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Review Article

THE PHARMACOLOGICAL EFFECTS OF *HELIANTHUS ANNUUS*- A REVIEW

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Abstract:

Helianthus annuus was used as food and medicine worldwide. It was cultivated basically for its seeds, which give the world's second most important source of edible oil. Phytochemical analysis showed that *Helianthus annuus* contained carbohydrates, phenolics, flavanoids, tannins, alkaloids, saponins, phytosterols, steroids, triterpenoids and fixed oils. It possessed many pharmacological effects included antiinflammatory, analgesic, antimicrobial, anti-plasmodial, antidiabetic, anti-ulcer, antidiarrheal, antihistaminic, reproductive, anticancer, antioxidant, anti-obesity, central nervous system effects and hepato-, nephro- and cardio- protective effects. This review highlighted the chemical constituents and pharmacological effects of *Helianthus annuus*.

Keywords: chemical constituents, pharmacology, *Helianthus annuus*

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INTRODUCTION:

Medicinal plants are the Nature's gift to human beings to help them pursue a disease-free healthy life. Plants have been used as drugs by humans since thousands of years ago. As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine. Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives [1-30]. *Helianthus annuus* was used as food and medicine worldwide. It was cultivated basically for its seeds, which give the world's second most important source of edible oil. Phytochemical analysis showed that *Helianthus annuus* contained carbohydrates, phenolics, flavanoids, tannins, alkaloids, saponins, phytosterols, steroids, triterpenoids and fixed oils. It possessed many pharmacological effects included antiinflammatory, analgesic, antimicrobial, anti-plasmodial, antidiabetic, anti-ulcer, antidiarrheal, antihistaminic, reproductive, anticancer, antioxidant, anti-obesity, central nervous system effects and hepato-, nephro- and cardio- protective effects. This review was designed to highlight the chemical constituents and pharmacological effects of *Helianthus annuus*.

Plant profile:**Synonyms:**

Helianthus tubaeformis Nutt., *Helianthus platycephalus* Cass. *Helianthus ovatus* Lehm., *Helianthus multiflorus* Hook., *Helianthus macrocarpus* DC., *Helianthus macrocarpus* DC. & A. DC., *Helianthus lenticularis* Douglas, *Helianthus lenticularis* Douglas ex Lindl., *Helianthus jaegeri* Heiser, *Helianthus indicus* L., *Helianthus erythrocarpus*, *Helianthus aridus* Rydb., *Helianthus annuus* var. *texanus* [Heiser] Shinnars, *Helianthus annuus* subsp. *Texanus* Heiser, *Helianthus annuus* var. *macrocarpus* [DC.] Cockerell, *Helianthus annuus* subsp. *lenticularis* [Douglas ex Lindl.] Cockerell, *Helianthus annuus* var. *lenticularis* [Douglas ex Lindl.] Steyerm and *Helianthus annuus* subsp. *jaegeri* [Heiser] Heiser [31].

Taxonomic classification:

Kingdom: Plantae, Subkingdom: Viridiplantae, **Infra kingdom:** Streptophyta, **Superdivision:** Embryophyta, **Division:** Tracheophyta, **Subdivision:** Spermatophytina, **Class:** Magnoliopsida, Superorder: Asteranae, **Order:** Asterales, **Family:** Asteraceae, **Genus:** *Helianthus*, **Species:** *Helianthus annuus* [32].

Common names:

Arabic: Dawar El Shams, Zahrat El Shams; **English:** Sunflower; **French:** Grand soleil, Tournesol; **German:** Sonnenblume; **Hindi:** Surajmukhi; **Italian:** Girasole; **Japanese:** himawari; **Korean:** Haebaragi; **Portuguese:** Girassol; **Spanish:** Girasol; **Swedish:** solros [33].

Distribution:

It was native to United states, Mexico and Canada and now widely cultivated in countries of both tropical and temperate [33].

Description:

The sunflower is an erect, coarse, tap-rooted annual with rough-hairy stems 6-30 dm [100-300 cm] tall. The leaves are mostly alternate, egg-shaped to triangular, and entire or toothed. The flower heads are 7.5-15 cm [3-6 in] wide and at the ends of branches. Ray flowers are yellow and disk flowers are reddish-brown [34-35].

Traditional uses:

The seeds, flower petals and tender leaf petioles are edible. Flower petals can be eaten raw or cooked but are best eaten in the young bud stage when it has an artichoke flavour[36].

The sunflower was used as food and medicine worldwide. *Helianthus annuus* was cultivated basically for its seeds, which give the world's second most important source of edible oil. Sunflower oil was light in color, mild in taste, and low in saturated fats. It contained more of the antioxidant vitamin E than any other vegetable oil and is also high in vitamins A and D. Sunflower oil was able to withstand high temperatures and was thus a good choice when frying foods. Sunflower oil can be used instead of olive oil in salads and dressings [37-38].

The oil was also used in cosmetic formulation. The seed oil, shoots, and herb tincture was employing as anti-inflammatory, anti-oxidant, antitumor, antiasthmatic, antipyretic, astringent, anti-hypoglycemic, cathartic, diuretic, stimulant, vermifuge, antimicrobial and for vulnerary purposes [38]. Seeds were used as diuretic, expectorant, for colds, coughs and throat and lung ailments. The flowers and seeds were used in Venezuela in folk remedies for the treatment of cancer [39]. A tea made from the leaves was astringent, diuretic and expectorant; it was used in the treatment of high fevers. The crushed leaves were used as a poultice on sores, swellings, snakebites and spider bites. A tea made from the flowers was used in the treatment of

malaria and lung ailments. The flowering head and seeds were febrifuge, nutritive and stomachic. A decoction of the roots was used as a warm wash on rheumatic aches and pains [40]. A tincture of the flowers and leaves was recommended in combination with balsamics in the treatment of bronchiectasis. The seeds, if browned in the oven and then made into an infusion are admirable for the relief of whooping cough [41].

Parts used medicinally:

Seeds, flowers, roots and bark [36-40].

Physicochemical characteristics:

Physicochemical properties of sunflower seed oil: free fatty acid: 0.042%, acid value: 0.953mgKOH/g, ester value: 182.138mg KOH/g, saponification value: 182.233 mg KOH/g, iodine value: 119.921 mgI₂/100g, peroxide value: 6.322mg O₂/kg, appearance: light amber oil, and specific gravity: 0.915 at 25°C [42].

Chemical constituents:

Phytochemical analysis showed that *Helianthus annuus* contained carbohydrates, phenolics, flavanoids, tannins, alkaloids, saponins, phyosterols, steroids, triterpenoids and fixed oils [43-45].

Quantitative phytochemical analysis of ethanolic leaf extract of *Helianthus annuus* showed that it contained alkaloid 1.23%, glycosides 0.04%, saponin 1.46%, flavonoids 0.03%, terpenoids 0.64% and phenolic compound 0.34% [46].

Fatty acids identified in sunflower oil were included: palmitic 5.8%, palmitoleic 0.1%, stearic 3.9%, oleic 15.9%, linoleic 71.7%, alpha linoleic 0.6 %, gamma linoleic 0.1%, arachidic 0.3%, gadoleic 0.2%, tetracosanoic 0.5%, and behenic acid 0.7% [47].

Eighty four volatile components were isolated from sunflowers of different varieties by Gas chromatography, among which 20 terpene hydrocarbons, 9 alcohols, 3 phenols, 6 esters, and 19 oxygenated compounds. Terpene hydrocarbons accounted for more than 93% of the extracts. They were included α -pinene, β -pinene, camphene, limonene, *p*-cymene, α -terpinene and 17 other compounds [47].

Sixty nine compounds were identified in the essential oil of leaves and capitula of two cultivars of *Helianthus annuus* grown in the coastal region of Tuscany [Italy], these compounds included [*E*]-3-hexen-1-ol, [*E*]-2-hexen-1-ol, tricyclene, α -thujene,

α -pinene, camphene, thuja-2,4[10]-diene, sabinene, β -pinene, myrcene, 2,3-dehydro-1,8-cineole, pseudolimonene, α -terpinene, *p*-cymene, limonene, β -phellandrene, 1,8-cineole, phenylacetaldehyde, [*E*]-ocimene, α -terpinene, *cis*-sabinene hydrate, terpinolene, *trans*-Sabinene hydrate, *cis-p*-mentha-2-en-1-ol, *trans-p*-mentha-2,8-dien-1-ol, α -campholenal, *trans-p*-mentha-2-en-1-ol, *cis*-verbenol, *trans*-verbenol, inocarvone, *p*-mentha-1,5-dien-8-ol, borneol, 4-terpineol, *p*-cymen-8-ol, α -terpineol, myrtenol, safranal, decanal, verbenone, 2-methyl-2-nonen-4-one, *trans*-carveol, -cyclocitral, isobornyl acetate, 2-undecanone, *trans*-pinocarvyl acetate, methyl geranate, α -copaene, β -bourbonene, β -cubebene, β -elemene, β -caryophyllene, β -gurjunene, *trans*- α -bergamotene, [*E*]-geranyl acetone, α -humulene, germacrene D, bicyclogermacrene, α -muurolene, *trans*- γ -cadinene δ -cadinene, *trans*-nerolidol, dendrolasin, spathulenol, germacrene D-4-ol, caryophyllene oxide, T-cadino, desmethoxy enecalinal, *epi*-13-manoyl oxide [48].

The protein content of the defatted meal ranged from 28 to 32%. Analysis of amino acid contents [g/100g] showed that the range of contents in the defatted meal and dehulled defatted meal of E122 and F2 BRS varieties were [g/100g]: lysine: 1.19-1.48, histidine: 0.64-0.88, arginine: 2.01- 3.00, aspartic acid: 2.37- 3.28, threonine: 0.96-1.20, serine: 1.14- 1.46, glutamic acid: 5.34- 7.72, proline: 0.73-1.65, glycine: 1.41-1.87, alanine: 1.13-1.52, cystine: 0.64-0.81, valine: 1.28-1.75, methionine: 0.59- 0.78, isoleucine: 1.07-1.52, leucine: 1.65-2.19, tyrosine: 0.57-0.83 and phenylalanine 1.21-1.69 [49].

Nutritional values of sunflower seed kernels [dried] from Pakistan, per 100 g were: energy: 2,385 kJ [570 kcal], carbohydrates: 18.76 g, sugars: 2.62 g, dietary fiber 10.5 g, fat: 49.57 g, saturated 5.20 g, monounsaturated 9.46 g, polyunsaturated: 32.74 g, protein: 22.78 g, thiamine 2.29 mg [199%], riboflavin 0.25 mg, niacin 4.5 mg, pantothenic acid: 6.75 mg, vitamin B6: 0.77 mg, folate [vit. B9]: 227 μ g, vitamin C: 1.4 mg, vitamin E: 34.50 mg, calcium: 116 mg, iron 6.77 mg, magnesium: 354 mg, manganese: 2.02 mg, phosphorus: 705 mg, sodium 3 mg and zinc: 5.06 mg [37].

Ent-kaurane glycoside [helikauranoside A] and ent-kaurane-type diterpenoids: [-]-kaur-16-en-19-oiic acid, grandifloric acid, and paniculose IV were isolated from the aerial parts of *Helianthus annuus* [50].

Germacranolide with α -methylene- γ -lactone moiety, the heliangolide niveusin B and its ethoxy derivative were isolated from the methanolic extract of *Helianthus annuus* [51-52].

Benzyl alcohol β -D-apiofuranosyl-[1 \rightarrow 6]- β -D-[4-O-caffeoyl] glucopyranoside, together with eight phenolic compounds: caffeic acid, methyl caffeoate, chlorogenic acid, 4-O-caffeoylquinic acid, 3-O-caffeoylquinic acid, methyl chlorogenate, 3,5-di-O-caffeoylquinic acid, eriodictyol 5-O- β -D-glucoside cinnamic acid and monoester of quinic acid were isolated from the seed of sunflower [*Helianthus annuus*][53-54].

[2R]-2-hydroxy-N-[[2S,3S,4R,10E]-1,3,4-trihydroxyicos-10-en-2-yl]docosanamide, [2R,3R]-2,3-dihydroxy-N-[[2S,3S,4R,10E]-1,3,4-trihydroxyicos-10-en-2-yl] docosanamide, N-[2-phenylethyl] tetracosanamide, [2R]-N-[[2S,3S,4R,8E]-1- β -D-Glucopyranosyloxy]-3,4-dihydroxyoctadec-8-en-2-yl]-2-hydroxyhexadecanamide were isolated from acetone extract of flower disc of *Helianthus annuus* [55].

Flavonoids, tambulin, the chalcones kukulcanin B, heliannone A, heliannones B and C were also isolated from *Helianthus annuus* [56-57].

Sixteen compounds were isolated from the seeds of *Helianthus annuus* included 3,4-dimethoxycinnamic acid, 3-hydroxy-1-[4-hydroxy-3-methoxy-phenyl]-1-propanone, 3-[hydroxyl-acetyl]-1H-indole, 6-acetyl-7-hydroxy-2,3-dimethylchromone, ayapin, p-hydroxybenzoic acid, vanillic acid, ferulic acid, trans-caffeic acid, coumaric acid, nicotinic acid, indole-3-carboxaldehyde, indole-3-carboxylic acid, stigmasterol, β -sitosterol, and β -daucosterol [58].

Furanoheliangolide derivative, 4,5-dihydroniveusin A, as well as niveusin B, argophyllin A and B and three diterpene acids [grandifloric acid, ciliaric acid and 17-hydroxy-*ent*-isokaur-15[16]-en-19-oic acid] were isolated from a Texas population of *Helianthus annuus* [59]. Oleanane-type triterpene glycosides, helianthosides 1, 2, 3, 4, 5 and B were isolated from an *n*-butanol-soluble fraction of a methanol extract of sunflower [*Helianthus annuus*] petals [60]. Fractionation of a petroleum ether extract of *Helianthus annuus* led to the isolation of three diterpene acids: grandiflorolic, kaurenic and trachylobanoic acids [61].

Pharmacological effects:

Antiinflammatory and analgesic effects:

The antiinflammatory effect of helianthosides compounds isolated from an *n*-butanol-soluble fraction of a methanol extract of sunflower was studied against 12-*O*-tetradecanoylphorbol-13-acetate [TPA]-induced inflammation [1.7 nmol/ear] in mice, all of the compounds tested exhibited marked anti-inflammatory activity, with ID50 values in the range 65-262 nmol per ear [60].

Three diterpene acids [grandiflorolic, kaurenic and trachylobanoic] were studied for potential anti-inflammatory activity on the generation of inflammatory mediators in lipopolysaccharide [LPS]-activated RAW 264.7 macrophages. At non-toxic concentrations, these compounds reduced, in a concentration-dependent manner nitric oxide [NO], prostaglandin E₂ [PGE₂] and tumor necrosis factor [TNF- α] production, as well as expression of inducible nitric oxide synthase [NOS-2] and cyclooxygenase-2 [COX-2]. All diterpenoids displayed significant *in vivo* anti-inflammatory activity and suppressed the 12-*O*-tetradecanoylphorbol-13-acetate [TPA]-mouse ear edema. In addition, inhibition of myeloperoxidase [MPO] activity, an index of cellular infiltration, was observed [61].

The anti-inflammatory and analgesic effects of the ethanol extract of leaves of *Helianthus annuus* [0.5, 2 and 4 g/k] were investigated in rats using the albumin induced paw edema model of inflammation as well as the hot plate and tail immersion analgesic test methods. The treatment with the tested doses of the extract effectively inhibited paw edema induced by egg albumin. This effect was comparable if not better than 10 mg/kg of indomethacin orally. Treatment with the extract was also significantly increased the mean tolerance time of rats to thermal noxious stimuli compared to control animals and appeared to be more effective than 10 mg/kg of indomethacin treatment [62].

The methanol extract of seeds of *Helianthus annuus* was evaluated for analgesic activity using acetic acid induced writhing and hot plate methods. In acetic acid-induced writhing test, the extract showed significant [P<0.05] analgesic potential at doses of 100 and 200 mg/kg bw [50.35 and 57.85% inhibition, respectively]. In the hot plate method, increase [P<0.05] of latency period was also observed in comparison to standard aspirin. At 60 minutes, the latency period of two different doses [100 and 200

mg/kg bw] was found at 13 ± 0.91 and 16.5 ± 1.55 second[45].

Antimicrobial effects:

The antimicrobial properties of sunflower seed oil were investigated against different pathogenic microorganisms [*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus subtilis* and *Candida albicans*]. The results revealed that the oil possessed antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Candida albicans* [42].

The antimicrobial properties of the ethanol stem extract of *Helianthus annuus* was evaluated against *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus Niger* and *Candida albicans*. Ethanolic extract of *Helianthus annuus* stem possessed antimicrobial activities against *Staphylococcus aureus*, *Aspergillus niger* and *Candida albicans*, while *Escherichia coli* resisted the extract. MIC and MBC/MFC of the ethanol stem extract of *Helianthus annuus* against *Staphylococcus aureus* were 70 and 90 mg/ml, against *Aspergillus niger* were 80 and 80 mg/ml, and against *Candida albicans* were 50 and 70 mg/ml respectively[44].

The antibacterial effect of the aqueous and ethanolic leaf extracts of *Helianthus annuus* was evaluated using disc diffusion method and agar well diffusion method. In the disc diffusion method, the aqueous extract had an inhibition zone [mm] of 1.1 ± 0.5 on *Staphylococcus aureus*, 1.2 ± 0.1 on *Klebsiella pneumoniae*, 1.6 ± 0.3 on *Pseudomonas aeruginosa*, 1.7 ± 0.5 on *Bacillus subtilis*, 1.3 ± 0.5 on *Escherichia coli*, 1.1 ± 0.2 on *Salmonella typharium*, and 1.1 ± 0.3 on *Micrococcus luteus*, while the ethanol extract had 6.1 ± 0.2 on *Staphylococcus aureus*, 5.88 ± 0.7 on *Klebsiella pneumoniae*, 6.12 ± 0.3 on *Pseudomonas aeruginosa*, 7.1 ± 0.5 on *Bacillus subtilis*, 5.5 ± 0.1 on *Escherichia coli*, 5.6 ± 0.2 on *Salmonella typharium* and 5.3 ± 0.2 on *Micrococcus luteus*. For the agar well diffusion method, the aqueous extract had inhibition zone [mm] of 1.9 ± 0.5 on *Staphylococcus aureus*, 1.3 ± 0.2 on *Klebsiella pneumoniae*, 1.67 ± 0.2 on *Pseudomonas aeruginosa*, 2.1 ± 0.1 on *Bacillus subtilis*, 1.3 ± 0.1 on *Escherichia coli*, 1.1 ± 0.5 on *Salmonella typharium* and 1.7 ± 0.1 on *Micrococcus luteus*. The ethanol extract had 5.8 ± 0.1 on *Staphylococcus aureus*, 5.71 ± 0.5 on *Pseudomonas aeruginosa*, 5.7 ± 0.1 on *Bacillus subtilis*, 5.8 ± 0.2 on *Escherichia coli*, 5.2 ± 0.1 on *Salmonella typharium* and 5.5 ± 0.3 on *Micrococcus luteus*[46].

The antimicrobial activity of methanolic extract of seeds from *Helianthus annuus* was studied against *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhi*, *Vibrio cholera*, *Rhizopus stolonifer*, *Aspergillus fumigatus*, *Fusarium oxysporium* and *Candida albicans*. The seed extract of *Helianthus annuus* showed high activity against *Salmonella typhi*, moderate activity against *Staphylococcus aureus* and *Vibrio cholera* and less activity against *Bacillus subtilis*. The extract also showed high activity against *Rhizopus stolonifer* and *Aspergillus fumigates*, moderate activity against *Candida albicans*, while, *Fusarium oxysporium* resisted the extract [43].

The effect of topical application of sunflower seed oil 3 times daily to preterm infants <34 weeks gestation, on skin condition, rates of nosocomial infections and mortality was studied in Kasr El-Aini neonatal intensive care unit at Cairo University. Treatment with sunflower seed oil resulted in a significant improvement in skin condition [P=0.037] and a highly significant reduction in the incidence of nosocomial infections [adjusted incidence ratio: 0.46; 95%, confidence interval: 0.26-0.81; P= 0.007] compared with infants not receiving topical prophylaxis. No adverse effects were recorded as a result of topical therapy [63].

The effect of polar oil extract from the seeds of *Helianthus annuus* in Napkin dermatitis and its antimicrobial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus vulgaris* and *Candida albicans* were studied. The extract was efficient as topical treatment in Napkin dermatitis. The results also showed that the extract inhibited the growth of all the tested microorganisms at different concentrations [64].

Sunflower oil was easily absorbed by the skin and provides deep nourishment and moisturizing. For these reasons, it was a popular ingredient in over the counter and homemade beauty products including lotions, creams and massage oils. It can retain moisture in the skin. It may also provide a protective barrier that resisted infection in premature infants. Infants receiving a daily skin treatment of sunflower oil were 41% less likely to develop infections in the hospital[65].

Anti-plasmodial effect:

The anti-plasmodial effect of the ethanol extract of the leaves of *Helianthus annuus* [2g and 4g / kg bw/ day for 3 days] was investigated in *Plasmodium berghei* infected Swiss albino mice. The chemo-

suppression of the infection was found to be 98.1 and 98.3% for 2g and 4g / kg BW respectively [66].

Among many plants, *Helianthus annuus* showed good to moderate antiplasmodial activity. *Helianthus annuus* seeds showed 50% inhibitory concentration [IC₅₀] of 0.1µg/ml [methanol extract] and 0.6 µg/ml [petroleum ether extract] against *Plasmodium falciparum* K1 strain[67].

Hepato- , nephro- and cardio- protective effects:

The hepatoprotective activity of ethanolic and aqueous extracts of *Helianthus annuus* flowers was studied in CCl₄ induced hepatotoxicity in wistar rats. Treatment with the *Helianthus annuus* flower extracts significantly [P<0.001] reduced elevated serum enzymatic level of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and total bilirubin in CCl₄ induced rats treated with 200mg/kg bw. The biochemical effects of the ethanolic and aqueous extracts of *Helianthus annuus* flowers were further confirmed by histopathological examinations of liver [68].

The effect of aqueous and ethanolic extracts [500 mg for each for 10 days] of *Helianthus annuus* leaves on calcium oxalate nephrolithiasis was studied in male rats. Ethylene glycol and ammonium chloride feeding resulted in hyperoxaluria as well as increased renal excretion of calcium and phosphorus. The increased deposition of stone forming constituents in the kidneys of calculogenic rats was significantly lowered by treatment with aqueous and ethanolic extracts [69].

Oil of *Helianthus annuus* at doses of 20 mg/kg for two weeks, protected New Zealand rabbits from myocardial infarction induced by epinephrine [70].

Applying 12% sunflower seed oil in rat food pellet for 4 weeks decreased the incidence of reperfusion-induced ventricular fibrillation both after 6 min [2/15 vs. 7/11] and 12 min [0/11 vs. 2/8] of myocardial ischemia and the incidence of other arrhythmias was also decreased. The number of animals developing no arrhythmias during reperfusion was increased [8/15 after 6 min of ischemia, 4/11 after 12 min of ischemia vs. 0/11 and 0/8 in controls, respectively][71].

Antidiabetic effect:

The antihyperglycemic effect of ethanol seed extract [250 mg/kg and 500 mg/kg, po] was studied in normal, glucose loaded hyperglycemic and streptozotocin [STZ] induced Type 2 diabetic rats. Alcoholic seed extract of *Helianthus annuus* showed

less significant changes in blood glucose level of normoglycemic rats [P<0.05], while, it caused much reduction in blood glucose levels [P<0.01] in diabetic rats. Administration of extract in streptozotocin-nicotinamide induced diabetic rats, significantly decreased the blood glucose level [P<0.001], restored the lipid profile, showed improvement in body weight, liver glycogen content, glycosylated haemoglobin, plasma malondialdehyde, glutathione level and serum insulin levels[72].

The crude methanol extract of *Helianthus annuus* was separated into fractions and evaluated for antidiabetic effect. The extract yielded thirteen fractions. Bioactivity screening of the fractions [60 mg/kg] using alloxan-induced hyperglycemic rats showed that fraction 8, 9, 10 and 13 caused various degrees of reduction in fasting blood glucose in time-dependent manner. The activities of the fractions were compared to the crude extract [600 mg/kg]. The crude extract, glibenclamide, fractions 8, 9, 10 and 13 caused 66.74%, 57.43%, 61.36%, 59.80%, 70.63% and 78.03% reductions in fasting blood glucose, respectively, at 6 h[73].

The antidiabetic, oral glucose tolerance test [OGTT], and antioxidant effects of methanol extract of *Helianthus annuus* leaves were investigated using alloxan-induced diabetic rats. The extract [150, 300, and 600 mg/kg] showed a significant [P<0.05] dose- and time-dependent decrease in blood glucose level of alloxan-induced diabetic rats. At 6 h posttreatment, there was a significant [P<0.05] decrease in blood glucose level at 600 mg/kg extract [66.74 %] compared with the negative control group [10 mg/kg distilled water]. The OGTT in normoglycemic rat showed no significant [P>0.05] difference in blood glucose level among the treatment groups. In diabetic OGTT, the blood glucose level of the extract [600 mg/kg]- treated group was significantly [P<0.05] lower when compared to the that of the negative control group at 120 min post glucose load, but there was no significant [P>0.05] difference between the extract- and glibenclamide [2 mg/kg]-treated groups. The extract also produced concentration-dependent increase in antioxidant activity [74].

Among three plants, the sunflower sprout exhibited the strongest inhibitory effects against the formation of advanced glycation end products [AGEs]. At a concentration of 1.0 mg/ml, its inhibitory rate achieved 83.29%, which was stronger than that of aminoguanidine [1 mM], a well-known synthetic antiglycative agent [with an inhibitory rate of 80.88%]. The antioxidant capacity of *Helianthus annuus* was also much stronger than other sprout

samples in terms of free radical scavenging and reducing properties. An active ingredient contributing to these activities was identified as cynarin [1,5-dicaffeoylquinic acid]. Sunflower sprout rich in cynarin may be regarded as a beneficial food choice for diabetic patients[75].

Anti-ulcer and antidiarrheal effects:

The anti-ulcer activity of hydroalcoholic extracts of *A. indicum*, *Helianthus annuus* and a combination of both was evaluated against ethanol induced gastric ulcer and pyloric ligation induced gastric ulcer in Albino Wistar Rats. All extracts showed significant anti-ulcer activity. The protective effect was found to be in the following order: combined hydro alcoholic extract of *A. indicum* and *Helianthus annuus* > hydro alcoholic extract of *Helianthus annuus* > hydro alcoholic extract of *A. Indicum* [76].

The antidiarrheal activity of ethanolic extract of the leaves of *Helianthus annuus* was evaluated using castor oil induced diarrhoea model and gastrointestinal transit model in mice. Ethanolic extract of the leaves of *Helianthus annuus* [250 and 500mg/kg bw] significantly decreases the severity of diarrhea [77].

Antihistaminic effect:

The antihistaminic activity of ethanolic extract of the leaves of *Helianthus annuus* was evaluated in histamine induced bronchoconstriction on guinea pigs and microshock model in rabbits for antihistaminic activity. *Helianthus annuus* possessed marked antihistaminic potential [77].

Central nervous system effects:

The central nervous system activity of methanolic extract of *Helianthus annuus* seeds was evaluated in mice model. The results revealed that the methanol extract of *Helianthus annuus* seeds at 100 and 200 mg/kg caused a significant increase in the spontaneous activity [general behavioural profile]. *Helianthus annuus* showed significant increase in grip strength and pain responses at dose of 200 mg/kg. It also showed strong movement response in spontaneous activity, pinna reflex and touch response at dose 200 mg/kg. There was also moderate increase in awareness and alertness at dose 200 mg/kg. The methanolic extract of *Helianthus annuus* seeds also caused moderate anxiolytic activity [light-dark box and elevated plus maze test]. *Helianthus annuus* showed moderate increase in the latency of entry into the light box with peak effect produced at the dose of 200 mg/kg [72±0.85 seconds] compared to control [34±5.63 seconds]. In respect of latency of entry into the light box and number of entries, *Helianthus*

annuus showed moderately significant anxiolytic effect at the dose of both 100 mg/kg [63±0.62 seconds] and 200 mg/kg [72±0.85 seconds]. *Helianthus annuus* produced a significant increase in the time spent in the open arms model with peak effect at the dose of 100 mg/kg [51±0.62 seconds] relative to control [30.23±0.62 seconds]. In respect of entry into open arms, the extract at the dose of 100 mg/kg significantly [P<0.05] increased the number of entries compared to control. The number of entries into the closed arms was reduced by *Helianthus annuus* at doses of 100 and 200 mg/kg. The methanolic extract of *Helianthus annuus* seeds also caused remarkable antidepressant activity [tail suspension test]. *Helianthus annuus* showed significant antidepressant activity [P<0.05] by decreasing the immobility time [*Helianthus annuus* 100mg/kg: 93±0.47; *Helianthus annuus* 200mg/kg: 78±1.3] as compared with imipramine [60mg/kg: 30.2±0.64] and control [190.8±0.75][78].

The antidepressant [tail suspension test] and anxiolytic activity [light-dark box test and elevated plus maze test] of methanolic extract of *Helianthus annuus* seeds were investigated in mice. The efficacy of extract [100-200 mg/kg] was compared with standard antidepressant drug, imipramine 60 mg/kg and anxiolytic drug diazepam [1mg/kg]. The results revealed that the methanol extract of *Helianthus annuus* seeds possessed a significant result in tail suspension test at 100 mg/kg [93 ± 0.47 seconds] and 200 mg/kg [78 ± 1.3 seconds] and moderate result in light-dark box test at 100 mg/kg [63±0.62] and 200 mg/kg [72±0.85], in elevated plus maze test at 100 mg/kg [51± 0.58 seconds] and 200 mg/kg [60±0.62 seconds]. Accordingly, the methanol extract of *Helianthus annuus* exhibited significant antidepressant and moderate anxiolytic activity[79].

Reproductive effects:

The effects of ethanol extract of leaves of *Helianthus annuus* [0.5 g/kg of orally for 2 weeks] on the fecundity was studied in rats. The results showed that coital frequency was unaffected by the extract treatment but pregnancy rate and number of pups per rat and per group were reduced significantly. The histo-degenerative changes induced by the ethanol extract in the gonads may be responsible for the reduced fecundity observed in treated adult rats[80].

In studying the effects of the ethanol extract of the leaves of *Helianthus annuus* on the histology of the testes, blood level of some reproductive hormones and epididymal sperm properties in Wistar rats, it

appeared that the extract possessed some anti-fertility effects[81].

Anticancer effect:

The antiproliferative effect of *Helianthus annuus* chloroform root extract was studied against HeLa, MCF-7 and A-431 cell lines. MIC50 of the extract was 3.51, 3.36 and 4.19 µg/ml against the three cell line respectively [82].

Antioxidant effect:

In studying the antioxidant activity of methanolic extract of seeds from *Helianthus annuus*, the results revealed that the extract possessed very significant DPPH [1, 1-diphenyl-2-picrylhydrazyl] radical scavenging activity compared to standard antioxidant. The DPPH radical scavenging activity of the extract was increased with the increasing concentration [43].

Lutein, which identified in the hexane extract of *Helianthus annuus* effectively inhibited peroxidation of lipids, hydroxyl radical formation and DPPH radical formation 86%, 92% and 90% respectively at concentration of 20µg/ml, it showed more antioxidant activity than α-tocopherol, curcumin and butylated hydroxy anisole, which, when used at dose ~12 times more [400µM] than lutein, they showed 75–95% inhibition of lipid peroxidation and scavenging of hydroxyl and DPPH radicals[83].

The crude methanol extract of *Helianthus annuus* was separated into fractions and evaluated for antioxidant effect. The extract yielded thirteen fractions. *In vitro* anti-oxidant tests at the concentration of 400 µg/ml showed that the crude methanol extract, fraction 8, 9,10 and 13 gave 89.00%, 30.42%, 47.90%, 88.03% and 92.72% anti-oxidant activity, respectively, in DPPH model; and 3.69, 0.95, 0.23, 0.67 and 0.28 µM anti-oxidant potential, respectively, in FRAP model[73].

Anti-obesity activity:

The anti-obesity activity of the methanolic extract of *Helianthus annuus* seeds was studied in mice model. The mice received cafeteria diet, atorvastatin [10 mg/kg] and *Helianthus annuus* 200 mg/kg daily for 6 weeks. Parameters such as food consumption, locomotor activity, body weight, body mass index [BMI], lee index of obesity [LIO], total cholesterol, triglyceride, LDL, HDL and glucose were studied. The the methanolic extract of *Helianthus annuus* seeds significantly increased locomotor activity [rearing, grooming, ambulation] with HDL and significantly decrease food consumption, body weight, BMI, LIO, total cholesterol, triglyceride, LDL and glucose[84].

Side effect and toxicity:

The LD50 of the ethanol extract of leaves of *Helianthus annuus* was found to be 14g/kg in rats[55]. The methanol extract of *Helianthus annuus* leaves at the dose range of 300-3600 mg/kg was tolerated by the rats[74].

Health risks or side effects following the proper administration of designated therapeutic dosages of sunflower oil in human, were not recorded[86]. No adverse events were recorded as a result of topical therapy in infants [63].

Sunflower seeds were a rare source of allergy, however, several cases of occupational allergies to sunflowers were described [87].

Ethanol extract of leaves of *Helianthus annuus* reduced the fertility and fecundity of rats [80].

CONCLUSION:

The review highlighted the chemical constituent, pharmacological and therapeutic effects of *Helianthus annuus* as promising source of drugs because of its safety and effectiveness.

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