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RESEARCH ARTICLE

ADVANCES OF PHARMACOLOGICAL ACTIVITIES OF THE PLANT *Cajanus cajan* L. (FABACEAE): A REVIEW

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ABSTRACT

The perennial legume *Cajanus cajan (L),* also known as the Bengali Tur, Hindi Arhar, English Pigeon Pea, and Sanskrit Adhaki, is widely grown around the world in tropical and semitropical climates. Red gram is mostly produced and consumed in India. It has a high quantity of proteins and essential amino acids including methionine, lysine, and tryptophan and is both a food crop and a cover/probe crop. It has been conventionally used in various medicinal practices for the treatment of different pabulum. The plant has been traditionally used to treat a range of ailments, including cough, fever, diarrhea and skin infections. Modern research has also shown that pigeon pea may have potential in the treatment of diabetes, hypertension, and cancer. These are attributed to its various phytochemical ingredients similar as alkaloids, tannins, flavonoids etc. In addition to general information, this review paper provides an account of the pharmacological effects, clinical trials, and biological conditioning of each part of the plant *Cajanus cajan*.

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INTRODUCTION

The Sumerian civilization left behind the earliest historical accounts of herbs. Plants have been used by humans for therapeutic purposes throughout history and are still the basis for many medications that are currently in use (Pal *et al*., 2011). In order to protect themselves from environmental stress, plants develop an endless array of secondary metabolites. The diverse secondary metabolites that plants produce have long been used therapeutically in medicine (Pal *et al*., 2007). Many plant-derived phytochemicals, many of which are still in use today even though they were first described in the early history of modern medicine, served as the foundation for many medications that are still in use today (Mohammed *et al*., 2009). *It belongs to the perennial Fabaceae family.* The seeds are rich in protein, fiber, and various minerals and are used in variety of dishes including soups, stews, curries and salads (Pal *et al*., 2005). It is extensively farmed for its edible seeds, which are used in a variety of culinary applications, throughout tropical and subtropical areas of the world. Arhar has been grown for at least three thousand years (Pal *et al*., 2006). Most likely, it originated in Asia, went to East Africa, and then was traded to the American continent as slaves. Pigeon pea is highly adaptable to different growing conditions and is a popular crop in low- input husbandry systems, and is relatively drought tolerant and can fix atmospheric nitrogen, thereby improving soil fertility. It is branched, hairy shrub, 1-2 meters high.

It is also used as livestock feed and as a soil-improving crop due to its ability to fix nitrogen in the soil. India is a major producer of pigeon peas, accounting for roughly 90% of global output. Currently, it covers 3.86 million hectares and produces 2.67 million tons annually (Kumar *et al*., 2010). It is frequently consumed as a dal. Its leaves are raised silkworms in India, and some cultures also eat the leaves and young shoots as vegetables. Amongst its many medicinal uses, *in traditional Chinese medicine, C. cajan* is recommended for pain alleviation (Ahsan and Islam, 2009). It has also been investigated in more recent years as a potential therapy for bedsores, wound healing, and aphtha. Chemical investigations have found the two globulins cajanin and concajanin (Ambasta, 2004). It has been used to treat a range of ailments, including cough, fever, diarrhea and skin infections, stabilizing menstrual period. The goal of the current review article is to draw researchers' attention to the unknown and unstudied areas of *C. cajan.*

Scientific classification

Kingdom: Plantae
Class: Magnoliopsida
Order: Fabales
Family: Fabaceae
Genus: Cajanus
Species: *cajan* (L.) Huth.

Botanical description: There are only a few types of pigeon pea, which are also referred to as Congo pea, no eye pea, dhal, red

gramme, gungo pea, gandul, gandure, frijol de árbol, and pois cajan, among others. Older cultivars and semi-cultivars are short-lived, semi-deciduous shrubs with a base stem diameter that varies from 1 to 4 cm in the West Indies. They typically have a single stem, are freely branching, and after a few months, turn woody. These woods may be more brittle and hard. They have nodulated fine roots, lateral roots, and deep roots that can reach depths of up to 3 meters. The sparsely spaced, trifoliate leaves contain narrowly elliptic, lanceolate, or oblong leaflets that are 2.5 to 9 cm long, with the center leaflet being somewhat longer than the laterals. The branches and tiny twigs support the sparse yellowish-green foliage. Axial racemes range in size from five to twelve blooms. Outside, 2 cm long, yellow flowers are typical, with orange to purple blossoms becoming more prevalent. The 4 to 8 cm long, mottled bronze-purple legumes are flattened and constricted between the seeds. As they develop, they turn brown. The leaves of the plant are green and compound with three leaflets. It is bright yellow five petaled flower with a red center. The flowers bloom in clusters and are typically found at the ends of the branches. The fruit of the *cajanus* plant is a pod that is oblong in shape and can be up to 10 cm in length. The seeds are small, round can be various colors including white, brown and black.

Geographical source: It has been grown in ancient Egypt, Africa, and Asia from the beginning of time. America eventually received it. It now adapts in a number of tropical nations. India is the main producer, accounting for 90% of global output. Its altitude ranges from 0-3000 m in India and Columbia to 1250 m in Hawaii. Although it has a wide range of adaptability, it is mostly a plant of the semi-dry lowlands (Duke, 2004).

Cultivation: The ideal seed beds for *C. cajan* are those that have been deeply excavated and carefully tended to keep weeds at bay. Pigeon peas can either be a perennial kind with a harvest that can last three to five years (although the seed yield dramatically drops after the first two years) or they can be an annual variation better suited for seed production. It responds typically to phosphorus and requires enough calcium, potash, and magnesium.

To enable mechanized harvesting and inter-row cultivation, it is sown in rows. It is usually intercropped with sesame in India, maize in Malawi, and forage grasses in Hawaii. It can be sown in holes spaced about 2 meters apart. The performance of the seedling is greatly enhanced by weed management during the first two months of growth (Morton, 1976).

Pharmacological activities and active constituents of *C. cajan body parts*

- **Leaf**: Chloroform-extract leaf part of *Cajanus cajan* shows antibacterial activity. The active chemical constituent is Cajanus lactone (coumarin). Ethanol-extract leaf part shows hypocholesterolemic activity. Its active chemical constituents are cajanin, longistylin C, longistylin A. Some ethanol-extract leaf part shows ant plasmodial activity and its active chemical constituents are betulinic acid, longistylin C, longistylin A. Pinostrobin, chemical constituent shows anti-inflammatory and neuroactive activity. Cajaninstilbene acid, orientin, vitexin constituents shows antioxidant activity. Cajaninstilbene acid, vitexin and pinostrobinshows antimicrobial activity. Methanol-extract and hydroalcohol-extract leaf aerial parts shows hepatoprotective and anthelmintic activity and chemical constituents are protein fraction Cl-1, phenolics (flavonoids, tannins).

- **Root**: Ethanol-extract root part shows antiplasmodial activity and the active constituents are betulinic acid, longistylin C, longistylin A. Ethanol-water (70:30 v/v) extract root part shows antioxidant activity and the active constituents are genstein, genistin. Ethanol extract root shows anticancer activity; active constituent is cajanoliso flavonoids.

Ethnopharmacological importance: *C. cajan* has long been utilized as a significant treatment for a number of ailments as a feed crop. It is used by the Garo, a tribal group in Bangladesh, to cure diabetes and as an energy booster (Pal *et al*., 2011). In Trinidad and Tobago, *C. cajan* leaves are used to cure constipation, colic, and food poisoning (Lans, 2007). Pigeon pea leaves are used in Chinese folk medicine to stop bleeding, as an anesthetic, and to remove parasites. The leaf, seeds, and young stems are used as a toothbrush, a remedy for gingivitis, and to treat stomatitis in various regions of Tamil Nadu, India (Ganeshan, 2008). It is a significant folk remedy in the eastern portion of Rajasthan, where fresh juice and boiling leaves are taken orally to relieve constipation and counteract the effects of intoxication. Inflammations and ulcers of the mouth are treated with leaf paste. To encourage breastfeeding, leaves and seeds are put to the breast as a poultice (Upadhyay *et al*., 2010).

Pharmacological action: Since the beginning of time, many sections of *C. cajan* have been used for their biological functions, and some of them have experimental support. There are several reports on the pharmacological activities of *C. cajan* based on contemporary scientific investigations, in addition to their usage in traditional remedies.

Pharmacological activity of leaf part of *Cajanus cajan:*

Antimicrobial Activity: The *Cajanus cajan* extracts shown potential action against eight pathogenic species, including *Candida albicans, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, Proteus vulgaris,* and *Staphylococcus epidermidis*. The SFE extracts of *Cajanus cajan* have a significant inhibitory impact on *S. epidermidis. B. subtilis* and *S. aureus*. The antibacterial action was shown in mice that had been infected with *S. aureus* in vivo, and histopathology was used to determine the exact mechanism by which the plant extract combats these pathogens (Yuan-gang *et al*., 2010). The ethanol and supercritical fluid extraction extracts of *Cajanus cajan* were assessed for their antibacterial activities. The plant extracts had substantial antibacterial effects both in vivo and in vitro, indicating that they might be effective against MRSA and *S. aureus.* Qi *et al*., 2014 conducted a study in which, the essential oil obtained through hydro distillation and solvent-free microwave extraction has demonstrated excellent activity against *B. subtilis* and *P. acnes*, as well as gram positive and gram negative bacteria (Qi *et al*., 2014).

Antibacterial Activity: New natural coumarins were isolated through the bioassay-guided fractionation of chloroform using extracts from *C. cajan* leaves: cajanuslactone and two phytoalexins: cajaninstilbene acid and pinostrobin. Cajanuslactone was found to have a high level of activity against the bacteria *S. aureus.* Test results indicated that the extract of pigeon pea leaves could successfully stop the growth of the pathogen *Salmonella typhi*. These extracts have been shown to be effective against some pathogenic bacteria. The gram (-ve) bacteria *Salmonella typhi* is responsible for the infectious disease typhoid, which is prevalent in many developing nations. There are two main groups of *C. cajan's* major components: Stillbene, flavonoids, and an extract of this plant may be able to effectively stop *S. typhi, S. aureus,* and *E. coli* from growing (Kong *et al*., 2010).

Antidiabetic Effects: Alloxan-induced diabetic rats and oral glucose-loaded rats were used to investigate the methanolic extract of *C. cajan* leaf extract's antidiabetic properties. The extract's phytochemical analysis and acute toxicity and lethality (LD_{50}) were also evaluated (Pal, 2008). According to the findings, alloxan diabetic rats' fasting blood sugar was significantly reduced by the extract in a dose-dependent manner, with the maximum hypoglycemic effect occurring after four to six hours (Ezike *et al*., 2010).

Hypocholesterolemic Effects: Stilbenes-containing extract-fraction from *C. cajan* (SECC) was discovered to have an impact on diet-induced hypercholesterolemia in Kunming mice. Mice's dietary cholesterol's atherogenic properties were reduced by the SECC. Hepatic low density lipoprotein-receptor and cholesterol-7-alpha-hydroxilase expression levels as well as bile acid synthesis may

increase as a result of its hypocholesteromic effects. Petroleum ether, chloroform, and methanol were separated from *C. cajan* seed extract for research. When compared to the control, Swiss Albino mice induced by streptozotocin had significantly lower lipid profiles when the methanol fraction was present. The extract was then subjected to chromatographic examination, and a substance named CCA1 was discovered that, for the first time, had pronounced hypolipidemic activity. The *C. cajan* diet has reduced cholesterol levels in hypercholesterolemic hamsters at doses between 200 and 800 g/kg feed by converting cholesterol to bile acids, increasing CPT-1, LDL receptor, cholesterol-7-alpha hydroxylase, antioxidant enzymes, and further increasing lipid peroxidation. It has been demonstrated that feeding male Sprague Dawley rats *C. cajan* drinks at doses comparable to human consumption - 30 grammes daily reduces total cholesterol levels by 19.78 percent in diabetic-hypercholesterolemic rats.

Glycemic activity: Streptozocin-induced Type 2 diabetic rats were used to test the aqueous extract of *C. cajan* leaves to see how it affected blood sugar levels. Normal rats' fasting blood glucose levels significantly increased with this extract. Based on previous reports of *C. cajan* seeds' hypoglycemic activity, the study of the leaves was considered. However, the observed results were exactly the opposite, suggesting that it may be useful for managing hypoglycemia, brought on by an overdose of insulin or other hypoglycemic medications (Jaiswal *et al*., 2008).

Neuroactive properties: Pinostrobin, a flavanone replacement from *C. cajan,* was evaluated for its in vitro neuroactive characteristics. Pinostrobin prevented the voltage-gated Na-channels of mammals' brains from suppressing the depolarizing effects of the Na-channel selective activator veratridine in a synapto neurosomal preparation produced from mouse brain. The pharmacological profile of pinostrobin has been observed to be comparable to that of Na-channel-blocking depressant drugs. In his study, Lui *et al*, 2015 also mentioned that stilbenes in *C. cajan* leaves have neuroprotective activity because they reduce cognitive impairment and neuron apoptosis in mice (Lui *et al*., 2015). Contrarily, it has been shown that the prevention of oxidative stress gives all four stillbenes—cajaninstilbene acid, longistyline A, longistyline C, and cajanolactone A—extracted from *C. cajan* leaves neuroprotective properties to shield PC12 cells from damage brought on by corticosterone and glutamate. The central nervous system (CNS) of mammals is largely composed of voltage-gated sodium channels, which use sodium ions to maintain neural firing. The substituted flavanone pinostrobin, which is derived from the *Cajanus cajan* plant and has been used as a sedative in traditional Chinese medicine (Nicholson *et al*., 2010), appears to have inhibitory effect on sodium channels.

Hepatoprotective effects: Methanolic extracts of *C. cajan* were tested for their ability to protect the liver against carbon tetrachloride (CCl4)-induced liver damage in Swiss albino mice. Because it decreased serum levels of alanine aminotransferase (ALT), also known as serum glutamate pyruvate transaminase (SGPT), aspartate aminotransferase (AST), also known as serum glutamate oxaloacetate transaminase (SGOT), and cholesterol, the same extract was found to have a significant protective effect (Ahsan *et al*., 2009).

Antioxidant activity: The antioxidant activities of *C. cajan* leaf extracts in aqueous, ethanol, ethyl acetate, and petroleum ether were evaluated using the 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay (Pal *et al*., 2008) and the -beta carotene-linoleic acid test. The four main constituents of the ethanol extract of *C. cajan* (3-hydroxy-4-prenylmethoxystilbene-2-carboxylic acid), pinoxtrobin, vitexin, and orientin, were also tested. The results of the tests revealed that *C. cajan* leaf extracts can be useful natural antioxidants and likely have medicinal potential, making them suitable for use in the food or health industries (Wu *et al*., 2009). It was also suggested to use a novel technique called negative pressure cavitations extraction (NPCE) to extract the primary isoflavonoids, genistein and genistin, from pigeon pea root (Pal and Mitra, 2010). Antioxidant activity was significantly concentration-dependent with this method. Syringolin, also known as 2,6-dimethoxyphenol, has been reported to have a profile that appears to have anti-oxidative effects and to inhibit oxidative stress. Stilbenes, flavones, coumarins, phytosterols, and other chemical constituents of *C. cajan* leaves have been identified as having anti-oxidant properties in previous research (Pal *et al*., 2010). The metabolites of *C. cajan* plants were examined, and it was discovered that they contain organic substances such as phytohormone, phenolics, fatty acids, aminopyrimidines, and tripeptides, which have metabolites that are anti-oxidant and iron-chelating. In the study, a variety of extraction methods were used to extract a large quantity of enriched flavanoids and stilbenes from *C. cajan* to determine which method produces more anti-oxidant properties. Aqueous two-phase extraction and negative pressure cavitations work together to maximize the yield of flavanoids and stillbenes, which results in relatively high anti-oxidant activity.

Anticancer activity: An important phytoalexin is cajanol, an isoflavanone derived from the roots of *C. cajan*. Cajanol's anticancer effects on MCF-7 human breast cancer cells were investigated and tested. To determine the mechanism by which cajanol inhibits cell growth, additional parameters including DNA fragmentation assay, cell cycle distribution and morphological assessment of nuclear change, mitochondrial membrane potential disruption, ROS generation and expression, Bcl-2, PARP, and Cytochrome-C levels were measured. It has been demonstrated that cajanol inhibits the development of MCF-7 cells in a dose- and time-dependent manner. Cajanol have demonstrated the ability to induce apoptosis through a mitochondria-dependent pathway and to stop the cell cycle in the G2/M phase. Cajanin-stillbene acid, which was isolated from Pigeon Pea (*Cajanus cajan*) and has anti-estrogenic properties and structural similarities to estrogens, has shown cytotoxic effects on estrogen receptor-alpha and offers promising therapeutic effects against breast cancer cells. The methanol extract of *Cajanus cajan* has been shown to be highly cytotoxic against a variety of cancer cell lines (Luo *et al*., 2010).

Antiplasmodial and Anti-malarial: There are two significant compounds found in the pigeon pea plant (*Cajanus cajan*): Betulinic acid, logistylin A, and C, which have anti-plasmodial properties and all of which work effectively against *Plasmodium falciparum* (Grover *et al*., 2002). Extracts of the roots and leaves of pea plant showed moderately high in vitro activity against *P. falciparum* which is the main causative agent of Malaria (Mathew *et al*., 2017).

Pharmacological activity of aerial part of *Cajanus cajan:*

Anthelmintic activity: Indian adult earthworms (*Pheretima posthuma*) were employed to evaluate the hydro-alcoholic extracts of the aerial portions of the *Cajanus cajan* plant for their anthelmintic effects (Pal *et al*., 2007) because of their physical and physiological similarities to intestinal parasites and round worms. Flavonoids and tannins, which are said to have good anthelmintic properties, were thought to be responsible for this feature.

Anti-Mutagenic properties: The phytochemical constituents of *Cajanus cajan* include tannins, reducing sugars, anthraquinone, triterpenoids, alkaloids, phenols, saponins, and flavonoids among other bioactive substances. In animals induced by mutagen, this plant's flavonoid fraction extraction enhanced its cytotoxic and genotic effects. Quercetin, a highly potent molecule that fights against mutagen-induced cells and mutagenicity in rat liver cells, is one of the flavonoids that can be isolated from *C. cajan*. Therefore, it protects somatic and germ cells against chromosomal alterations and DNA deterioration.

Tyrosinase inhibitory activity: The ability of *C. cajan* roots, stems, and seeds to suppress tyrosinase activity was also examined, and water, dichloromethane, and methanol extracts were made for this purpose. The IC_{50} ranged between 3.55 and 12.43 mg/mL for the extracts, with the methanolic root extract having the highest inhibitory potency (IC_{50} = 3.55 mg/mL) (Rinthong and Maneechai, 2018).

Fig A

Fig B

Fig C

Fig D

Fig- 1. A. Seeds, B. Leaves and raw fruits, C. Flowers D. Mature fruits of *Cajanus cajan*

Phytochemical Constituents: In order to comprehend the mechanism underlying the advantageous effects of *Cajanus cajan*, extensive scientific investigation is being conducted to extract and identify the active components in pigeon pea leaves. It is believed that polyphenols, especially flavonoid compounds, have the most important therapeutic effect on human health (Tekale *et al*., 2016). Lutein, apigenin, quercetin, and isorhamnetin are the four flavonoids identified in the extracts of pigeon pea leaves (Singh *et al*., 2009) and have shown good pharmacological activities. Pigeon pea leaves have been found to contain cajaninstilbene acid and pinostrobin, which are members of the stilbenes and flavanones classes, respectively. They also have been found to have good pharmacological activities. Cajaninstilbene Acid is a very minor amount of the stilbene-2-carboxylic acid that is present in plants (Duker- Eshun *et al*., 2004). It has hypoglycemic, hypotriglycerimic activity (Liogier*et al*., 1998) and is also active in the treatment of postmenopausal osteoporosis. Then again, it is an antioxidant. The powerful flavonoid inducer pinostrobin has a remarkable capacity to activate antioxidant and phase 2 detoxication enzymes in mammals. Additionally, it can suppress the growth of MCF-7 cells, which are stimulated by dehydroepiandrosterone sulphate and 17b-estradiol, and inhibit the human placental aromatase (Pal *et al*., 2009). Most flavonoids and stilbenes are natural antioxidants (Cooksey *et al*., 1982). Cajanol, an isoflavone found in Pigeon pea root extracts (Sarkar *et al*., 2009) with three other phenolic hydroxyls and methoxyl groups. Numerous scientific experiments have found the antispasmodic and antifungal activity of cajanol along with cytotoxic activity towards human breast cancer (Fu *et al*., 2015). Cajanin, Longistylin A, and Longistylin C are the three components present in stilbenes containing extract-fraction from *C. cajan*, and they also exhibit estrogenic activity (Le *et al*., 2000), hypocholesterolemic effects, and anti-oxidative capabilities. A new coumarin called cajanuslactone (7-hydroxy-5-O-methyl-8- (3-methyl-2- butylene)-4-phenyl-9,10-dihydro-benzopyran-2-one) was found during bioassay-guided fractionation of the $CHCl_3$ extract of pigeon pea leaves (Luo *et al*., 2008). Genistein and Genistin, two isoflavanoids that exhibit strong antioxidant activity, have been isolated from the roots of the pigeon pea plant. Additionally, the ethanolic extracts of leaves include vitexin and orientin, both of which have strong antioxidant capabilities (Yuan *et al*., 1999). Additionally, Pigeon pea leaf extracts contain hordenine, Juli Florine, botulinic acid, stigmasterol, beta-sitosterol, and other substances.

CONCLUSION

Pigeon pea plants are widely used for consumption due to their availability and abundance in many nations, as well as their excellent nutritional content. Its countless medical benefits have also been employed traditionally in many regions of the world, but its identify as a medicinal plant is still unknown. In addition to its use as a food and animal feed crop, this plant is also used for soil improvement and erosion control. Its deep taproot system helps to improve soil structure and fertility. The bioactive properties of proteins and peptides produced from pulse seeds have recently drawn increased interest in the domains of food science and nutrition due to their possible benefits in treating and/or delaying the onset of disease.

Since lectins and protease inhibitors, which were previously considered to be protein anti-nutritional compounds, have shown promise in the treatment and/or prevention of several cancers, obesity, and hypertension, the term "anti-nutritional" needs to be reevaluated. Furthermore, pulse peptides may serve as primary therapeutic agents or supplemental therapies for some cardiovascular disorders because of their ACE inhibitor capabilities. As a result, techniques are needed for the efficient extraction and separation of these proteins and peptides. Pulse seeds have the potential to be a wonderful source of beneficial bioactive proteins and peptides. In order to further understand the mechanisms underlying the absorption of biologically active chemicals obtained from dry peas, chickpeas, and lentils into the bloodstream as well as their target tissues and tissue-specific activities, additional study is also required.

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