mice were able to be restored to the normal level.[30] Apart from the study, karanjin could also normalize lipid peroxidation and antioxidant enzyme catalase by interrupting with oxidative stress. Karanjin has been evaluated for an anti-ulcerogenic property by employing adult male albino rats at 10 and 20 mg/kg b.w. Karanjin inhibited 50 and 74% of ulcers induced by the forced swim. H^+, K^+-ATPase activity, which was increased 2-fold in ulcer conditions, was normalized by karanjin in both swim/ethanol stress-induced ulcer models. Karanjin could inhibit oxidative stress as evidenced by the normalization of lipid peroxidation and antioxidant enzyme (i.e., catalase, peroxidase and superoxide dismutase) levels.[5] The above results imply that karanjin can be an effective anti-ulcer agent. Further, being non-toxic, it may also be used in combination with other nutraceuticals for effective management of oxidative stress-induced disease conditions.

Anti-inflammatory activity

The recent study stated that karanjin may be useful for its anti-inflammatory properties. Karanjin can lower down collagen and cartilage malfunction and one of the methods is by reduction of proinflammatory cytokine TNFα that are produced by macrophages

if there is articular inflammation. Besides, it can avoid joint damage and this is proved from arthritis score, radiographic and analysis of histopathology.[31] Karanjin shows immunomodulatory properties by reducing the secretion of inflammatory mediators which is produced by immune cells. However, the anti-inflammatory response that was produced from this compound mostly against bradykinin and PGE1-induced inflammation and only minimum inhibition against histamine and 5-HT-induced inflammation. The modulation of inflammation is mainly to be eicosanoid-events in inflammation.[32] In a later experiment, treatment with karanjin on rats showed inhibition of NO, the potent inflammatory mediator that caused tissue damage and peroxynitrite ($ONOO^-$). The researcher concluded that karanjin might be used as a treatment for intestinal inflammation.[30] Administration of *P. pinnata* leaves extract that contain karanjin by mouth exhibits significant anti-inflammatory properties in acute, subacute and chronic inflamed rats. Positively, karanjin did not produce any sign of gastric injury in the model.[33] Hence, this agent can be used as a treatment for inflammation for different types of inflammatory diseases.

Antibacterial activity

The potential for antibacterial properties for this plant is varied depending on the solvent used during the extraction process of phytoconstituents.[34] For instance, the methanol and ethanol extract of the seed of the tree with a dose of 100 µg/ml have shown definite antibacterial activity on certain pathogens in clinical settings such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Micrococcus luteus*.[35] In an earlier experiment, by Ujwal *et al.*[36] the team investigated the antimicrobial activity against different microorganisms and used different solvent during the extraction process. They stated that the strongest zone of inhibition was observed from the seed of the *P. pinnata* and it might be due to the content of the karanjin. Later, the treatment of karanjin against the bacterial strain of *Staphylococcus aureus* and *Escherichia coli* enterotoxin caused some morphological changes towards the organism. There were shrinking, membrane disruption and break down of the cell wall was observed in the bacterial cells. The researcher concluded that this compound might cause lysis of both organisms due to the significant membrane disruption and interruption of cell wall architectures.[37]

The extract of this compound can fight with tested dental pathogens which are *Staphylococcus aureus*, *Streptococcus mutans*, *Enterococcus faecalis*, *Escherichia coli*, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa* and a yeast, *Candida albicans*. In this test, all of the plates show inhibition against these organisms as compared to the control plate.[38] The efficacy of the antimicrobial activity of this compound is based on its concentration. Therefore, a higher concentration produces a higher zone of inhibition.[39] However, this compound still shows strong broad-spectrum activity against certain bacteria and also certain fungi.[40] Further investigations should be done in regard to these findings although it has been claimed to portray antibacterial property.

Anti-Alzheimer's disease activity

Pongamia pinnata is traditionally used for the treatment of mental problems and also used as a brain tonic in different parts of India.[41] Previous studies on *Pongamia pinnata* showed antistress, neuroprotective and antianxiety activities.[7, 15, 42, 43] Anti-Alzheimer's activity of karanjin was evaluated through elevated plus maze and Morris water maze model on Swiss albino mice by Saini *et al.*[44] Results of this study showed significant ($P<0.01$) anti-Alzheimer's activity of karanjin (25 and 50 mg/kg) and demonstrated improvement in learning, memory and inhibited the symptoms of diazepam induced memory loss in experimental animals. The findings of this study suggested that karanjin may be useful in the treatment of the patients suffering from Alzheimer's disease and memory-related disorders.

INDUSTRIAL USES OF KARANJIN

Pesticides

Karanjin is used in agricultural practices for its pesticidal, insecticidal and acaricidal activities. Raghav *et al.*[45] provide insights for understanding the binding interactions of karanjin with bovine serum albumin (BSA) and its possible toxicological effects on mammalian cell lines and bacteria. The results of this study indicated that karanjin had a very mild inhibitory effect on the growth of microorganisms and that the exposure to karanjin might not affect the useful microbes present in the environment. Karanjin had caused an effect on the growth of larvae of *Tribolium castaneum* (Hbst.) and juvenile hormone. The larvae could not develop into bugs as the inhibition took at the larval and pupal stages of the organism. Different concentrations of this active ingredient produced a different time of inhibition in this experiment.[46]

Mathur *et al.*[47] had done an experiment of karanjin against the larva of flesh fly. The increment in karanjin concentration (2000 - 3500 ppm) causing an increase in the mortality rate of the larva. As for lower concentration (1000 – 2000 ppm), deformed pupal-adult intermediates were observed. In another study, Verma *et al.*[48] had proved the ability of karanjin against termites. In the study, the researcher used a model named *Odontotermes obesus* and karanjin was introduced in a form of oil that was inedible. The 100% mortality rate was achieved after 6 hours of karanjin exposure on the termites. According to Dang *et al.*[49], insecticide activity of karanjin was observed as it halted the effect of ecdysteroids thus, acting as an insect growth regulator (IGR) and antifeedant. Apart from that, karanjin interrupted with cytochrome P-450 in certain insects and mites, disrupting bodily function. The study of multiple plant compounds against *Helicoverpa armigera* (Hub.) showed that karanjin inhibited the growth of this insect. However, this compound was not effective in reducing the fruit damage which caused no change in crop yield as compared to other plant compounds.[50] All these findings demonstrated that karanjin can be used as a potent pesticide.

Nutrition for farm animals

Previously in studying nutrition regarding this molecule, karanjin was included in a cake ingredient to make a karanj cake. Solvent extracted karanj cake did not cause any digestion problem to lambs, however, the lambs which were fed with 50% expeller pressed karanj cake showed the lower percent of digestibility of dry matter, organic matter, crude protein, total carbohydrate, neutral detergent fiber and acid detergent fiber. Hence, solvent extracted karanj cake could be given to the lambs without causing any harm for 98 days but not for expeller-pressed karanj cake as it might disrupt nutrient intake and digestibility.[51]

In other studies, the researcher found out that the usage of detoxified karanja cake for farm animals could be added as a replacement of soybean meal, but only at low levels as the higher level of replacement might cause danger. Findings suggested that there was no interruption at total protein levels, including enzymes.[52] In an experiment conducted by Soren *et al.*[53], the lambs that were given with damage-causing extract cake that was washed by water did not show any adverse effects. After the experiment was done for 196 days, several organs were collected to see the function. It showed normal activities in serum enzymes, no damage features of tissues in the liver, intestine, parathyroid gland and testis. There was no rupture or lesion in the organ. Karanjin infused in the ingredient of the cake as nutrition for the farm animal is an excellent alternative in regards to its quality attributed.

Biodiesel

Significant improvement in the performance of the engine and exhaust emission had been shown when using a lower blend of karanja oil

when it was used preheating or without preheating the machines. When karanja oil blended with diesel for up to 50% v/v could be used for diesel replacement with the improved performance of the engine.[54] Moreover, the investigation using methyl and ethyl esters of Karanja oil was done by Baiju *et al.*[55] Overall, both of these fuels can be used without any adjustment made to the engine. The differences were just in the form of viscosity and cold flow properties. The viscosity and cold flow properties of ethyl esters karanjin fuel were higher and much better than methyl esters karanjin fuel. However, both fuels still could be used as alternative diesel fuels in the future.

Besides, the emission of carbon monoxide gas and hydrocarbon produced from biodiesel made from this compound was lower than diesel fuel.[56] Verma *et al.*[57] had produced Karanja biodiesel fuel with a different type of alcohol as a solvent. In the analysis, all the biodiesel produced from different alcohols meets the Indian Standard 15607. The most reliable fuel was Karanja Oil Pentyl Ester (KOPnE) as it had cold flow properties and higher viscosity as compared to other biodiesel produced. Thus, this compound might be potential to be used as commercial as there are plenty of articles stated the advantages and methods in yielding karanjin biofuel on the internet.

Other activities

Perumalsamy *et al.*[58] were demonstrated that the karanjin may be used to control the mosquito populations. Further, the study showed that karanjin was produced potent toxicity towards *Culex pipiens pallens, Aedes aegypti,* and *Aedes albopictus* larvae. Molecular docking studies of karanjin was carried out with the receptors responsible for psoriasis (IL-17A, IL-17F, IL-23, RORγt, and TLR-7). The docking score result of karanjin was well comparable with Methotrexate, a known drug used for treating Psoriasis. Overall, the results suggested that Karanjin could be used as a natural and better alternative in curing psoriasis without any side effects.[18]

Pharmacokinetic and bioavailability of karanjin

Due to the limited research focus on the pharmacokinetic characteristics of karanjin, a complete overview of the absorption, distribution, metabolism and excretion profiles of karanjin is still relatively lacking. To date, there have been only one report on pharmacokinetic studies of karanjin in rats. Shejawal *et al.*[59] investigated pharmacokinetics of karanjin in experimental animals by RP-HPLC method and the parameters were analyzed using non compartmental model. The absorption of karanjin was rapid in animals with Tmax of 2.307 ± 0.11 h and $t_{1/2}$ value of 3.78 ± 0.30 h. Further, the pharmacokinetic results designated that the karanjin has been eliminated from systemic circulation at 24 h. Findings of this study recommended that the results would be valid for the future study on karanjin for its different therapeutic uses and also beneficial for justifying the dosage and route of administration from its formulations.

CONCLUSION

To date, karanjin can only be isolated from various parts of *P. pinnata* plant. However, it would be superb if this molecule can be explored from other plants as well. Previous excelled findings in regards to *P. pinnata* is possible due to existing inherent karanjin which may act as a good catalyst in amplifying the pharmacological effect. Although karanjin is initially recognized as an antioxidant, several kinds of research have proven that it is truly multifaceted in other industries as well. This precious molecule requires further understanding to fully capture its mechanism in many terms and benefits. Hence, this review has provided a comprehensive view concerning the initial ideas of the medicinal and agricultural purposes of karanjin. Additional investigations may, therefore, help in exploiting its properties and emerging phytopharmaceuticals based on it. Soon, more mechanistic oriented basic research is needed to illuminate the mechanisms of actions. Karanjin with highly interesting biological effects is worth to be studied more carefully considering the folklore uses of the plants possessing this active ingredient.

CONFLICTS OF INTEREST

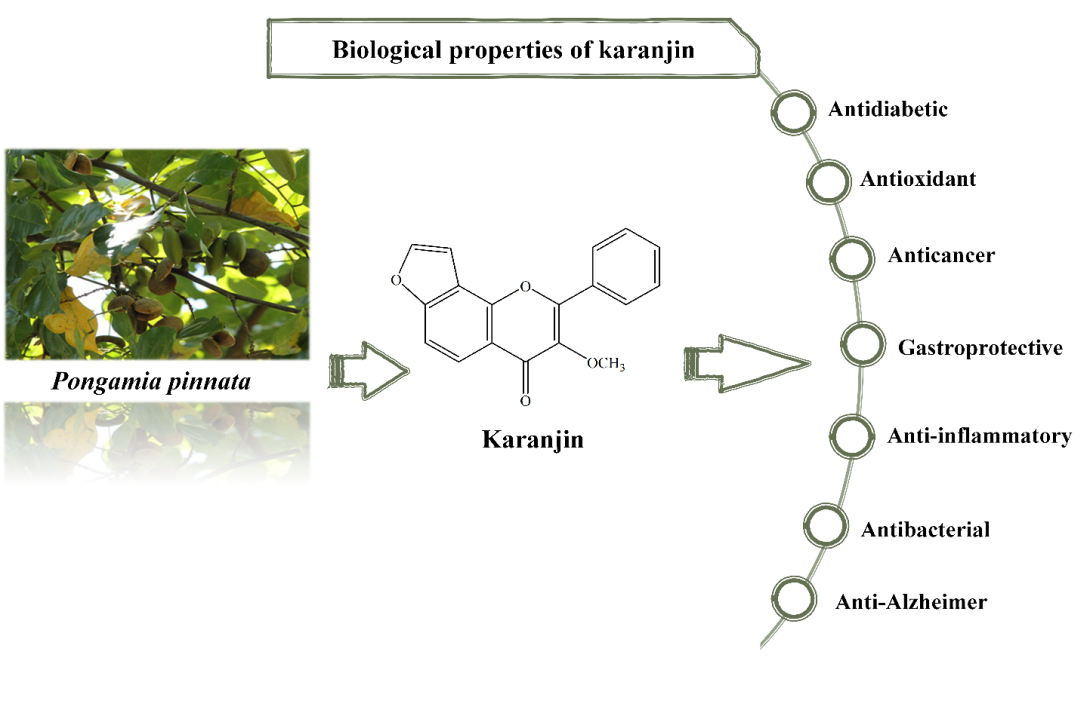
Authors declared that there is no competing interests exist.

REFERENCES

1. Csurhes S, Hankamer C. Weed Risk Assessment: Pongamia: The State of Queensland. Australia: Department of Empolyment, Economic Development and Innovation, 2010;1-16.
2. KV Naturals. Karanjin: KV Natural Ingredients Pvt Ltd. India. http://kvnaturals.com/karanjin.html
3. Arote S, Yeole P. *Pongamia pinnata* L: a comprehensive review. International Journal of PharmTech Research. 2010;2:2283-90.
4. Pandey A, Nivedika G, Pankaj B, Sharma D. Evaluation of *Pongamia pinnata* (L.) Pierre. progenies for their growth performance in Madhya Pradesh, India. World Applied Sciences Journal. 2010;10:225-33.
5. Vismaya, Eipesona WS, Manjunathab JR, Srinivasb P, Kanyaa TCS. Extraction and recovery of karanjin: A value addition to karanja (*Pongamia pinnata*) seed oil. Industrial Crops and Products. 2010;32:118-22.
6. Dhanmane SK, Salih FA. Isolation of Karanjin from *Pongamia pinnata* and its identification by different analytical techniques. Kurdistan Journal of Applied Research. 2018:156-60.
7. Sangwan S, Rao D, Sharma R. A review on *Pongamia pinnata* (L.) Pierre: A great versatile leguminous plant. Nature and Science. 2010;8:130-9.
8. Pulipati S, Babu PS, Lakshmi DN, Navyasri N, Harshini Y, Vyshnavi J, *et al.* A phyto pharmacological review on a versatile medicinal plant: *Pongamia pinnata* (L.) pierre. Journal of Pharmacognosy and Phytochemistry. 2018;7:459-63.
9. Mandal B, Maity CR. Hypoglycemic action of karanjin. Acta Physiologica et Pharmacologica Bulgarica. 1986;12(4):42-6.
10. Punitha R, Manoharan S. Antihyperglycemic and antilipidperoxidative effects of *Pongamia pinnata* (Linn.) Pierre flowers in alloxan induced diabetic rats. Journal of Ethnopharmacology. 2006;105:39-46.
11. Punitha R, Vasudevan K, Manoharan S. Effect of *Pongamia pinnata* flowers on blood glucose and oxidative stress in alloxan induced diabetic rats. Indian Journal of Pharmacology. 2006;38:62-3.
12. Tamrakar AK, Yadav PP, Tiwari P, Maurya R, Srivastava AK. Identification of pongamol and karanjin as lead compounds with antihyperglycemic activity from *Pongamia pinnata* fruits. Journal of Ethnopharmacology. 2008;118:435-9.
13. Jaiswal N, Yadav PP, Maurya R, Srivastava AK, Tamrakar AK. Karanjin from *Pongamia pinnata* induces GLUT4 translocation in skeletal muscle cells in a phosphatidylinositol-3-kinase-independent manner. European Journal of Pharmacology. 2011;670:22-8.
14. Badole SL, Bodhankar SL. Investigation of antihyperglycaemic activity of aqueous and petroleum ether extract of stem bark of *Pongamia pinnata* on serum glucose level in diabetic mice. Journal of Ethnopharmacology. 2009;123:115-20.
15. Sikarwar MS, Patil M. Antidiabetic activity of *Pongamia pinnata* leaf extracts in alloxan-induced diabetic rats. International Journal of Ayurveda Research. 2010;1:199-204.
16. Joshi P, Sonawane VR, Williams IS, McCann GJP, Gatchie L, Sharma R, *et al.* Identification of karanjin isolated from the Indian beech tree as a potent CYP1 enzyme inhibitor with cellular efficacy *via* screening of a natural product repository. Medchemcomm. 2018;9(2):371-82.
17. Guo JR, Chen QQ, Lam CWK, Zhang W. Effects of karanjin on cell cycle arrest and apoptosis in human A549, HepG2 and HL-60 cancer cells. Biological Research. 2015;48:40.
18. Roy R, Pal D, Sur S, Mandal S, Saha P, Panda CK. Pongapin and Karanjin, furanoflavanoids of *Pongamia pinnata*, induce G2/M arrest and apoptosis in cervical cancer cells by differential reactive oxygen species modulation, DNA damage, and nuclear factor kappa - light - chain - enhancer of activated B cell signaling. Phytotherapy Research. 2019;33:1084-94.
19. Michaelis M, Rothweiler F, Nerreter T, Sharifi M, Ghafourian T, Cinatl Jr J. Karanjin interferes with ABCB1, ABCC1, and ABCG2. Journal of Pharmacy and Pharmaceutical Sciences. 2014;17:92-105.
20. Hazra B, Sarkar R, Biswas S, Mandal N. Antioxidant and iron chelating potential of Pongammia pinnata and its role in preventing free radical induced oxidative damage in plasmid DNA. International Journal of Phytomedicine. 2011;3:240-53.
21. Ghosh A, Tiwari GJ. Role of nitric oxide-scavenging activity of Karanjin and Pongapin in the treatment of Psoriasis. Biotechnology. 2018;8:338.

22. Parul R, Kundu SK, Saha P. *In vitro* nitric oxide scavenging activity of methanol extracts of three Bangladeshi medicinal plants. The Pharma Innovation. 2013;1:83-8.
23. Arshad N, Rashid N, Absar S, Abbasi M, Saleem S, Mirza B. UV-absorption studies of interaction of karanjin and karanjachromene with ds. DNA: Evaluation of binding and antioxidant activity. Open Chemistry. 2013;11:2040-7.
24. Supreeth Shankar K. Phenolics and furano-flavonoids from karanja (*Pongamia pinnata*) seed oil and their Antioxidant Activities. ePrints@CFTRI, 2010; http://ir.cftri.com/9540/
25. Mohamed Essa M, Subramanian P. *Pongamia pinnata* modulates the oxidant–antioxidant imbalance in ammonium chloride-induced hyperammonemic rats. Fundamental & Clinical Pharmacology. 2006;20:299-303.
26. Patel PP, Trivedi ND. Effect of karanjin on 2, 4, 6-trinitrobenzenesulfonic acid-induced colitis in Balb/c mice. Indian Journal of Pharmacology. 2017;49:161-7.
27. Prakash P, Prasad K, Nitin M, Sreenivasa R. Anti-ulcer and anti-secretory properties of the *Pongamia pinnata* root extract with relation to antioxidant studies. Research Journal of Pharmaceutical Biological and Chemical Sciences. 2010;1:235-44.
28. Prabha T, Dorababu M, Goel S, Agarwal P, Singh A, Joshi V, *et al*. Effect of methanolic extract of *Pongamia pinnata* Linn seed on gastro-duodenal ulceration and mucosal offensive and defensive factors in rats. Indian Journal of Experimental Biology. 2009;47:649-59.
29. Prabha T, Babu MD, Priyambada S, Agrawal V, Goel R. Evaluation of *Pongamia pinnata* root extract on gastric ulcers and mucosal offensive and defensive factors in rats. Indian Journal of Experimental Biology 2003;41:304-10.
30. Patel PP, Trivedi ND. Karanjin ameliorates DSS induced colitis in C57BL/6 mice. International Journal of PharmTech Research. 2012;6:4866-74.
31. Bose M, Chakraborty M, Bhattacharya S, Mukherjee D, Mandal S, Mishra R. Prevention of arthritis markers in experimental animal and inflammation signalling in macrophage by karanjin isolated from *Pongamia pinnata* seed extract. Phytotherapy Research. 2014;28:1188-95.
32. Singh R, Pandey B. Anti-inflammatory activity of seed extracts of Ponamia pinnata in rat. Indian Journal of Physiology and Pharmacology. 1996;40:355-8.
33. Srinivasan K, Muruganandan S, Lal J, Chandra S, Tandan S, Prakash VR. Evaluation of anti-inflammatory activity of *Pongamia pinnata* leaves in rats. Journal of Ethnopharmacology. 2001;78:151-7.
34. Gahlaut A, Chhillar AK. Evaluation of antibacterial potential of plant extracts using resazurin based microtiter dilution assay. International Journal of Pharmacy and Pharmaceutical Sciences. 2013;5:372-6.
35. Rani MS, Dayanand C, Shetty J, Vegi PK, Kutty AM. Evaluation of antibacterial activity of *Pongamia Pinnata* linn on pathogens of clinical isolates. American Journal of Phytomedicine and Clinical Therapeutics. 2013;1:645-51.
36. Ujwal P, Kumar M, Naika HR, Hosetti B. Antimicrobial activity of different extracts of *Pongamia pinnata*. Medicinal and Aromatic Plant Science and Biotechnology 2007;1:285-7.
37. Singh A, Jahan I, Sharma M, Rangan L, Khare A, Panda AN. Structural Characterization, In Silico studies and *in vitro* antibacterial evaluation of a furanoflavonoid from Karanj. Planta Medica Letters. 2016;3:e91-5.
38. Pulipati S, Babu PS, Sampath R, Sree NB. Antimicrobial efficacy of *Pongamia pinnata* (L) pierre against dental caries pathogens of clinical origin. Indo American Journal of Pharmaceutical Sciences. 2016;3:546-51.
39. Kesari V, Das A, Rangan L. Physico-chemical characterization and antimicrobial activity from seed oil of *Pongamia pinnata*, a potential biofuel crop. Biomass and Bioenergy. 2010;34:108-15.
40. Badole SL, Bodhankar SL, Raut CG. Protective effect of cycloart-23-ene-3 β, 25-diol (B2) isolated from *Pongamia pinnata* L. Pierre on vital organs in streptozotocin-nicotinamide induced diabetic mice. Asian Pacific Journal of Tropical Biomedicine. 2011;1:S186-90.
41. Badole SL, Patil KY. *Pongamia pinnata* (Linn.) Pierre and inflammation. Polyphenols in Human Health and Disease: Elsevier, 1st Edn, pp1-1488;2014.
42. Manigauha A, Patel S, Monga J, Ali H. Evaluation of anticonvulsant activity of *Pongamia pinnata* Linn in experimental animals. International Journal of PharmTech Research. 2009;4:1119-21.
43. Tiwari SK, Pandey YK. Ayurvedic drugs in prevention and management of age related cognitive decline: a review. Int J Pharm Sci Drug Res. 2012;4:183-90.
44. Saini P, Lakshmayya L, Bisht VS. Anti-alzheimer activity of isolated karanjin from *Pongamia pinnata* (L.) pierre and embelin from *Embelia ribes* Burm. f. Ayu. 2017;38:76-81.
45. Raghav D, Mahanty S, Rathinasamy K. Biochemical and toxicological investigation of karanjin, a bio-pesticide isolated from Pongamia seed oil. Pesticide Biochemistry and Physiology. 2019;157:108-21.
46. Rao A, Niranjan B. Juvenile-hormone-like activity of'karanjin against larvae of red flour beetle Tribolium castaneum H. Comparative Physiology and Ecology. 1982;7:234-6.
47. Mathur Y, Srivastava J, Nigam S, Banerji R. Juvenomimetic effects of karanjin on the larval development of flesh fly, *Sarcophaga ruficornis* Fabr. (Cyclorrhapha: Diptera). Journal of Entomological Research. 1990;14:44-51.
48. Verma M, Pradhan S, Sharma S, Naik S, Prasad R. Efficacy of karanjin and phorbol ester fraction against termites (*Odontotermes obesus*). International Biodeterioration & Biodegradation. 2011;65:877-82.
49. Dang QL, Lim CH, Kim JC. Current status of botanical pesticides for crop protection. Research in Plant Disease. 2012;18:175-85.
50. Sarkar S, Patra S, Samanta A. Evaluation of bio-pesticides against red cotton bug and fruit borer of okra. Evaluation. 2015;10:601-4.
51. Ravi U, Singh P, Garg A, Agrawal D. Performance of lambs fed expeller pressed and solvent extracted karanj (*Pongamia pinnata*) oil cake. Animal Feed Science and Technology. 2000;88:121-8.
52. Rao S, Kumar DD. Effect of substitution of soybean meal by detoxified karanja cake on diet digestibility, growth, carcass and meat traits of sheep. Small Ruminant Research. 2015;126:26-33.
53. Soren NM, Sharma AK, Sastry VR. Biochemical and histopathological changes in sheep fed different detoxified karanj (*Pongamia glabra*) seed cake as partial protein supplements. Animal Nutrition. 2017;3:164-70.
54. Agarwal AK, Rajamanoharan K. Experimental investigations of performance and emissions of Karanja oil and its blends in a single cylinder agricultural diesel engine. Applied Energy. 2009;86:106-12.
55. Baiju B, Naik M, Das L. A comparative evaluation of compression ignition engine characteristics using methyl and ethyl esters of Karanja oil. Renewable Energy. 2009;34:1616-21.
56. Dwivedi G, Sharma M. Prospects of biodiesel from Pongamia in India. Renewable and Sustainable Energy Reviews. 2014;32:114-22.
57. Verma P, Sharma M, Dwivedi G. Prospects of bio-based alcohols for Karanja biodiesel production: An optimisation study by Response Surface Methodology. Fuel. 2016;183:185-94.
58. Perumalsamy H, Jang MJ, Kim J, Kadarkarai M, Ahn Y. Larvicidal activity and possible mode of action of four flavonoids and two fatty acids identified in *Millettia pinnata* seed toward three mosquito species. Parasites & Vectors. 2015;8:237.
59. Shejawal N, Menon S, Shailajan S. Bioavailability of karanjin from *Pongamia pinnata* L. in Sprague dawley rats using validated RP-HPLC method. Journal of Applied Pharmaceutical Science. 2014;4(03):10-4.

GRAPHICAL ABSTRACT



ABOUT AUTHORS

Mahendran Sekar is currently working as Associate Professor in Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Health Sciences, Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh, Perak, Malaysia. His research is mainly in the field of drug discovery and development of natural products. His research interest is isolation of active constituents from medicinal plants and study about its biological properties.

Aina Akmal Mohd Noor worked as research assistant at Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh, Perak, Malaysia. She is currently pursuing Ph.D in Medical Immunology in School of Medical Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian, Malaysia. Her research interest is mapping the immune cells in an immune-mediated inflammatory disease.

Siti Nurul Najiha Othman pursuing Master of Pharmacy (By Research) at Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh, Perak, Malaysia. Her research interest is isolation of active constituents from medicinal plants and study about its biological properties.

Pei Teng Lum is currently pursuing Ph.D in Pharmacy at Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh, Perak, Malaysia. Her research interest is isolation of active constituents from medicinal plants and study about its effect on neurodegenerative disorders.

Shankar Mani is currently working as Associate Professor in Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, Karnataka, India. His research interest is mainly in synthesis of medicinally important compounds and study about its biological properties. He also interest in the research of drug discovery and development of natural products.

Mohd. Farooq Shaikh is currently working as a Senior Lecturer and leader of Neuropharmacology Research Strength at Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Selangor, Malaysia. He is a trained pharmacologist with special interest in neurosciences. His personal interest is experimental epilepsy and the discovery of anti-epileptic drugs from diverse sources including medicinal plants. Currently, his team is working on epilepsy and Alzheimer's disease-related cognitive dysfunctions.

Cite this article: Noor AAM, Othman SNN, Lum PT, Mani S, Shaikh MF, Sekar M, *et al.* Molecules of Interest – Karanjin – A Review. Pharmacogn J. 2020;12(4):938-45.