International Journal of Pharmaceutical Science and Research
ISSN: 2455-4685
Impact Factor: RJIF 5.28
www.pharmacyjournal.net
Volume 3; Issue 2; April 2018; Page No. 27-37

Pharmacological and phytochemical properties of *Cajanus cajan* (L.) Huth. (Fabaceae): A review

Proma Roy Orni[1], Sazzad Zaman Ahmed[2], Marzana Monefa[3], Tanzim Khan[4], Pritesh Ranjan Dash[5*]
[1- 4] Department of Pharmacy, BRAC University, Mohakhali, Dhaka, Bangladesh
[5] Department of Pharmacy, Jahangirnagar University, Savar, Dhaka, Bangladesh

Abstract
Cajanus cajan which is also known as 'pigeon pea' is used as food crop in tropical and subtropical areas of the world which is a great source of protein, vitamin B and minerals for human as well as animals and has a great contribution over medicinal uses. It belongs to the Fabaceae family and it has many medicinal properties such as anti-bacterial, anti-microbial, anti-inflammatory, hypocholesterolemic effects, anti-diabetic, anti-cancer, neuroactive properties, antioxidant, hepatoprotective, anthelmintic, glycemic and many more. Its extracts such as polyphenols, quercetin, luteolin, apigenin, isorhamnetin, flavonoids, cajaninstilbene acid etc. are very useful for the treatment of jaundice, diarrhea, sores, cough, bronchitis, bladder-stones and diabetes. From ancient period to present time, pigeon pea is used by different population for different purposes such as food, agricultural and treatment. The ethno-pharmacological importance of pigeon pea is utilized in various ways among the tribal community 'Garo' of Bangladesh, Chinese people, people of West Indies and people of Tamil Nadu and Rajasthan. This study has mainly focused on various pharmacological actions and medicinal uses through review study of different studies done on pigeon pea.

Keywords: *Cajanus cajan*, pharmacological properties, phytoconstituents

Introduction
Cajanus cajan (L.) Huth. (Family: Fabaceae), generally known as "Pigeon pea" (English), an individual from the Cajanus variety, is a standout amongst the most significant lasting or yearly leguminous sustenance trims in Asia, Africa and a few sections of South America [1, 2, 3], broadly circulated in different parts of tropical and subtropical territories of the world, and assuming a vital part in the field of agribusiness and nourishment [1]. *Cajanus cajan* is a beneficial nontoxic grain that provides both food supplement and a wide range of medicinal applications [4]. Pigeon pea is a wellspring of protein, vitamin B and minerals for veggie lover populaces and creatures. The plant *C.cajan* contains many bioactive constituents such as stilbenes, flavones, phytosterols, coumarins and many more which possess therapeutic applications for diabetes, hepatitis, malaria, cancer, hyperglycemia etc. [20, 2, 5, 6]. This plant is also considered to have anti-oxidant, anti-cancer, anti-tumor, anti-malarial and anti-bacterial properties [20, 26]. Concentrates of pigeon pea leaves are useful for jaundice, looseness of the bowels, wounds, hack, bronchitis, bladder-stones and diabetes [15]. In the folk medicine of China, pigeon pea leaves are used to arrest blood, relieve pain and kill worms [66]. The young leaves of the pigeonpea can be chewed for treating aphtha, and the decoction of the leaves has been proved to treat cough and diarrhea effectively [66]. In recent years, pigeonpea leaves have been used to treat traumatism, burnt infection, bedsore etc. [39]. It was also found that pigeon pea leaves exhibit notable anti-inflammatory, antibiotic and abirritation effects and inhibit capillary permeability [23, 24, 50]. Especially in China, it is considered as an excellent traditional Chinese medicine (TCM) in the market for the therapy of ischemic necrosis of femoral head. This paper is a comprehensive and an up-to-date review of the plant – *Cajanus cajan* and this review paper mainly focused on the pharmacological properties and further scope in the therapeutic uses of this plant.

Scientific Classification
Kingdom: *Plantae*
Class: *Magnoliopsida*
Subclass: *Rosidae*
Order: *Rosidae*
Family: *Fabaceae*
Genus: *Cajanus*
Species: *Cajanus cajan* (L.) Huth.

Botanical Description
Pigeon pea occurs in several varieties and known as congo pea, no eye pea, dhal, red gram, gungo pea, gandul, gandure, frijol de árbol and pois cajan etc. Varieties that are old in cultivation and semi-cultivation in the West Indies treated are semi-deciduous, short-lived shrubs which are generally 1 to 4 cm in basal stem diameter. They are usually single stemmed, freely branching and become woody after a few months. These woods can be more hard and brittle. They have deep root (up to 3m) as well as lateral roots and nodulated fine roots. The branches and fine twigs support abundant yellowish green foliage which are sparingly arranged, silky-pubescent, trifoliolate leaves have narrowly elliptic, lanceolate or oblong leaflets, 2.5 to 9 cm long, and the center leaflet being slightly longer than the laterals. The five- to 12-flowered racemes are axillary. Flowers are about 2 cm long, yellow, the standard often being orange to purple outside. The legumes, which are flattened, somewhat constricted between seeds, and 4 to 8 cm

long, are mottled bronze-purple when immature, drying to brown. They contain 2 to 9 mottled brown (white, red, brown, gray, or black in improved varieties) seeds, 7 to 8 mm long by 6 mm broad. There are 2n = 22, 44, or 66 chromosomes [51].

a.

b.

Fig 1: a. Flowers (b) Immature and mature pods of *Cajanus cajan*

Pharmacological Properties

Different parts of *Cajanus cajan* are used for their biological activities from ancient times and most of them have been experimented with solid grounds of their therapeutic values. Besides their uses in folkloric medicines, there are wide availability of modern scientific study conducted on the biological activities and pharmacological actions of *C. cajan*.

Antimicrobial Activity

The extracts of *Cajanus Cajan* were showed potential activity against eight microbial strains: *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Aspergillus niger* and *Candida albicans* [16, 18, 21]. A great inhibitory effect of the SFE extracts of *C.cajan* was seen against *S. epidermidis*, *S. aureus* and *B. subtilis* [64]. *In vivo*, the antimicrobial activity was observed in mice which was inoculated with *S. aureus* and the pathway through which the plant extract works again these microorganisms was studied by histopathology [64]. The ethanol extracts and supercritical fluid extraction extracts from *Cajanus Cajan* were evaluated from its antimicrobial activities and the plant extracts showed significant antimicrobial activities both in vivo and in vitro and this might be a potential candidate for the treatment of *S. aureus* and might also work against MRSA [18]. In a study conducted by Qi *et al*., the essential oil extracted from solvent-free microwave extraction and hydrodistillation have showed excellent activity against gram positive and gram negative bacteria, *B. subtilus* and *P. acnes* [21].

Anti-plasmodial and Anti-malarial

Pigeon pea plant (Cajanus Cajan) constituents two important compounds: logistylin A, C and betulinic acid which possess anti-plasmodial characteristics and all works well against *Plasmodium falciparum* [42]. Extracts from roots and leaves of pea plant contains have showed moderately high *in vitro* activity against *P. falciparum* which is that main causative agent of Malaria [22].

Antibacterial Activity

Extracts from *C.cajan* leaves in the bioassay-guided fractionation of chloroform resulted into the isolation of new natural coumarins: Cajanuslactone and two phyto alexins: Pinostrobin and cajaninstilbene acid [24]. It was seen that cajanuslactone have high antibacterial activity against the bacteria, *S. aureus* [50]. The extracts of pigeon pea leaves have shown to be effective against some pathogenic bacteria and test result reported that the extract could successfully inhibit the proliferation of bacteria *Salmonella Thypi* [16]. Thyphoid is an infectious disease that is caused by the gram (-ve) bacteria *Salmomella Thypi* and it this disease is a burden in many developing countries. The major component in *C. cajan* are classified into two groups: stillbene and flavonoids and the extract of this plant could effectively inhibit growth of *S. thypi*, *S. aureus* and *E. coli* [16].

Anthelmintic Activity

The HA (hydro-alcoholic) extraction from the aerial parts of *Cajanus cajan* were studies for anthelmintic properties using the adult earthworm found in India (*Pheretima posthuma*) as their anatomical and physiological characteristics resembles closely with intestinal parasites and round worms [56, 58]. This property was thought for the presence of phenolics compound such as flavanoids and tannins which shows good anthelmintic property [59]. The seed extracts of *C.cajan* shows high content of bioactive compounds which possess anti-helmintic activities [23].

Anticancer Activity

C. cajan roots contains Cajanol, an isoflavanone which is an important phytoalexin. The anticancer properties of cajanol towards MCF-7 human breast cancer cells were studied and experimented [53]. In order to determine the mechanism of cell growth inhibition of cajanol, other parameters like DNA fragmentation assay, cell cycle distribution and morphological assessment of nuclear change, mitochondrial membrane potential disruption, reactive oxygen species (ROS) generation and caspase-3 and caspase-9 expression, Bcl-2, PARP and cytochrome-C were quantified [17, 53]. Cajanol have showed to inhibit the growth of MCF-7 cells in a time- and dose-dependent manner [53]. Cajanol have showed to arrest the cell cycle in the G2/M phase and have also induced apoptosis via a reactive oxygen species (ROS)-mediated mitochondria-dependent pathway [53]. Cajanin stillbene acid isolated from Pigeon Pea (*Cajanus Cajan*) is structurally similar to estrogens which have showed cytotoxic effects to estrogen receptor-alpha and possess anti-estrogenic properties, promising therapeutic effects against breast cancer cells [17]. The methanol extract of *Cajanus Cajan* shows high cytotoxicity against many cancer-cell lines [19].

Anti-Mutagenic properties

Phytochemical compounds in *Cajanus cajan* contains many bioactive compounds such as tannins, reducing sugars, anthroquinone, triterpenoids, alkaloids, phenols, saponins and flavonoids where flavonoid fraction extraction from this plant improved cytotoxic and genotic effects in mutagenic agents induced animals [20]. Quercetin is one of the extracted flavonoids from *C. cajan* which is a very active compound to work against mutagen induced cells and mutagenicity in rats' hepatic cells, thus providing protection against DNA damage and chromosomal changes in germ and somatic cells [20].

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 [53]. Research using methanol extract of *C.cajan* seeds were fractionated into petroleum ether, chloroform, and methanol. The methanol fraction significantly decreased lipid profiles of streptozotocin-induced Swiss Albino mice compared to control. The extract was then subjected to chromatographic analysis and a compound (CCA1) was isolated which possessed first prominent hypolipidemic activity [12].

C. cajan diet at doses of 200-800 (g/kg feed) has improved cholesterol level of hypercholesterolemia hamsters by converting cholesterol to bile acids and by increasing CPT-1, LDL receptor, cholesterol-7-alpha hydroxylase, antioxidant enzymes and further increasing lipid peroxidation [10]. The C. cajan beverages administration at doses equivalent to human consumption of 30 grams/day to Sprague Dawley male rats has confirmed to have potential to reduce total cholesterol levels by 19.78 % of diabetic-hypercholesterolemia rats [14].

Antidiabetic Effects

Study carried out to test the effect of roasted and unroasted seeds of *C. cajan* on serum glucose levels of normal and alloxan diabetic mice. The result indicated unroasted seeds have a hypoglycemic effect on diabetic rats, but roasting causes loss of hypoglycemic property of the seeds [11]. 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 [56, 58]. 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 [3]. The effects of different fractions of the methanolic extracts of *C. cajan* on the fasting blood sugar were investigated in the streptozotocin-induced diabetic Swiss Albino mice. Hypoglycemia was observed in animals treated with methanol fraction, whereas, the petroleum ether and chloroform fractions of *C. cajan* had no effect [12]. Study was carried out to evaluate antihyperglycemic potential of different solvent extracts of leaves of *Cajanus cajan* in alloxan induced diabetic Swiss albino mice. Among the four solvent extract was Petrolium ether, Chloroform, Ethyl acetate and methanol extract. Two extracts namely ethyl acetate and methanol extract significantly reduced the blood glucose level by 27.09 and 37.68% respectively in diabetic mice after daily oral administration for 10 days at a dose of 250 mg/kg. These two extracts also potentiated the action of insulin. The other two extract did not significantly reduce blood glucose level of the diabetic mice [13].

Research has shown there is hypoglycemic activity of C. cajans roots extract [5] leave extract [2, 3], roots and leaves extracts [7]. Research conducted using C. cajan drink diet given at doses equivalent to human consumption of 30 grams/day to diabetic-hypercholesterolemia Sprague dawley rats. The beverage caused decrease in plasma glucose by 33.86 and improvement of the plasma antioxidant of the diabetic hypercholesterolemia rats. This result indicated the probable of *C. cajan* beverage as an anti-diabetic functional drink. [14].

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 [4, 13].

Neuroactive properties

Pinostrobin is a substitute of flavanone from *C.cajan* and its in vitro neuroactive properties were estimated. Voltage-gated Na-channels of mammals' brain were inhibited by pinostrobin on the ability of the substance to suppress depolarizing effects of Na-channel selective activator veratidine in a synaptoneurosomal preparation from mouse brain. It has been seen that pharmacological profile of pinostrobin is similar to the depressant drugs which block Na-channel [55]. Lui (2015), also mentioned in his study that stilbenes found in C.cajan leaves have ameliorate cognitive defects and neuron apoptosis in mice and thus having neuroprotective activity [29]. Then again, it has been seen that all the four stillbenes extracted from C.cajan leaves (cajaninstilbene acid, longistyline A, Longistyline C and cajanolactone A posses neuro-protective properties against the damaged induced by corticosterone and glutamate in PC12 cells by the inhibition of oxidative stress [29]. Voltage-gated sodium channel are widely present CNS of mammals where sodium ions play an important role in the maintenance of the neural firing in the central nervous system. A substituted flavanone, pinostrobin which can be found in *Cajanus Cajan* seem to have inhibitory activity of the sodium channels and has been used as a sedative in traditional Chinese medicine [55].

Antioxidant activities

2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay and β-carotene-linoleic acid test were done on aqueous, ethanol, ethyl acetate and petroleum ether which are the extracts of *C.cajan* leaves to find out the antioxidant activities. Additionally, those test were also done on cajaninstilbene acid

(3-hydroxy-4-prenylmethoxystilbene-2-carboxylic acid), pinoxtrobin, vitexin and orientin which are the four main compounds of ethanol extract of *C.cajan* [58]. After the tests were carried out, it was seen that the leaf extracts of *C.cajan* can be valuable natural antioxidants and likely usable as medicine and can be used in food or health industry [62]. Negative pressure cavitations extraction (NCPE), a new method was introduced and genistein and genistin which are the extraction of the main isoflavonoids of *C.cajan* was suggested. This method showed notable concentration-dependent antioxidant activity. The profile of Syringol, also known as 2,6-dimethoxyphenol, seem to have anti-oxidative properties and is found to have suppress oxidative stress [24]. Previous studies have found the chemical constituents in *C. cajan* leaves to have stilbenes, flavones, coumarins, and phytosterols that seem to possess anti-oxidant properties [26, 27]. Metabolites analysis of C.cajan plants showed the presence organic compounds, phenolics, fatty acids, aminopyrimidines, tripeptides, phytoharmone are some of the important metabolites which have anti-oxidant and iron chelating activity [32]. Wang *et al*. (2015), in the study extracted large amount of enrich flavanoids and stilbenes from C.cajan where different extraction techniques were used to determine which technique yields greater anti-oxidant properties [33]. Negative-pressure cavitations in addition with aqueous two-phase extraction tend to optimize yield flavanoids and stillbenes and thus provide relatively high anti-oxidant activity [33].

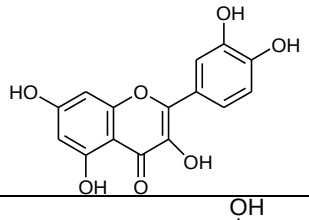
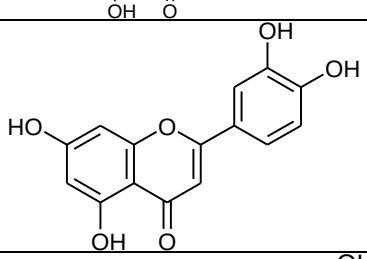
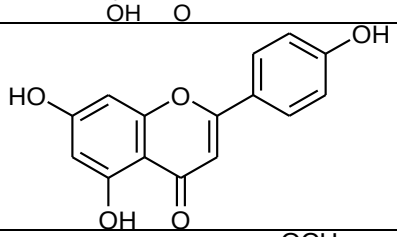
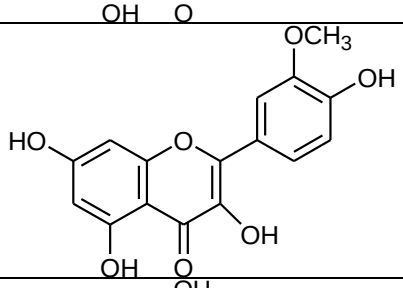
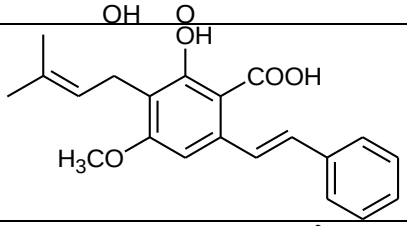
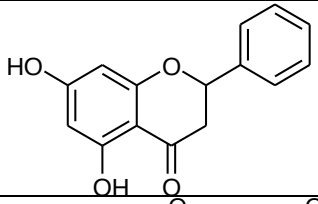
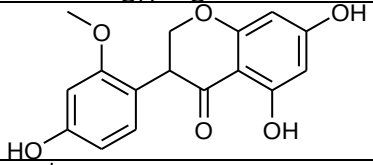
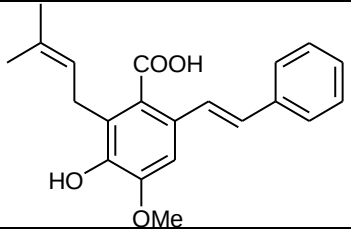
Hepatoprotective Effects

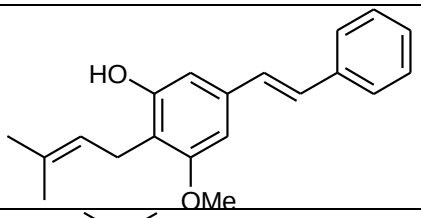
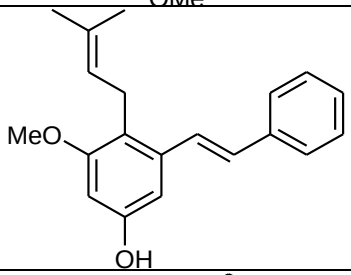
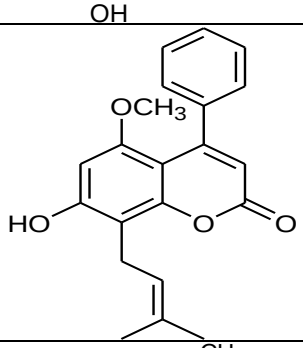
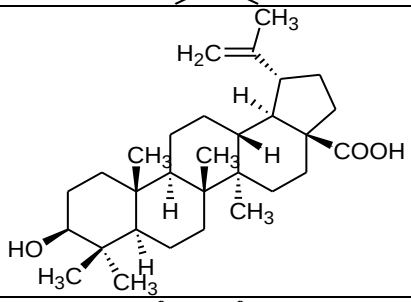
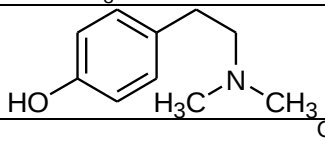
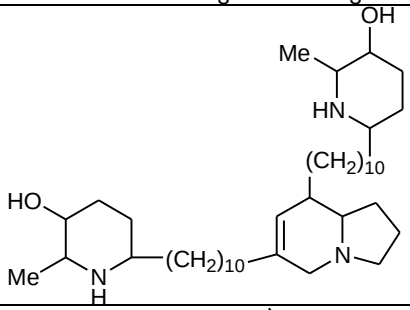
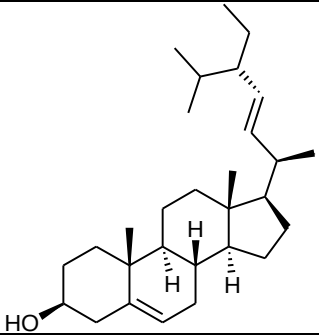
An experiment is done on damaged liver Swiss albino mice induced by carbon tetrachloride (CCl_4) to see the hepatoprotective activity of the methanol extracts of *C.cajan.* It was found that the sane extract showed a little protective effect by decreasing the serum levels of alanine aminotransferase (ALT) or serum glutamate pyruvate transaminase (SGPT), aspartate aminotransferase (AST) or serum glutamate oxaloacetate transaminase (SGOT), and cholesterol to a significant extent [37]. Alcohol induced liver damage of rat can prevented by the methanol-aqueous fraction (MAF2) of the leaf extract. After co-administration of MAF2, it decreases the activity of liver maker enzymes and augmented antioxidant enzyme activities. Thus, it shows a promise in therapeutic use in alcohol-induced liver dysfunction [37]. Glutamic oxaloacetic transaminase and glutamic pyruvic transaminase indicates liver functioning status that is if the activity of these two enzymes are low, the better the liver functionality [31]. In the study conducted by Das (2018), extracted from C.cajan greatly reduced bilirubin content in cells and rats and this shows a clear indication of hepatoprotective properties. Methanol-aqueous fraction of *Cajanus Cajan* leaf extract prevented chronically alcohol induced rat with chronic liver damage [34]. It has been observed that alcohol induced liver damage is mainly due to the result of oxidative stress and UGT (UDP glucoronosyl transferease) gene expression is an important cytoprotectant. Prolonged intake of alcohol causes the down-regulation of UGT expression where Methanol-aqueous fraction *C.cajan* leaf extraction prevents this downregulation- thus, permitting cytoprotection and treating alcohol induced liver dysfuction [34].

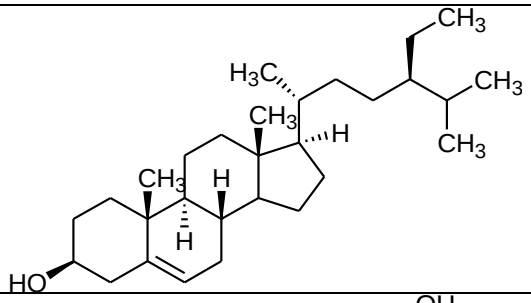
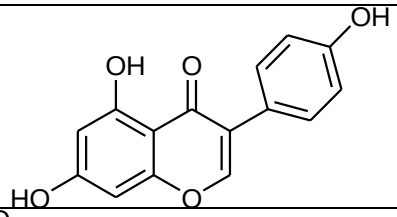
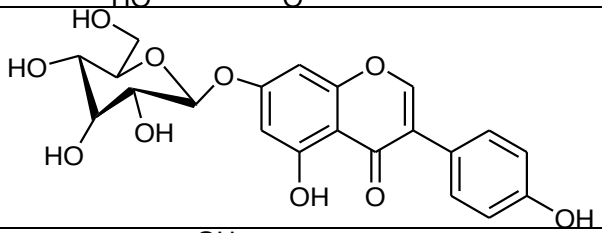
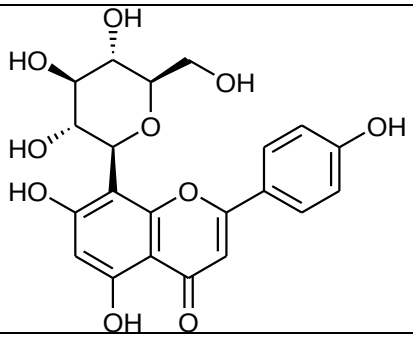
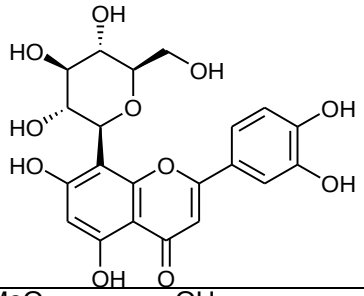
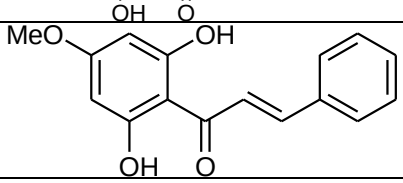
Photochemical Constituents

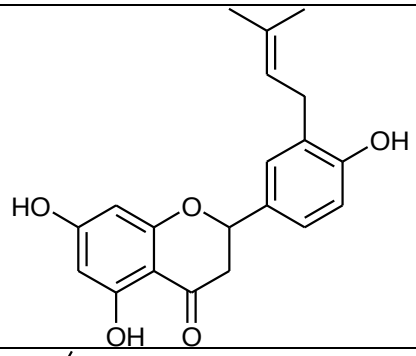
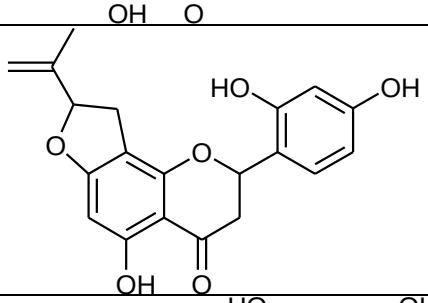
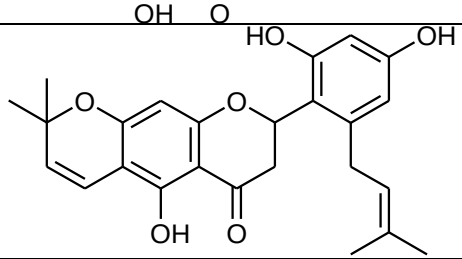
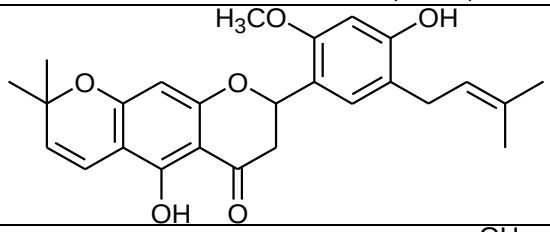
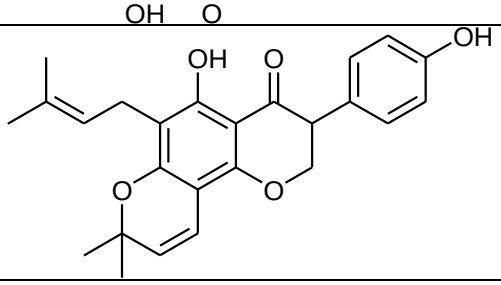
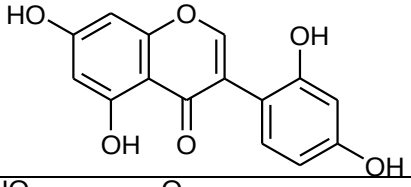
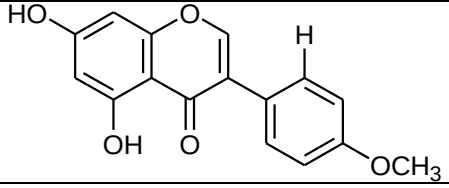
For determine the mechanism that is involved with the beneficial effects of *Cajanus Cajan*, a great deal of scientific study is conducted for isolating and identifying the active components in pigeon pea leaves. Polyphenols, especially the flavonoid compounds is thought to play the main compound for the therapeutic effect on human health [28, 43]. The four flavonoids found in the extracts of pigeon pea leaves are:- luteolin, apigenin quercetin, and isorhamnetin [39, 33, 32, 24], which have showed good pharmacological properties. In other studies, it has been seen that pigeon pea leaves have cajaninstilbene acid and pinostrobin and these belong to stilbenes and flavonones groups respectively [24, 28]. They also have been found to have good pharmacological activities. Cajaninstilbene acid is stilbene-2- carboxylic acid, which is found in plants in very slight amount [40]. It has hypoglycemic, hypotriglycerimic activity [49] and is also active in the treatment of postmenopausal osteoporosis [68]. Then again, it is an antioxidant [63]. Pinostrobin which is a potent flavonoid inducer have great ability to induce mammalian phase 2 detoxication enzymes and antioxidant enzymes.It also holds the ability to inhibit the human placental aromatase and reduce proliferation of MCF-7 cells which is induced by the dehydroepiandrosterone sulphate and 17b-estradiol [54]. Most flavonoids and stilbenes are natural antioxidants [38]. Cajanol, an isoflavone found in pigeonpea root extracts [24] with three other phenolic hydroxyl and a methoxyl groups. Many scientific experiments have found the antiplasmoidal and antifungal activity of cajanol [15] along with cytotoxic activity towards human breast cancer [53]. There are three components found in stilbenes containing extract-fraction from *C. cajan*, i.e., Cajanin, Longistylin A and Longistylin C which also shows estrogenic activity [68], hypocholesterolemic [52] and anti-oxidative properties. A new coumarin, named cajanuslactone (7-hydroxy-5-O-methyl-8- (3-methyl-2-butylene)-4-phenyl-9,10-dihydro-benzopyran-2-one) was isolated from the bioassay-guided fractionation of the $CHCl_3$ extract of pigeon pea leaves [50]. Two isoflavanoids genistein and genistin have been isolated from the roots of pigeon pea plant that possess good antioxidant activity [67]. Moreover, vitexin and orientin from the ethanolic extracts of leaves also possess high antioxidant properties [63]. Pigeonpea leaves extracts also have other components such as hordenine, juliflorine, betulinic acid, stigmasterol, beta-sitosterol and others [41, 42, 46].

Table 1: The major constituents of *Cajanus cajan*

SN.	Chemical Constituent	Structure
1	Quercetin	
2	luteolin	
3	Apigenin	
4	Isorhamnetin	
5	Cajaninstilbene acid	
6	Pinostrobin	
7	Cajanol	
8	Cajanin	

9	Longistylin A	
10	Longistylin C	
11	Cajanuslactone	
12	Betulinic acid	
13	Hordenine	
14	Juliflorine	
15	Stigmasterol	

16	Beta-sitosterol	
17	Genistein	
18	Genistin	
19	Vitexin	
20	Orientin	
21	Pinotrobin chalcone	

22	Isoprenylated genistein	
23	Isoflavonoid phytoalexin	
24	Cajanone	
25	2-O-methylcajanone	
26	Cajaflavonone	
27	2-Hydroxygenistein	
28	Biochanin A	

Conclusion

The abundance and availability of pigeon pea plants in many countries, in addition with their high nutritional value, have made Pigeon pea plant one of the vast usage for consuming and . Pulse crops have long been known for their nutritional and health-promoting properties, such as being an excellent source of protein, fiber, carbohydrates, and for their role in decreasing the risk of certain cancers, managing obesity, lowering cholesterol and type-2 diabetes [20]. Recently, the bioactive properties of proteins and peptides derived from pulse seeds have gained increased recognition in the areas of food science and nutrition for their potential benefits in treating and/or reducing the onset of disease. Lectins and protease inhibitors which were traditionally considered as protein anti-nutritional compounds have shown potential in the treatment and/or prevention of various cancers, obesity and hypertension which has necessitated a reconsideration of the use of the term ‘‘anti-nutritional”. Additionally, the ACE inhibitor properties of pulse peptides could make them primary therapeutic agents or adjuncts to treatment for certain cardiovascular diseases. Pulse seeds may, therefore, be potentially excellent source of beneficial bioactive proteins and peptides, and techniques for the efficient extraction and fractionation of these proteins and peptides are needed [24]. Further research is also needed to improve our understanding of the mechanisms involved in the absorption into the blood stream, target sites and their activity in various tissues of biologically active compounds derived from dry peas, chickpeas and lentils.

Reference

1. Luo, QF, Sun, L, Si JY, *et al*. Hypocholesterolemic effect of stilbenes containing extract-fraction from *Cajanus cajan* L. on diet-induced hypercholesterolemia in mice. Phytomedicine. 2008; 15:932-939.
2. Aja PM, Igwenyi IO, Okechukwu PCU, Orji OU, Alum EU. Glob Vet. 2015; 14(3):439-47.
3. Ezike AC, Akah PA, Okoli CC, Okpala CB. Experimental evidence for the antidiabetic Activity of Cajanus cajan leaves in rats. J Basic Clin Pharm [Internet], 2010, 81-4.
4. Nahar L, Nasrin F, Zahan R, Haque A, Haque E, Mosaddik A. Pharmacognocy Res. 2014; 6(2):180-187.
5. Cestele S, Catterall WA. Molecular mechanism of neurotoxin action on voltage-gated sodium channels. Biochimie. 2000; 82:833-892.
6. Anwar MM, Kalpana MA, Bhadra B, Rahman S, Sarker S, Chowdhury MH, *et al*. Adv Nat Appl Sci. 2010; 4(3):311-6.
7. Acevedo BA, Avanza MV, Cháves MG, Ronda F. J Food Eng. 2013; 119(1):65-71.
8. Dai FJ, Hsu WH, Huang JJ, Wu SC. Food Chem Toxicol. 2013; 53:384-91.
9. Amalraj T, Ignacimuthu S. Indian J Exp Biol. 1998; 36(10):1032-3.
10. Habib A, Anisuzzaman AS, Khan RI, Gafur A. 2010. J Bangladesh Pharmacol Soc. 1998; 5:34-38.
11. Dolui AK, Sengupta R. Antihyperglycemic effect of different solvent extracts of leaves of Cajanus cajan and HPLC profile of the active extracts. Asian Journal of Pharmaceutical and Clinical Research. 2012; 5(2):116-119
12. Ariviani S, *et al*. IOP Conf. Ser.: Earth Environ. Sci. 2018; 102 012054
13. Duker-Eshun G, Joroszewski JW, Asomaning WA, Oppong-Boachie F, Christensen SB. Antiplasmodial constiotuents of *Cajanus cajan*. Phytother Res. 2004; 18(2):128-130.
14. Agus S, Achmadi SS and Mubarik NR. Antibacterial activity of naringenin-rich fraction of pea leaves towards *Salmonella thypi*. Asian Pacific Journal of Tropical Biomedicine. 2017; 7(8): 725-728
15. Fu Y, Kadioglu O, Wiench B, Wei Z, Wang W, Luo M, *et al*. Activity of the antiestrogenic cajanin stilbene acid towards breast cancer. The Journal of Nutritional Biochemistry. 2015; 26(11):1273-1282.
16. Zu Y, Liu X, Fu Y, Wu N, Kong Y, Wink M. Chemical composition of the SFE-CO2 extracts from *Cajanus cajan* (L.) Huth and their antimicrobial activity in vitro and in vivo. *Phytomedicine*. 2010; 17(14):1095-1101.
17. Ashidi J, Houghton P, Hylands P, Efferth T. Ethnobotanical survey and cytotoxicity testing of plants of South-western Nigeria used to treat cancer, with isolation of cytotoxic constituents from Cajanus cajan Millsp. leaves. Journal of Ethnopharmacology. 2010; 128(2):501-512.
18. Mona AMA, Negm SAS, Ayman AF, Emad MH. Flavonoid fraction of *Cajanus cajan* prohibited the mutagenic properties of cyclophosphamide in mice *in vivo*. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 2018; 826:1-5.
19. Qi X, Ting-Ting L, Wei Z, Guo N, Luo M, Wang W. Zu Solvent-free microwave extraction of essential oil from pigeon pea leaves [*Cajanus cajan* (L.) Millsp.] and evaluation of its antimicrobial activity. Industrial Crops and Products. 2014; 58:322-328.
20. Titanji VPK, Zofou D, Ngemenya MN. The Antimalarial Potential of Medicinal Plants Used for the Treatment of Malaria in Cameroonian Folk Medicine. African Journal of Traditional, Complementary and Alternative Medicines. 2008; 5(3):302-321.
21. Pratima H, Mathad P. Comparative study on pharmacohnostic and phytochemical composition of seed-coat and cotyledon of *Cajanus Cajan* L, 2017, 2320-5148
22. Mathew D, Lidiya JP, Manila TM, Divyasree P, Sandhya RVTK. Therapeutic molecules for multiple human diseases identified from pigeon pea (*Cajanus cajan* L. Millsp.) through GC-MS and molecular docking. Food Science and Human Wellness. 2018; 6:202-216.
23. Das S, Teja KC, Mukherjee S, Seal S, Sah RK, Duary B, *et al*. Impact of edaphic factors and nutrient management on the hepatoprotective efficiency of Carlinoside purified from pigeon pea leaves: An evaluation of UGT1A1 activity in hepatitis induced organelles. Environmental Research. 2018; 161:512-523.
24. Sarkar R, Hazra B, Mandal S, Biswas S, Mandal N. Assessment of in vitro antioxidant and free radical scavenging activity of Cajanus cajan J Complement Inte Med. 2009; 6(1):1-19.

25. Wu N, Fu K, Fu YJ, Zu YG, Chang FR, Chen YH, *et al*. Antioxidant activities of extracts and main components of pigeonpea [Cajanus cajan (L.) Millsp.] leaves. Molecules. 2009; 14:1032-1043.
26. Liu YM JB, Shen SN, Guo Z, Li ZY, Si JY, Pan RL. Chemical constituents from leaves of *Cajanus cajan*. Chin Tradit Herb Drugs. 2014; 45:466-470.
27. Lui YM, Shen SN, Xia FB, Chang Q, Lui XM, Pan RL. Neuroprotective of Stillbenes from Leaves of Cajanus Cajan against Oxidative Damage Induced by Corticosterone and Glutamate in Differentiated PC12 Cells: Chinese Herbal Medicines. 2015; 7(3):238-246.
28. Tekale S, Jaiwal B, Padul M. Identification of metabolites from an active fraction of Cajanus cajan seeds by high resolution mass spectrometry. Food Chemistry. 2016; 211:763-769.
29. Das S, Teja K, Mukherjee S, Seal S, Sah R, Duary B, *et al*. Impact of edaphic factors and nutrient management on the hepatoprotective efficiency of Carlinoside purified from pigeon pea leaves: An evaluation of UGT1A1 activity in hepatitis induced organelles. Environmental Research. 2018; 161:512-523.
30. Tekale S, Jaiwal B, Padul M. Identification of metabolites from an active fraction of Cajanus cajan seeds by high resolution mass spectrometry. Food Chemistry. 2016; 211:763-769.
31. Wang X, Wei W, Zhao C, Li C, Luo M, Wang W, *et al*. Negative-pressure cavitation coupled with aqueous two-phase extraction and enrichment of flavonoids and stilbenes from the pigeon pea leaves and the evaluation of antioxidant activities. Separation and Purification Technology. 2015; 156:116-123.
32. Kundu R, Dasgupta S, Biswas A, Bhattacharya A, Pal B, Bandyopadhyay D, *et al*. *Cajanus cajan* Linn. (Leguminosae) prevents alcohol-induced rat liver damage and augments cytoprotective function. Journal of Ethnopharmacology. 2008; 118(3):440-447.
33. Stevens PF. onwards. Angiosperm Phylogeny Website, 2001-2008, 9.
34. Doyle JJ, Luckow MA. The Rest of the Iceberg. Legume Diversity and Evolution in a Phylogenetic Context. Plant Physiology. 2003; 131(3):900-10.
35. Ahsan R, Islam M. Hepatoprotective activity of methanol extract of some medicinal plants against carbon tetrachloride-induced hepatotoxicity in rats. Euro J Sci Res. 2009; 37:302-10.
36. Alen-Ruiz F, Garcia-Falcon MS, Perez-Lamela MC, Martinez-Carballo E, Simal-Gandar J. Influence of major polyphenols on antioxidant activity in Mencia and Brancellao red wines. Food Chemistry. 2009; 113:53-60.
37. Chen DH, Li HY, Lin H. Chin Tradit & Herb Drugs. 1985; 16:134-136.
38. Cooksey CJ, Dahiya JS, Garratt PJ, Strange RN. Phylochemistry. 1982; 21:2935.
39. Cooksey CJ, Dahiya JS, Garratt PJ, Strange RN. Science. 1983; 220:1398.
40. Duker-Eshun G, Jaroszewski JW, Asomaning WA, Oppong-Boachie F, Brogger-Christensen S. Antiplasmodial constituents of *Cajanus cajan*. Phytotherapy Research. 2004; 18(2):128-130.
41. Fan YG, Xu CY, He W. Chin J Basic Med in Tradit Chin Med. 2002; 8:35-37.
42. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. Journal of Ethnopharmacology. 2002; 81(1):81-100.
43. Duker-Eshun G, Jaroszewski JW, Asomaning WA, Oppong-Boachie F, Brogger Christensen S. Antiplasmodial constituents of *Cajanus cajan*, Phytother. Res. 2004; 18:128-130.
44. Green PW, Stevenson PC, Simmonds MS, Sharma HC. Phenolic compounds on the pod-surface of pigeonpea, *Cajanus cajan*, mediate feeding behavior of Helicoverpa armigera larvae. Journal of Chemical Ecology. 2003; 29(4):811-821.
45. Chang HM, H PP. But, Pharmacology and Applications of Chinese Materia Medica, World Scientific Publishing, Singapore 1986, 1(2).
46. Hélène LC, Toby PR, Quentin CB. An apparent reversal in floral symmetry in the legume Cadia is a homeotic transformation. PNAS. 2006; 103(32):12017-12020.
47. Inman WD, Hoppe DC. In: Compositions containing hyportrigly ceridemically active stilbenenoids. WIPOI. Bureau, 2002.
48. Kong Y, Fu YJ, Zu YG, Chang FR, Chen YH, Liu XL, *et al*. Cajanuslactone a new coumarin with anti-bacterial activity from pigeon pea leaves. Food Chem. 2010; 121:1150-1155
49. Liogier HA. Descriptive flora of Puerto Rico and adjacent islands, Spermatophyta. Editorial de la Universidad de Puerto Rico, Río Piedras,1998; PR. 481.
50. Luo QF, Sun L, Si JY, Chen DH. Hypocholesterolemic effect of stilbenes containing extract fraction from *Cajanus cajan* on diet induced hypercholesterolemia in mice. Phytomedicine 2008;15:932-9
51. Luo M, Liu X, Zu Y, Fu Y, Zhang S, Yao L, *et al*. Cajanol, a novel anticancer agent from Pigeonpea [*Cajanus cajan* (L.) Millsp.] roots, induces apoptosis in human breast cancer cells through a ROS-mediated mitochondrial pathway. Chem. Biol. Interac. 2010; 188:151-60.
52. Le Bail JC, Aubourg L, Habrioux G. Effects of pinostrobin on estrogen metabolism and estrogen receptor transactivation. Cancer Letters. 2000; 156:37-44.
53. Nicholson RA, David LS, Pan RL, Xin Min Liu. Pinostrobin from *Cajanus cajan* (L.) Millsp. Inhibits sodium channel-activated depolarization of mouse brain synaptoneurosomes. Fitoterapia. 2010; 81:826-9.
54. Pal DK, Sannigrahi S, Mazumder UK. Analgesic and anticonvulsant effects of saponin isolated from the leaves of Clerodendrum infortunatum Linn. In mice. Indian J Exp. Biol. 2009; 47:743-7.
55. Pal DK, Sahoo M, Mishra A. Analgesic and anticonvulsant effects of saponin isolated from the stems of Opuntia vulgaris Mill in mice. Euro Bull Drug Res. 2005; 13:91-7.
56. Pal DK. Evaluation of CNS activities of aerial parts of *Cynodon dactylon* Pers. in mice. Acta Pol Pharm Drug Res. 2008; 65:37-43.
57. Singh S, Mehta A, John J, Mehta P. Anthelmintic

potential of Andrographis paniculata, Cajanus cajan and Silybum marianum. Pharmacog J. 2010; 2:71-3.
58. Smartt J. Tropical pulses. Longman Group Limited, London, 1976, 348.
59. Upadhyay B, Parveen, Dhaker AK, Kumar A. Ethnomedicinal and ethnopharmaco - statistical studies of Eastern Rajasthan, India. J Ethnopharmacol. 2010; 129:64-86.
60. Wu D, Nair MG, DeWitt DL. Novel compounds from Piper methysticum Forst (Kava Kava) roots and their effect on cycloxygenase enzyme. J Agric Food Chem. 2002; 50:701-5.
61. Wu N, Fu K, Fu YJ, Zu YG, Chang FR, Chen YH, *et al*. Antioxidant activities of extracts and main components of pigeonpea [*Cajanus cajan* (L.) Millsp.] leaves. Molecules. 2009; 14:1032-43.
62. Yuan-gang Zu, Xiao-lei, Yu-jie Fu, NanWu, YuKong, Michael W. Chemical composition of the SFE-CO2 extracts from *Cajanus cajan* (L.) Huth and their antimicrobial activity in vitro and in vivo. Phytomed. 2010; 17:1095-101.
63. Yuan H, Li X, He W. Chin J Tradit Med Traum & Orthop. 1999; 17:4-8.
64. Yuan J, Zhang J, Lin J, Xiong YH. Tradit Chin Drug Res & Clin. Pharm. 2004; 15:429-431.
65. Zhang DY, Zhang S, Zu YG, Fu YJ, Kong Y, Gao Y, *et al*. Negative pressure cavitation extraction and antioxidant activity of genistein and genistin from the roots of pigeon pea. Separation and Purification Tech. 2010; 74:261-70
66. Zheng YY, Yang J, Chen DH, Sun L. Effects of the stilbene extracts from *Cajanus cajan* L. on ovariectomy-induced bone loss in rats. Acta Pharmaceutical Sinica. 2007; 42:562-565.