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A Review on Phytochemistry and Phytopharmaclogy of *Cajanus cajan* (L) Millsp for the future Challenges and Perspective

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A B S T R A C T

Cajanus cajan (family: Fabaceae) more commonly known as pigeon pea, is a drought-resistant crop important for small scale farmers in semi-arid areas where rainfall is low. Pigeon pea contains high levels of protein and important B vitamins and is therefore especially important for people living on subsistence diets. In India, pigeon pea seeds come in a huge variety of flavours and colours, ranging from bitter to sweet and from black to creamy white. It contained several vitamins like thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), vitamin B6, folate (B9), choline, vitamin C, vitamin E, vitamin K and amino acids like tryptophan, threonine, isoleucine, leucine, lysine, methionine, cystine, phenylalanine, tyrosine, valine, arginine, histidine, alanine, aspartic acid, glutamic acid, glycine, minerals and several phytoconstituents like polyphenols, tannins, terpines, glycosides etc. Due to the present of diverse bioactive compounds, considerable progress of C. cajan had been achieved regarding its pharmacological activities and therapeutic applications. This review article gives an overview on the biological activities of the compounds isolated, pharmacological actions and clinical studies of C. cajan extracts apart from its general details.

Keywords: Fabaceae, Pigeon pea, Drought-resistant, Phytoconstituents, Pharmacological etc.

A R T I C L E I N F O

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1. Introduction

Throughout history plants have been used by human beings for medicinal purposes and even in modern times have formed the basis of many pharmaceuticals in use. Plants produce a vast array of secondary metabolites as defense against environmental stress or other factors like pest attacks, wounds, and injuries. The complex secondary metabolites produced by plants have found various therapeutic uses in medicine from time immemorial [1-3]. The early history of modern medicine contains descriptions of plant-derived phytochemicals, many of which are still in use [4-6]. *Cajanus cajan* (L) Millsp. (In Sanskrit: Adhaki, Hindi: Arhar, English: Pigeon pea, Bengali: Tur) is a perennial member of the family fabaceae. Other common names are red gram, congo pea, gungo pea, and no-eye pea [7]. The cultivation of arhar goes back at least 3000 years. The centre of origin is most likely Asia, from where it travelled to East Africa and by means of the slave trade to the American continent. It is an erect, branched, hairy shrub, 1-2 meters high. Leaves are oblong-lanceolate to oblanceolate with three leaflets. Flowers are yellow, in sparse peduncled racemes, about 1.5-cm long. Pod is hairy, 4-7 cm long, 1 cm wide, containing two to seven seeds. India is a principal pigeon pea-growing country contributing nearly 90% of the total world production. Currently, it occupies an area of 3.85 million hectares with an annual production of 2.68 million tones [8]. It is a multipurpose plant as it is extensively eaten as a dal. It is rich in proteins. In India its leaves are used for rearing silkworms; green pods are used as a vegetable; husk, green leaves and tops are used as fodder and also as green manure [9]. Amongst its many medicinal uses, *C. cajan* is indicated in the relief of pain in traditional Chinese medicine and as a sedative [10]. In recent years it has also been explored for the treatment of ischemic necrosis of the caput femoris, aphtha, bedsore and wound healing. Chemical investigations have revealed the presence of two globulins, cajanin and concajanin [9]. It has been used widely for many years for treating diabetes, sores, skin irritations, hepatitis, measles, jaundice, dysentery and many other illnesses; for expelling bladder stones and stabilizing menstrual period [11].

Taxonomy

Kingdom: Plantae
Order: Fabales
Family: Fabaceae
Genus: Cajanus
Binomial name: *Cajanus cajan* (L.)

Common names: The pigeon pea is known by numerous names with different etymologies. In the languages of India: tubarika in Sanskrit, thuvaram paruppu in Tamil, thuvara parippu in Malayalam[1], togari bele in Kannada, tuver' in Gujarati, toor Dal in Marathi, toor dal or arhar dal two equally popular names in Hindi. The original word in Hindi and other northern / eastern languages is arhar, but the southern toor has been widely accepted over the past century or so., orhor dal in the Bengali language, rohor dail in Assamese, harada dali in the Odia language, kandi bedalu in Telugu, behliang in the Zomi/Mizo language and Towar or Tovar or Tover ki dal in Common or widely spoken Hindi and Urdu in India [12, 13].

Habitat: Pigeon pea grows in tropical and subtropical regions. The crop thrives when annual rainfall is 600–1000 mm, but it is tolerant of drought and can be grown in areas with less than 600mm rainfall. Pigeon pea can grow on a wide range of soil types.

Geography and distribution: Pigeon pea was first domesticated in India where it has been growing for thousands of years. Around 2,000 BC, a second centre of pigeon pea diversity was developed in East Africa and from there, probably as a result of the slave trade, the crop was brought to the Americas. Today pigeon pea is grown throughout tropical and subtropical regions of the world; the largest producer is India, followed by East Africa and Central America [14].

Description [15-18]

Overview: Cajanus cajan is an erect shrub up to 4 metres tall, with roots that extend up to 2 metres into the soil. Its main stem is erect, ribbed and the plant has many secondary branches.

Leaves: The leaves are alternate along the stems and are composed of three leaflets (tri-foliolate) and they are positioned alternately along the stem. The petiole (the stalk which connects the leaf to the stem) is 1-8 cm long and grooved above. The leaflets are elliptical (like a stretched circle when flat) to lance-shaped (lanceolate) and are 2.5-13.5 cm long to 1-5.5 cm wide. The leaflets are green above and a silvery grey-green beneath and are covered on their lower surfaces in small yellow glands.

Figure 1: Flowering plant

Figure 2: Plant with flowers and seeds.

Flowers:
The stalked flowers are arranged along an unbranched axis (a raceme). The racemes are axillary (arising from the point between the main stem and a leaf). The flowers are yellow and are papilionaceous, typical of species belonging to the Leguminosae subfamily Papilionoideae, and resemble, for example, the pea (Pisum sativum) flower. Each flower has 10 stamens, 9 of which are fused into a partial tube, with the tenth stamen free. The ovary is positioned above the sepals, petals and stamens. The style is curved.

Fruit:
The fruit is a straight or sickle-shaped pod 2-13 cm long x 0.5-1.5 cm wide containing up to 9 seeds. The seeds are 4-9 mm x 3-8 mm and can be white, brown, purplish, black or mottled.

Cultivation [19-22]
It is a short-day plant. Gooding (1962) reported two groups of plants in Trinidad one group spans 60 to 106 days in the time taken from sowing to podding, the other up to 237 days. It flowers over about two months as days become shorter, and has flowers and ripe pods on the plant at the same time. It flowers in 98 days in the Kimberley district in northern Australia (lat. 15°S) with pods maturing in 178 days. It flowers in eight months in the Bombay district in India (lat. 20°N). Too much shading causes the plant to make spindly growth and to bear thin, pale green foliage and few pods (Krause, 1932). The growing period lasts from 60 to 235 days, depending on cultivar and latitude.

Temperature:
Cajanus cajan is very heat-tolerant. Prefers hot moist conditions. Under Hawaiian conditions grows between 18 and 30°C. Will grow at temperatures above 35°C under adequate soil conditions of moisture and fertility. Does not tolerate frost, but will grow in temperatures to just above frost level. Will seed as a perennial at 1840 m down to a minimum night temperature of 10°C (Krause, 1932). Subject to frost damage (Schofield, 1945). Tall plants may escape light frosts because of the height of the foliage.

Water:
Cajanus cajan is one of the most drought tolerant legume crops, with a wide range of rainfall tolerance, but prefers more than 625 mm and in elevated areas exceeding 2 000 m cold nights and cloudy weather interfere with fertilization of flowers. Flowers well where rainfall is 1 500 to 2 000 mm. On deep, well-structured soil will grow where rainfall is 250 to 375 mm (Krause, 1932).

Soil: Tolerates a wide range of soils, from sands to heavy black clays. Tolerates a wide range of pH, but the most favourable range is pH 5.0 to 7.0. It is sensitive to salt spray, high salinity and to water logging. Will grow in sand provided it does not contain more than 0.0005 g of sodium chloride per gram of soil (Krause, 1932).

Cultivated area:
Of unknown origin, probably Indian and African. Cultivated in ancient Egypt, Africa and Asia since prehistoric times, later introduced to America. Now acclimatized in several tropical countries. The major producer is India with over 100 cultivars, 2.4 million ha cultivated and 90% of world production. Its altitude range is 1250 m in Hawaii (Ripperton and Hosaka, 1942), at heights of 1230 to 1500 m it fails to set seed; 0 to 3000 m in India (Krause, 1932) and Colombia (Crowder, 1960). Essentially a plant of the semi-dry lowlands but has wide adaptability. Generally should not be planted above 770 m. Latitudinal limit is 30° N and S, the optimal being 15-20° for most cultivars.

2. Methods of Pigeon Peas Cultivation

Sowing: Pigeon pea plants grow from seeds. The seeds should be planted 1 to 2 inches deep in the ground maintain a distance of 3 to 4 inches between them. The months of June and July are ideal for planting this crop. Pigeon peas grow well on all types of soils ranging from fine textured to coarse and infertile soils. Their deep roots enable them with greater adaptability to even grow well on semiarid lands. The salinity or soil pH for this plant is best kept between 5.0 and 7.0. The plant is tolerant of herbicides. [23-26]

Watering:
After six hours from planting the seeds, the area around the seeds to a depth of 5 centimeters should be soaked with water.

Caring:
Adding fertilizers to the soil does not significantly affect the growth of the plants. Pigeon peas grow well in Phosphorus-rich soil. If there are any weeds, they should be removed by hand. The seedlings should be thinned when they become 2 inches tall. This is to be done to keep a distance of 12 to 18 inches between the plants.

Temperature:
The temperature of the soil should be at least 60 degrees Fahrenheit while the seeds are being planted. The plants are generally not frost tolerant. The optimum temperature for growing pigeon peas should range between 18 °C and 38 °C. Annual rainfall sufficient for smooth growth of this plant should range between 600mm to 1000mm. It can also tolerate dryer and drought conditions and grow in places with low annual rainfall.

Harvesting:
The crop is harvested during the months of December and January in India and in the months of June and July in Africa. Flowering of the plants can start anywhere between 56 to 210 days after the seeds are sown. The plant takes around 95 to 256 days to mature.

Pigeon Pea Diseases
It is observed that when pigeon pea is used for producing green manure, the plant is safe from pests. However, if pods are formed, then insects such as Agromyza Fruit Flies and Heliothis Borers (pod borers) may cause health problems for the pigeon pea plant. Pigeon pea plants in Hawaii are frequently threatened by attacks from

1. Coccus elongatus
2. Lycaena boetica
3. A stem borer
4. Leaf-eating caterpillars

Some cultivars of pigeon pea plant can be hosts to Rotylenchulus reniformis (reniform nematodes) and root knot nematodes like Meloidogyne spp. and Meloidogyne incognita among others. The ‘FL81d’ and ‘Norman’ cultivars of this plant are able to resist the root knot nematodes. In India, Fusarium udum causes Fusarium wilt,

a vascular wilt fungal disorder these plants commonly suffer from. It is a highly damaging disease. In order to control the disease, the crops should be rotated on regular intervals. Root rot is caused by the fungus Phaeolus manihotis. Pathogens like Physalospora cajanae, a fungus, causes stem cankers and leaves dead and diseased areas on branches and stems of the plant. Witch's broom is sometimes found in these pea plants. This is caused by polymorphic Mycoplasma-like organisms. Under close observation, Rhabdovirus-like particles are also found in the affected areas. Symptoms of this disease include excessive spreading of shoots coming out of axillary buds accompanied by stunted growth of leaves and shortening of internodes.

Ethnopharmacological Importance

C. cajan being a forage crop has been utilized as an important remedy for various ailments. The garo tribal community of Bangladesh utilizes it for the treatment diabetes and as an energy stimulant [1] In Trinidad and Tobago the leaves of C. cajan are used in food poisoning, as colic and in constipation [27]. In Chinese folk medicine pigeon pea leaves are used to staunch blood, as an analgesic and to kill parasites. In some parts of Tamil Nadu, India, the leaf, seeds and young stems are used to cure gingivitis, stomatitis and as a toothbrush [28]. It is also an important folk medicine in eastern Rajasthan as fresh juice/boiled leaves are given orally to nullify the effect of intoxication and as a laxative. Leaf paste is applied in oral ulcers and inflammations. Leaves and seeds are applied as poultice over the breast to induce lactation [29].

3. Chemistry

Chemical constituent investigations have indicated that C. cajan leaves are rich in flavonoids and stilbenes. They also contain saponins, conspicuous amount of tannins, and moderate quantities of reducing sugars, resins and terpenoids. Chemical studies reveal 2'-2' methyl cajanone, 2'-hydroxy genistein, isoflavones, cajanin [Figure 3], cahanones etc., which impart antioxidant properties [30]. Roots are also found to possess genistein and genistin. It also contains hexadecanoic acid, α amyrin, β-sitosterol, Pinostrobin [Figure 4], longistylin A [Figure 4] and longistylin C [Figure 5] which imparts anticancer activity. Presence of cajanuslactone [Figure 6], a coumarin imparts antibacterial activity. Presence of cajaninstilbene acid [Figure 7], pinostrobin, vitexin [Figure 8] and orientin [Figure 9] is responsible for antiplasmodic activity.

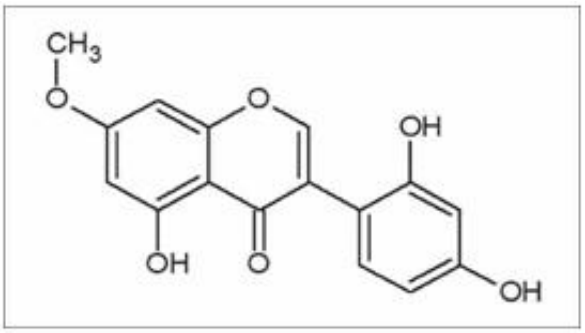

Figure 3: Cajanin

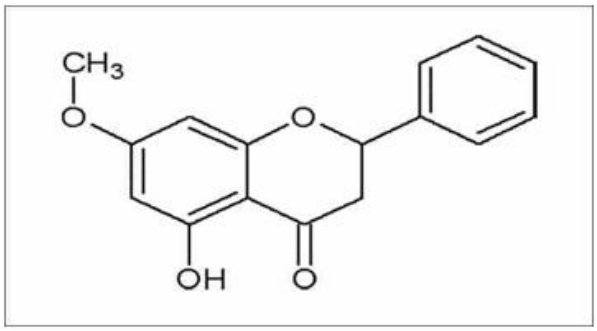

Figure 3: Pinosrobin

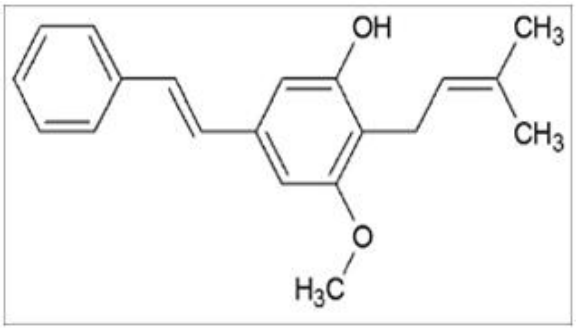

Figure 4: Longistylin A

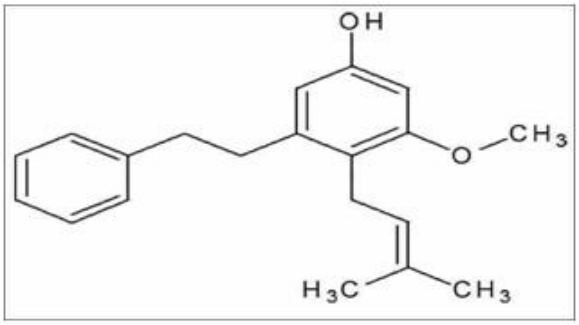

Figure 5: Longistylin C

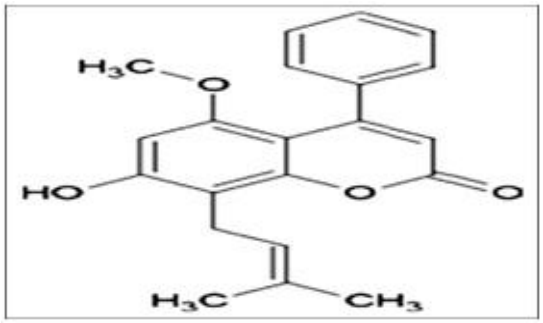

Figure 6: Cajanuslactone

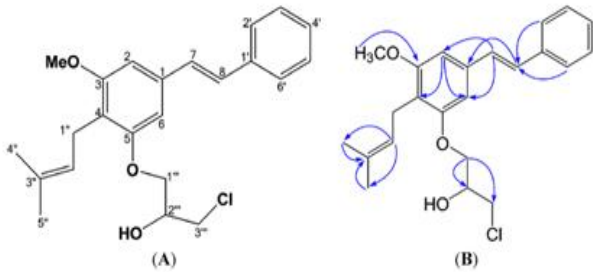

Figure 7: Haloginated cajaminstilbene

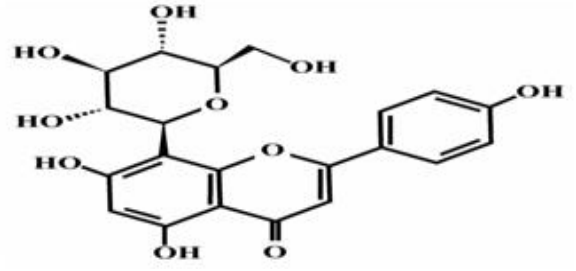

Figure 8: Vitexin

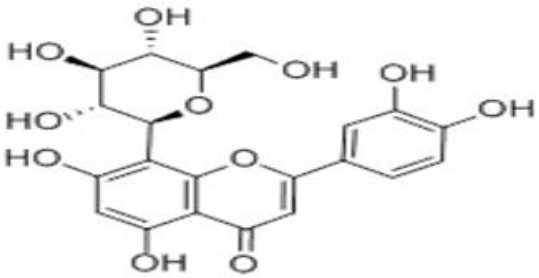

Figure 9: Orientin

4. Biological Activities

During the last few decades a large number of compounds have been isolated from C. cajan and some of them have got excellent biological activities. A new natural coumarin cajanuslactone has been isolated from the leaves of C. cajan which is a potential antibacterial agent against Gram-positive micro-organisms [31]. The three stilbenes, cajanin, longistylin C and longistylin A from leaves have been found to possess hypocholesterolemic effects [32] Anti-plasmodial activities have also been confirmed in betulinic acid isolated from roots and longistylin A and C obtained from leaves.[33]. Pinostrobin, a substituted flavanone isolated from leaves possesses anti-inflammatory activity and inhibits sodium channel-activated depolarization of mouse brain synaptoneurosomes [34]. Two isoflavanoids genistein and genistin isolated from the roots were found to possess antioxidant activity [35]. Cajanol an isoflovanone found in the roots is found to possess anticancer activity Four important compounds, pinostrobin, cajaninstilbene acid, vitexin and orientin isolated from ethanolic extracts of leaves were found to possess significant antioxidant properties. Isoflavanoids isolated from ethanolic extract of leaves also showed significant antimicrobial activities. Some protein fraction isolated from leaves also showed hepato-protective effects [36] and the presence of phenolics (flavanoids and tannins) impart anthelmintic activity [37].

Pharmacological Actions

Different parts of C. cajan have been utilized for their biological activities since time immemorial and some of them have experimental grounds for their acceptance. Apart from their uses in folkloric medicines, there are several reports on the biological activities and pharmacological actions of C. cajan based on modern scientific investigations.

Antimicrobial Activity:

The in vitro and in vivo antimicrobial activities of SFE-CO2 (supercritical fluidextraction) extracts and ethanol extracts from C. cajan were investigated. In vitro antimicrobial activities of the extracts were evaluated against eight microbial strains: Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis, Proteus vulgaris, Pseudomonas aeruginosa, Escherichia coli, Aspergillus niger and Candida albicans. A marked inhibitory effect of the SFE extracts was observed against S. epidermidis, S. aureus and B. subtilis. In vivo antimicrobial activity was studied in mice that had been inoculated with S. aureus and the potential mechanism of antimicrobial activity was studied by histopathology.

Antibacterial Activity:

The bioassay-guided fractionation of chloroform extract from pigeon pea leaves led to isolation of new natural coumarins: Cajanuslactone and two phyto alexins: Pinostrobin and cajaninstilbene acid. It was found that cajanuslactone possessed good antibacterial activity against S. aureus [30].

Hypocholesterolemic Effects:

The effects of the stilbenes containing extract-fraction from C. cajan (SECC) on diet-induced hypercholesterolemia in kunming mice were identified. The SECC reduced the atherogenic properties of dietary cholesterol in mice. Its hypocholesterolemic effect may involve enhancement of the hepatic Low Density Lipoprotein-receptor and cholesterol-7-alpha-hydroxylase expression levels and bile acid synthesis [32].

Antidiabetic Effects:

The antidiabetic activity of methanolic extract of leaves of C. cajan was studied in alloxan-induced diabetic and oral glucose-loaded rats. The acute toxicity and lethality (LD50) and phytochemical analysis of the extract were also evaluated.[26,27] The results showed that the extract significantly reduced the fasting blood sugar of alloxan diabetic rats in a dose-related manner with maximum hypoglycemic effect at 4-6 h [33,41].

Neuroactive Properties:

In-vitro neuroactive properties of pinostrobin, a substituted flavanone from C. cajan were estimated. It was demonstrated that pinostrobin inhibits voltage-gated sodium channels of mammalian brain based on the ability of this substance to suppress the depolarizing effects of the sodium channel selective activator veratridine in a synaptoneurosomal preparation from mouse brain. The pharmacological profile of pinostrobin resembles that of depressant drugs that block sodium channels [34].

Antioxidant Activities:

Antioxidant activities of the aqueous, ethanol, ethyl acetate, n-butanol, petroleum ether extracts of C. cajan leaves and the four main compounds separated from the ethanol extract, i.e. cajaninstilbene acid (3-hydroxy-4-prenylmethoxystilbene-2-carboxylic acid), pinostrobin, vitexin and orientin, were examined by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay [42-44] and β-carotene-linoleic acid test. Based on the results obtained, it was concluded that the pigeon pea leaf extracts may be valuable natural antioxidants and potentially applicable to medicine and the health food industry. A new method–negative pressure cavitations extraction (NPCE)–was also proposed and extraction for the main isoflavonoids, namely genistein and genistin from pigeon

pea roots was suggested. NPCE extract possessed notable concentration-dependent antioxidant activity [40].

Anticancer Activity:

Cajanol, an isoflavanone from C. cajan roots is an important phytoalexin. The anticancer activity of cajanol towards MCF-7 human breast cancer cells was investigated. In order to explore the mechanism of cell growth inhibition of cajanol some parameters like cell cycle distribution, DNA fragmentation assay and morphological assessment of nuclear change, reactive oxygen species (ROS) generation, mitochondrial membrane potential disruption and expression of caspase-3 and caspase-9, Bcl-2, PARP and cytochrome c were measured. Cajanol inhibited the growth of MCF-7 cells in a time- and dose-dependent manner. Cajanol arrested the cell cycle in the G2/M phase and induced apoptosis via a reactive oxygen species (ROS) - mediated mitochondria-dependent pathway [36].

Hepatoprotective Effects:

The methanol extracts of C. cajan were studied for hepatoprotective activity against Swiss albino mice with liver damage induced by carbon tetrachloride (CCl_4). It was found that the same extract exhibited a moderate protective effect by lowering the serum levels of alanine aminotransferase (ALT) or serum glutamate pyruvate transaminase (SGPT), aspartate aminotransferase (AST) or serum glutamate oxaloacetate transaminase (SGOT), and cholesterol to a significant extent [37]. The methanol-aqueous fraction (MAF2) of the leaf extract was also used to prevent alcohol induced rat liver damage. Co-administration of MAF2 reversed the liver damage; it decreased the activities of liver marker enzymes and augmented antioxidant enzyme activities and showed a promise in therapeutic use in alcohol-induced liver dysfunction.

Anthelmintic Activity:

The hydro-alcoholic extracts of the aerial parts of C. cajan were evaluated for anthelmintic properties using Indian adult earthworm (Pheretima posthuma) due to their anatomical and physiological resemblance with intestinal parasites and round worms [45, 46] This property was supposed to be due to the presence of phenolics (flavanoids and tannins) which are reported to have good anthelmintic property [38].

Glycemic Activity:

The glycemic profile of the aqueous extract of C. cajan leaves in streptozocin-induced Type 2 diabetic rats was evaluated. This extract showed significant increment in fasting blood glucose levels of normal rats. The study of leaves was taken into consideration on the basis of earlier reported hypoglycemic activity of C. cajan seeds. However, the results observed were found to be just opposite and therefore it may be useful in controlling hypoglycemia occasionally caused due to excess of insulin and other hypoglycemic drugs [41].

5. Conclusion

C. cajan is the rich source of protein and a most important forage and cultivated crop. It has also been used traditionally in many parts of the world due to various pharmacological and microbiological properties but its identity as a medicinal plant for various disease and ailments has not yet been established. Recently several flavonoids, isoflavonoids, tannins and protein fractions have been purified, isolated and elucidated their structures from its different parts and their therapeutic uses have been established, but many bioactive constituents and pure compounds have so far been neglected by phytochemist, medicinalchemist and pharmacologists and a large amount of work has been done only on extracts and not the isolated fractions which shows scope for further study in this direction. The present review article aims at focusing the attention of research scholars on the unexplored and untouched areas of C. cajan for the future Challenges and Perspective and may act as an promising step towards the establishment of C. cajan (L) Millsp. as a potential medicinal plant.

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