



# Bardana

## *Arctium lappa*

### Nome botanico

*Arctium lappa* L. (*Compositae*)

### Parti usate

Radice.

### Componenti principali

Acidi caffeilchinici. Lignani. Inulina. Composti acetilenici solforati. Poliacetileni. Guaianolidi. Acido costusico. Acido  $\gamma$ -guanidino-n-butirrico.

### Attività farmacologica

Attività epatoprotettiva. Attività antidermopatica. Attività ipoglicemizzante e antiuricemia. Azione antiinfiammatoria e antiossidante.

### Impiego clinico

Acne e dermatopatie. Insufficienza epatica. Iperuricemia.

### Controindicazioni

Ipersensibilità nota a piante della famiglia delle *Compositae*.

### Avvertenze e speciali precauzioni d'uso

Non sono noti studi clinici controllati in donne in gravidanza e durante allattamento: in conformità con la prassi medica generale, il prodotto non deve essere impiegato senza prima avere sentito il parere del medico.

### Interazioni

Nessuna nota.

### Effetti indesiderati

Nessuno degno di nota.

# Note Bibliografiche

## Composizione

I componenti principali della radice di Bardana (*Arctium lappa*) sono rappresentati da acidi caffeilchinici, quali acido clorogenico, acido caffeico e acido isoclorogenico e da lignani tra cui arctigenina e il suo glucoside arctiina<sup>1</sup>, diartigenina<sup>2</sup>, neoartina B, metilarctigenina, phylligenina, pinosresinolo<sup>3</sup>, daucosterolo, matairesinolo e lappaolo<sup>4</sup>. Sono inoltre presenti elevate quantità di polimeri di inulina, in misura del 30-45%, e mucillagini, per un totale nella radice di circa il 70% di polisaccaridi. La droga contiene poi una quindicina di poliacetileni; dieci composti acetilenici solforati diversi, quali acido aretico, arctinone, arctinolo, arctinale; un olio essenziale ricco di acidi amari; acido costusico; principi amari come i guaianolidi deidrocostusicolattone e 11,13-diidrodeidrocostusicolattone e il lattone sesquiterpenico arctiopicrina; sitosterolo, stigmasterolo e acido  $\gamma$ -guanidino-n-butirrico<sup>5</sup>.

## Attività biologiche ed impieghi clinici descritti in letteratura

Le attività biologiche ed i più noti impieghi clinici descritti per il fitocomplesso della *Arctium lappa* sono:

**Medicina popolare.** Nella medicina popolare europea la Bardana era soprattutto utilizzata come diuretico (“depurativo del sangue”), contro la calcolosi biliare o urinaria, come diaforetico e nel trattamento della gotta e dei reumatismi. Esternamente, la radice veniva impiegata come cataplasma per eczemi, ulcere e ferite a cicatrizzazione torpida, mentre il cataplasma di foglie fresche serviva per mitigare i dolori delle articolazioni nell’artrite e per i catarri polmonari. Di notevole interesse anche l’utilizzo nei disturbi a carico dell’apparato gastrointestinale per facilitare le funzioni digestive

<sup>1</sup> “A simple method involving polyamide column chromatography in combination with HPLC-PAD and HPLC-ESI/MS for isolating and identifying two kinds of lignans, **arctiin and arctigenin**, in the leaves of burdock (*Arctium lappa* L.) has been established.” (Liu S, Chen K, Schliemann W, Strack D. Isolation and identification of arctiin and arctigenin in leaves of burdock (*Arctium lappa* L.) by polyamide column chromatography in combination with HPLC-ESI/MS. *Phytochem Anal.* 2005 Mar-Apr;16(2):86-9).

<sup>2</sup> Han BH, Kang YH, Yang HO, Park MK. A butyrolactone lignan dimer from *Arctium lappa*. *Phytochemistry* 1994; 37(4):1161-1163.

<sup>3</sup> Boldizsár I, Füzfai Z, Tóth F, Sedlák E, Borsodi L, Molnár-Perl I. Mass fragmentation study of the trimethylsilyl derivatives of arctiin, matairesinoside, arctigenin, phylligenin, matairesinol, pinosresinol and methylarctigenin: their gas and liquid chromatographic analysis in plant extracts. *J Chromatogr A.* 2010 Mar 5;1217(10):1674-82.

<sup>4</sup> “In this work the bioactive metabolic profile, the antioxidant activity and total phenolic content of burdock (*Arctium lappa*) seeds, leaves and roots were obtained. (...) **The main compounds of burdock extracts were caffeoylquinic acid derivatives, lignans (mainly arctiin) and various flavonoids.** The occurrence of some phenolic acids (caffeic acid, chlorogenic acid and cynarin) in burdock seeds; **arctiin, luteolin and quercetin rhamnoside in burdock roots**; phenolic acids, quercetin, quercitrin and luteolin in burdock leaves was reported for the first time.” (Ferracane R, Graziani G, Gallo M, Fogliano V, Ritieni A. Metabolic profile of the bioactive compounds of burdock (*Arctium lappa*) seeds, roots and leaves. *J Pharm Biomed Anal.* 2010 Jan 20;51(2):399-404).

<sup>5</sup> Ferracane R, Graziani G, Gallo M, Fogliano V, Ritieni A. Metabolic profile of the bioactive compounds of burdock (*Arctium lappa*) seeds, roots and leaves. *J Pharm Biomed Anal.* 2010 Jan 20;51(2):399-404.

e stimolare l'appetito, in quanto la droga favorisce la secrezione di succhi gastrici e in particolare della bile. La radice era infine impiegata come blando lassativo per la presenza di inulina. I medici eclettici americani del XIX secolo consideravano la Bardana un eccellente diuretico e la prescrivevano per infezioni dell'apparato urinario, disturbi renali e minzione dolorosa, oltre che per infezioni cutanee ed artrite (King's American Dispensatory, 1898). Nella tradizione della medicina cinese, la radice della Bardana elimina l'eccesso di energia "nervosa", le tossine e le infezioni (riduce lo yang); per questa sua attività decongestionante viene utilizzata come rimedio per le sindromi da raffreddamento quali raffreddore e influenza<sup>6</sup>.

**Attività antinfiammatoria e decongestionante.** L'estratto di Bardana radice ha dimostrato una significativa attività antinfiammatoria<sup>7</sup> e antiossidante<sup>8</sup> in diversi modelli sperimentali quali, rispettivamente, l'infiammazione plantare da carragenina nel ratto e il test di epatotossicità indotta da tetracoloro di carbonio e da altri agenti epatotossici; l'estratto ha mostrato in particolare un notevole effetto scavenger sul radicale superossido e sul radicale idrossilico e perossidico<sup>9</sup>. I componenti del fitocomplesso principalmente responsabili dell'attività antiflogistica sembrano

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<sup>6</sup> **"The fruits of *Arctium lappa* L. is an often-used herbal drug in traditional Chinese medicine for the treatment of common cold caused by wind and heat.** This drug contained many constituents, principally arctiin, with arctigenin in smaller amount. In this work, arctiin has been isolated from the fruits of *Arctium lappa*, and then enzymolyzed into arctigenin." (Sun WJ, Sha ZF, Gao H. Determination of arctiin and arctigenin in *Fructus Arctii* by reverse-phase HPLC. *Acta Pharmaceutica Sinica* 1992; 27: 549-51).

<sup>7</sup> **"The effects of *Arctium lappa* L. (root) on anti-inflammatory and free radical scavenger activity were investigated. Subcutaneous administration of A. lappa crude extract significantly decreased carrageenan-induced rat paw edema. When simultaneously treated with CCl<sub>4</sub>, it produced pronounced activities against CCl<sub>4</sub>-induced acute liver damage.** The free radical scavenging activity of its crude extract was also examined by means of an electron spin resonance (ESR) spectrometer. The IC<sub>50</sub> of A. lappa extract on superoxide and hydroxyl radical scavenger activity was 2.06 mg/ml and 11.8 mg/ml, respectively. These findings suggest that *Arctium lappa* possess free radical scavenging activity. The inhibitory effects on carrageenan-induced paw edema and CCl<sub>4</sub>-induced hepatotoxicity could be due to the scavenging effect of A. lappa." (Lin CC, Lu JM, Yang JJ, Chuang SC, Ujiie T. Anti-inflammatory and radical scavenge effects of *Arctium lappa*. *Am J Chin Med.* 1996;24(2):127-37).

<sup>8</sup> **"Five antioxidative caffeoylquinic acid derivatives were isolated from the roots of burdock (*Arctium lappa* L.)...** Their structures were established as 1-O-,5-O-dicaffeoylquinic acid (1), 1-O-,5-O-dicaffeoyl-3-O-succinylquinic acid (2), 1-O-,5-O-dicaffeoyl-4-O-succinylquinic acid (3), 1-O-,5-O-dicaffeoyl-3-O-,4-O-disuccinylquinic acid (4), and 1-O-,3-O-,5-O-tricaffeoyl-4-O-succinylquinic acid (5) on the basis of chemical and spectral (NMR, MS) evidence. (...) The antioxidant efficiency increased in the order of α-tocopherol < chlorogenic acid < caffeic acid < (1) = (2) = (3) = (4) < (5)." (Maruta Y, Kawabata J, Niki R. Antioxidative caffeoylquinic acid derivatives in the roots of burdock (*Arctium lappa* L.). *J Agric Food Chem.* 1995; 43(10):2592-2595).

<sup>9</sup> "...To evaluate the anti-inflammatory, antinociceptive and antioxidant activities of aqueous and ethanol extracts prepared from the leaves of *Arctium minus* (Hill) Bernh. ssp. *minus* (Asteraceae), the ethanolic and aqueous extracts from the leaves of *Arctium minus* were evaluated in mice for anti-inflammatory activity using carrageenan-induced hind paw edema model and for antinociceptive activity using p-benzoquinone-induced abdominal contractions test. Our results showed that **only the ethanol extract exhibited a dose-dependent anti-inflammatory activity** ranging between 11.1 and 23.6% at 200mg/kg dose as well as displayed a significant antinociceptive activity without inducing any gastric damage. Although, **both extracts were shown to possess significant DPPH radical-scavenging activity**, that of aqueous extract was found to have more pronounced activity. In FIA-CL system, the ethanol extract was shown to possess a significant scavenger activity against H<sub>2</sub>O<sub>2</sub> while the aqueous extract was much more potent antioxidant activity against HOCl-luminol CL than ethanol extract. ... In this study, in vivo experimental results have also supported its folk medicinal utilization." (Erdemoglu R. et al. Estimation of anti-inflammatory, antinociceptive and antioxidant activities on *Arctium minus* (Hill) Bernh. ssp. *Minus*. *J Ethnopharmacol.* 2009; 121(2):318-23).

essere i lignani come l'arctigenina<sup>10</sup>, che agisce inibendo in maniera dose-dipendente la secrezione di citochine proinfiammatorie<sup>11</sup>, tra cui TNF- $\alpha$  e IL-6, nonché l'espressione di enzimi proinfiammatori, come l'ossido nitrico sintetasi (iNOS), da parte dei neutrofili attivati; la molecola non sembra invece interferire con l'espressione di COX-2. In maniera analoga sembrano agire anche la diartigenina, il lappaolo e gli altri lignani butirrolattonici del fitocomplesso, capaci di inibire significativamente la produzione di NO indotta dal LPS in macrofagi di ratto tipo RAW264.7 con una IC<sub>50</sub> di appena 9,5 microM<sup>12</sup>. Diversi studi suggeriscono che l'attività antinfiammatoria di questi composti si espliciti attraverso l'inibizione della via di traduzione del fattore centrale che regola la risposta infiammatoria nei leucociti, il cosiddetto "fattore nucleare kappaB" (NF-kappaB), complessa molecola proteica che è inattiva in condizioni fisiologiche ma che si attiva sotto l'impulso di stimoli esterni alla cellula - come batteri, virus, radicali liberi, ecc. - inducendo a livello nucleare il risveglio di geni che codificano per molteplici potenti proteine infiammatorie. In particolare, l'inibizione riscontrata per i lignani della Bardana sembra verificarsi attraverso l'inibizione del legame di NF-kappaB ai suoi siti specifici sul DNA<sup>13,14</sup>. Il Nuclear Factor kappaB (NF-kB) controlla, direttamente o con la cooperazione

<sup>10</sup> "Arctigenin, a bioactive constituent from dried seeds of *Arctium lappa* L. (Compositae), was found to exhibit anti-inflammatory activities and its molecular mechanism (was studied). ... **Arctigenin suppressed lipopolysaccharide (LPS)-stimulated NO production and pro-inflammatory cytokines secretion, including TNF-alpha 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. **These results indicated that potent inhibition on NO, TNF-alpha and IL-6, but not COX-2 expression and COX-2 activity, might constitute the anti-inflammatory mechanism of arctigenin. Arctigenin suppressed the overproduction of NO through down-regulation of iNOS expression and iNOS enzymatic activity in LPS-stimulated macrophage.**" (Zhao F, Wang L, Liu K. *In vitro* anti-inflammatory effects of arctigenin, a lignan from *Arctium lappa* L., through inhibition on iNOS pathway. *J Ethnopharmacol.* 2009 Apr 21;122(3):457-62).

<sup>11</sup> "...Previously, we showed that arctigenin potently inhibited the induction of nitric oxide synthase (iNOS) by lipopolysaccharide (LPS), which involved suppression of NF-kappaB activation. **In the present study, we examined the effects of arctigenin on mitogen-activated protein (MAP) kinase activation in Raw264.7 cells and MAP kinase kinase (MKK) activity. The effect of arctigenin on activator protein-1 (AP-1) activation was also studied in association with tumor necrosis factor-alpha (TNF-alpha) expression. (...). Arctigenin blocked TNF-alpha production and decreased the level of TNF-alpha mRNA in the cells exposed to LPS. These results showed that arctigenin inhibited activation of MAP kinases including ERK1/2, p38 kinase and JNK through the inhibition of MKK activities, leading to AP-1 inactivation, which might, at least in part, contribute to the inhibition of TNF-alpha production.**" (Cho MK, Jang YP, Kim YC, Kim SG. *Arctigenin, a phenylpropanoid dibenzylbutyrolactone lignan, inhibits MAP kinases and AP-1 activation via potent MKK inhibition: the role in TNF-alpha inhibition. Int Immunopharmacol.* 2004 Oct;4(10-11):1419-29).

<sup>12</sup> Park SY, Hong SS et al. *Lignans from Arctium lappa and their inhibition of LPS-induced nitric oxide production. Chem Pharm Bull (Tokyo)* 2007; 55(1):150-2).

<sup>13</sup> "The effects of arctigenin and demethyltraxillagenin on the nuclear factor-kappaB (NF-kappaB)-mediated inducible nitric oxide synthase (iNOS, EC1.14.13.39) gene expression were studied in Raw264.7 cells. (...) These results demonstrated that **arctigenin potently inhibited LPS-inducible iNOS expression in murine macrophages through suppression of I-kappaBalpha phosphorylation and nuclear translocation of p65. Potent inhibition of LPS-inducible NO production in macrophages may constitute anti-inflammatory effects of the dibenzylbutyrolactone lignans.**" (Cho MK, Park JW, Jang YP, Kim YC, Kim SG. *Potent inhibition of lipopolysaccharide-inducible nitric oxide synthase expression by dibenzylbutyrolactone lignans through inhibition of I-kappaBalpha phosphorylation and of p65 nuclear translocation in macrophages. Int Immunopharmacol.* 2002 Jan;2(1):105-16).

<sup>14</sup> *Diartigenin, a lignan constituent from Arctium lappa, down-regulated zymosan-induced transcription of inflammatory genes through suppression of DNA binding ability of nuclear factor-kappaB in macrophages. J Pharmacol Exp Ther.* 2008 Nov;327(2):393-401.

di altri fattori di trascrizione, l'attività di oltre 100 geni coinvolti nel controllo di processi fisiologici di primaria importanza, quali la regolazione della risposta immunitaria alle infezioni, l'apoptosi, il ciclo cellulare, lo sviluppo e la funzione di numerosi organi e tessuti, compresi quelli del sistema emolinfopoietico. Come conseguenza di tale molteplicità di funzioni, la deregolata attivazione di NF-kappaB è associata a malattie infiammatorie croniche, patologie autoimmuni, infezioni virali e malattie del sistema immunitario, malattie linfoproliferative.

Ricordiamo a questo proposito che i corticosteroidi inibiscono NF-kappaB e che l'aspirina, ma non gli altri FANS, è un potente inibitore del NF-kappaB. È interessante notare, infine, che sembrano esplicarsi attraverso un meccanismo simile a quello sopra descritto anche l'azione antinfiammatoria di diversi altri composti naturali come il partenolide - lattone sesquiterpenico estratto dal *Chrysanthemum parthenium*, la curcumina (*Curcuma longa*) e la silibina (*Sylibum marianum*)<sup>15</sup>. Infine, può contribuire all'effetto decongestionante della radice di Bardana anche l'attività immunomodulante svolta dalla componente polisaccaridica del fitocomplesso<sup>16</sup>.

**Attività detossificante ed epatoprotettiva.** La Bardana ha mostrato una significativa attività protettiva nei confronti dell'epatotossicità indotta sperimentalmente dal consumo cronico di etanolo; la somministrazione della droga ha inoltre marcatamente inibito il danno epatico indotto da altri agenti epatotossici quali tetracloruro di carbonio (CCl<sub>4</sub>) e paracetamolo (acetaminofene), contrastando la perossidazione lipidica, l'aumento delle transaminasi e la perdita di glutazione

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<sup>15</sup> "Natural products and some extracts are reviewed and assessed for their activity and potency as NF-kappaB inhibitors. **A large number of compounds are currently known as NF-kappaB modulators and include the isoprenoids, most notably kaurene diterpenoids and members of the sesquiterpene lactones class, several phenolics including curcumin and flavonoids such as silybin.** (...) In addition, where enough data exists some conclusions on structure-activity relationship are provided." (Bremner P, Heinrich M. *Natural products as targeted modulators of the nuclear factor-kappaB pathway. J Pharm Pharmacol.* 2002 Apr;54(4):453-72).

<sup>16</sup> "....The methods employed in structural determination were methylation analysis and <sup>1</sup>H and <sup>13</sup>C NMR spectral measurements. In tests for antitussive activity in cats the fructan was found to be equally active as some non-narcotic, synthetic preparations used in clinical practice to treat coughing, and in mitogenic and comitogenic tests its biological response was comparable to that of the commercial Zymosan immunomodulator." (Kardosová A, Ebringerová A, Alföldi J, Nosál'ová G, Franová S, Hribalová V. *A biologically active fructan from the roots of *Arctium lappa* L., var. *Herkules*. Int J Biol Macromol.* 2003 Nov; 33(1-3):135-40).

cellulare<sup>17,18</sup>. Poiché nelle epatopatie acute e croniche lo stress ossidativo sembra avere un ruolo patogenetico importante, è molto probabile che l'attività antiossidante, particolarmente evidente a livello epatico, rappresenti uno dei meccanismi più significativi alla base della discreta capacità epatoprotettiva del fitocomplesso di *Arctium lappa*. E va sottolineato che una parte consistente di questa attività scavenger contro i radicali liberi è legata alla presenza di derivati caffeilchinici, presenti in misura significativa nel fitocomplesso della droga<sup>19</sup>. Per tali composti è in effetti già stata descritta una potente attività protettiva nei confronti di molti agenti epatotossici<sup>20</sup>. Contribuisce inoltre all'azione epatoprotettiva anche l'inibizione del fattore nucleare NF-κB a livello dell'epatocita. Le fibre solubili contenute nella Bardana sono in grado di legare composti tossici, eventualmente

<sup>17</sup> **"In order to evaluate the hepatoprotective effects of *Arctium lappa* (burdock)**, a group of rats (n = 10) was fed a liquid ethanol diet (4 g of absolute ethanol/ 80 ml of liquid basal diet) for 28 days and another group (n = 10) received a single intraperitoneal injection of 0.5 ml/kg carbon tetrachloride (CCI(4)) in order to potentiate the liver damage on the 21st day (1 day before the beginning of *A. lappa* treatment). Control group rats were given a liquid basal diet which did not contain absolute ethanol. When 300 mg/kg *A. lappa* was administered orally 3 times per day in both the 1-day and 7-day treatment groups, some biochemical and histopathological parameters were significantly altered, both in the ethanol group and the groups receiving ethanol supplemented with CCI(4). ***A. lappa* significantly improved various pathological and biochemical parameters which were worsened by ethanol plus CCI(4)-induced liver damage**, such as the ethanol plus CCI(4)-induced decreases in total cytochrome P-450 content and NADPH-cytochrome c reductase activity, increases in serum triglyceride levels and lipid peroxidation (the deleterious peroxidative and toxic malondialdehyde metabolite may be produced in quantity) and elevation of serum transaminase levels. (...). These results tended to imply that the **hepatotoxicity induced by ethanol and potentiated by CCI(4) could be alleviated with 1 and 7 days of *A. lappa* treatment. The hepatoprotective mechanism of *Arctium lappa* could be attributed, at least in part, to its antioxidative activity, which decreases the oxidative stress of hepatocytes, or to other unknown protective mechanism(s).**" (Lin SC, Lin CH, Lin CC, Lin YH, Chen CF, Chen IC, Wang LY. *Hepatoprotective effects of *Arctium lappa* Linne on liver injuries induced by chronic ethanol consumption and potentiated by carbon tetrachloride. J Biomed Sci. 2002 Sep-Oct;9(5):401-9*).

<sup>18</sup> **"In order to investigate the hepatoprotective effects of the root of *Arctium lappa* L. (Compositae), male ICR mice were injected with carbon tetrachloride (CCI4, 32 microl/kg, i.p.) or acetaminophen (600 mg/kg, i.p.). *A. lappa* suppressed the SGOT and SGPT elevations induced by CCI4 or acetaminophen in a dose-dependent manner and alleviated the severity of liver damage based on histopathological observations. (...)**From these results, **it was suggested that *A. lappa* could protect the liver cells from CCI4 or acetaminophen-induced liver damages, perhaps by its antioxidative effect on hepatocytes, hence eliminating the deleterious effects of toxic metabolites from CCI4 or acetaminophen.**" (Lin SC, Chung TC, Lin CC, Ueng TH, Lin YH, Lin SY, Wang LY. *Hepatoprotective effects of *Arctium lappa* on carbon tetrachloride- and acetaminophen-induced liver damage. Am J Chin Med. 2000;28(2):163-73*).

<sup>19</sup> **"...The antioxidant and anticarcinogenic properties of chlorogenic acid have been established in animal studies.** (...) Further studies indicated that chlorogenic acid could stimulate the nuclear translocation of Nrf2 (NF-E2-related factor) as well as subsequent induction of GSTA1 antioxidant response element (ARE)-mediated GST activity. The phosphatidylinositol 3-kinase pathway might be involved in the activation of Nrf2 translocation. **These results provide the first evidence that chlorogenic acid could protect against environmental carcinogen-induced carcinogenesis and suggest that the chemopreventive effects of chlorogenic acid may be through its up-regulation of cellular antioxidant enzymes and suppression of ROS-mediated NF-κappaB, AP-1, and MAPK activation.**" (Feng R, Lu Y, Bowman LL, Qian Y, Castranova V, Ding M. *Inhibition of activator protein-1, NF-κappaB, and MAPKs and induction of phase 2 detoxifying enzyme activity by chlorogenic acid. J Biol Chem. 2005 Jul 29;280(30):27888-95*).

<sup>20</sup> "Hepatoprotective activity guided chemical analyses led to the isolation of two dicaffeoyl quinic acid derivatives, methyl 3,4-di-O-caffeoyl quinate (1) and 3,4-di-O-caffeoyl quinic acid (2)... **These compounds were stronger antihepatotoxic agents than glycyrrhizin.**" (Basnet P, Matsushige K, Hase K, Kadota S, Namba T. *Potent antihepatotoxic activity of dicaffeoyl quinic acids from popolis. Biol Pharm Bull 1996; 19: 655-7*).

assorbiti per via orale o inalati, quali ipoclorobenzoni (PCB), e di facilitarne l'eliminazione<sup>21</sup>. Anche questo meccanismo, insieme con la capacità della droga di esercitare direttamente sull'epatocita i suoi effetti, potrebbe contribuire all'attività antitossica della radice di Bardana. Inoltre, la Bardana riduce l'assorbimento intestinale di colesterolo e di lipidi, ma l'aspetto più interessante è la ridotta formazione di acido litocolico (LCA) dagli acidi colico edeossicolico (DCA). Poiché l'acido litocolico è epatotossico, mutageno e potenzialmente cancerogeno, il rapporto LCA/DCA nella bile e nell'intestino è preso da alcuni AA. come indice di rischio per il cancro coloretale. La Bardana, come altre fibre dietetiche, riduce questo indice<sup>22</sup>.

**Acne e dermatopatie.** La Bardana viene tradizionalmente utilizzata nel trattamento di diverse dermatopatie, quali acne, dermatite seborroica e foruncolosi, sia per la sua azione disintossicante, stimolante la secrezione epatobiliare e la diuresi, sia per la sua attività antiinfiammatoria e antiossidante<sup>23,24</sup>. È ben noto, infatti, che un'eccessiva produzione di sostanze ossidanti nella cute

<sup>21</sup> "We investigated the binding of PCB by dietary fiber in vivo and in vitro. Forty male rats consisting of four rats a group were housed and rats of each group were given a treatment diet containing rice-bran fiber, spinach fiber, burdock fiber, cabbage fiber, soybean fiber Japanese-radish fiber, carrot fiber, corn fiber and cellulose for five days... **A significant correlation existed between the amounts of binding PCB in vitro and fecal PCB output in rats by eight types of dietary fiber** ( $r = 0.986, p < 0.01$ )." (Morita K, Hamamura K, Iida T. Binding of PCB by several types of dietary fiber in vivo and in vitro. *Fukuoka Acta Medica* 1995; 86: 212-7).

<sup>22</sup> "This study was conducted to evaluate the effects of different types of dietary fibers (DF) under the conditions with or without cholesterol (Chol) loading on the amount and composition of steroids in rat feces... Although **the lithocholic acid (LCA)/deoxycholic acid (DCA) ratio, a risk index for colorectal cancer, was significantly lower in the bamboo, burdock and apple groups** than in the CP or corn groups when given the diet without Chol, the differences disappeared with the addition of Chol... **These results suggest that the intake of some DF by host animals works beneficially for the microbial conversion of BA and Chol in the large intestine but that the addition of Chol acts to cancel such beneficial effects.**" Shimizu J, Yamada N, Nakamura K, Takita T, Innami S. Effects of different types of dietary fiber preparations isolated from bamboo shoots, edible burdock, apple and corn on fecal steroid profiles of rats. *Journal of Nutritional Science and Vitaminology* 1996; 42: 527-39).

<sup>23</sup> "To delve into the anti-aging effects and mechanism of Niubanggen (**Radix Arctii Lappae**), the activity of SOD and the content of MDA and lipofuscin in the tissues of the liver, brain and blood serum of the lab rats were observed 30 days after they had been fed with the Niubanggen decoction. Result: **The activity of SOD in the liver tissue and blood serum of the decoction-fed lab rats was improved dramatically ( $P < 0.05$  or  $P < 0.01$ ), the content of MDA in the brain tissue and blood serum lowered obviously ( $P < 0.05$  or  $P < 0.01$ ), and the content of lipofuscin dropped distinctly ( $P < 0.01$ ).** Conclusion: **The mechanism of the anti-aging effects of the Niubanggen is mainly obtained by raising the activity of SOD and reducing the contents of MDA and lipofuscin.**" Liu S, Li Y, Li S, Luo M, Liu X. An experimental research into the anti-aging effects of *Radix Arctii Lappae*. *J Tradit Chin Med*. 2005 Dec; 25(4): 296-9).

<sup>24</sup> "...To gain deeper insight in this field, we examined the effects of **3,5-di-O-caffeoylquinic acid (DCA), its methyl ester (DCE) and epigallocatechin gallate (EGCG) in nitrate and oxidative processes.** These compounds were found to be strong inhibitors of the nitration of tyrosine residues induced by ONOO- in bovine serum albumin, with their  $IC_{50}$  values (10-40  $\mu$ M) notably decreasing in the presence of bicarbonate. (...) This ability seems to be due to a direct interaction with ONOO- or with the species generated by leukocytes. The possible interference with the production of NO was also studied: **both DCA and EGCG inhibited nitrite production in LPS-stimulated macrophages by 24% and 40%, respectively, and the expression of nitric oxide synthase-2 (NOS-2), as well. DCA and EGCG reduced by 52% and 59%, respectively, the NF-kappaB transcriptional activity. In contrast, DCE did not show any effect.**" (Olmos A, Giner RM, Recio MC, Ríos JL, Gil-Benito R, Máñez S. Interaction of dicaffeoylquinic derivatives with peroxynitrite and other reactive nitrogen species. *Arch Biochem Biophys*. 2008 Jul 1; 475(1): 66-71).

ha un ruolo importante nella patogenesi dell'acne e di altre dermatiti<sup>25</sup>. Studi recenti dimostrano poi che gli estratti di *Arctium lappa* (ma non l'arctiina) possiedono anche attività antiallergica, in quanto inibiscono la degranolazione mastocitaria e antagonizzano la liberazione di leucotrieni ed altri mediatori chimici della flogosi, riducendo la reazione cutanea immediata nell'animale sensibilizzato e ostacolando l'amplificazione delle reazioni infiammatorie<sup>26</sup>. D'altra parte, la radice di *Arctium lappa* contiene almeno due importanti classi di composti ad azione antinfiammatoria quali i lignani butirrolattonici, come l'arctigenina, e gli acidi caffeilchinici, come l'acido clorogenico<sup>27</sup>. Tali sostanze agirebbero inibendo l'attivazione di NF-kappaB a livello macrofagico e del TNF- $\alpha$ , nonché bloccando la formazione di specie reattive dell'ossigeno mediante inibizione della ossido nitrico

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<sup>25</sup> "Skin antioxidant network protects cells against oxidative injury and prevent the production of oxidation products, ... When oxidative stress overwhelms the skin antioxidant capacity the subsequent modification of cellular redox apparatus leads to an alteration of cell homeostasis and a generation of degenerative processes. (...) Based on these findings, the review summarises **the possible correlations between antioxidant imbalance, lipid oxidative breakage and inflammatory skin diseases (such as psoriasis or acne)**, from both a pathological and therapeutic points of view." (Briganti S, Picardo M. *Antioxidant activity, lipid peroxidation and skin diseases. What's new. J Eur Acad Dermatol Venereol.* 2003 Nov;17(6):663-9).

<sup>26</sup> "In this study, the inhibitory effects of *Arctium lappa* Linne (Compositae) (AL) on degranulation and the release of mediators as well as on inhibition of cys-leukotriene biosynthesis by basophils were investigated. AL was selected out of 10,000 herbal extracts in a set-up for high throughput screening in which the degree of degranulation was monitored by the release of beta-hexosaminidase from rat basophil leukemia (RBL-2H3) cells(...). Although arctiin, the active component of AL that has been described in the literature, was not able to reduce degranulation in RBL-2H3 cells, a single high-performance liquid chromatography (HPLC) fraction from the AL extract inhibited beta-hexosaminidase release (IC<sub>50</sub>) = 22.2 microg/ml). Topical administration of an aqueous extract of AL (5 mg/ear) on the ear of whey-sensitized mice 4 hrs before challenge with whey in the ear inhibited acute ear swelling by 50% in an in vivo cow's milk allergic model. The extract had no effect in this model when administered orally. In conclusion, the active component present in the active HPLC fraction of the **Arctium lappa extract was able to significantly reduce the release of inflammatory mediators through inhibition of degranulation and cys-leukotriene release in vitro. In addition, this active component was able to inhibit acute skin response in mice in vivo, indicating that AL is a very promising natural component for use in anti-allergic treatment.**" (Knipping K, van Esch EC, Wijering SC, van der Heide S, Dubois AE, Garssen J. *In vitro and in vivo anti-allergic effects of Arctium lappa L. Exp Biol Med (Maywood).* 2008 Nov;233(11):1469-77).

<sup>27</sup> "...**The active phenolic components, chlorogenic acid and caffeic acid, existed mainly in the skin of burdock root, and the content of chlorogenic acid was much higher than that of caffeic acid. Burdock possessed significant free radical scavenging activity, which was mainly attributed to chlorogenic acid**, whose free radical scavenging activity was similar to that of caffeic acid and higher than that of vitamin E." (Chen FA, Wu AB, Chen CY. *The influence of different treatments on the free radical scavenging activity of burdock and variations of its active components. Food Chemistry* 2004; 86(4):479-484).



sintetasi<sup>28,29</sup>. Oltre ad un effetto antiinfiammatorio diretto e ad un'azione protettiva dei fibroblasti dall'azione citossica dei radicali liberi, ricerche recenti dimostrano poi per i lignani di *Arctium lappa*, in particolare l'arctiina, anche un'attività stimolante della neosintesi di collagene nonché dell'espressione della ialuronano sintetasi<sup>30</sup>, elementi centrali nell'organizzazione tridimensionale dei componenti della matrice extracellulare del derma. La matrice extracellulare è una rete gelatinosa di proteine e carboidrati che fa da impalcatura all'interno dei tre strati della pelle – derma, ipoderma ed epidermide – composta prevalentemente da acqua, collagene, elastina, glicoproteine e mucopolisaccaridi. Per l'estratto di radice di Bardana è stata inoltre evidenziata anche una specifica attività anti-elastasi<sup>31</sup>. Ancora, è stato studiato sperimentalmente l'effetto protettivo degli acidi

<sup>28</sup> "The protective effects of burdock (*Arctium lappa* Linne) on oxidation of low-density lipoprotein (LDL) and nitric oxide production were investigated. The results showed that **methanolic extracts of burdock (MEB) and their major components, chlorogenic acid (CHA) and caffeic acid (CA), showed marked antioxidant activity against oxidative damage of liposome ( $p < 0.05$ ), deoxyribose ( $p < 0.05$ ) and protein ( $p < 0.05$ )**. In addition, at a concentration of 500 µg/ml, the inhibitory effect of MEB on LDL oxidation was 66.9% compared to the control ( $p < 0.05$ ). MEB, at 200 µg/ml, not only enhanced GSH levels, but also increased activity of GSH reductase, GSH peroxidase, GSH transferase and catalase, which were 3.82-, 24.9-, 4.35- and 3.02-fold compared to the control ( $p < 0.05$ ), respectively. MEB directly scavenged nitric oxide in a concentration-dependent fashion ( $p < 0.05$ ). (...). Reverse transcription-polymerase chain reaction (RT-PCR) analysis revealed that the expression of iNOS and COX-2 mRNA in activated macrophages were suppressed by a high concentration (500 µg/ml) of MEB. Furthermore, a downregulated degradation of IκB-α by MEB was found, indicating that MEB reduced iNOS enzyme expression as a result of preventing NF-κB activation. These results suggest that **MEB displays an inhibitory action on biomolecules and has a bioactive action for attenuating excessive NO generation at inflammatory site as well as in cardiovascular disease.**" (Bor-Sen Wang, Gow-Chin Yen, Lee-Wen Chang, Wen-Jye Yen, Pin-Der Duh. *Protective effects of burdock (Arctium lappa Linne) on oxidation of low-density lipoprotein and oxidative stress in RAW 264.7 macrophages. Food Chemistry* 2007; 101(2):729–738.

<sup>29</sup> Cho MK, Jang YP, Kim YC, Kim SG. Arctigenin, a phenylpropanoid dibenzylbutyrolactone lignan, inhibits MAP kinases and AP-1 activation via potent MKK inhibition: the role in TNF-α inhibition. *Int Immunopharmacol.* 2004 Oct;4(10-11):1419-29.

<sup>30</sup> "...This study aims to screen for an active ingredient with anti-inflammatory (i.e., reduction of interleukin-6 and tumor necrosis factor-α) and matrix-stimulating efficacy which improves the clinical signs of skin aging in vivo. **In vitro studies with pure Arctiin were performed investigating the inhibition of cytokine induction and stimulation of collagen neosynthesis.** In vivo home-in-use studies using an *Arctium lappa* fruit extract-containing formulation were carried out to determine procollagen and hyaluronan synthesis, hyaluronan synthase-2 gene expression, and reduction of wrinkle volume after treatment. Results. In vitro studies on human dermal fibroblasts and monocyte-derived dendritic cells supplemented with pure Arctiin showed relative to untreated control cells a stimulation of collagen synthesis and a decrease in interleukin-6 and tumor necrosis factor-α concentration, respectively. **In addition, topical in vivo application of an A. lappa fruit extract-containing formulation for 12 weeks significantly stimulated procollagen synthesis and increased hyaluronan synthase-2 expression as well as hyaluronan levels compared to vehicle-treated control areas.** Similarly, after a 4-week treatment with an A. lappa fruit extract-containing formulation, wrinkle volume in the crow's feet area was significantly reduced as compared to treatment with the vehicle. Conclusions. Our data show that topical **treatment with a natural A. lappa fruit extract significantly improves the metabolism of the dermal extracellular matrix** and leads to a visible wrinkle reduction in vivo." (Knott A, Reuschlein K, Mielke H, Wensorra U, Mummert C, Koop U, Kausch M, Kolbe L, Peters N, Stäb F, Wenck H, Gallinat S. *Natural Arctium lappa fruit extract improves the clinical signs of aging skin. Journal of Cosmetic Dermatology* 2008; 7(4):281-289).

<sup>31</sup> "...The anti-ageing and anti-oxidant properties of 23 plant extracts (from 21 plant species) were assessed as anti-elastase and anti-collagenase activities and in selected anti-oxidant assays along with phenolic content. Results: **Anti-elastase activities were observed for nine of the extracts with inhibitory activity in the following order: white tea (approximately 89%), cleavers (approximately 58%), burdock root (approximately 51%), bladderwrack (approximately 50%), anise and angelica (approximately 32%).** Anti-collagenase activities were exhibited by sixteen plants of which the highest activity was seen in white tea (approximately 87%), green tea (approximately 47%), rose tincture (approximately 41%), and lavender (approximately 31%). Nine plant extracts had activities against both elastase (E) and collagenase (C) and were ranked in the order of white tea (E:89%, C:87%) > bladderwrack (E:50%, C:25%) > cleavers (E:58%, C:7%) > rose tincture (E:22%, C:41%) > green tea (E:10%: C:47%)

caffeilchinici – come l'acido caffeico<sup>32</sup> – nei confronti dell'eritema cutaneo indotto da radiazioni ultraviolette<sup>33</sup> e sulla degradazione del collagene tipo III indotta dai radicali liberi sulla pelle umana esposta ai raggi solari (UVA/UVB)<sup>34</sup>, nonché l'effetto inibitorio degli stessi sulla ialuronidasi<sup>35</sup>, enzima responsabile di gran parte del danno ai tessuti cutanei e sottocutanei che si osserva in corso di acne, dermatite seborroica ed altre affezioni cutanee di natura infiammatoria.

Alla luce delle proprietà fin qui esposte e a conferma degli impieghi descritti dalla medicina empirica, gli estratti di Bardana possono dunque rappresentare un valido coadiuvante nei processi flogistici a carico dell'epidermide e nel trattamento dermatologico della pelle secca, pruriginosa e screpolata, anche a causa dell'invecchiamento cutaneo.

**Attività ipoglicemizzante.** In studi sull'animale è stata dimostrata un'attività ipoglicemizzante dei lignani, importanti componenti del fitocomplesso di *Arctium lappa*<sup>36</sup>. La frazione dell'estratto

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> rose aqueous (E: 24%, C:26%) > angelica (E:32%, C:17%) > anise (E:32%, C:6%) > pomegranate (E:15%, C:11%). Total phenolic content varied between 0.05 and 0.26 mg gallic acid equivalents (GAE)/mL with the exception of white tea (0.77mg GAE/mL)." (Thring TS, Hili P, Naughton DP. School of Life Sciences, Kingston University, London, KT1 2EE, UK. *Anti-collagenase, anti-elastase and anti-oxidant activities of extracts from 21 plants. BMC Complement Altern Med.* 2009 Aug 4;9:27).

<sup>32</sup> "Caffeic acid (CA) and its analogues such as rosmarinic acid are well known as antioxidative agents. Exposure to UVA is known to generate reactive oxygen species (ROS) such as singlet oxygen (1O<sub>2</sub>) and superoxide anion radical (\*O<sub>2</sub><sup>-</sup>) in the skin of animals, which in turn induces skin photodamage and photoaging. Because CA and its analogues quench 1O<sub>2</sub>, these compounds were topically applied to the abdominal skin of live hairless mice and were found to suppress ROS generation upon UVA exposure. Furthermore, **the generation of UVA-induced ROS was also suppressed in the skin of mice that were orally given CA. In order to understand the mechanism by which CA blocks ROS production in UVA-exposed skin, the pharmacokinetics of CA upon oral administration to mice was followed and CA was found to efficiently distribute in the skin. These results suggest that skin damage by UVA-induced ROS generation is reduced by oral supplementation of CA, which has a scavenging and quenching activity against ROS.**" (Yamada Y, Yasui H, Sakurai H. *Suppressive effect of caffeic acid and its derivatives on the generation of UVA-induced reactive oxygen species in the skin of hairless mice and pharmacokinetic analysis on organ distribution of caffeic acid in ddY mice. Photochem Photobiol.* 2006 Nov-Dec;82(6):1668-76).

<sup>33</sup> Saija A, Tomaino A, Trombetta D, De Pasquale A, Uccella N, Barbuzzi T, Paolino D, Bonina F: *In vitro and in vivo evaluation of caffeic and ferulic acids as topical photoprotective agents. Int J Pharm* 2000;199:39-47.

<sup>34</sup> "The protective effect of caffeoyl derivatives on the free radical-induced degradation of Type III collagen has been investigated. ... **These results indicate that this representative class of polyphenols protects collagen from free radical damage through a scavenging effect on reactive oxygen species and/or C-, N-, S-centered secondary radicals, and provide an indication for their topical use for the prevention/treatment of photodamage of the skin by UVA/UVB radiation, in which oxidative stress plays a crucial role.**" (Facino RM, Carini M, Aldini G, Saibene L, Pietta P, Mauri P. *Echinacoside and caffeoyl conjugates protect collagen from free radical-induced degradation: a potential use of Echinacea extracts in the prevention of skin photodamage. Planta Med* 1995;61: 510-4)

<sup>35</sup> "Among these caffeoyl conjugates, chicoric and caftaric acids had the greatest antihyaluronidase activity." (Facino RM, Carini M, Aldini G, Marinello C, Arlandini E, Franzoi L, Colombo M, Pietta P, Mauri P. *Direct characterization of caffeoyl esters with antihyaluronidase activity in crude extracts from Echinacea angustifolia roots by fast atom bombardment tandem mass spectrometry. Farmaco* 1993; 48: 1447-61).

<sup>36</sup> "The antidiabetic activity of the total lignan from the plant *Fructus Arctii*, used in China for the control of diabetes, was investigated in models of alloxan-induced diabetic mice and hyperglycemic-hyperlipidemic diabetic rats. The biochemical parameters studied were: blood glucose, glucose tolerance, serum insulin, serum triglycerides, total cholesterol and high density lipoprotein (HDL). Total lignan was given to mice and rats daily for 10 days at doses of 2.0, 1.0, 0.5 g/kg and 1.38, 0.69, 0.35 g/kg respectively. **The alloxan-diabetic animals showed significant reductions in plasma glucose, triglycerides**

metanolico della droga solubile in etile acetato riduce poi l'attività dell' $\alpha$ -glucosidasi<sup>37</sup>, un enzima presente nell'orletto a spazzola della mucosa intestinale che nell'intestino tenue è deputato alla scissione dei carboidrati complessi. Inoltre, per il suo elevato contenuto in inulina – un polimero del fruttosio contenuto nella radice (fino al 45%) non digeribile dal corredo enzimatico gastrointestinale e che quindi non viene assorbito dall'organismo – la radice di Bardana viene utilizzata per rallentare la digestione dei carboidrati. Ritardando la digestione dei carboidrati ritarda il passaggio del glucosio in circolo così da consentire alla  $\beta$ -cellula pancreatica di aumentare la secrezione insulinica con una riduzione del picco glicemico post-prandiale.

**Attività antiurolitiasica.** L'iperuricemia può portare alla formazione di cristalli di urato che si depositano nelle articolazioni e nei reni. Quando questa condizione si manifesta nelle articolazioni provocando dolore e infiammazione, prende il nome di "gotta". L'iperuricemia è poi strettamente associata allo sviluppo di ipertensione, malattia renale e progressione della malattia.

Secondo alcuni AA. la Bardana ha una moderata attività diuretica ed antiurolitiasica, ed è probabilmente per questa attività che viene utilizzata nella medicina popolare nell'iperuricemia e nelle calcolosi urinarie<sup>38</sup>. Studi recenti documentano poi che gli acidi dicaffeilchinici identificati nel fitocomplesso della radice di *Arctium lappa* inibiscono l'enzima xantina-ossidasi contribuendo a ridurre i livelli plasmatici di acido urico e giustificando l'impiego tradizionale della droga nei pazienti con iperuricemia e gotta<sup>39</sup>.

**Altre attività.** Tra i meccanismi identificati alla base dell'attività antiinfiammatoria del fitocomplesso di *Arctium lappa* è stata dimostrata l'inibizione dell'attivazione del fattore nucleare kappaB, che potrebbe rappresentare un possibile bersaglio di nuovi e più selettivi farmaci antiinfiammatori. Il Nuclear Factor kappaB (NF-kB) è un fattore di trascrizione nucleare presente in tutte le cellule

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**and total cholesterol after treatment with the total lignan from the plant Fructus Arctii and glibenclamide (used as standard) compared with the diabetic controls**, while the glucose tolerance, serum insulin level and HDL-cholesterol were elevated without the risk of hypoglycemia. In conclusion, the total lignan from the plant Fructus Arctii has been proven to be a safer antidiabetic agent and might help to prevent diabetic complications. It can serve as a good adjuvant in the present armamentarium of antidiabetic drugs." (Xu Z, Wang X, Zhou M, Ma L, Deng Y, Zhang H, Zhao A, Zhang Y, Jia W. *The antidiabetic activity of total lignan from Fructus Arctii against alloxan-induced diabetes in mice and rats. Phytother Res.* 2008 Jan;22(1):97-101).

<sup>37</sup> **"Methanol extract from Arctium lappa L. showed an inhibitory activity of  $\alpha$ -glucosidase. The methanol extract was re-extracted with ethyl acetate and water. The ethyl acetate extract showed inhibitory activity. The inhibitory compound was isolated from the ethyl acetate extract and identified as sitosterol- $\beta$ -D-glucopyranoside (1) by EI-MS, FAB-MS, IR, 1H and 13C NMR spectroscopy. Compound 1 inhibited 97.3% of  $\alpha$ -glucosidase activity at a concentration of 200.0  $\mu$  mol/mL, and the ID50 (50% inhibition dose) value was 30  $\mu$  mol/mL. (..)"** (Miyazawa M, Yagi N, Katsuya Taguchi K. *Inhibitory Compounds of  $\alpha$ -Glucosidase Activity from Arctium lappa L. Journal of Oleo Science* 2005; 54(11):589-594).

<sup>38</sup> *Grases F, Melero G, Costa-Bauza A, Prieto R, March J G. Urolithiasis and phytotherapy. International Urology and Nephrology* 1994; 26: 507-11.

<sup>39</sup> *Nguyen MT, Awale S, Tezuka Y, Shi L, Zaidi SF, Ueda JY, Tran QL, Murakami Y, Matsumoto K, Kadota S. Hypouricemic effects of acacetin and 4,5-o-dicaffeoylquinic acid methyl ester on serum uric acid levels in potassium oxonate-pretreated rats. Biol Pharm Bull.* 2005 Dec;28(12):2231-4.

che producono citochine, fattori di crescita, chemochine, molecole di adesione e proteine di fase acuta, sia in condizioni normali che patologiche. Una volta attivato, esso controlla, direttamente o con la cooperazione di altri fattori di trascrizione, l'attività di oltre 100 geni che regolano numerosi processi cellulari di vitale importanza per la flogosi e la risposta immunitaria.

La sua inappropriata e aberrante attivazione può essere pertanto correlata con la patogenesi di numerose malattie fra cui asma, artrite reumatoide ed altre malattie autoimmuni o infiammatorie croniche, fibrosi polmonare, glomerulonefrite<sup>40</sup>, shock settico, aterosclerosi, neoplasie<sup>41</sup>. Altre patologie dove il ruolo eziopatogenetico svolto da NF-kappaB è ben documentato sono poi i processi infiammatori associati all'infezione da Herpes virus e l'AIDS<sup>42</sup>.

La Bardana possiede poi un'azione protettiva a livello dello stomaco: l'estratto in cloroformio della radice esercita attività antigastrica e antiulcerosa; tale azione sembra dovuta ad una riduzione della secrezione acida per inibizione dell'enzima gastrico H<sup>+</sup>/K<sup>+</sup>-ATPasi, che favorisce la riepitelizzazione della mucosa lesa<sup>43</sup>. Infine, i derivati caffeilchinici come tutti gli acidi aromatici, sono anche dotati di una forte azione batteriostatica e fungicida, come del resto gli idrocarburi

<sup>40</sup> "(...) **In this study, the ameliorative effects of arctiin, a natural compound isolated from the fruits of *Arctium lappa*, on rat glomerulonephritis induced by cationic bovine serum albumin (CBSA) were determined.** After oral administration of arctiin (30, 60, 120 mg/kgd) for three weeks, the levels of serum creatinine (Scr) and blood urea nitrogen (BUN) and 24-h urine protein content markedly decreased, while endogenous creatinine clearance rate (ECcr) significantly increased. The parameters of renal lesion, hypercellularity, infiltration of polymorphonuclear leukocyte (PMN), fibrinoid necrosis, focal and segmental proliferation and interstitial infiltration, were reversed. In addition, we observed that **arctiin evidently reduced the levels of malondialdehyde (MDA) and pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor (TNF-alpha), suppressed nuclear factor-kappaB p65 (NF-kappaB) DNA binding activity, and enhanced superoxide dismutase (SOD) activity. These findings suggest that the ameliorative effects of arctiin on glomerulonephritis is carried out mainly by suppression of NF-kappaB activation and nuclear translocation and the decreases in the levels of these pro-inflammatory cytokines, while SOD is involved in the inhibitory pathway of NF-kappaB activation.** Arctiin has favorable potency for the development of an inhibitory agent of NF-kappaB and further application to clinical treatment of glomerulonephritis, though clinical studies are required." (Wu JG, Wu JZ, Sun LN, Han T, Du J, Ye Q, Zhang H, Zhang YG. *Ameliorative effects of arctiin from *Arctium lappa* on experimental glomerulonephritis in rats. Phytomedicine. 2009 Nov;16(11):1033-41.*

<sup>41</sup> *Matsumoto T, Hosono-Nishiyama K, Yamada H. Antiproliferative and apoptotic effects of butyrolactone lignans from *Arctium lappa* on leukemic cells. Planta Med. 2006 Feb;72(3):276-8.*

<sup>42</sup> *Eich E, Pertz H, Kaloga M, Schulz J, Fesen MR, Mazumder A, Pommier Y. (-)-Arctigenin as a Lead Structure for Inhibitors of Human Immunodeficiency Virus Type-1 Integrase. J Med Chem. 1996; 39(1):86-95.*

<sup>43</sup> "*Arctium lappa* L. is used in folk medicine as a diuretic, depurative and digestive stimulant and in dermatological conditions. **The objective of this study was to evaluate the effect and the possible mechanisms involved in the gastroprotective effects of a chloroform extract (CE) of the roots from *A. lappa* and its fractions.** Oral pretreatment with CE (10, 30 and 100 mg kg(-1)) significantly reduced gastric lesions induced by ethanol by 61%, 70% and 76%, respectively. Oral administration of CE (100 mg kg(-1) per day for 7 days) reduced the chronic gastric ulceration induced by acetic acid by 52%. Intraduodenal CE (100, 300 and 600 mg kg(-1)) reduced the total acidity of gastric secretion by 22%, 22% and 33%, respectively, while i.p. administration (10, 30 and 100 mg kg(-1)) inhibited total acidity by 50%, 60% and 67%, respectively. In-vitro, CE inhibited H<sup>+</sup>, K<sup>+</sup>-ATPase activity with an EC50 of 53 microgmL(-1) and fraction A (30 and 100 microgmL(-1)) reduced this by 48% and 89%, respectively. CE had no effect on gastrointestinal motility. CE (250 microgmL(-1)) and fraction B (100 and 250 microgmL(-1)) had free-radical scavenging ability, inhibiting 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical activity by 50%, 20% and 55%, respectively. Collectively, **the results show that the CE protects animals from gastric lesions by reducing gastric acid secretion via inhibition of gastric H<sup>+</sup>, K<sup>+</sup>-ATPase.**" (Dos Santos AC, Baggio CH, Freitas CS, Lepieszynski J, Mayer B, Twardowschy A, Missau FC, dos Santos EP, Pizzolatti MG, Marques MC. *Gastroprotective activity of the chloroform extract of the roots from *Arctium lappa* L. J Pharm Pharmacol. 2008 Jun;60(6):795-801.*

acetilenici del fitocomplesso<sup>44</sup>; tali evidenze potrebbero supportare l'impiego degli estratti della droga nei disturbi di natura infettiva<sup>45</sup>.

**Tollerabilità.** Da studi tossicologici su animali la Bardana risulta essere una droga caratterizzata da una elevata tollerabilità e priva di rilevanti effetti collaterali. Tra gli eventi avversi, sono stati segnalati ad oggi solo tre casi di dermatite da contatto quando la Bardana è stata usata topicamente, ed è stato registrato un caso di anafilassi in seguito a somministrazione orale<sup>46</sup>. Non sono noti dalla letteratura studi clinici controllati in donne in gravidanza e durante l'allattamento: alcuni AA. riferiscono tuttavia una possibile azione sulla muscolatura uterina<sup>47,48</sup>, per cui in caso di gravidanza è opportuno utilizzare il prodotto con prudenza<sup>49</sup>.



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<sup>44</sup> "...**The phytotherapeutic agent extracted from an ethyl acetate fraction (AcOEt) of Arctium lappa** inhibited the growth of all the microorganisms (a mixed bacterial suspension of *Pseudomonas aeruginosa*, *Escherichia coli*, *Lactobacillus acidophilus*, *Streptococcus mutans* and *Candida albicans*) in this study." (*Gentil M, Pereira JV, Sousa YT, Pietro R, Neto MD, Vansan LP, de Castro França S. In vitro evaluation of the antibacterial activity of Arctium lappa as a phytotherapeutic agent used in intracanal dressings. Phytother Res. 2006 Mar;20(3):184-6.*)

<sup>45</sup> *Holetz FB, Pessini GL, Sanches NR, Cortez DA, Nakamura CV, Filho BP. Screening of some plants used in the Brazilian folk medicine for the treatment of infectious diseases. Mem Inst Oswaldo Cruz. 2002 Oct;97(7):1027-31.*

<sup>46</sup> *Sasaki Y, Kimura Y, Tsunoda T, Tagami H. Anaphylaxis due to burdock. Int J Dermatol. 2003 Jun;42(6):472-3.*

<sup>47</sup> *Farnsworth NR. Potential value of plants as sources of new antifertility agents I. J Pharm Sci. 1975; 64:535-98.*

<sup>48</sup> *Xie LH, Ahn EM, Akao T, Abdel-Hafez AA, Nakamura N, Hattori M. Transformation of arctiin to estrogenic and antiestrogenic substances by human intestinal bacteria. Chem Pharm Bull (Tokyo) 2003; 51:378-384.*

<sup>49</sup> *Ward WE, Jiang FO & Thompson LU. Exposure to flaxseed or purified lignan during lactation influences rat mammary gland structures. Nutrition and Cancer 2000; 37:187-192.*