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The medical Importance of *Cicer arietinum* - A review

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Abstract: The phytochemical analysis of *Cicer arietinum* seeds revealed the presence of carbohydrates, proteins, amino acids, fixed oils, phytosterols, alkaloids, phenolic compounds and tannins, flavonoids, glycosides, saponins, amino acids, iron, phosphate, sulphate, and chloride. *Cicer arietinum* possessed aphrodisiac, estrogenic, antioxidant, ACE- inhibition, antidiabetic, anti-inflammatory, hypocholesterolaemic, antidiarrhoeal antidiarrhoeal, anticonvulsant, hepatoprotective, anticancer, diuretic, anti-nephrolithiasis and many other pharmacological effects. This review was designed to highlight the chemical constituents and pharmacological effects of *Cicer arietinum*.

Keywords: *Cicer arietinum, constituents, pharmacology*

I. INTRODUCTION

During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world[(1)]. There are hundreds of significant drugs and biologically active compounds developed from the traditional medicinal plants. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects[(2-60)]. The seeds of *Cicer arietinum* as well as their consumption as a food, they were used traditionally as aphrodisiac, for bronchitis, catarrh, cholera, constipation, diarrhea, dyspepsia, flatulence, snakebite, sunstroke, and warts. Acids (malic and oxalic acids) are supposed to lower the blood cholesterol levels. In India these acids were harvested by spreading thin muslin over the crop during the night. In the morning the soaked cloth is wrung out, and the acids are collected and used as hypolipidemic. Seeds were also considered antibilious. The phytochemical analysis of *Cicer arietinum* seeds revealed the presence of carbohydrates, proteins, amino acids, fixed oils, phytosterols, alkaloids, Phenolic compounds and tannins, flavonoids, glycosides, saponins, amino acids, iron, phosphate, sulphate, and chloride. *Cicer arietinum* possessed aphrodisiac, estrogenic, antioxidant, ACE- inhibition, antidiabetic, anti-inflammatory, hypocholesterolaemic, antidiarrhoeal antidiarrhoeal, anticonvulsant, hepatoprotective, anticancer, diuretic, anti-nephrolithiasis and many other pharmacological effects. This review was designed to highlight the chemical constituents and pharmacological effects of *Cicer arietinum*.

Plant profile:

Synonyms:

Cicer album hort., *Cicer arientinium*, *Cicer arietinum* subsp. *arietinum*, *Cicer edessanum* Bornm., *Cicer grossum* Salisb., *Cicer nigrum* hort., *Cicer physodes* Rchb., *Cicer rotundum* Alef., *Cicer sativum* Schkuhr and *Cicer sintenisii* Bornm[(61)].

Taxonomic classification:

Kingdom: Plantae; **Division**: Magnoliophyta; **Class**: Magnoliopsida; **Order**: Fabales; **Family**: Fabaceae; **Subfamily**: Faboideae; **Genus**: *Cicer;* **Species**: *Cicer arietinum*[(62-63)].

Common names:

Arabic: hummus, hommos, lablabi; **Chinese:** ying zui dou**; English:** Bengal gram, chickpea, garbanzo**; French:** pois chiche**; German:** kichererbse**; India:** kala chana, Bengal gram**; Italian:** cece**; Portuguese:** grão-de-bico**; Spanish**: garbanzo; **Swedish:** kikärt; **Turkish**: nohut[(63)].

Distribution:

It was a cultivated crop grown in tropical, sub-tropical and temperate regions. It was believed that the species originated in the southern Caucasus and northern Persia, southeastern Turkey and Syria[(64-67)]. However, botanical and archeological evidence showed that chickpea was first domesticated in the Middle East and was widely cultivated in India, Mediterranean area, the Middle East, and Ethiopia since antiquity. Wild species are most abundant in Turkey, Iran, Afghanistan, and Central Asia[(68)].

Now, it was cultivated in **Africa**: Algeria, Egypt, Ethiopia, Kenya, Libya, Madeira, Morocco, Somalia, Sudan, Tanzania, Tunisia, Uganda, Zaire, Zimbabwe; **Asia** : Afghanistan, Armenia, Azerbaijan, Bhutan, China, Gruzia, India, Indonesia, Iran, Iraq, Java, Kazakhstan, Kirgizstan, Mongolia, Myanmar, Nepal, Pakistan, Russia in Asia, Sri Lanka, Taiwan, Turkmenistan, Uzbekistan; **Middle East**: Cyprus, East Aegean (Greek), Jordan, Lebanon,

Oman, Syria, Turkey, Yemen; **Europe**: Albania, Balearic Is, Belarus, Bulgaria, Corsica, Crete, Estonia, former Yugoslavia, France, Greece, Italy, Lithuania, Moldova, Portugal, Romania, Russia in Europe, Sardinia, Sicily, Spain, Ukraine; **Australasia**; **Caribbean**: Caribbean-TRP, Dominican Republic, Haiti; **Central America**: Costa Rica, Guatemala, Mexico; **South America**: Argentina, Bolivia, Chile, Colombia and Peru[69].

Description:

Stems are branched, erect or spreading, sometimes shrubby much branched, 0.2-1 m tall, glandular pubescent, olive, dark green or bluish green in color. Root system is robust, up to 2 m deep, but major portion up to 60 cm. Leaves imparipinnate, glandular-pubescent with 3-8 pairs of leaflets and a top leaflet (rachis ending in a leaflet); leaflets ovate to elliptic, 0.6-2.0 cm long, 0.3-1.4 cm wide; margin serrate, apex acuminate to aristate, base cuneate; stipules 2-5 toothed, stipules absent. Flowers solitary, sometimes 2 per inflorescence, axillary; peduncles 0.6-3 cm long, pedicels 0.5-1.3 cm long, bracts triangular or tripartite; calyx 7-10 mm long; corolla white, pink, purplish (fading to blue), or blue, 0.8-1.2 cm long. The staminal column is diadelphous (9-1) and the ovary is sessile, inflated and pubescent. Pod rhomboid ellipsoid, 1-2 with three seeds as a maximum, and inflated, glandular-pubescent. Seed color cream, yellow, brown, black, or green, rounded to angular, seedcoat smooth or wrinkled, or tuberculate, laterally compressed with a median groove around two-thirds of the seed, anterior beaked [66,68,70].

Traditional uses:

The seeds were used traditionally as aphrodisiac, for bronchitis, catarrh, cholera, constipation, diarrhea, dyspepsia, flatulence, snakebite, sunstroke, and warts. Acids (malic and oxalic acids) are supposed to lower the blood cholesterol levels. In India these acids were harvested by spreading thin muslin over the crop during the night. In the morning the soaked cloth is wrung out, and the acids are collected and used as hypolipidemic. Seeds were also considered antibilious[8]**.** *Cicer arietinum* which is generally consumed as a seed food is a good source of protein and traditionally used in pacifying the burning sensation in stomach, hepatomegali, stomatitis, inflammations, skin diseases and bronchitis[71].

Chickpeas have also been widely used in traditional Uighur medicine to treat and prevent hypertension, hyperlipidemia, diabetes, itchy skin, flatulence, low libido, tumor formation and osteoporosis[72].

Part use: Leaves, seeds and seedpod[68,71-72].

Physicochemical (%w/w):

Roots: alcohol soluble extractive 16.24, water soluble extractive 7.36, chloroform soluble extractive 3.28, petroleum ether soluble extractive 0.72, acetone soluble extractive 3.76, moisture content13.33, total ash 19.83, acid insoluble ash 13.96 and water soluble ash14.46. **Seeds**: alcohol soluble extractive 3.7- 4.5, water soluble extractive 5.5- 6.2, total ash 6.8 6.9, acid-insoluble ash 1.8- 1.9, water-soluble ash 1.5- 1.9 and swelling index 3ml/g[73-74].

II. CHEMICAL CONSTITUENTS

The preliminary phytochemical screening of *Cicer arietinum* seeds revealed the presence of carbohydrates, proteins, amino acids, fixed oils, phytosterols, alkaloids, Phenolic compounds and tannins, flavonoids, glycosides, saponins, amino acids, iron, phosphate, sulphate, and chloride [73-76].

Chickpeas were an excellent source of carbohydrates and proteins, which constitute about 80% of the total dry seed weight. Dried chickpeas contain about 20% protein. The bulk of the seed was made up of carbohydrates (61%) and 5% fat. Crude fiber is mostly located within the seed coat. The seeds were relatively rich in lecithin, potassium, phosphorus, calcium, folate and vitamin C, and also have small quantities of vitamins A and B. 100 g of chickpeas can supply about 350 calories[62,77-78]. Raw whole seeds contain per 100 g: 357 calories, 4.5-15.69% moisture, 14.9-24.6 g protein, 0.8-6.4 % fat, 2.1-11.7 g fiber, 2-4.8 g ash, 140-440 mg Ca, 190-382 mg P, 5.0-23, 9 mg Fe, 0-225 m g b-carotene equivalent, 0.21-1.1 mg thiamin, 0.12-0.33 mg riboflavin, and 1.3-2.9 mg niacin [68,77].

The chemical composition of (Kabuli)-type chickpea (*Cicer arietinum* L.) developed in Argentina was evaluated for nutritional purpose. Protein, oil and ash contents, fatty acid, tocopherol and mineral element compositions were studied. Among the studied genotypes, protein content ranged from 18.46 to 24.46 g/100g, oil content ranged from 5.68 to 9.01 g/100g and ash from 3.55 to 4.46 g/100g. Linoleic, oleic and palmitic acids were the most abundant fatty acids. The average oleic-to-linoleic ratio was 0.62 and average iodine value was 117.82. Tocopherols were found in chickpea seeds in relatively similar amounts across all genotypes. Mineral element analysis showed that chickpea was rich in macronutrients such as K, P, Mg and Ca[79].

The amino acid composition (%) of seed proteins were: 7.2 g lysine, 1.4 g methionine, 8.8 g arginine, 4.0 g glycine, 2.3 g histidine, 4.4 g isoleucine, 7.6 g leucine, 6.6 g phenylalanine, 3.3 g tyrosine, 3.5 g threonine,

4.6 g valine, 4.1 g alanine, 11.7 g aspartic acid, 16.0 g glutamic acid, 0.0 g hydroxyproline, 4.3 g proline, and 5.2 g serine [68,77,80].

Fatty acid compositions of Desi-type included: oleic 52.1, linoleic 38.0, myristic 2.74, pactic 5.11, and steatic 2.05, and of Kabuli-type: oleic 50.3, linoleic 40.0, myristic 2.28, palmitic 5.74, stearic 1.61, and arachidic 0.07%[68].

The volatile compounds identified in the Roasted Chickpea (*Cicer arietinum* L) included 61 aroma-active compounds. They are consisted of aldehydes (25%), hydrocarbons (25%), terpenoids (20%), esters (8%), ketones (8%), alcohols (8%) and heterocyclic (8%)[81].

Phyto-oestrogen content of *Cicer arietinum* (daidzein, genistein and secoisolariciresinol) were 11–192, 69–214, 7–8 μg/100 g dry weight[82].

Further studies showed that chickpea seeds and sprouts. They contain at least the following 8 phytoestrogens: biochanin A, formononetin, genistein, biochanin A-7-O-β-D-glucoside, calycosin, trifolirhizin, ononin, and sissotrin[83].

The influence of different germination conditions on isoflavone contents in chickpea sprouts was investigated. Chickpea sprouts were germinated under different experimental conditions, including germination in the dark (GD), in the light (GL), under ethanol stress (GE), or under salt stress (GS) in the dark. The results demonstrated that the isoflavone contents in chickpea sprouts germinated with these various conditions was significantly increased ($p<0.05$) compared to those in untreated chickpea seeds. The maximum amount of total isoflavones was obtained from chickpea sprouts in the GL group on day 8. The contents of formononetin and biochanin A in this group were 154 and 130 times higher, respectively, than in untreated seeds and 1.2 times higher than in sprouts in the GD group. Moreover, the isoflavone contents of chickpea sprouts in the GE and GS groups were also higher ($p < 0.05$) than those in the GD group. A solution of 3% ethanol and 0.03 mol/l salt seemed to be the most optimal for isoflavone production among selected solutions. Most of the isoflavone contents were significantly increased ($p<0.05$), especially formononetin and biochanin A, while the genistein content decreased with germination. Ononin, pseudobaptigenin, and glycitein acetylated glucoside were only detected in germinated chickpeas[84].

The effects of soaking, cooking and industrial dehydration on the phenolic profile, and antioxidant capacity in two chickpea varieties (Sinaloa and Castellano) were studied. Chromatographic analysis identified a total of 24 phenolic components, being isoflavones the main phenolics in raw and processed Sinaloa and Castellano flours. The impact of the industrial dehydration was different depending on the chickpea variety. Although Castellano chickpea exhibited the highest levels of phenolic compounds (103.1 μg/g), significant reductions were observed during processing; in contrast, the dehydration did not cause any further effects in Sinaloa flours. Interestingly, Sinaloa variety showed high thermal stability of isoflavones during processing. The levels of antioxidant capacity were in accordance with the behavior of phenolic compounds exhibiting noticeable reductions in Castellano chickpea and not relevant changed in Sinaloa chickpea[85].

Seed coat, cotyledon and embryonic axe fractions of chickpea (*Cicer arietinum* L.) were evaluated for their phenolic composition in relation to antioxidant activities. Compositional analysis of phenolics by HPLC revealed a wide variation in the distribution of flavonols, isoflavones, phenolic acids and anthocyanins among fractions. Although cotyledon fractions were rich in phenolic acids, the concentrations of flavonols such as quercetin, kaempferol, and myricetin were significantly ($p< 0.05$) lower than the embryonic axe and seed coat fractions. Ferulic, chlorogenic, caffeic, and vanillic acids were the principal phenolic acids found in cotyledons. The most striking difference was the predominance of isoflavones in embryonic axe fractions. The isoflavone genistein was detected in all three fractions of chickpea. Seed coat fractions having higher total phenolic indexes which were found to be the most active 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavengers (IC_{50} 13.1 to 18.6 microg/ml) followed by embryonic axe and cotyledon fractions (IC_{50} 15.4 to 34.2 microg/ml). Hydrogen peroxide (H_2O_2) scavenging capacities of cotyledons, embryonic axe and seed coats of chickpea were 12.3, 34.1 and 78.6% [86].

III. PHARMACOLOGICAL EFFECTS

Effects on Reproductive systems

Aphrodisiac effect:

The potential aphrodisiac effect of seeds of methanolic extract of *Cicer airetinum* (MECA) was studied in sexually sluggish male albino rats. Sexual behavioral parameters like mount frequency (MF), intromission frequency (IF), ejaculation frequency (EF), ejaculation latency (EL), mount latency (ML) and intromission latencies (IL) were observed in male rats. The male serum cholesterol and testosterone concentrations were also estimated. Oral administration of MECA at 200 and 400 mg/kg body weight was significantly increased the MF, IF, EF and EL ($P < 0.05$) in comparison to control groups, while, ML and IL were significantly decreased ($p<0.05$). The extract also significantly ($p<0.05$) increased the serum cholesterol and testosterone levels. From these effects, MECA possessed significant increase in the sexual activity in male rats. The authors postulated

that the augmented sexual behavior in male rats might be due to the presence of alkaloids, saponins and flavonoids in MECA[87].

Estrogenic effects:

Aqueous, alcoholic and chloroform extract of *Cicer arietinum* were tested for abortifacient activity in female albino rat, it was given from day 11 to 15 of pregnancy at the dose level of 100, 200 and 400 mg/kg body weight. The aqueous extract at a dose of 400mg/kg was found to be most effective abortifacient. Similarly it was also found to increase the reproductive organ weight and possess estrogenic activity when tested in immature ovariectomised female albino rats[88]. Isoflavones, the important chemical components of the seeds and sprouts of chickpea, have drawn attention due to their potential therapeutic use. The estrogenic activity of isoflavones extracted from chickpea *Cicer arietinum* L sprouts (ICS) was observed recently. MTT assay showed that ICS at the low concentration ranges (10^{-3} /mg/l) promoted MCF-7 cell growth, while at high concentrations, (>1 mg/l) inhibited cell proliferation, indicating that ICS worked at a diphasic mechanism. Flow cytometric analysis further calculated the proliferation rate of ICS at low concentration (1 mg/l). ERα/Luc trans-activation assay and then semi-quantitative RT-PCR analysis indicated that ICS at low concentrations induced ERα-mediated luciferase activity in MCF-7 cells and promoted the ER downstream target gene pS2 and PR trans-activation. These effects were inhibited by ICI 182,780, a special antagonist of ER, indicating that an ER-mediating pathway was involved. Alkaline phosphatase (AP) expression in Ishikawa cells showed that ICS at low concentrations stimulated AP expression. Accordingly, ICS has significant estrogenic activity *in vitro*. ICS may be useful as a supplement to hormone replacement therapy and in dietary supplements[89].

Isoflavones extracted from chickpea sprouts (ICS) stimulated estrogen responsive element (ERE)-promoter activity in cells, and concurrent treatment with the nonselective estrogen receptor antagonist ICI 182,780 abolished the estrogenic activity induced by ICS[90].

The estrogenic activities of the isoflavones extracted from chickpea sprouts (ICS) was studied in ovariectomized rats (OVX). The rats were administered via intragastric gavage 3 different doses of ICS (20, 50, or 100 mg/kg/day) for 5 weeks. Their uterine weight and serum levels of 17β-estradiol (E2), follicle stimulating hormone (FSH) and luteinizing hormone (LH) were measured. The epithelial height, number of glands in the uterus, and number of osteoclasts in the femur were histologically quantified, and the expression of proliferating cell nuclear antigen (PCNA) was assessed immunohistochemically. Bone structural parameters, including bone mineral density (BMD), bone volume/tissue volume (BV/TV), trabecular thickness (Tb.Th) and trabecular separation (Tb.Sp) were measured using Micro-CT scanning. Treatments of OVX rats with ICS (50 or 100 mg/kg/day) produced significant estrogenic effects on the uteruses, including the increases in uterine weight, epithelial height and gland number, as well as in the expression of the cell proliferation marker PCNA. The treatments changed the secretory profile of ovarian hormones and pituitary gonadotropins: (serum E2 level was significantly increased, while serum LH and FSH levels were decreased) compared with the vehicle-treated OVX rats. Furthermore, the treatments significantly attenuated the bone loss, increased BMD, BV/TV and Tb.Th and decreased Tb.Sp and the number of osteoclasts. Treatment of OVX rats with the positive estrogen control drug E2 (0.25 mg/kg/day) produced similar, but more prominent effects[91].

Antioxidant effects:

The free radicals scavenging, antioxidant properties and intestinal α-glucosidase inhibitory activity of methanol extract of two varieties of *Cicer arietinum* were evaluated. Compared with raw seeds increase in total polyphenol and flavonoids concentration in green gram sprouts and Kabuli Chana sprouts (KCs) were recorded. Total protein concentrations in sprouts did not differ from non-sprouted grains. 2,2'- Azinobis (3-ethyl benzthiazoline-6-sulphonic acid) cation scavenging activity was more than twice in Bengal gram sprouts of (BGs) and KCs than their raw seeds. 2,2-diphenyl-1-picrylhydrazyl, hydrogen peroxide scavenging, nitro blue tetrazolium reducing and glucose-induced Hb-glycation inhibitory activity did not differ from non-sprouted raw grains. Increase in rat intestinal α-glucosidase inhibitory activity was observed in BGs and KCs. BGs significantly mitigated first 30 min starch-induced postprandial glycemic excursions and reduced 2 h postprandial glycemic load[92].

The extent of free radical scavenging properties and antioxidant effects of crude extracts of sprouted *Cicer arietinum* (Chick pea/Chana/Bengal gram) seeds were evaluated. Two main varieties of *Cicer arietinum* seeds viz. Kabuli-Chana (cream seed-coat) and Bengal gram (brown seed-coat) were examined and compared for their free radical scavenging properties and antioxidant effects. Free radical scavenging properties were evaluated against stable 2, 2-diphenyl-1-picrylhydrazyl radical (DPPH) and hydrogen peroxide radical and the extent of antioxidant effect was assessed by lipid peroxidation induced by ferrous sulphate on the lipid present in the liver homogenate. The results showed that the two *Cicer arietinum* extracts were differed in their capacities to quench or inhibit DPPH, hydrogen peroxide and lipid peroxide. Brown colored *Cicer arietinum*

sprouts showed the greatest activity against DPPH radicals, hydrogen peroxide radicals and lipid peroxide compared to the cream variety[93].

The root of *Cicer arietinum* was extracted using solvents of different polarities and explored for *in vitro* free radical scavenging activity. Preliminary assays of three different extracts of *Cicer arietinum* root showed that the extracts possess electron donating ability and reduction of ferric ion to ferrous in a cell free system at pH-7.4. It has also been found from total antioxidant capacity as assessed by reduction of molybdate showed *Cicer arietinum* root extracts to possess (standard) ascorbic acid equivalents per milligrams of the extracts. Hydroalcoholic root extract was found more effective when compared to alcoholic and water extracts in scavenging 1, 1-diphenyl-2-picrylhydrazyl, reducing ferric ion and molybdate reduction in antioxidant capacity. A significant correlations exist between extract concentrations and percentage scavenging activity of radicals in all models[94].

The lectin was isolated from the seeds of *Cicer arietinum*. The antioxidant activity of the eluted fractions containing lectin was determined. DPPH scavenging activity of isolated lectin from *Cicer arietinum* Linn. at concentration of 10, 100, 250,500 and 1000 (µg/ml) were 19.5 ±4.29, 34.2 ± 0.77, 42.0 ±0.35 54.3 ± 1.14 and 69.2 ± 3.67(% Inhibition)[95].

Extract and its different fractions of mature pod wall of *Cicer arietinum* Linn. were assessed for their antioxidant activity by *in vitro* methods. Antioxidant activity was studied using 1, 1- Diphenyl-2-Picrylhydrazyl (DPPH), nitric oxide scavenging activity, hydrogen peroxide scavenging activity, reducing power assay. Results showed that extracts and fractions exhibited significant DPPH, nitric oxide and hydrogen peroxide activity[96].

Rats treated with CCl_4 showed a significant decrease in superoxide dismutase, catalase, GSH, increased MDA levels. The group of rats treated with petroleum ether extract of *Cicer arietinum* (200mg/kg, po, once daily) showed no significance increase in catalase, GSH, SOD and no significant decrease in MDA levels. Whereas group treated with low doses of methanol and aqueous extracts (200mg/kg) showed a significant increase in the catalase, GSH, GST and a significant decrease in MDA. On the other hand, 250 and 500 mg/kg of ethanolic seeds extract of *Cicer arietinum* showed hepatoprotective against the paracetamol induced hepatotoxicity in rats [76, ,97].

ACE- inhibition:

Treatment of legumin of *Cicer arietinum* with alcalase yielded a hydrolysate that inhibited the angiotensin I converting enzyme with an IC_{50} of 0.18 mg/ml. Fractionation of this hydrolysate by reverse phase chromatography afforded six inhibitory peptides with IC_{50} values ranging from 0.011 to 0.021 mg/ml. All these peptides contain the amino acid methionine and are also rich in other hydrophobic amino acids. Hydrolysates of chickpea legumin obtained by treatment with alcalase are a good source of peptides with angiotensin-1converting enzyme inhibitory activity[98].

Antidiabetic effect:

It was reported that the seeds reduced postprandial plasma glucose and were useful in the treatment of diabetes[99-100]. The antihyperglycaemic activity of petroleum ether extract of *Cicer arietinum* (PEECA) seeds was evaluated at three different doses i.e. 100, 200 and 400 mg/kg po in alloxan (70 mg/kg iv) induced diabetic mice. In both acute and subacute studies serum glucose level (SGL) was measured. The change in body weight was noted during subacute study. Oral glucose tolerance test (OGTT) was performed in both diabetic and non-diabetic mice previously loaded with (2.5 g/kg po) glucose. Glyburide (10 mg/kg) was used as a standard drug. The maximum reduction in SGL was observed in PEECA (400 mg/kg) group at 6h (137.17 mg/dl) in acute study and on 21st day (217.79 mg/dl) in subacute study respectively. In glyburide treated mice the maximum reduction in SGL was observed at 6h (194.97 mg/dl) and on 21st day (267.40mg/dl) respectively. PEECA (400 mg/kg) and glyburide (10 mg/kg) prevented loss of body weight in diabetic mice. OGTT showed increased glucose threshold in non-diabetic and diabetic mice. Accordingly, PEECA showed antihyperglycaemic activity comparable with glyburide[101].

Anti-inflammatory effects:

The anti-inflammatory potency of methanolic and ethanolic extracts of *Cicer arietinum* seeds at different doses (250 mg/kg and 500 mg/kg body weight) were investigated against carrageenan and histamine induced paw edema in rats. All doses of the extracts showed a significant ($p<0.001$) anti-inflammatory activity when compared to control groups and with standard drug (Indomethacin 10 mg/kg, orally). Both the methanolic and ethanolic extracts showed the dose dependant activity. Among these extracts, the methanolic 500 mg/kg and ethanolic 500 mg/kg extracts of *Cicer arietinum* showed maximum anti-inflammatory activity[102].

Hypocholesterolaemic effect:

The hypocholesterolaemic and antioxidant activities of chickpea protein were studied. All hydrolysates tested exhibited better hypocholesterolaemic activity when compared with chickpea protein isolate. The highest cholesterol micellar solubility inhibition (50%) was found after 60 min of treatment with alcalase followed by 30 min of hydrolysis with flavourzyme. To test antioxidant activity of chickpea proteins three methods were used: β-carotene bleaching method, reducing power and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging effect. Chickpea hydrolysates showed better antioxidant activity in all assays, especially reducing power and DPPH scavenging effect than chickpea protein isolate[(103)].

Antidiarrhoeal effect:

The antidiarrhoeal activity of the hydroalcoholic extract of *Cicer arietinum* roots and its acetone and methanol fraction was studied based on their effect on Castor oil induced diarrhea in mice. The results showed that the highest reduction in diarrhoea was observed in hydroalcoholic extract (24.63 %), while Loperamide (5 mg/kg) inhibited the castor oil induced diarrhoea by 75.37 %[(75)].

Anticonvulsant effect:

A dichloromethane extract was prepared from fruits of *Cicer arietinum* by percolation. Different doses of the extract were administered to the mice and pentylenetetrazole induced clonic seizure occurrence and latency were recorded 30 min thereafter. The extract protected mice against clonic seizures induced by pentylenetetrazole, dose-dependently (ED_{50}= 3g/kg) with no toxic and lethal effects[(104-105)].

Hepatoprotective effect:

The Hepatoprotective activity of petroleum ether, methanol and aqueous extracts of aerial parts (except fruits) of *Cicer arietinum* L was studied against CCl_4 induced hepatotoxicity in rats. The plant extracts were administered to the experimental rats (200 and 400 mg/kg/day po for 20 days). The Hepatoprotective activity of these extracts was evaluated by liver function biochemical parameters (serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, serum alkaline phosphatase, total bilirubin, lipid peroxidation, superoxide dismutase, catalase, reduced glutathione) and histopathological studies of liver. Pre-treatment of the rats with petroleum ether, methanol and aqueous extract prior to CCl_4 administration caused a significant reduction in the values of SGOT, SGPT, SALP, LPO, total bilirubin and significant increase in SOD, CAT, GSH ($P<0.01$), almost comparable to the Silymarin. The hepatoprotective activity was confirmed by histopathological examination of the liver tissue of control and treated animals. Histology of liver sections of the animals treated with the extracts showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration[(76)].

Antimicrobial effects:

The antibacterial activities of the extracts obtained from *Cicer arietinum* L. varieties (seed extract, fruit skin extract and aerial part extract) were studied *in vitro*. Chickpea seed extracts (Cse) showed varying antibacterial activity against Gram negative strains (*E. coli*, *P. aeruginosa*, *K. pneumoniae*) in MIC range 16–64 μg/ ml, but were less active against gram-positive (*S. aureus*, *B. subtilis*, *E. faecalis*) strains with MIC of 64 μg/ ml. Statistically different MICs were observed between the extracts of the fruit skin (Cfs) and the aerial part (Cap) ($p<0.05$). The antibacterial activity of Chickpea fruit skin (Cfs) and Chickpea aerial parts (Cap) extracts were not statistically different ($p>0.05$) as they showed the same degree of inhibition against Gram-negative (*E. coli* and *K. pneumoniae*) bacteria and gram positive bacterium, (*E. faecalis* at the concentration of 32 μg/ml). Additionally, they were both less effective against *P. aeruginosa*, *S. aureus*, and *B. subtilis* at a concentration of 64 μg/ml. Of all the Chickpea extracts, Chickpea seed extract (Cse; $p < 0.05$). exhibited the strongest antifungal activity against *C. albicans* at a concentration of 8 μg/ml. Even at a concentration of 16 μg/ml, fruit skin (Cfs) and aerial part (Cap) extracts showed lower antifungal activity than the seed extract[(106)].

The hydroalcoholic extract and its acetone and methanol fractions of the root of *C. arietinum* were studied for their antibacterial activity by disc diffusion method against different gram positive (*Staphylococcus aureus* and *Bacillus subtilis*) and gram negative (*Escherchia coli*) bacteria. It was observed that the hydroalcoholic extract and its acetone and methanol fraction showed significant activity against all the tested microorganisms [*E. coli* (NCIM - 2831), *S. aureus*, (NCIM - 2079) *B. subtilis* (NCIM - 2439)] and the hydroalcoholic extract showed the highest activity (13 mm) against *S. aureus*[(107)].

Cicer arietinum L ferritin was successfully isolated with two subunits with molecular weights of 20.1- kDa and 29- kDa respectively. The antibacterial effect of ferritin extracted from Chick pea (*Cicer arietinum* L.*)* was evaluated against Gram negative microorganisms (*Escherichia coli, Pseudomonas aeruginosa, Kliebsiella pneumonia, Proteus vulgaris*), as well as Gram-positive microorganism (*Staphylococcus aureus, Staphylococcus epidermis*). Among all the test pathogens *E. coli* was found susceptible (with zone of inhibition 8 mm) to the purified ferritin extract[(108)].

Several proteins, including a glucanase, a chitinase, an antifungal cyclophyllin-like protein, and three antifungal peptides designated cicerin, arietin, and cicearin were isolated from the chickpea (*Cicer arietinum* L)[(109)].

Two antifungal peptides with novel N-terminal sequences were isolated from chickpea. Although the two chickpea peptides, cicerin and arietin, were similar in molecular weight (5-8 kDa), they differed somewhat in antifungal activity. Arietin was more potent against *M. arachidicola*, *B. cinerea*, and *F. oxysporum* while cicerin exhibited a higher cell-free translation-inhibiting activity than arietin[(110)].

An antifungal protein, was isolated from *Cicer arietinum* and purified by gel filtration and tesred using agar diffusion method against human pathogenic fungi of ATCC strains and against clinical isolates of *Candida krusei, Candida tropicalis* and *Candida parapsilosis*. MIC values were varied from 1.56 to 12.5 µg/ml. Protein isolated from *Cicer arietinum* also inhibited the growth of fungal strains which are resistant to fluconazole[(111)].

The crude water extract of *Cicer arietinum* showed most significant antifungal activity against *Drechslera tetramera* even at lower concentration of 5%. In dichloromethane fraction, the inhibitory effect was found to be proportional with the applied concentration[(112)].

The antiviral activities of the extracts from the seed, fruit skin and aerial parts of ten varieties of *Cicer arietinum* (Chickpea) were evaluated against Herpes simplex type 1 *(*HSV-1*)* and Parainfluenza-3 *(*PI-3*)* viruses. Madin-Darby Bovine Kidney and Vero cell lines were employed for antiviral assessment of the *Citer arientinum L.* extracts, in which acyclovir for HSV-1 and oseltamivir for PI-3 were tested as reference drugs. *Cicer arietinum* seed extracts (Aydin 92 variety) possesses significant antiviral activity against both DNA (max to min CPE inhibitory conc: 32-4 µg/ ml) and RNA (max to min CPE inhibitory conc: 32-16 µg/ ml) viruses compared to the fruit skin and aerial part extracts as well as the controls. Besides, the extracts of fruit skin (Menemen 92 variety) and aerial parts (Aydin 92 variety) showed remarkable activity against DNA viruses at 32 - 1 µg/ ml concentration[(113)].

Anticancer effect:

Cytotoxic activity of C-25 protein isolated from *Cicer arietinum* was studied on oral cancer cells and normal cells. It reduced the cell proliferation of human oral carcinoma cells with IC_{50} of 37.5 µg/ml and no toxic effect was found on normal human peripheral blood mononuclear cells even at higher concentration of 600 µg/ml[(59)]. Results of the cytotoxicity evaluation of isoflavones isolated from *Cicer arietinum* (10, 20, 40, 80, 160 and 360 µg/ml) against MCF-7 breast cancer cell line showed a dose dependent inhibition of cell growth[(114)].

Diuretic and anti-nephrolithiasis effects:

The diuretic and anti-nephrolithiasis activities of *Cicer arietinum* ethanolic seed extract were evaluated in albino rats. The activity was studied by using ethylene glycol induced nephrolithiasis model. Cystone was used as standard drug. Two test doses of *Cicer arietinum* ethanolic seed extract were used. The total duration of evaluation was 28 days. Urine volume, urine analysis, serum analysis were used to assess the efficacy of test drug. The results revealed that the extract decreased urinary stones in the kidney with good diuretic property[(115)].

Pharmacological effects of Allantoin:

Cicer arietinum is one of the plant sources of allantoin[(116-117)]. The allantoin, 5-ureide-hydantoin, has been widely reviewed in literature as a pharmacological active compounds, its pharmacological effects included wound healing, regulation of inflammatory response, stimulation of fibroblastic proliferation, enhancement extracellular matrix synthesis, anti-irritating, hydrating and remover of necrotic tissue, stimulating the cell mitosis, promoter of epithelial stimulation, analgesic action and keratolytic activity[(118-123)].

Side effects and toxicity:

In acute toxicity studies, no mortality was observed even at highest dose of 2 g/kg, orally in rats[(16,42)]. Adult Swiss albino mice of female sex were subjected to acute toxicity studies. The mice were observed continuously for 2 h for behavioral, neurological and autonomic profiles and for any lethality or death for the next 48 h. The results indicated that petroleum ether extract of *Cicer arietinum* was safe up to the dose of 5000 mg/kg body weight. No lethality or any toxic reactions were occurred up to the end of study period[(101)].

IV. CONCLUSION

This review discuss the chemical constituent, pharmacological and therapeutic effects of *Cicer arietinum* as promising herbal drug because of its safety and effectiveness.

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