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Review Article

MEDICAL IMPORTANCE OF HELIANTHUS TUBEROSUS- A REVIEW

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Abstract:

Phytochemical analysis of Helianthus tuberosus showed that it contained coumarins, unsaturated fatty acids, polyacetylenic derivatives, phenols, flavonoids, sesquiterpenes, protein, amino acid, reducing sugars, organic acids, lactones and cardiac glycoside. The pharmacological investigations revealed that Helianthus tuberosus exerted antioxidant, anticancer, antidiabetic, antifungal and α-Glucosidase inhibitory activity, as well as it produced inulin which used as functional food and possessed many medical benefits. This review will highlight the chemical constituents and pharmacological and therapeutic effects of Helianthus tuberosus.

Keywords: Helianthus tuberosus, pharmacology, therapeutic, chemical constituents

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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 pharmaceuticals, agrochemicals, flavours. biopesticides fragrances, colours, and food additives[1-20]. Phytochemical analysis showed that it contained Helianthus tuberosus coumarins, unsaturated fatty acids, polyacetylenic derivatives, phenols, flavonoids, sesquiterpenes, protein, amino acid, reducing sugars, organic acids, lactones and cardiac glycoside. The pharmacological investigations revealed that Helianthus tuberosus exerted antioxidant, anticancer, antidiabetic. antifungal and α -Glucosidase inhibitory activity, as well as it produced inulin which used as functional food and possessed many medical benefits. This review was designed to highlight the chemical constituents and pharmacological and therapeutic effects of Helianthus tuberosus.

Plant profile:

Synonyms:

Helianthus esculentus Warsz., Helianthus serotinus Tausch, Helianthus tomentosus Michx., Helianthus tuberosus var. subcanescens A. Gray, Helianthus tuberosus f. tuberosus and Helianthus tuberosus var. tuberosus[21].

Taxonomic classification:

Kingdom: Plantae; Phylum: Spermatophyta, Subphylum: Angiospermae, Class: Dicotyledonae, Order: Asterales, Family: Asteraceae, Genus: Helianthus, Species: Helianthus tuberosus[22].

Common names:

Arabic: Taffahh Al-Ardh; Tartuf; English: Earthapple, Jerusalem-artichoke, Sunchoke, Topinambur; French: Artichaut de Jérusalem, Topinambur; German: Erdbirne, Indianerknolle, Topinambur; Italy: Girasole di Canadá, Tartufo diCanna, Topinambur; Japanese: Kiku-imo; Portuguese: Batata-tupinambá, Girassol-de-batata, Tupinambá, Tupinambor; Russian: Podsolnečnik Klubenosnij, Topinambur, Zemljanaja gruša; Spanish: Aguaturma, Castaña de tierra, Námara, Pataca, Patata de caña; Swedish: Jordärtskocka; Thailand: Thantawan-hua; Vietnam: Quyf doji[22-23].

Distribution:

It was native to Canada and United states, and naturalized in Africa, Asia [Russian Federation, Turkey, Iraq, Republic of Korea, China and Japan]. Australasia [Australia and New Zealand], Europe [Belarus, Estonia, Latvia, Lithuania, Moldova, Russia Federation-European part, Ukraine, Austria, Belgium, Czech Republic, Germany, Hungary, Netherlands, Poland, Slovakia, Switzerland, Norway, Sweden, United Kingdom, Albania. Bulgaria, Croatia, Italy, Macedonia, Romania, Slovenia, France and Spain], Southern America [Argentina and Uruguay], and it was cultivated widely in the temperate regions[22-23].

Description:

Robust, erect, perennial herb, in cultivation usually grown as an annual, up to 3 m tall, scarcely to moderately branched in upper half of stem, hirsuta in most above-ground parts. Roots adventitious [in plants not grown from seed], fibrous, spreading deeply. Tubers formed by thickening of short and stout or long and slender underground stolons, ellipsoid to globose, 2-8[-15] x 3-6 cm, whitish, yellow, red or purple, with small scale leaves and axillary buds. Leaves opposite or in whorls of three in lower plant part, in upper part alternate, simple; petiole 2-4 cm long, winged above; blade ovate to ovate-lanceoliate, 10-20 cm long, base tapering into petiole, margin irregularly serrate, apex acute, veins prominent with three main veins. Inflorescence a head, 4-8 cm in diameter, few together in a leafy panicle 8-20 cm long; involucral bracts in several rows, lanceolate, long acuminate, subequal, 15-17 x 4 mm, ciliate, blackish outside; receptacle flat, 1.5-2 cm in diameter; outer ray florets sterile, with goldenyellow, ligulate corolla, elliptical to oblong, 2.5-4.5 x 1 cm; disc florets bisexual, with tubular bright yellow corolla, 6-7 mm long; sterile bracts pale, 8-9 mm long, with greenish-yellow apex; five stamens; style slender, with two-lobed stigma. Fruit an achene, oblongoid, 5-7 mm long, flattened at the sides, brownish with dark stripes, thinly hairy[22].

Traditional uses:

Jerusalem artichoke was considered as one of the primary sources for inulin in higher plants. Its protein has high food value due to the presence of almost all essential amino acids, it was used as livestock feed[24]. Tubers of *Helianthus tuberosus* were utilized as a diuretic, spermatogenic, tonic,

galactagogue, aphrodisiac, antihemorrhoidal, collagogue and to decrease diabetes symptoms[25-27]. Leaves were used as a natural medicine for the treatment of skin wound, bone fracture and swelling[28-29].

Part used medicinally:

Whole plant, tubers and leaves [24-29].

Chemical constituents:

Phytochemical analysis of *Helianthus tuberosus* showed that it contained coumarins, unsaturated fatty acids, polyacetylenic derivatives, phenols, flavonoids, sesquiterpenes, protein, amino acid, reducing sugars, organic acids, lactones and cardiac glycoside[25,28,30-31].

The tubers comprised about 80% water, 15% carbohydrate, and 1 to 2% protein. The tubers contained little or no starch and small amount of fat included trace amounts of monounsaturated and polyunsaturated fatty acids, but no saturated fatty acids. The polyunsaturated fatty acids linoleic [24 mg/100g raw tuber] and α -linoleic acid [36 mg/100g raw tuber][32-33].

It contained inulin 7 to 30% of fresh weight [8 and 21% inulin of fresh weight is considered typical][34-35].

The root of *Helianthus tuberosus* contained inulin 20%, fructose amount 91.9 %, glucose amount 8.1 %[36].

The composition of *Helianthus tuberosus* tubers [per 100 g fresh weight]: water: 7-80.1%, energy: 38-76 kcal, protein: 0.5-8.0 g, total carbohydrate: 10.6-17.3 g, dietary fiber: 1.3-4g, total sugars: 1-1.6g, sucrose: 0.6 g, lactose: 0 g, total starch: trace- 7.2g, total fat: 0.1-<1 g, total fatty acids: <0.1-<1 g, saturated fatty acids: 0-0.17g, monounsaturated fatty acids: <0.1-<1 g, polyunsaturated fatty acids: <0.1- <1 g, cholesterol: 0-0.3 mg, total sterols: 5.2 mg, ash: 1.2 g, nitrogen: 0.25-0.38g, calcium: 14-37 mg, iron: 0.4-3.7 mg, magnesium: 14.4-17 mg, potassium: 420-657 mg, sodium: 1.8- 4mg, phosphorus: 63-78 mg, copper: 0.10-0.12 mg, boron: 0.21-0.24 mg, manganese 0- 0.3 mg, sulfur: 22-27mg, chlorine: 0 mg, zinc: 0.1-12 mg, aluminum:4 mg, barium: 0.33mg, silicon: 4.4mg, nickel: 0-16µg, iodine: 0-0.1 μg, chromium: 0-6.4 μg, selenium: 0-0.2 μg, lead 6.3µg, cadmium 1.1µg, vitamin A [retinol]: 0.6-1µg, carotenoids: 9-28.9 µg, vitamin B1 [thiamin]: 0.07-0.2 mg, vitamin B 2[riboflavin]: 0-0.16 mg, niacin 0.5-1.3mg, vitamin B6: 0.09 mg, pantothenic acid: 0.38 mg, biotin: 0.5 µg, folates: 13-22 µg, vitamin B 12 [cobalamin]: 0 μg, vitamin C: 2-6 mg, vitamin D: 0 μg, vitamin E: <0.1-2 mg, vitamin K: 1.44 μg and tryptophan: 0.23mg. Amino Acid composition of crude protein of *Helianthus tuberosus* tubers [% of dry weight] were: asparatic acid 0- 0.86, threonine 0.20- 0.30, serine 0- 0.19, glutamic acid 0-0.83, glycine 0- 0.21, alanine 0- 0.23, cysteine 0-0.06, valine 0.22- 1.33, methionine 0- 0.06, isoleucine 0-0.19, leucine 0.27- 0.85, tyrosine 0.12, phenylalanine 0- 0.23, histidine 0.17- 0.21, lysine 0.30- 0.33, arginine 0.46- 0.65 and proline 0- 0.30[37-39].

However, the contents of essential amino acids in Jerusalem artichoke tubers of Rote Zonenkugel variety [mg/g protein] were included: histidine: 17, isoleucine: 29, leucine: 40, lysine: 45, methionine + cystine: 23, phenylalanine + tyrosine: 44, threonine: 29, valine: 33 and the sum of essential amino acids was 260[40].

The chemical constituents of the leaf, stem and total aerial parts [% dry weight] were: leaf protein 26.9-29.4, stem protein: 8.8-11.9, total aerial parts protein: 7-9; leaf sugars: 0.8-2.4 stem sugar: 5-6; total aerial parts fructose: 1.8-2.2; total aerial parts glucose: 1.2-2.1; total aerial parts sucrose: 1.2-2.1; total aerial parts inulin [fructan] 2-4.5; leaf cellulose: 6.6-7.3, stem cellulose: 13.1-14.2, total aerial parts cellulose 17-20; leaf hemicelluloses: 4.3-4.5, stem 9.3-9.6. total hemicelluloses: aerial hemicelluloses: 21; leaf lignin: 17.9-21.7, stem lignin 10.8-14.1, total aerial parts lignin: 12-14; leaf uronides: 13.2-15.8, stem uronides: 9.2-10.9, leaf ash: 13.4-14.9, stem ash: 6.8-9.4, total aerial parts ash: 8-10[37, 41-42].

The total phenol content of the ethanol extract of tubers of *Helianthus tuberosus* was 7.91 mg GAE/g and total flavonoid content was 29.60 ± 5.23 mg QE/g[27].

The 70 % ethanol extracts of tubers of different varieties and wild populations of *Helianthus tuberosus* grown on territory of Bulgaria, possessed the highest total phenolic content [6-17 mg GAE/g dry weight][43].

Ethyl acetate fraction of *Helianthus tuberosus* leaves contained the highest total phenolic content [266.69 \pm 2.51 mg GAE/g dry extract]. Six phenolic compounds were also isolated, among them 3-O-caffeoylquinic acid and 1,5-dicaffeoylquinic acid. The content of 3-O-caffeoylquinic acid in n-butanol fraction was 74.58 \pm 1.05 mg/g, while 1,5-dicaffeoylquinic acid in ethyl acetate fraction was 104.51 ± 2.86 mg/g[44].

Ten chlorogenic acids were identified from the leaves of three *Helianthus tuberosus* [3-O-

caffeoylquinic acid, two isomers of caffeoylquinic acid, caffeic acid, *p*-coumaroyl-quinic acid, feruloylquinic acid, 3,4-dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, 1,5-dicaffeoylquinic acid, and 4,5-dicaffeoylquinic acid][45]

Naturally occuring isomers of caffeoylquinic acid namely neo-chlorogenic acid, chlorogenic acid and crypto-chlorogenic acid, 4 isomeric di-caffeoylquinic acids [3,5-O-dicaffeoyl, 3,4-O-dicaffeoyl, 4,5-O-dicaffeoyl and 1,3-O-dicaffeoyl esters] were identified from *Helianthus tuberosus* tubers[46].

Eleven sesquiterpene lactone and two flavones were isolated from *Helianthus tuberosus* leaves[47].

Eight components were detected in the methanolic extract of Jerusalem Artichoke tuber extract from Folurd region included: cyclopentanol, hexadecanoic acid, 9-octadecenoic acid, 9-octadecenoic acid, 9octadadecinoic acid, octadeconic acid. octadecenal and 9-octadeconic acid. Ten components were identified in the methanolic extract Jerusalem Artichoke tuber extract from Polsefid region included: utero-noenen-1-ol-3; 2-propen-1-ol; 3-deoxy-d-manneolclactone; heyadecanic acid; 1pyrrolin,3-ethyl; 9-octadecnoic acid; octadelenoic acid; 13-octa decnal; 1,2-epoxy-1-vinylcyclode coene and cycloprtadecanon c, 2-hydroxy, and ten compounds were isolated from the methanolic extract of Jerusalem artichoke tuber extract from Bandar Torkaman region included: 2-furan carboxaldehyde; 2-furan carboyaldehyde; Dodecane1,1-oxybis; Glycine,n-methyl-n-1-oxadodecyl; hexa-decaneic acid; 9-octadecenoic acid; oleic acid; 9-octadecenal; 9-octadecenal and phthalic acid disoo ctvl ester[48]. Nine compounds: ent-17-oxokaur-15[16]-en-19-oic acid, ent-17-hydroxykaur-15[16]-en-19-oic acid, ent-15β-hydroxykaur-16[17]-en-19-oic acid methyl ester, ent-15-nor-14-oxolabda-8[17],12E-dien-18-oic acid, 4,15-isoatriplicolide angelate, 4,15-isoatriplicolide methylacrylate, [+]-pinoresinol, [-]-loliolide, and vanillin were isolated from the chloroform-soluble subfraction of a methanol extract of the whole plant of Helianthus tuberosus collected in Ohio, USA[25].

The major component in leaves and tubers oils was[-]- β -bisabolene with the highest concentration among other volatile compounds concentrations of 70.7% and 63.1%, respectively. Other components in leaves present in significant contents being: α -copaene [1.50%], β -bourbonene [0.59%], [E]- α -bergamoten [0.47%], geranyl acetate [0.39%], β -sesquiphellandrene [3.18%], β -ionon [2.35%], caryophyllene oxide [4.95%], [Z]- α -bisabolene epoxide [12.65%], neophytadiene [1.60%], and

hexahydrofarnesylacetone[1.68%]. However. chemical constituents of the essential oil from leaves Helianthus tuberosus [g/100g] and tubers of respectively were included: p-mentha-1,5- dien-8-ol: - and 0.00013, Verbenone: - and 0.00020, Bornyl acetate: – and 0.00017, α -Copaene: 0.00074 and - , Phenylacetaldehyde: – and 0.00011, β-bourbonene: 0.00029 and -, [E]- α -bergamoten: 0.00023 and -, Geranyl acetone: 0.00019 and -, Calarene: - and 0.00027, β -ionone: 0.00116 and -, -[-] β -bisabolene: 0.03486 and 0.00205, β-sesquiphellandrene: 0.00157 and -, Caryophyllene oxide: 0.00244 and -, [Z]- α bisabolene epoxide: 0.00624 and -, neophytadiene: 0.00079 and -, hexahydrofarnesylacetone: 0.00083 and - and squalene: - and 0.00032[49].

Pharmacological effects:

Antioxidant effect:

The radical scavenging activities of Jerusalem artichoke [Helianthus tuberosus] leaves were investigated in vitro. The results indicated that the ethyl acetate fraction contained the highest total phenolic content [266.69 ± 2.51 mg GAE/g dry extract] accompanied with strongest free radical scavenging abilities. Following an in vitro radical scavenging activity-guide fractionation procedure, six phenolic compounds which strongly quenched free radicals were separated from ethyl acetate fraction. Among them, 3-O-caffeoylquinic acid and 1,5dicaffeoylquinic acid played a dominant role due to their strong free radical scavenging abilities and their high contents. The content of 3-O-caffeoylquinic acid in n-butanol fraction was 74.58 ± 1.05 mg/g, while 1,5-dicaffeoylquinic acid in ethyl acetate fraction was $104.51 \pm 2.86 \,\mathrm{mg/g}[44]$.

Antioxidant activity of the ethanol extract of tubers of Helianthus tuberosus was evaluated in vitro. cation radical scavenging activity of the ethanol extract of tubers of Helianthus tuberosus was 20.25 ± 4.97 and 1.38 ± 0.58 at concentration of 1000 and 570 µg/ml respectively, DPPH radical scavenging activities of ethanol extract was 13.58 \pm 2.54 18.24±1.80% at concentration of 1000 and 570 µg/ml respectively. Reducing power [absorbance] of the ethanol extract of tubers of Helianthus tuberosus was 0.0030 ± 0.0010 , 0.0038 ± 0.0001 0.0089±0.0003 at concentration of 3000, 1000 and 570 µg/ml respectively, and the metal chelating capacity [Inhibition] was >100, 95.12±1.33 and 94.27±2.33 at concentration of 3000, 1000 and 570 μg/ml respectively[27].

The total fructans, phenolic content and radical scavenging activities of the extracts were investigated using ABTS and CUPRAC methods. The 70% ethanol extracts possessed the highest total phenolic

content [6-17 mg GAE/g dry weight]. The water extracts characterized by higher fructan levels, 32 to 69 g/100 g/ dry weight. The flour obtained from tubers of Scorospelcu variety and wild population of *Helianthus tuberosus* were evaluated as a valuable source of total polyphenols and soluble dietary fibers, because of the rich fructan content. The results revealed that flours possessed radical scavenging activity and were suitable for human and animal nutrition to prepare foods with health benefits[43].

Anticancer effect:

The cytotoxic activities of eleven sesquiterpene lactone and two flavones compounds isolated from the leaves of Helianthus tuberosus were tested against MCF-7, A549 and HeLa cancer cells lines. The results revealed that sesquiterpene lactones exhibited consistent cytotoxicity against all three cancer cell lines, while flavones showed selective inhibitory activity against HeLa cell lines. Among them, one of the sesquiterpene lactone compounds, exhibited strong growth inhibitory activity against all three cell lines. Its IC50 values against MCF-7, A549 1.97 ± 0.04 , 7.79 ± 0.44 , and HeLa were $9.87 \pm 0.20 \,\mu\text{g/ml}$, respectively[47].

Nine compounds [ent-17-oxokaur-15[16]-en-19-oic acid, ent-17-hydroxykaur-15[16]-en-19-oic acid, ent-15β-hydroxykaur-16[17]-en-19-oic acid methyl ester, ent-15-nor-14-oxolabda-8[17],12E-dien-18-oic acid, 4,15-isoatriplicolide angelate, 4,15-isoatriplicolide methylacrylate, [+]-pinoresinol, [-]-loliolide, and vanillin] isolated from the chloroform-soluble subfraction of a methanol extract of the whole plant of *Helianthus tuberosus* were tested for cytotoxic activity against MCF-7 human breast cancer cell line. The results revealed that two germacrane-type sesquiterpene lactones [4,15-isoatriplicolide angelate and 4,15-isoatriplicolide methylacrylate] possessed cytotoxic activity[25].

Cytotoxic effects of different substances isolated from *Helianthus tuberosus* were tested against four cell lines [Hp G2- cells, HCT-116, MCF-7 and 1301-cells]. Total sesquiterpenes were potent cytotoxic followed by heliangine, while inulin did not exhibit cytotoxic effect[50].

Antidiabetic effect:

The ethanol extracts of tubers of *Helianthus tuberosus* [250 and 500 mg/kg bw] showed antidiabetic effect in streptozotocin induced diabetic rats, it also possessed an inhibitory effect on kidney tissue TBARS levels [24.5%][51].

Effect on carbohydrate digestive enzymes:

 α -Glucosidase inhibitory activity of the tubers of *Helianthus tuberosus* was 13.60 \pm 2.54% and α -amylase inhibitory activity was $0.49 \pm 0.03\%$ [27].

Antifungal effect:

The extracts and phenolic acids from Helianthus tuberosus leaves were investigated for antifungal effect and potential use in enhancing preservation of fruits and vegetables in storage. Either crude leaf extract or n-butanol fraction was active against Botrytis cinerea, Colletotrichum gloeosporioides, Phytophthora capsici Leonian and Rhizoctonia cerealis, with the values of IC50 ranging from 2.166 to 2.534 g/l for the crude leaf extract and 0.232-1.911 g/l for n-butanol fraction. The severity of grey mould caused by B. cinerea was significantly reduced by nbutanol fraction applied at 1 and 2 g/l [the control efficiency of 71.3% and 77.8%, respectively, compared with commercial preparation carbendazim. Six phenolic acids were separated from n-butanol Among fraction. them, caffeic acid. dicaffeoylquinic acid and 1,5-dicaffeoylquinic acid played a dominant role and were active in bioassays against Gibberella zeae, with respective minimum inhibitory concentrations [MIC] being 108, 60 and 4.2 µg/ml respectively[52].

The antifungal activities of *Helianthus tuberosus* leaves extracts was studied against *Rhizoctonia solani*, *Gibberella zeae*, *Alternaria solani* and *Botrytis cinerea*. The results showed that the extracts exerted antifungal activity against *Rhizoctonia solani*, *Alternaria solani* and *Botrytis cinerea*, the inhibitory effects of aqueous extracts were significantly less than those of extracts of organic solvents, the extract of ethyl acetate possessed the highest inhibitory activity, and its lowest inhibitory rates were 77.91%, 100 and 100% to *Rhizoctonia solani*, *Alternaria solani* and *Botrytis cinerea* respectively at a concentration of 20 mg/ml[30].

Medical benefit of inulin:

Inulin was used as functional food. Functional food was defined as food that demonstrated to affect at least one target function in the body beyond basic nutritional effects, in a way to either enhance stage of well-being and health and/or reduce the risk of disease. Experimental studies have shown that inulin, stimulating the immune system of the body, decreasing the pathogenic bacteria in the intestine, relieving constipation, decreasing the risk of osteoporosis by increasing mineral absorption, especially of calcium, reducing the risk of

atherosclerosis by lowering the synthesis of triglycerides and fatty acids in the liver and decreasing their level in serum, modulating the hormonal level of insulin and glucagon, thereby regulating carbohydrate and lipid metabolism by lowering the blood glucose levels, lowering the blood urea and uric acid levels, thereby maintaining the nitrogen balance and also reduced the incidence of colon cancer. Furthermore, inulin with the β [2,1] linkages between the fructose monomers cannot be digested by human intestinal enzymes, giving rise to important applications in functional foods suitable for management of type 2 diabetes, obesity and other blood sugar-related health conditions[53-57].

When inulin used orally, it passed the stomach and small intestine without metabolism, when it reached the large intestine, it fermented by the colonic microflora, therefore it caused no effect on blood sugar levels. Furthermore, the non-digestible nature of inulin resulted in a caloric value significantly lower than typical carbohydrates[58-59].

Inulin regularised the occurrence of intestinal contractions of high amplitude which are more effective in propelling the residual food, debris, secretions and bacterial cells in elderly rats. It decreased translocation of bacteria [total aerobic, anaerobic and the Enterobacteriaceae] to the mesenteric lymph nodes and liver, in DSS-colitis induced rats. It also restored the barrier function of the epithelium inducing lower protection of the mucosa to carcinogenic substances. Inulin and oligofructose were completely fermented by the colonic microbiota and selectively stimulated bifidobacteria and lactobacilli growth and activity at the expense of pathogenic bacteria [e.g. clostridia]. The intestinal microbiota can be considered as a metabolically adaptable and rapidly renewable organ of the body. However, unbalances in its microbial community and activities were found to be implicated in disease initiation and progression, such as chronic inflammatory bowel diseases and colonic cancers. Restoration of this balance by increasing bifidobacteria levels was used to reduce disease severity of patients and to improve well-being in healtly volunteers. The health benefits associated to the induction of high bifidobacteria levels in the colon by the use of prebiotics [inulin and oligofructosel were documented. It also reduced intestinal yeast densities after oral challenge of mice with Candida albicans, resulting in an enhanced survival rate. Clinical studies in humans have also shown that inulin-type fructans can protect against pathogen colonization and infection[60-64].

The effect of Jerusalem artichoke [JA], as a source of inulin, was evaluated on intestinal pH, some blood parameters and liver enzymes. Inulin effectively modified intestinal characteristics, blood metabolites and liver enzymes. Furthermore, 10% JA reduced serum glucose as well as fructose levels. Serum ALP levels was decreased [P<0.05] by 10% JA[65].

CONCLUSION:

This review discussed the chemical constituent, pharmacological and therapeutic effects of *Helianthus tuberosus* as promising herbal drug because of its safety and effectiveness.

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