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REVIEW ARTICLE

The Pharmacological Importance and Chemical Constituents of *Arctium Lappa*. A Review

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ABSTRACT

Arctium lappa is a common medicinal herb in China, Europe, North America and Asia. It was used for the treatment of many health complains. Many active chemical groups were isolated from *Arctium lappa;* include volatile oils, lignans, sesquiterpene lactones, polyynes, polysaccharides, phytosterols, tannins, flavonoids, amino acids, trace elements and many other contents. Pharmacological studies showed that *Arctium lappa* exerted many pharmacological effects including enhancement of sexual behavior, anti-fatigue, antidiabetic, antioxidant, anticancer, anti-inflammatory, gastroprotective, hepatoprotective and antimicrobial effects. The present review will highlight the chemical constituents and the pharmacological and therapeutic effects of *Arctium lappa*.

KEYWORDS

Arctium Lappa, Sesquiterpene Lactones, Gastroprotective, Hepatoprotective

INTRODUCTION

Synonym

Arctium majus Bernh., *Lappa communis* var. *major* Cosson et Germ., *Lappa major* GAERTN., *Lappa officinalis* ALL., *Lappa vulgaris* Hill., *Lappa vulgaris* var. *major* Neilr[2-4,9].

English Names

Beggars button, burdock, cockle-bur, cockle-button, common burdock, cuckold-dock, great but, great clotbur, greater burdock, hardock, hare burr, hurr-bur, stick-button and bat weed[2].

Family

Compositae; Asteraceae

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Plant Description

Burdock's stem has multiple branches, each of which is topped by many crimson-violet flower heads that produce the famous (burrs) that give burdock its name. The biennial grows to three to nine feet in height. The root has a very hard, horny, brown, longitudinally wrinkled bark and a white interior. The plant is readily grown from seed in moist, rich soil and full sun[2].

Distribution

Burdock was distributed in Europe, Northern Asia and North America. It was very commonly met along roadsides and in all waste places[2,4].

Traditional Use

Preparations of Burdock Root were used for ailments and complaints of the gastrointestinal tract, as a diaphoretic and diuretic, and for blood purifying. Externally, it was used for ichthyosis, psoriasis and seborrhea of the scalp. It was also used in China for the treatment of carbuncles,

ulcers and erythema of the skin as well as sore throats[3].

Part Used

The ripe seed and the fresh or dried roots were used medicinally[3].

Chemical Constituents

The plant contained volatile oil (small amounts including, among others, phenylacetaldehyde, benzaldehyde, and 2-alkyl-3-methoxy-pyrazines), lignans: (neoarchtiin A , and arctigenin), sesquiterpene lactones, polyynes (chief components are trideca-l, ll-dien-3, 5,7,9-tetrain, as well as sulfur derivatives, caffeic acid derivatives: including chlorogenic acid, isochlorogenic acid), polysaccharides (fructose), mucilage's (xyloglucans, acidic xylans), riterpenes: including alpha-amyrin, omega-taraxasterol, acetic acid ester, phytosterols: beta-sitosterol, stigmasterol, campesterol and their esters, and tannins. Lignans were isolated from different parts of the plant, arctigenin (from the leaves, fruits, seeds, and roots), arctiin (from the leaves, fruits, and roots), trachelogenin (from the fruits), lappaol F (from the fruits and seeds), and diarctigenin (from the fruits, roots and seeds). Terpenoids, beta-eudesmol, 3α-hydroxylanosta-5, 15-diene and 3α-acetoxy-hop-22(29) -ene were isolated from the fruits. Polyphenols, caffeic acid (from the stems, leaves, and the skin of roots), chlorogenic acid (from the leaves and the skin of roots), and tannin (from the roots). Inulin and sterols were isolated from the roots. Amino Acid, metal elements (potassium, calcium, iron, magnesium, manganese, sodium, zinc and copper), vitamins (C, A, B1 and B2) and crude fiber, phosphorus and carotene were also isolated from the plant[1-12]. Sulfur-containing acetylenic compounds were also isolated from *A. lappa*[13]. Total phenolic content of *A. lappa* in different extracts were : in dichloromethane hot extract 0.12%, in ethanolic hot extract 6.39%, in aqueous hot extract 2.87%, in dichloromethanic extract 0.10%, in ethanolic extract 4.45%, in aqueous extract 3.51%, and in hydroethanolic extract 10.25%[14].

Pharmacological Effects

Effects on Reproductive Systems

In Traditional Chinese Medicine, *Arctium lappa* L. root is recommended as an aphrodisiac agent, and used for the treatment of impotence and sterility, while Native Americans included the root in herbal preparations for women in labor[15].

The aqueous extract of *Arctium lappa* L. roots enhanced sexual behavior in male rats. Oral administration of *Arctium lappa* L. roots extract at 600 and 1,200 mg/kg body weight significantly increased the frequencies of mount, intromission, and ejaculation frequency ($p < 0.05$). Administration of the extract also reduced the post-ejaculatory interval[11,16-18]. *In vivo A. lappa* induced uterine stimulant activity[17].

Antidiabetic Effects

The antidiabetic effect of the ethanolic extract of the root of burdock (*Arctium lappa* L.) was investigated in streptozotocin- induced diabetic rats. Oral administration of the root ethanolic extract was significantly decreased blood glucose and increased insulin level in diabetic rats compared to the control diabetic group. Meanwhile, the levels of serum total cholesterol, triglycerides and low density lipoprotein in the root ethanolic extract treated diabetic rats were lower, and the high density lipoprotein level was higher than that index of the control diabetic rats. Furthermore, oral administration of root ethanolic extract was significantly decreased serum urea and creatinine as well as malondialdehyde levels of liver and kidney tissues, while body weight gain and tissue glycogen content were elevated in diabetic rat, all of which indicate an improvement in diabetic state. In addition, 400 mg/kg body weight of root ethanolic extract had a marked improvement of the glucose tolerance in normoglycemic rats[19].

Silver *et al* investigated the effect of burdock powder on normal and diabetic patients, and found out that burdock root possess hypoglycemic effects. The antidiabetic effect of burdock root was related to polysaccharides, the main component of the root. Root extract

maintained the blood glucose level constant, therefore improving the tolerance to high glucose level[20].

Antioxidant and Anticancer Effects

The cytotoxic and genotoxic effects of *A. lappa* root aqueous extract were examined on the root meristem cells of *Allium cepa*. Onion bulbs were exposed to 12, 62.5 and 125 mg/ml concentrations of the extracts of A. *lappa*. All the tested extracts have been observed to have cytotoxic effects on cell division in *A. cepa*. *A. lappa* root extract induced the total number of chromosomal aberrations and micronuclei (MNC) formations in *A. cepa* root tip cells significantly. Two of the tested concentrations were observed to have mitodepressive effects on cell division and induced mitotic spindle disturbance in *Allium cepa*[21].

Higher radical scavenging activity was found for the hydroethanolic extract of *A. lappa*. The higher phenolic contents were found in the dichloromethane extract hydroethanolic extracts. These phenolic compounds included arctigenin, quercetin, and chlorogenic acid and caffeic acid compounds. The dichloromethane extracts were the only extracts that exhibited activity against cancer cell lines, especially for K562, MCF-7 and 786-0 cell lines[14].

The free radical scavenging activities of *A. lappa* were attributed to the presence of caffeoyl quinic acid derivatives. However, the lignans from *A. lappa* exerted antiproliferative and apoptotic effects for leukemic cells. Arctgenin possessed antitumor effects on pancreatic cancer cell lines[11,12,18,22-23]. Foldeak and Dombradi also confirmed the antitumor activity of *A. lappa*[24]. Arctigenin, one of the major bioactive components of *Arctium lappa* L was reported to exhibit antioxidant, antitumor and anti-inflammatory activities[25].

The antiproliferative activity of the crude extract of *Arctium lappa*, and semipurified fractions, and isolated compounds from the leaves of *A. lappa* was tested by bioassay-guided testing in Caco-2 cells. The crude extract was obtained with a 50% hydroethanolic extract and then partitioned with hexane, ethyl acetate, and *n*-butanol. The ethyl-acetate fraction (EAF) showed antiproliferative activity[26].

Bioassay-guided cytotoxicity fractionation isolated the compounds lappaol A, C, and F, with cytotoxic activity, their IC_{50} values were 8, 16, and 40 ug/ml, respectively[27].

Onopordopicrin, a sesquiterpene lactone isolated from the leaves of *A. lappa* also inhibited the tumor necrosis factor and showed antitumor activity with IC_{50} of 15 umol/L by MTT and PTP assays against a cell line of promyelocytic leukemia (HL60)[28-30].

Antiinflammatory Effects

Arctium lappa decreased edema in the rat-paw model of carageenan-induced inflammation[22]. Its extract was significantly reduced the release of inflammatory mediators through inhibition of degranulation and cys-leukotriene release[31]. Cultured macrophage RAW 264.7 was used to investigate the anti-inflammatory mechanism of arctigenin of *A. lappa*. Arctigenin suppressed lipopolysaccharide (LPS)-stimulated NO production and pro-inflammatory cytokines secretion, including TNF-α and IL-6 in a dose-dependent manner. Arctigenin also strongly inhibited the expression of iNOS and iNOS enzymatic activity, whereas the expression of COX-2 and COX-2 enzymatic activity were not affected by arctigenin[32].

Chlorogenic acid, as one of the constituents of A. *lappa* , inhibited lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 cells, inhibited staphylococcal exotoxin-induced production of IL-1β, TNF, IL-6, INF-γ, monocyte chemotactic protein-l, macrophage inflammatory protein (MIP)-lα, and MIP-lβ in human peripheral blood mononuclear cells. Chlorogenic acid also inhibited lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 cells, and decreased LPS-induced up-regulation of cyclooxygenase-2 at the protein and mRNA levels resulting in the inhibition of prostaglandin E2 release from LPS-treated RAW 264.7 cells[33-34]. Butanol extract of *A. lappa* caused significant inhibition

of β-hexosaminidase release in RBL-2H3 cells and suppressed mRNA expression and protein secretion of IL-4 and IL-5 induced by ConA-treated primary murine splenocytes. 100 μg/ml of butanol extract of *A. lappa* suppressed not only the transcriptional activation of NF-κB, but also the phosphorylation of MAPKs in ConA-treated primary splenocytes[35].

When BALB/C female mice were treated with *Arctium lappa* L polysaccharide(ALP) at low, medium and high dose, the immunological analysis showed that the number of antibody-producing cells at all doses, the phagacytosis index at medium dose and the weight of spleen and thymus at all doses was significantly increased after 20 days[36].

Gastrointestinal Effects

The chloroform extract fraction of the roots protected animals from chronic gastric ulceration by reducing gastric acid secretion *via* inhibition of gastric H^+, K^+-ATPase[37]. Oral administration of 100 mg/kg daily of *Arctium lappa* powder for 7 days in dextran sulfate induced colitis in mice prevented mucosal edema, submucosal erosions, ulceration, inflammatory cell infiltration and colon damage. In addition, immunohistochemistry analysis showed that the levels of the inflammatory cytokines, IL-6 and TNF-α were also decreased in *Arctium lappa* -treated groups[38].

Oral (1% in drinking water, or 400 mg/d) administration of inulin (one of the constituents of A. *lappa*) in rats was found to ameliorate DSS-induced colitis. It also induced an acidic environment (pH < 7.0) from the cecum to the left colon and increased lactobacilli counts. In addition, it increased the number of fecal bifidobacteria and lactobacilli in the cecal content of rats[39-40].

Burdock was shown to suppress the CCl_4 or acetaminophen-intoxicated mice as well as the ethanol plus CCl4-induced rat liver damage. The underlying hepatoprotective ability of burdock could be related to the decrease of oxidative stress on hepatocytes by increasing glutathione (GSH), cytochrome P-450 content and NADPH-cytochrome C reductase activity and by decreasing malondialdehyde (MDA) content, hence alleviating the severity of liver damage based on histopathological observations[41-42].

Anti-fatigue Effect

The anti-fatigue effect of the extract of *Arctium lappa* L. was studied in male mice by forced swimming test. The swimming time of mice treated by 4 and 6 g/kg of an extract of *Arctium lappa* was significantly prolonged as compared with control group. The hepatic glycogen storage in the groups treated with 2, 4 and 6 g/kg of *Arctium lappa* extract was significantly increased. Lactic acid clearance in the groups treated with 4, and 6 g/kg of *Arctium lappa* extract was significantly accelerated after mice swimming[43].

Antimicrobial Activity

Antibacterial activity against Gram negative (*E. coli, Shigella flexneri, and Shigella sonnei*), Gram positive (*Staphylococcus aureus, Bacillus subtilis*) and Mycobacterium, have been documented for *A. lappa*[44].

The lyophilized extract of *A. lappa* was effective against *B. subtilis* and *C. albicans*. Ethyl acetate fraction was used as intracanal medication for 5 days in teeth infected with *C. albicans*, *E. coli*, *L. acidophylus*, *P. aeruginosa* and *S. mutans*. It inhibited microbial growth after 14 days[45-46].

The antimicrobial activity of rough extracts from leaves of *Arctium lappa* and their phases was tested *in vitro* against microorganisms commonly found in the oral cavity, specifically in endodontic infections, *Enterococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Candida albicans*. The *Arctium lappa* constituents exhibited a great microbial inhibition potential against the tested endodontic pathogens[46].

Contraindications and Side Effects

No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. There was a

slight potential for sensitization via skin contact with the drug. Excessive dose may interfere with existing hypoglycemia. It should be avoided during pregnancy and lactation[3,8].

Dosage

Dried root: 2-6 g by infusion three times daily. Decoction (1:20) 500 ml per day[8].

CONCLUSION

The paper reviewed *Arctium lappa* as promising natural medicinal plants with wide range of pharmacological activities which could be utilized in several medical applications because of their effectiveness and safety.

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