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Anti-cancer and anti-tumor activity of Glycyrrhiza uralensis Fisch

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ABSTRACT

Glycyrrhiza uralensis Fisch is an herbaceous perennial legume native to southern Europe and parts of Asia, such as India. The aim of this study is to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases up to 2016. Totally, of 68 found articles, 42 articles were included. The search terms were "Glycyrrhiza uralensis Fisch.", "therapeutic", "pharmacological", Various studies have shown that Glycyrrhiza uralensis Fisch possess antimutagenic effect, anticancer effect, Chemopreventive effects, and antitumoral effects. Glycyrrhiza uralensis Fisch is widely used for its curative activities causing its significant value. This plant showed that it can be a potential anti-cancer and anti-tumor plant replacing someday for chemical anti-carcinoma drug. Further studies are needed to prove and diagnose the other useful and unknown properties of this multipurpose plant.

Keywords: Glycyrrhiza uralensis Fisch**,** therapeutic, pharmacological, alternative and complementary medicine

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INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many diseases[1-20].The Glycyrrhiza uralensis Fisch plant is an herbaceous perennial legume native to southern Europe and parts of Asia, such as India[21]. It is not botanically related to anise, star anise, or fennel, which are sources of similar flavoring compounds. It is an herbaceous perennial, growing to 1 m in height, with pinnate leaves about 7–15 cm long, with 9–17 leaflets. The flowers are 0.8–1.2 cm long, purple to pale whitish blue, produced in a loose inflorescence. The fruit is an oblong pod, 2–3 cm long, containing several seeds[22]. Glycyrrhizin has also demonstrated antiviral[23], antimicrobial[24], anti-inflammatory[25], hepatoprotective[22], and blood pressure-increasing effects *in vitro* and *in vivo*, as is supported by the finding that intravenous glycyrrhizin [as if it is given orally very little of the original drug makes it into circulation] slows the progression of viral and autoimmune hepatitis[26]. In one clinical trial liquorice demonstrated promising activity, when applied topically, against atopic dermatitis[27]. Additionally, liquorice may be effective in treating hyperlipidemia [a high amount of fats in the blood][28]. Liquorice has also demonstrated efficacy in treating inflammation-induced skin hyperpigmentation[29]. Liquorice may also be useful in preventing neurodegenerative disorders and dental caries. Liquorice has been traditionally known and used as medicine in Ayurveda for rejuvenation. Liquorice extract is used as a home remedy for skin lightening [30, 31].

Pharmacological Activities

Anticancer effect

Antimutagenesis against N-nitroso compounds contribute to prevention of human cancer was investigated. It was found that Glycyrrhiza aspera ethanolic extract exhibits antimutagenic activity against N-methyl-N-nitrosourea [MNU].The inhibitory activity of glabridin and licochalcone A was more effective than that of liquiritigenin. Thus, Glycyrrhiza contains antimutagenic components against DNA alkylating, direct-acting carcinogens [32].

It was determined whether and by what mechanism HEGU and its active component, isoangustone A, inhibit cell-cycle progression in DU145 human prostate and 4T1 mouse breast cancer cells. The addition of HEGU to drinking water significantly suppressed the orthotopic growth of 4T1 allografts and the expression of the proliferating nuclear cell antigen, CDK2 and CDK4 proteins in the tumor tissues. These results demonstrate the potential of HEGU containing isoangustone A as an antitumor agent [33].

The cytotoxicity of the selected compounds and their aglycones were evaluated against HeLa and MCF-7 cancer cell lines, and the preliminary structure-activity relationship was also elucidated .four new triterpene glucuronides, namely uralsaponins C-F [1-4], an artificial product, namely the methyl ester of glycyrrhizin [5], as well as six known triterpene glucuronides was isolated [34].

Licorice root extract for effects on Bcl-2 to identify novel cytotoxic derivatives was assessed. the result demonstrated that licorice root contains beta-hydroxy-DHP, which induced Bcl-2 phosphorylation, apoptosis, and G2/M cell cycle arrest, in breast and prostate tumor cells, similarly to the action of more complex [MW >800] antimicrotubule agents used clinically[35].

The in vitro immunomodulatory and antitumor potential of Glycyrrhiza uralensis polysaccharides fractions of high molecular weight [fraction A], low molecular weight [fraction B] and crude extract [fraction C] was investigated. The result indicate that G. uralensis polysaccharides especially those of low molecular weight have a potential as anticancer agents. is the ability of the polysaccharides to up-regulate anticancer cytokine IL-7, which is important in proliferation and maturation of immune cells and it is associated with better prognosis in cancer[36].

It was examined whether HEGU and licoricidin inhibit metastasis using the 4T1 mammary cancer model. The result demonstrates that the licoricidin in HEGU inhibits lung metastasis of 4T1 mammary carcinoma cells, which may be mediated via inhibition of cancer cell migration, tumor angiogenesis, and lymph angiogenesis [37].

The effects of an ethanol extract Glycyrrhiza glabra on the expression of HSP90, growth and apoptosis in the HT-29 colon cancer cell line was evaluated. Results showed that Glycyrrhiza glabra inhibited proliferation of the HT-29 cell line at a concentration of 200 μg/ml and this was confirmed by the highest rate of cell death as measured by trypan blue and MTT assays [38].

The three authenticated medicinal species of licorice [Glycyrrhiza glabra [GG], G. uralensis [GU], and G. inflata [GI]] tested .the results suggest that, of the three licorice species that are used in botanical supplements, GI represents the most promising chemopreventive licorice extract for women's health. Additionally, the differential effects of the Glycyrrhiza species on estrogen metabolism emphasize the importance of standardization of botanical supplements to species-specific bioactive compounds [39].

Isoflavonoid calycosin showed the best potency against human T-cell leukaemia cells MT-4. Pterocarpans medicarpin and homopterocarpin exhibit anticancer activity in micromolar range with selectivity on the human monocyte cells U-937. The isoflavan [3R]-vestitol [16] was highly selective on the lymphoblastoid leukaemia cells CEM-13 and was more active than the drug doxorubicin [40].

Treatment with LigC alone did not induce NQO1 in vivo most likely due to its conversion to LigF, extensive metabolism, and its low bioavailability in vivo. These data show the chemopreventive potential of licorice species in vitro could be due to LigC and LicA and emphasize the importance of chemical and biological standardization of botanicals used as dietary supplements. It must be emphasized that menopausal women take these supplements for extended periods of time and long-term beneficial effects are quite possible [41].

Antitumoral effects

The mechanism of action of LRE was investigated. Analysis of cell cycle distribution after treatment of MCF-7 cells with TCDD showed that LRE inhibited the proliferation of MCF-7 cells via G2/M phase arrest. Result revealed that LRE dose-dependently increased the expression of the tumor suppressor genes p53 and p27 and down-regulated the expression of cell cycle-related genes. The finding suggest that LRE can mitigate the tumorigenic effects of TCDD in breast cancer cells by suppression of AhR expression and cell cycle arrest. Thus, LRE can be used as a potential toxicity-alleviating agent against EDC-mediated diseases [42].

CONCLUSION

Glycyrrhiza uralensis Fisch is widely used for therapeutic and purposes that trigger its significant value. Various combinations and numerous medicinal properties of its extract, essential oils, its stems and leaves demand further and more studies about the other useful and unknown properties of this multipurpose plant.

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