

 polinacea™

the most
innovative
immunobooster

from Echinacea

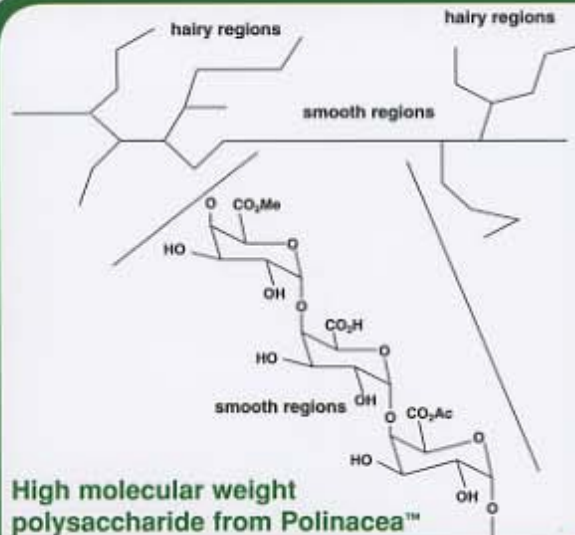


 indena
science is our nature™

What is Polinacea™?

Polinacea™ is the new immunomodulating herbal product developed by Indena. Obtained through an innovative extraction procedure (patent pending) from the roots of *Echinacea angustifolia*, Polinacea™ is characterized by a unique triple standardization that makes it different from all other echinacea derivatives. Due to its biological profile, it is reported to be totally safe and effective.

High molecular weight polysaccharide from Polinacea™



Standardized compound	Chemical nature	Content
Echinacoside	Caffeic acid derivative	≥ 4%
IDN 5405	Polysaccharide	≥ 5%
Isobutylamides	Amides	≤ 0.1%

Chemically defined because of the echinacoside (≥ 4%) and IDN 5405 (≥ 5%) content, the latter being a polysaccharide highlighted for the very first time in the *Echinacea angustifolia* root alone, it is devoid of isobutylamides as they do not add any biological contribute to the product.

Polinacea™ is an immunological response modulator that, through direct action on T cells, increases the immune functions showing superior effectiveness even when compared with very well known echinacea based specialities sold as drugs in Europe.

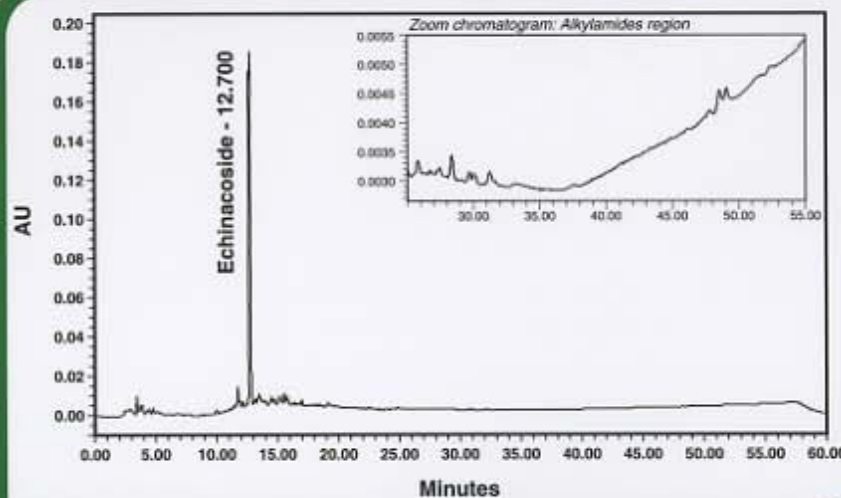


figure 1

Echinacea: Tradition and Uses

Echinacea angustifolia was used by native Americans to treat a variety of maladies including wounds, burns, insect bites, toothaches, infections and snake bites.

According to the *US Dispensatory* (1960 edition), Echinacea has been credited with ability to increase the resistance of the body to infection. From 1916 to 1950, Echinacea was included in the *National Formulary of the United States*. In the 1920s Echinacea was introduced into Europe as a drug. In recent years it has gained popularity worldwide through healthfood and dietary supplement channels.

Polinacea™: chemical profile

Polinacea™ is a standardized extract from *Echinacea angustifolia* selected species cultivated by Indena. The extract from its roots is obtained using only "food solvents". Besides echinacoside ($\geq 4\%$, by HPLC, see figure 1), Polinacea™ contains a very unique high molecular weight polysaccharide (characterized by a backbone of a polygalacturonic acid partially carboxymethylated and partially acetylated with a hairy region of rhamnogalacturonan) named IDN 5405 ($\geq 5\%$, by HPLC, see figure 2).

Polinacea™ contains also a low molecular weight polysaccharide identified to be inulin, enriching the product with a prebiotic profile.

Further to this, the isobutylamide fraction has been taken out of the product ($\leq 0.1\%$ in the finished extract). Recent data(*) show that this group of products is not relevant for the pharmacological effect of the extract. Furthermore toxicological *in vitro* and *in vivo* results suggest to reduce the isobutylamide content in the extract below 0.1% in relation with the possible chronic use of the product.

(*) Indena internal file

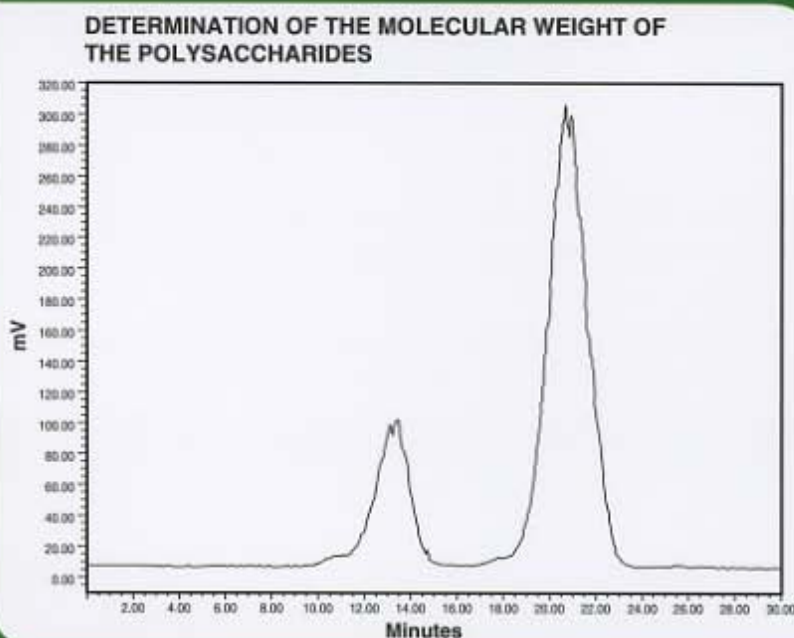


figure 2

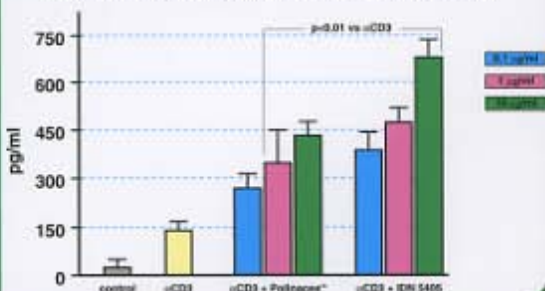
biological profile

Polinacea™ can be considered a very good immune response improver on the basis of the results obtained in several experimental models. In immunocompetent mice challenged with *Leishmania major* (one of the most representative experimental animal models utilized to check the immunobooster capability of drugs) Polinacea™ reduces by 25% the experimentally induced leishmaniasis. Moreover, Polinacea™ reduces by 30% and 40% the *Candida albicans* induced mortality in immunocompetent and in cyclosporin A treated mice, respectively (being cyclosporin A the standard drug utilized to suppress the immune-system) (see figure 3). In the same animal model, a reference product (the best selling European

POLINACEA™ (20mg/mouse i.p.) ACTIVITY ON CANDIDA ALBICANS INFECTED MICE IMMUNOSUPPRESSED OR NOT WITH CYCLOSPORIN A (CSA)		
Treatment	n	Survivors
<i>Candida albicans</i> (vehicle) 350000/mouse i.v.	20	0
<i>Candida albicans</i> (vehicle) 350000/mouse i.v. + Polinacea™	20	6 (p<0.01)
<i>Candida albicans</i> (vehicle) 290000/mouse i.v. + CSA (1mg i.p.)	10	0
<i>Candida albicans</i> (vehicle) 290000/mouse i.v. + CSA (1mg i.p.) + Polinacea™	10	4 (p<0.05)

Echinacea) compared to a placebo, has not given statistically significant results. In terms of mechanisms of action the hypothesis of a direct action on T cells can be done. In fact, both Polinacea™ as well as IDN 5405, after complete removal of LPS, give no rise to any macrophage activation. On the contrary, in culture both with murine and with human T cells co-stimulated with anti-CD3, they give rise to a very good response in terms of proliferation and IFN-gamma production (see figure 4).

Interferon production in purified T cells stimulated with α CD3, Polinacea™ and IDN 5405



Polinacea™: safety profile

The results of the studies conducted on Polinacea™ (oral acute and sub-chronic toxicity) indicate that the product has no toxic effect at all being the LD₅₀ > 2000 mg/kg. No signs of a clear toxicological effect were seen at any of the dose levels investigated (the high dose 1g/kg/die may be considered the "no observed adverse effect level" (NOAEL) in this study). This specific characteristic of Polinacea™ entitles it to be considered a high-profile candidate as a "functional ingredient"

in the enhanced food category in several countries.

Dosage

Dosage will be defined depending on the applications of the product. In health food application, 100-200 mg Polinacea™/die are suggested.

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