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Review

A review of the pharmacological effects of *Arctium lappa* (burdock)

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Abstract

Arctium lappa, commonly known as burdock, is being promoted/recommended as a healthy and nutritive food in Chinese societies. Burdock has been used therapeutically in Europe, North America and Asia for hundreds of years. The roots, seeds and leaves of burdock have been investigated in view of its popular uses in traditional Chinese medicine (TCM). In this review, the reported therapeutic effects of the active compounds present in the different botanical parts of burdock are summarized. In the root, the active ingredients have been found to "detoxify" blood in terms of TCM and promote blood circulation to the skin surface, improving the skin quality/texture and curing skin diseases like eczema. Antioxidants and antidiabetic compounds have also been found in the root. In the seeds, some active compounds possess anti-inflammatory effects and potent inhibitory effects on the growth of tumors such as pancreatic carcinoma. In the leaf extract, the active compounds isolated can inhibit the growth of micro-organisms in the oral cavity. The medicinal uses of burdock in treating chronic diseases such as cancers, diabetes and AIDS have been reported. However, it is also essential to be aware of the side effects of burdock including contact dermatitis and other allergic/inflammatory responses that might be evoked by burdock.

Keywords *Arctium lappa* (burdock) – Traditional Chinese medicine – Anti-inflammatory – Pharmacology

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Introduction

Starting from the end of the twentieth century, the majority of people in developed countries have become wealthier and more health conscious. They tend to spend extra money on different functional foods or nutraceuticals to pursue healthy aging. Natural products have been used in the treatment of various chronic human pathological conditions because they are rich in antioxidants (Guo et al. 2008). In traditional Chinese medicine (TCM), it is believed that food and medicine stem from the same origin but with different uses and applications (Chan et al. 2010). Therefore, it is common for Chinese people to incorporate different medicinal herbs into their diet to produce various "healthy" food recipes to achieve better taste, more attractive appearance and improved texture of the food and most importantly to improve health.

Burdock, a perennial herb in the family of Compositae stores most of its nutrients during the first year. These nutrients are then used for the flower-blooming process afterward. The plant, which can be found worldwide, has been cultivated as a vegetable for a period of long time in Asia (Morita et al. 1993). Burdock, called "Niubang" in Chinese, has been used in China and some western countries for over 3,000 years and its therapeutic uses have been documented in *The Compendium of Materia Medica* (*Bencao gangmu* in Chinese) written by Li Shizhen, the most famous/important figure in the history and development of TCM, during the Ming dynasty (Yu et al. 2003).

Burdock is traditionally used to treat diseases such as sore throat and infections such as rashes, boils and various skin problems. According to TCM, these pathological events are mainly due to the accumulation of toxin in the body. The dried root of 1-year-old burdock (Fig. 1) is the major part used for different therapeutic purposes, although burdock leaves and fruit/seeds are also used. It is suggested that the root of this herb is particularly effective and invaluable in eliminating heavy metals from our body. Therefore, it appears to have the function of draining toxins in terms of TCM theory (Yu et al. 2003).

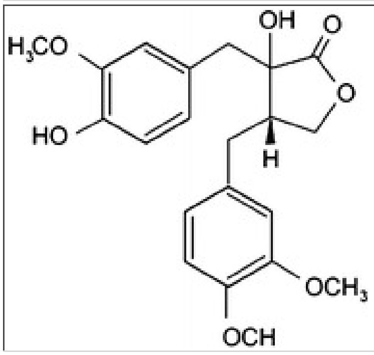
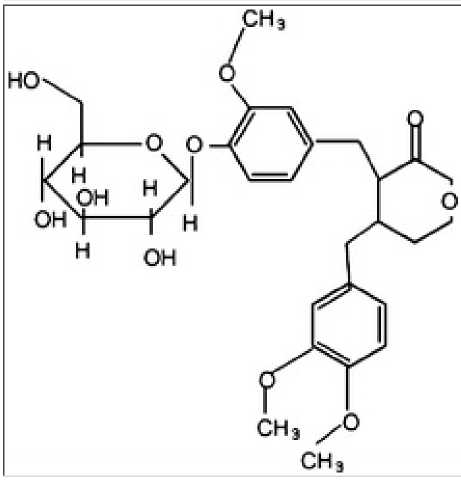
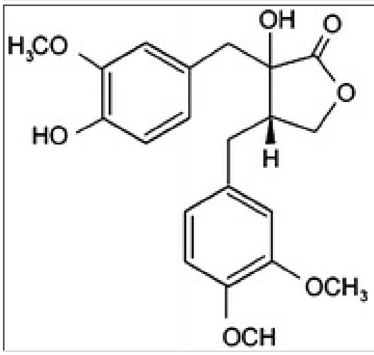
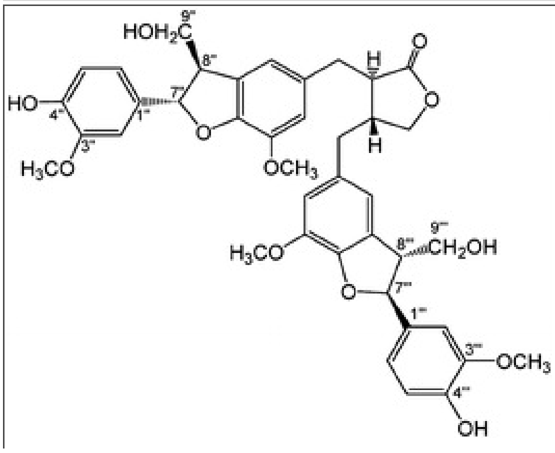
Fig. 1 The root of burdock

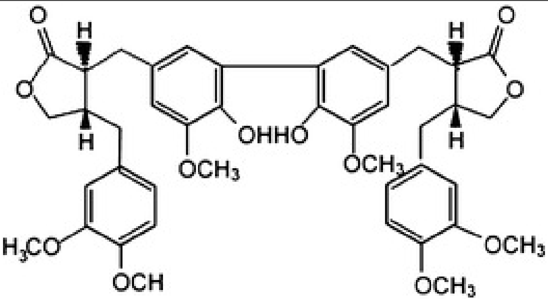
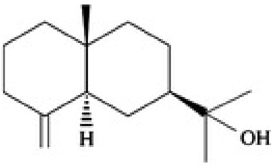
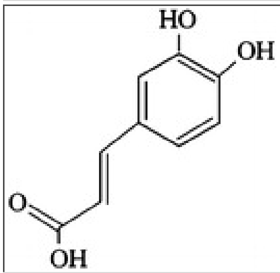
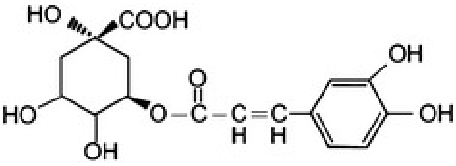
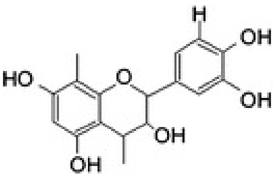
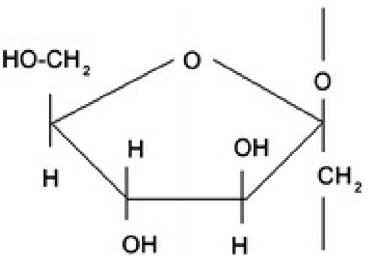
In contrast to some famous and expensive medicinal herbs such as *Ganoderma lucidum* (Lingzhi) and *Panax ginseng* (Ginseng) that have been used for a long period of time, with their rich and highly acclaimed nutritional values, burdock possesses various therapeutic values but is still sold at a low price. Moreover, it can be easily cultivated. In light of the aforementioned properties of this herb, the aim of this review is to summarize the currently available scientific information on burdock so as to provide a comprehensive overview of this herb.

Active ingredients found in burdock

With the advancement of different state-of-the-art analytical techniques, more active ingredients of burdock have been identified over the last decade (Park et al. 2007). The major active ingredients isolated from this herb are: tannin, arctigenin, arctiin, beta-eudesmol, caffeic acid, chlorogenic acid, inulin, trachelogenin 4, sitosterol-beta-D-glucopyranoside, lappaol and diarctigenin (Table 1). Apart from these compounds, burdock also contains various common nutrients (Table 2).

Table 1 General compounds and effects of burdock reported in the literature

Classification	Compound	Molecular formula	Parts of the plant	Effect
Lignans	 Arctigenin	$C_{12}H_{24}O_7$	Leaves, fruits, seeds, roots	Suppressor of heat shock; antitumor; anti-influenza virus
	 Arctiin	$C_{27}H_{34}O_{11}$	Leaves, fruits, roots	Antitumor-promoting activity; chemopreventi activity; antiproliferative activity against cell hybridoma cell, MH60
	 Trachelogenin	$C_{21}H_{24}O_7$	Fruits	Ca^{2+} antagonis activity; anti-HI properties
		$C_{40}H_{42}O_{12}$	Fruits, seeds	Inhibiting NO production

Classification	Compound	Molecular formula	Parts of the plant	Effect
	Lappaol F			
	 Diarctigenin	$C_{42}H_{46}O_{12}$	Fruits, roots, seeds	Inhibiting NO production
Terpenoids	 Beta-eudesmol	$C_{15}H_{26}O$	Fruits	Antibacterial; antiangiogenic
Polyphenols	 Caffeic acid	$C_9H_8O_4$	Stems, leaves, skin of roots	Antioxidative; free radical scavenging activity
	 Chlorogenic acid	$C_{16}H_{18}O_9$	Leaves; skin of roots	Neuroprotective antioxidative; anti-anaphylaxi and anti-HIV;
	 Tannin	$C_{76}H_{52}O_{46}$	Roots	Antitumor; immuno-modulator; hyaluronidase inhibition
Fructose	 Inulin	$(C_6H_{10}O_5)_n$	Roots	Prebiotic effectiveness; antihypertensio antidiabetes

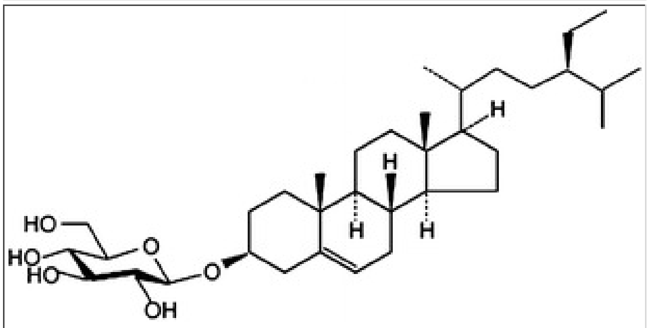
Classification	Compound	Molecular formula	Parts of the plant	Effect
Sterols	 Sitosterol-beta-D-glucopyranoside	$C_{35}H_{60}O_6$	Roots	Mammalian DN polymerase λ; anti-diabetes and obesity

Table 2 Major nutritional ingredients contained in the burdock roots

Types	Nutrient ingredients							
Amino Acid	Essential amino acids		Aspartic acid (25–28%)		Arginine (18–20%)			
Metal elements	Potassium	Calcium	Iron	Magnesium	Manganese	Sodium	Zinc	Copper
Vitamins	B1	B2	C	A				
Others	Crude fiber	Phosphorus	Carotene					

Pharmacological effects

The extracts from different parts of burdock have long been considered to be good for health. They help enhance the body's immune system and improve metabolic functions (Lin et al. 2002). Biological activities and pharmacological functions reported for the *Arctium* species include anti-inflammatory, anticancer, antidiabetic, antimicrobial and antiviral activities.

Anti-inflammatory effects

Inhibition of inducible nitric oxide synthase (iNOS) expression and nitric oxide (NO) production, suppression of pro-inflammatory cytokine expression, inhibition of the nuclear factor-kappa B (NF-κB) pathway, activation of antioxidant enzymes and scavenging of free radicals are the essential mechanisms of burdock's anti-inflammatory action.

The extract of burdock has been shown to exhibit anti-inflammatory response by inhibiting degranulation and release of cysteinyl leukotrienes (Cys-LTs) by peripheral blood mononuclear cells (PBMCs). Cys-LTs are synthesized inflammatory mediators such as histamine and prostaglandins. The blockade of Cys-LT is regarded as inhibition of inflammatory response. Also, the extract of burdock significantly inhibited acute mouse ear edema due to induced allergic response. Therefore, there has been evidence suggesting that burdock has significant anti-inflammatory effect (Knipping et al. 2008).

Lappaol F, diarctigenin and arctigenin, found in the seeds or leaves of burdock, are lignans that can inhibit NO production. The excessive production of NO by iNOS (EC1.14.13.39) is involved in various inflammatory diseases such as rheumatoid arthritis, autoimmune disease, chronic inflammation and atherosclerosis. Therefore, inhibition of NO production by iNOS in macrophages is a potential treatment for certain inflammatory diseases (Wang et al. 2007). Lappaol F and diarctigenin strongly inhibit NO production in lipopolysaccharide (LPS)-stimulated murine macrophage RAW264.7 cells with IC_{50} values of 9.5 and 9.6 μM, respectively (Park et al. 2007). Further study elucidated that diarctigenin could directly target NF-κB-activating signaling cascade by direct inhibition of the DNA binding ability of NF-κB and inhibition of NF-κB-regulated iNOS expression (Kim et al. 2008).

Arctigenin, a phenylpropanoid dibenzylbutyrolactone lignan, potently inhibits iNOS expression and NO production through suppression of NF-κB activation and inhibition of I-κBα phosphorylation and p65 nuclear translocation in LPS-activated macrophages (Cho et al. 2002). In addition, arctigenin strongly inhibits the expression of pro-inflammatory cytokines tumor necrosis factor-α (TNF-α) and IL-6, in LPS-stimulated RAW264.7 cells, THP-1 human monocyte-macrophage and differentiated human macrophage U937 (Cho et al. 2002; Zhao et al. 2009). Further study showed that arctigenin-induced inhibition of TNF-α production might be mediated by arctigenin's potent inactivation of mitogen-activated protein (MAP) kinases including ERK1/2, p38 kinase and JNK through the inhibition of MAP kinase kinase (MKK) activity, leading to inactivation of activator protein-1 (AP-1) (Cho et al. 2004; Zhao et al. 2009).

On the other hand, expression of inflammation-associated cyclooxygenase 2 (COX-2) and formation of prostaglandin E_2 (PGE_2) are the results of increased NO production. Inhibitor of COX-2 causes a potent inflammatory effect, since the prostaglandin family is associated with the onset of inflammation. The methanolic extract of burdock has been proven to be effective in inhibiting the expression level of COX-2 mRNA. Therefore, the anti-inflammatory effect of burdock is attributed to the lowered PGE_2 release (Wang et al. 2007).

In view of the inflammatory processes, inflammation has usually been investigated together with the pathway of free radicals. There have been many studies on the association between free radicals, oxidative stress and inflammation (Weber et al. 2005; Abreu et al. 2006; Pontiki et al. 2006). Instead of only studying the action of drugs/herbs on pro-inflammatory cytokines or/and other inflammatory mediators, their free radical scavenging capacities should also be considered. There are increasing studies focusing on both the effects of pro-inflammatory signaling and free-radical scavenging capacity of individual drug/herb, which may contribute to their resultant anti-inflammatory effect (Lee et al. 2007). Recent studies have demonstrated burdock's anti-inflammatory characteristics on carrageenan-induced rat paw edema and carbon tetrachloride (CCl_4)-induced hepatotoxicity. The carrageenan-induced rat paw edema assay is a widely used model for acute inflammatory testing. Burdock has shown to have significant inhibition on the growth of rat paw edema in a dose-related manner, thus suggesting some significant anti-inflammatory activities of burdock (Lin et al. 1996). Lin et al. (1996) demonstrated the antioxidant power of burdock extract by detecting the signal intensities of 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO)–OOH in relation to superoxide dismutase (SOD) concentration. Burdock was shown to have hepatoprotective effect by suppressing the CCl_4 or acetaminophen intoxication in mice, as well as the ethanol plus CCl_4-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 (Lin et al. 2000, 2002). In summary, the anti-inflammatory action of burdock is attributed to its high free radical scavenging capacities and antioxidant activity.

Anticancer activities

During the development of tumors, very large amounts of nutrients (oxygen and nutrients) are required to sustain the rapid proliferation of tumor cells. However, tumor cells can still survive under extreme conditions such as low oxygen and low carbohydrate availability due to their relatively high tolerance to hostile environment. Arctigenin, an active compound found in the seeds of burdock, has the ability to eradicate nutrient-deprived cancer cells (Awale et al. 2006). In addition to its broad spectrum of activities on different cancer cell lines, e.g., PANC-1 and AsPC-1, arctigenin seems to exhibit a highly preferential cytotoxicity to cancer cells that are bathed in glucose-deprived conditions (Awale et al. 2006). This is because arctigenin has a potent inhibitory effect on the phosphorylation of Akt (Guo et al. 2008), which is stimulated under glucose-deprived conditions. Hence, the rate of glucose formation in cancer cells is decreased, which in turn leads to cell death due to a lack of nutrients (Awale et al. 2006).

Protection of cells from harmful substances can greatly reduce the chance of tumor formation and thus suppresses cancer cell proliferation. Flavoniod-type antioxidants and some other active polyphenol antioxidants found in the root of burdock may account for the suppressive effects on cancer metastasis (Tamayo et al. 2000). It has been shown that extracts of the root protect cells from toxic substances and lower the mutations of cells (Miyamoto et al. 1993).

Tannin, a phenolic compound, is one of the most common active compounds found in the root of burdock. It induces macrophage responses, inhibits tumor growth and possesses immuno-modulatory properties (Miyamoto et al. 1993). However, tannin is potentially toxic in nature. It may cause stomach upset and at high concentrations has some dangerous side effects such as nephrotoxicity and hepatic necrosis (Miyamoto et al. 1993). Therefore, the use of tannin should be carefully monitored.

Antidiabetic activity

Burdock has been used to treat diabetes by TCM practitioners. Several studies have suggested that the root or/and fruit are possible parts with hypoglycemic effect. Sitosterol-beta-D-glucopyranoside is considered to be the most potent and efficacious substance among the large profile of active compounds found in the root of burdock. It has demonstrated potent inhibitory effects on alpha glucosidase activities. Alpha glucosidases are involved in the processing of glycoprotein and glycogenolysis. Inhibitors of glycosidase are potential therapeutic agents in treating diabetes mellitus and obesity (Mitsuo et al. 2005). In addition, gamma-glucoside-fructose ester, also known as inulin, can help to regulate blood glucose levels. Inulin, a natural carbohydrate present in the root of burdock, can act on cell surface receptors to keep the blood glucose level constant, therefore improving the tolerance to high glucose level. Also, the production of short chain fatty acids is also increased (Silver and Krantz 1931). The antidiabetic activity of total lignan from the fruit of burdock has been studied in a model of alloxan-induced diabetes in mice and rats. It has been proven that total lignan from burdock is a safe antidiabetic agent and may help prevent diabetic complications (Xu et al. 2008).

Antimicrobial and antiviral activity

It has been reported that the lyophilized extract of the leaves of burdock exhibits antimicrobial activity against oral micro-organisms and is most effective against bacteria related to endodontic pathogens such as: *Bacillus subtilis*, *Candida albicans*, *Lactobacillus acidophilus* and *Pseudomonas aeruginosa* (Pereira et al. 2005). Chlorogenic acid isolated from the leaves also show restraining effects on *Escherichia coli*, *Staphylococcus aureus* and *Micrococcus luteus* (Lin et al. 2004). Therefore, the leaves of burdock may be useful in treating tooth/gum diseases that are related to micro-organisms in the oral cavity. It is also a potential topical remedy for skin problems such as eczema, acne and psoriasis. In addition, the polyacetylene ingredients extracted from the root of burdock also possess potent antibacterial and antifungal activities (Takasugi et al. 1987).

Constituents of burdock have also demonstrated antiviral activity. Phenolic constituents such as caffeic acid and chlorogenic acid possess strong inhibitory effect on herpesvirus (HSV-1, HSV-2) and adenovirus (ADV-3, ADV-11) (Chiang et al. 2002). Arctigenin, one of the lignanoid ingredients, has demonstrated activities against human immunodeficiency virus type-1 (HIV-1) both in vivo and in vitro (Schroder et al. 1990; Eich et al. 1996). These suggest potential uses of these promising natural compounds isolated from burdock to treat infection by these viruses, especially HIV.

Other activities

Lignans isolated from burdock have been shown to be potent platelet-activating factor (PAF) receptor antagonists, calcium antagonists and hypotensive agent (Ichikawa et al. 1986; Iwakami et al. 1992). Arctiin, a lignin isolated from burdock seeds, has protective effect against 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP)-induced carcinogenesis (Hirose et al. 2000). Besides arctiin, polyphenolics in burdock, especially caffeic acid and chlorogenic acid, also have significant anti-mutagenic activity, which has a positive correlation with polyphenolic content (Liu and Tang 1997). The anti-decrepitude effect of burdock has also been noted. Li et al. (2004) have elucidated that the main mechanism of burdock's anti-decrepitude effect involves improvement of SOD activity and reduction of MDA and lipofuscin content. Furthermore, burdock has been used as an adjunctive therapy or alternative medicine for the treatment of gout, hypertension, arteriosclerosis and other inflammatory disorders (Li et al. 2004).

However, burdock has also been reported to have side effects. The most commonly reported side effect of burdock is the induction of contact dermatitis. Patients suffer from contact dermatitis after extended topical use of the root oil of burdock. Another reported case was a massage liniment containing burdock extracts that caused contact dermatitis (Paulsen 2002). There was also a case of development of anaphylaxis due to burdock consumption. A Japanese man had developed urticaria ten times after consuming cooked burdock, with redness occurring over his entire body. In addition, he experienced difficulties in breathing an hour after consuming it. It was found that this patient had a low blood pressure of 64/29 mmHg. He was diagnosed to be in anaphylactic shock (Sasaki et al. 2003). Therefore, it seems to be a misconception that herbs that are of natural sources have less side effect compared to drugs. It was suggested that adverse clinical effects for herbal drugs range from allergic skin reactions, the Stevens–Johnson syndrome and photosensitization to toxic dermatosis. Since most herbs are readily accessible by the general public, increasing number of cases of herb-induced adverse effects is expected (Niggemann and Gruber 2003). Therefore, public awareness about the possibility of adverse effects of medicinal herbs must be enhanced.

Conclusions

Burdock contains many active ingredients (isolated from different parts of the plant) that have been shown to possess many therapeutic effects for the treatment of various diseases. Multiple reports in the literature have demonstrated a wide range of possible clinical uses of this herb, because of its anti-inflammatory, antitumor/cancer, antidiabetic, antimicrobial and antiviral effects. In conclusion, the medicinal use of burdock in treating chronic diseases such as cancer, diabetes and AIDS is promising. However, it is also essential to be aware of the side effects of burdock including contact dermatitis and other allergic/inflammatory responses that might be evoked by burdock. It is expected that further investigations will lead to a better understanding of some other roles that burdock play in preventing and treating of human diseases, as well as the potential adverse effects and toxicity of the herb. It could provide us with more information on the beneficial effect and the potential risk of consuming burdock as a functional food.

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