

ROBITUS®

— Ribwort Extract
— Licorice Extract
— Thyme Extract

Plus

Cough
Syrup

روبیٹس پلس
کھانسی کا شربت

Composition:

Robitus Plus Syrup: Each 5ml contains:

Ribwort Extract 137.5mg

Thyme Extract 20mg

Licorice Extract 20mg

(Manufacturer Specs.)

RIBWORT PLANTAIN (*Plantago lanceolata*)

Plantago lanceolata belongs to the Plantaginaceae family. The flowering aerial parts or leaves are used for therapeutical purposes. The characteristic constituents are mucilage polysaccharides, flavonoids, and iridoid glycosides. It has therapeutical properties, such as anti-inflammatory, antioxidant, antifungal, immunostimulatory, and tissue regeneration. *Plantago lanceolata* is traditionally used for treating common cold and URTIs, and soothing and suppressing the cough. The ESCOP (European Scientific Cooperative on Phytotherapy) therapeutical indications for *Plantago lanceolata* extracts are catarrhs of the respiratory tract and mild inflammation of the oral and pharyngeal mucosae. The European Commission also approved its use for treating common cold and bronchitis-associated cough.

Based on literature and on the results of a survey in physicians according to Madaus (1976), *Plantago lanceolata* is administered in medical practice for the strengthening of mucosa and skin. It is given with very high success in diseases of the respiratory tract with severe mucous production.

Loew et al. (1997) mention *Plantago lanceolata* as mucilage drug which can be used against dry cough caused by pharyngitis. According to Hoppe (1975) *Plantago lanceolata* is used as a mucilage drug and mild expectorant. In folk medicine it is administered in catarrhs of the upper respiratory tract. Due to its positive benefit-risk-ratio *Plantago lanceolata* is recommended by Wegener and Kraft (1999) even for children for the treatment of moderate chronic irritative cough. Büechi and Wegener (2005) recommend the administration in moderate irritative cough as well as its topical application in cases of inflammation of the skin and mucosa.

Overview of available pharmacological data:

Plantago lanceolata has traditionally been regarded as a mucilage drug. The mucilage polysaccharides, mainly arabinose and galactose (Bräutigam and Franz 1985), are not resorbed and cover the mucosa with a protective layer against local irritations (Franz 1989, Müller-Limmroth 1980). Schmidgall et al. (2000) were the first to show moderate adhesive effects of polysaccharides from *Plantago lanceolata* extracts on mucus membranes.

Beyond this, pharmacological effects are attributed to the following constituents of *Plantago lanceolata* (Blaschek et al. 2008, Marchesan et al. 1998a):

- Iridoid glycosides: mainly aucubin and catalpol
- Mucilage polysaccharides
- Flavonoids: mainly apigenin and luteolin
- Phenylethanoids: acteoside, plantamajoside
- Phenol carboxylic acids
- Tannins

In vitro and in vivo pharmacological investigations have been performed with the total extract and with isolated agents from the total extract.

Anti-inflammatory, antioxidant, antibacterial, immunostimulant, epithelizing and antitoxic effects have been observed for extracts from *Plantago lanceolata* (Paper and Marchesan 1999, Büechi and Wegener 2005). In addition, spasmolytic and antiviral effects have been described by the authors for pure compounds of *Plantago lanceolata*.

Anti-inflammatory and antioxidant effects:

The anti-inflammatory efficacy of extracts from *Plantago lanceolata* has been investigated by means of the modified hen's egg chorioallantoic membrane test (HET-CAM) (Marchesan et al. 1998b). Four different freeze-dried liquid extracts (28% ethanol) were used. At a 10-fold higher concentration (500µg/pellet vs. 50µg) the anti-inflammatory activity of the extracts was comparable to that of hydrocortisone, phenylbutazone and diclofenac sodium. The *Plantago lanceolata* extract displayed significant efficacy concerning a dose-dependent inhibition of COX-2 activity. In vivo studies with dried frozen extracts from *Plantago lanceolata* leaves showed that in Wistar-Albino mice, the inflammatory effects caused by carrageenan and prostaglandin E1 were reduced (Shipochliev et al. 1981). Anti-inflammatory properties have also been established for single compounds of *Plantago lanceolata* by means of in vivo and in vitro experiments. The phenylethanoids acteoside and plantamajoside (Murai et al. 1995, Ravn et al. 1990, Hausmann et al. 2007, Hayashi et al. 1994, Molnár et al. 1989) and the iridoidglycosides, catalpol and aucubin (Recio et al. 1994) showed anti-inflammatory activity (in vitro and in vivo investigations). For flavonoids, anti-inflammatory effects have been described too (Spilková and Hubík 1988, Mascolo et al. 1988, Tordera et al. 1994). In connection with the anti-inflammatory activity of *Plantago lanceolata*, its antioxidant properties have also been studied, since free radicals may play a role in inflammatory diseases. Herold et al. (2003b) investigated the possible mode of action of the antioxidant potential of a hydroalcoholic extract from *Plantago lanceolata* leaves standardized to mucilaginous substances. The antioxidant property was measured using a colorimetric assay and the free radical scavenging potential by means of activated human polymorphonuclear neutrophils (PMNs). For the extract, a minor antioxidant status and the capacity of scavenging free radicals released by activated PMNs were observed.

The antioxidant activity of a methanol extract from the aerial parts of *Plantago lanceolata* was studied by Gálvez et al. (2005) using the DPPH scavenging test and lipid peroxidation inhibition assay, in which this extract was found to be the most active as compared to methanol extracts from other *Plantago* species. Antioxidant effects have also been observed for single compounds such as acteoside (Ji et al. 1993, Pan and Hori 1996, Wang et al. 1996; Li et al. 1996, Hausmann et al. 2007), various polysaccharides (Kardosová and Machová, 2006) and flavonoids (Catapano 1997, van Acker et al. 1996, Fraga et al. 1987).

Antibacterial effects:

In vitro investigations with pressed juice and aqueous extracts of *Plantago lanceolata* showed antibacterial effects against *Staphylococcus aureus*, *Streptococcus β-hemolyticus*, *Proteus vulgaris*, *Salmonella*, *Shigella*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Bacillus subtilis* (Háznagy 1970, Felklova 1958, Elich 1962).

Spasmolytic effects:

An ethanolic extract from *Plantago lanceolata* herba (DER 1:1) (Fleer et al. 1997) and an ethanolic (20%) soft extract of *Plantago lanceolata* (Fleer and Verspohl 2007) inhibited the ileum contractions caused by acetylcholine, histamine, potassium and barium ions and barium induced tracheal contractions in guinea-pigs. These effects were comparable to those of atropine and papaverine. Spasmolytic activity has been attributed to the iridoids, aucubin and catalpol (Urbina et al. 1994) and acteoside (Schapoval et al. 1998). Fleer and Verspohl (2007) observed antispasmodic effects for luteolin, acteoside, plantamajoside and catalpol peracetates.

Antiviral effects:

Abdin (2006) observed positive effects of tea from *Plantago lanceolata* leaves in one patient with AIDS related complex and suggests that further research might explore a possible role for *Plantago lanceolata* in the treatment of HIV-infection. Antiviral effects on aujeszky virus (Molnár et al. 1989) and RS-virus (Kernan et al. 1998) were observed for acteoside. Aucubin, as a prodrug for aucubigenin, inhibited in vitro DNS replication of hepatitis B virus (Chang 1997). Catalpol showed to be active against hepatitis B virus antigens (HBsAg) in HBsAg positive serum (Mehrotra et al. 1990). For caffeic acid and

chlorogenic acid (Chattopadhyay et al. 2008, Zanon et al. 1999, Chiang et al. 2002) as well as saponins and tanning agents (Büechi 1998, Büechi 1996) antiviral activity was shown, too.

Antitoxic effects:

Protective effects have been attributed to *Plantago lanceolata*. It has been reported that pressed juice from *Plantago lanceolata* had antitoxic effects on the damaging effects of 5-fluorouracil on the mucosa in mice with Ehrlich-tumours (Zueva and Yaremenko 1989, Borovskaya et al. 1987). Celik and Aslantürk (2006) also observed in vitro anti-mitotic and anti-genotoxic effects with aqueous extracts from *Plantago lanceolata* leaves. Antitumor activity was observed in vitro for acteoside and seems to be due at least in part to inhibition of protein kinase C (Herbert and Maffrand 1991). Flavonoids were shown to inhibit tumour promoter induced histamine release in a concentration-dependent manner (Middleton et al. 1987) and to inhibit hyaluronidase (Kuppusamy et al. 1990) and cyclic AMP phosphodiesterase (Kuppusamy and Das 1992). The hepatoprotective activity of an ethanolic extract from *Plantago lanceolata* leaves was investigated using pentobarbital-induced hypnosis model in mice treated with carbon tetrachloride as hepatotoxin. Significant hepatoprotective effects (25.5% inhibition) were observed (Deliorman et al. 1999).

Immunostimulant effects:

In vitro and in vivo, an aqueous extract from *Plantago lanceolata* leaves caused a significant increase of antibody formation and release of angiogenesis factor in lymphocytes of man and mouse (Strzelecka et al. 1995). An aqueous decoction of *Plantago lanceolata* leaves stimulated the production of interferon in mice (Plachcinska et al. 1984). Immunomodulatory effects were shown for several compounds of *Plantago lanceolata*: polysaccharides derived from *Plantago lanceolata* leaves (Bräutigam 1985, Ebringerová et al. 2003), aucubin and chlorogenic acid (Chiang et al. 2003), catalpol (Wegener and Kraft 1999, Garg et al. 1994) and acteoside (Marchesan et al. 1998).

Overall conclusions on clinical pharmacology and efficacy:

The traditional use is well documented. Apart from the results of one post-marketing study in 593 patients mainly with acute respiratory infections, among them 91 children and adolescents below 18 years of age (58 and 33 respectively), there is sufficient evidence in literature for the traditional internal use of *Plantago lanceolata* as a mucilage in the treatment of irritations of oral and pharyngeal mucosa and associated dry cough.

Conclusions:

The use of *Plantago lanceolata* as demulcent in the symptomatic treatment of oral and pharyngeal irritations and associated dry cough fulfils the requirement of at least 30 years of medicinal use (including at least 15 years with the European Union) according to the traditional use provisions of Directive 2001/83/EC as amended.

LICORICE (*Glycyrrhiza glabra*)

Glycyrrhiza glabra (family Fabaceae), commonly known as licorice, is a herbaceous perennial that has been used as medicinal remedies for thousands of years. Licorice root has been widely used around the world to treat cough since ancient times. It contains several active compounds including glycyrrhizin, glycyrrhetic acid, flavonoids, isoflavonoids, and chalcones. Glycyrrhizin and glycyrrhetic acid are considered to be the main active components and are potent inhibitors of cortisol metabolism, due to their steroid-like structures. The root of this plant has been used for treatment of coughs, colds, asthma, and COPD.

THYME (*Thymus vulgaris* L.)

Thyme (*Thymus vulgaris* L.), belonging to the Lamiaceae family, is a well-known spice plant possessing excellent medicinal properties. Thymus vulgaris oil and extract contain thymol, p-cymene, carvacrol, and γ -terpinene as the major components, which show very strong antibacterial, antifungal, and antioxidant activities; thus, Thyme is generally regarded as safe. Thyme (*Thymus vulgaris* L.) helps fight respiratory infections and is a natural

expectorant that serves as an antiseptic and helps expulse mucus. It's also good for soothing coughs and fighting nasal congestion.

Mechanism of action:

ROBITUS Plus as remedy for cold, mucus, cough, runny nose and sore throat, have anti-inflammatory and antibacterial effects, soothe a swollen mucous membrane of the throat and suppress cough, helps dissolve mucus and facilitates expectoration. In addition helps reduce swelling and allergic changes on the mucous membranes of the throat and nasopharynx.

Indications:

ROBITUS Plus Cough Syrup consists of natural plant extract based ingredients including Ribwort Plantain, Licorice, and Thyme that help to relieve cough, soothe throat, loosen phlegm, liquefies & removes mucus, promote healthy respiratory and bronchial functions; supports healthy mucous membrane.

Pregnancy and lactation:

In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Drug Interaction:

None Reported.

Dosage:

Dosage	
Age	Daily Dose
1 - 4 years	5ml 3 times
4 - 12 years	10ml 3 times
Above 12 years & Adults	10ml 4 times

Or as directed by the healthcare provider.

Overdose:

No case of overdose has been reported.

Contraindications:

Hypersensitivity to ribwort plantain, licorice and thyme or to any of the excipients.

Instructions:

Keep in a cool and dry place.
Protect from light, heat and moisture.
Keep out of the reach of children.

How Supplied:

- ROBITUS Plus syrup 120ml is available in a pet bottle and is sugar free.

Manufacturer's Enlistment No. 0078

Manufactured by:

Nutrimea
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Marketed by:

CENRJY
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Karachi