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Estrogenic activity of Humulus lupulus L

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ABSTRACT

Humulus lupulus or hop is a species of flowering plant in the Cannabaceae family, native to Europe, western Asia and North America. It is found in most countries of the North Temperate Zone. The aim of this study was to overview pharmacological properties of Humulus lupulus L.

***Methods**: This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 123 references. In this study, 66 studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of Humulus lupulus L. and dated mainly from the year 1999 to 2016.The search terms were "Humulus lupulus L", "therapeutic properties", "pharmacological effects".*

***Result**: The effects of Humulus lupulus L (Hop) in postmenopausal women was examined in this study. Humulus lupulus extract increased sexual motivation in hormone-primed female. Hops alleviate menopause-associated symptoms.*

***Conclusion**: based on the result of the study, Humulus lupulus is a potent estrogen with the potential to be used for the relief of menopausal symptoms in women. The endocrine properties of hops and hop products are due to the very high estrogenic activity of 8-prenylnaringenin and concern must be expressed about the unrestricted use of hops in herbal preparations for women.*

***Keywords**: Humulus lupulus L, Hop, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.*

INTRODUCTION

Herbal medicine is shown to contribute effectively in remedy and well-being of many diseases [1-24]. *Humulus lupulus* or hop is a species of flowering plant in the Cannabaceae family, native to Europe, western Asia and North America[25]. It is found in most countries of the North Temperate Zone [26].

It is a dioecious , perennial, herbaceous climbing plant which sends up new shoots in early spring[27] and dies back to a cold-hardy rhizome in autumn. Strictly speaking it is a bine rather than a vine, using its own shoots to act as supports for new growth [28].

The root is stout and perennial. The stem that arises from it every year is of a twining nature, reaching a great length, flexible and very tough, angled and prickly, with a tenacious fiber [29]. The leaves are heart-shaped and lobed, on foot-stalks, and as a rule placed opposite one another on the stem, though sometimes the upper leaves are arranged singly on the stem, springing from alternate sides [30]. The flowers spring from the axils of the leaves. The leaves and flower-heads have been used also to produce a fine brown dye.

Hops have tonic, nervine, diuretic, and anodyne properties [31]. Their volatile oil produces sedative [32] and soporific effects, and the Lupamaric acid or bitter principle is stomachic and tonic [33]. For this reason, Hops improve the appetite and promote sleep [34, 35].

It has proved of great service also in heart disease, fits, neuralgia, and nervous disorders, besides being a useful tonic in indigestion, jaundice, and stomach [36] and liver affections, menopause [37] generally. It gives prompt ease to an irritable bladder. Hops will often relieve toothache and earache and allay nervous irritation [38].

It is good for sluggish livers [39]. Hop juice cleanses the blood [40]. It removes pain and allays inflammation [41] and tumor [42] in a very short time. The drug Lupulin is an aromatic bitter and is reputed to be midly sedative, inducing sleep without causing headache [43]. *H.lupulus* contains myrcene, humulene, xanthohumol, myrcenol, linalool, tannins, and resin[44].

Estrogenic activity

The effects of hop in the management of Vasomotor Symptoms in postmenopausal women was reviewed. The result showed that dissemination actions are effective remedy in designing strategies aiming to boost women's health with vasomotor symptoms [45]. The efficacy of Hop on early menopausal symptoms and hot flashes was evaluated. The result showed Hop effectively reduced the early menopausal symptoms [46]. Some studies on exogenous estrogenic and estrogenic activity from soy and red clover suggest its medical efficacy [47].

The most estrogenic constituent is the prenylflavanone, 8-prenylnaringenin (8-PN).it was found in the strobiles of Humulus lupulus L. (Hops). Hops could be attractive for the development as herbal dietary supplements to attenuate menopause-associated symptoms [48].

Estrogenic botanical dietary supplement of an extract of hops was examined. Hop extracts are utilized as anxiolytics and hypnotics and possess estrogenic constituents. The estrogen-dependent induction of alkaline phosphatase in the Ishikawa cell line was observed. This process lead to an herbal extract suitable for the next researches of safety and efficacy [49].

In an animal study on female rats, the influence of Humulus lupulus extract on sexual behavior was evaluated. Humulus lupulus extract showed to increase sexual motivation in hormone-primed female rats [50].

The in vivo estrogenic effects of the Humulus lupulus was assessed. Findings suggest that while the H. lupulus extracts do not have an effect on the rat uterus, 8-PN at resembling doses to those formerly applied in humans did have an effect, and probably hold a deleterious effect in women [51].

It was shown that the exposure to the potent hop phytoestrogen 8-prenylnaringenin (8-PN) rely on intestinal bacterial activation of isoxanthohumol (IX), but this happen in solely one-third of tested patients. E. limosum consumption raised 8-PN production in low producers, resulting in similar 8-PN production in all rats [52].

In female rats, the effects of a prolonged consumption of Humulus lupulus on bone metabolism of long-term L-enriched diet investigated. It suggests that bone gains induced by exercise do not decrease instantly after ending of training and confirms the significance of the practice of physical activity during maturity and young adulthood to increase the climax bone density [53].

In a study, the result show that intestinal transformation of IX upon temperate beer consumption can lead to 8-PN presentation values that may pose within the range of human biological activity [54].

The absorption potent and metabolism of (8-PN) from hops were investigated. 8-PN is an estrogen to relieve the pain in women with menopausal symptoms. Although administered by mouth, 8-PN should unhesitatingly soak up from the intestine, its bioavailability should be reduced considerably by intestinal and hepatic metabolism [55].

The effect of different kinds of beer containing the prenylflavonoids was tested. Prenylflavonoids can modulate aromatase activity, decreasing estrogen synthesis; thus, able to prevent and treat estrogen-dependent disorders such as breast cancer [56].

The results show that the activity of the intestinal microbial community more than 10-fold can increase the exposure concentration [57]. The in vitro metabolism of 8-prenylnaringenin by human liver microsomes was investigated. A product formed by the B ring of 8-prenylnaringenin was observed. This product was probably an intermediate for the B ring cleavage product, 8-prenylchromone [58].

The results indicate that the endocrine properties of hops and hop products are due to the very high estrogenic activity of 8-prenylnaringenin and concern must be expressed about the unrestricted use of hops in herbal preparations for women [59]. The presence of 8-prenylnaringenin in hops may provide an explanation for the accounts of menstrual disturbances in female hop workers [60].

The influence of Humulus lupulus extract on sexual behavior of both naïve and sexually potent male rats was evaluated. Humulus lupulus extract exerted an anaphrodisiac effect only in naïve rats by prohibiting their mounting and ejaculating behavior. The presence of 8-PN in the extract could be only partially involved in the observed anaphrodisiac effect [61].

Anti-cancer

The results indicate that hop-derived prenylflavanones, but not prenylchalcones induce a caspase-independent form of cell death. Therefore, prenylflavanones seem to be encouraging candidates for better investigation in prostate anticancer therapy [62]. Hop flavonoids showed to probably have anti-breast cancer effects due to their ability to decrease estrogen synthesis [63].

Sedative effects

In an animal study, the sedative effect of hop on the rest activity was analyzed. The hop extract effectively attenuated nightly activity in the twenty-four-hour cycle activity rhythm. Non-alcoholic beer intake would be recommended due to containing hop content and consequent sedative action, aiding to overnight sleep [32].

Sedating activity of Ethanolic extracts of Humulus lupulus was examined. This sedating activity could be attributed to three categories of constituents of lipophilic hops extracts. Though the alpha-bitter acids proved to be most active constituents, the beta-bitter acids and the hop oil clearly contributed to the sedating activity of lipophilic Humulus extracts [64].

The anxiolytic effects of xanthohumol, a phytochemical constituent of Humulus lupulus, was investigated. Xanthohumol does not show significant modulation of the benzodiazepine receptor. Additional research should be investigated if xanthohumol acts as a benzodiazepine GABAA partial agonist or antagonist [65].

The morphological, phytochemical and ethnopharmacological aspects of Humulus lupulus L. was described. xanthohumol has been shown to exert cancer chemo preventive activity in in vitro experiments, while 8-prenylnaringenin has been characterized as one of the most potent phytoestrogens isolated until now. Nevertheless, further research is needed to open new biomedical application of these compounds [38].

The effects of Humulus lupulus CO2 extract and its fraction containing alpha-acids on the central nervous system of rats was investigated. The same effects were elicited by the administration of the Humulus lupulus fraction as its CO2 extract, containing alpha-acids, that is the major responsible agent for the enhanced pentobarbital effect and for the antidepressant property [66].

CONCLUSION

Based on the result of the study, *Humulus lupulus* is a potent estrogen with the potential to be used for the relief of menopausal symptoms in women. The endocrine properties of hops and hop products are due to the very high estrogenic activity of 8-prenylnaringenin and concern must be expressed about the unrestricted use of hops in herbal preparations for women.

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