

ABResearch

Inspired by nature... driven by biotechnology!

NEXT GENERATION BOTANICAL EXTRACTS

NOVEL FOOD

3.0 ecological approach with an
added-value for your food supplements

ECHINAN 4P

Echinacea angustifolia extract

- ▶ Immunity
- ▶ Antioxidant for sportsmen
- ▶ Titrated at 4% Echinacoside



/ ABR PRESENTATION

ABR stands for Active Botanicals Research. We are an Italian company, established in 2012, based in Brendola (North-East of Italy).

The decades-long solid background of ABR founder and the steady biotech experience of ABR researchers are employed to create unique ingredients devoted to the food supplements industry. With an open-innovation strategy, important collaborations with international research centres, accredited laboratories and customers are being carried out.

The revolutionary use of the plant cell cultures allows the production of high value and pure botanical extracts for the Nutraceuticals and the Nutricosmetics markets.

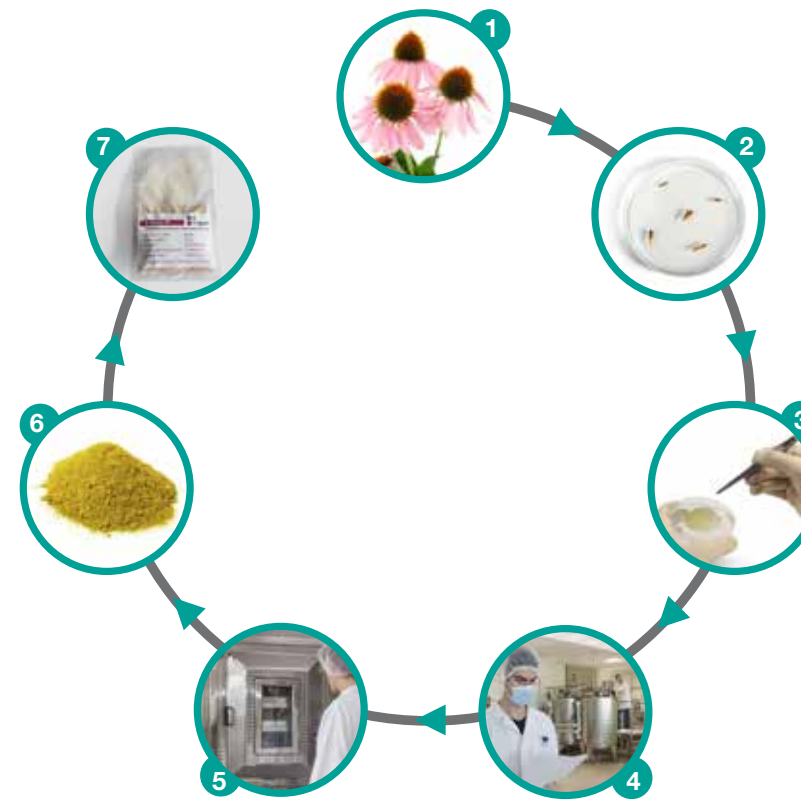
Food supplement manufacturers can now bring new benefits to the development of their products while respecting the regulatory requirements of Europe and USA, with a strong and relevant message for consumers: environmental protection, biodiversity of plants respect and health safety!

Our Mission

“ We are engaged with nature and entrust biotechnology to develop, manufacture and deliver top quality ingredients to support human health. ”



/ ECHINACEA ANGUSTIFOLIA CONCEPT



- 1 / Identification of a plant recognized for its content of rare and effective active molecules
- 2 / Isolation of the plant parts where the active molecules are expressed
- 3 / Induction of cells proliferation and *calli* induction
- 4 / After the selection of the most efficient cell population, among *calli*, the production of the active molecules is amplified in high volume sterile and highly controlled bioreactors
- 5 / Biomass water extraction, purification and lyophilization of actives
- 6 / *Echinacea angustifolia* extract, titrated in Echinacoside
- 7 / Finished and packed ingredient, ECHINAN 4P

Plant cell culture

BENEFITS OF MEDICINAL PLANT CELL CULTURES

Echinacea's story



At the end of the 1800s, Echinacea species, mainly *angustifolia*, was one of the most widely used medicinal plants in North America. The American Indians used it against infections of the upper respiratory tract and as a healing agent for wounds. Then, European colonists adopted it in turn for themselves and their cattle. In the 20th century, North America lost interest in the medicinal use of Echinacea and turned to new antibiotics.

In Europe, and more specifically in Germany, new researches carried out by physicians around 1920, helped to introduce the culture of Echinacea in Europe. Finally, by about the 1990s, a craze swept the United States for Echinacea, mainly because of the appearance of bacterial resistances to antibiotics.

There are nine species of Echinacea, three of them are exploited and are well known for their properties: *Echinacea purpurea*, *Echinacea pallida*, and *Echinacea angustifolia*. ABR has prioritized its work on *Echinacea angustifolia* which is the most difficult to cultivate and most historically valuable.

For manufacturers

- Strict control of the entire production chain parameters
- Secure and long-lasting supply of active ingredients / unlimited availability of ingredients all over the year
- No problem of harvesting nor seasonality
- Production of high-quality natural active ingredients
- Standardization of ingredients titre for an undiscussed repeatability of the manufacturing process

For the environment

- No impact on the environment nor on plant biodiversity
- Use of medicinal plants with no interference on the plants' ecosystem
- Possibility of using endangered or protected botanical species without putting them at risk
- No overexploitation of agricultural lands
- No use of fertilizer nor pesticide

/ ADVANTAGES FOR YOUR FINISHED PRODUCTS

The root of *Echinacea angustifolia* is naturally composed by phenolic compounds derived from caffeic acids as Echinacoside. *Echinacea angustifolia* root, in nature, contains between 0.5% and 1.3% of Echinacoside (C₃₅H₄₆O₂₀; M_r 786.5)¹. But its composition can change according to flowering period².

ABR cell culture from *Echinacea angustifolia* roots ensures the production of standardized extracts titrated at 4% Echinacoside.


PLANT FORM	POWDER	CONVENTIONAL EXTRACT	ECHINAN 4P
POSOLOGY	3 to 6 dosage forms / day	2 to 4 dosage forms / day	▶ 1 single dose / day
SUPPLY	Availability of raw material according to harvest and seasonality		▶ No supply scarcity
TECHNICAL CHARACTERISTICS	Density and volume of powder can change according to the batches	Constant concentration in active ingredients but the ratio Plant/Extract can vary	Consistent physicochemical characteristics of the powder from batch to batch
TITRATION IN ACTIVE INGREDIENTS	All the active ingredients are present even if concentration is mostly unchecked No selection of active ingredients	Standardized raw material with variable titration in active ingredients (0,5 to 4% in Echinacoside)	<i>Echinacea angustifolia</i> extract is mixed with maltodextrins to meet standard titration at 4% in echinacoside in each production batch. ▶ Titration at 4% Echinacoside (analyzed by HPLC and compared with a reference standard of pure Echinacoside)
PRICE	According to the supplier, the volume, the harvest and the seasonality		Fixed price
	Cheapest plant form but need to use high volume in dosage forms	Price according to the concentration in active ingredients	Slightly more expensive than conventional extract but with a commitment for the titration in Echinacoside (4%)
HEAVY METALS	Problems related to contaminants in the ground		Absence of cadmium, arsenic and mercury
CONTAMINANTS			Total absence of pesticides or fertilizers residues
PAH (POLYCYCLIC AROMATIC HYDROCARBONS)	Low risk but it depends if there is a stage of drying and the method in use	Variable content in PAH according to the harvest and the extraction	Dosage in compliance with the (EU) 2015/1933 Regulation

REGULATIONS: Novel Food Authorization in accordance with section 5 of Decree N°258/97. In compliance with European regulations.

¹ European Pharmacopoeia monograph ref.: 01/2008: 1821.


² Letchamo, W., J. Livesey, T.J. Arnason, C. Bergeron, and V.S. Krutilina. 1999. Cichoric acid and isobutylamide content in *Echinacea purpurea* as influenced by flower developmental stages. p. 494-498. In: J. Janick (ed.), Perspectives on new crops and new uses. ASHS Press, Alexandria, VA.





1 CAPSULE OR 1 TABLET
with only 70 to 100 mg of ECHINAN 4P daily

A SINGLE DOSE FOR CONSUMER



Echinan 4P is supplied lyophilized and 100% hydrosoluble
Aw: 0,415

HEALTH CLAIMS DOSES
for *Echinacea angustifolia*

- "It supports the immune system and the body's defense (antioxydant)".
- "It contributes to the oral well-being; a valid and efficient help during the cold season / a relief for the throat - it helps the upper respiratory tract".

A wide potential for your new development of food supplements and nutricosmetics: you can add other ingredients in your galenic forms to create new concepts for your nutraceuticals.

/ ANTIOXIDANT PROPERTIES

ORAC INDEX OF ECHINAN 4P

ORAC index (Oxygen Radical Absorbance Capacity) is a classification of foods according to their antioxidant power. Below is a short comparison of the ORAC index for ECHINAN 4P compared to some other plants and foods.

	ORAC VALUE (µM Trolox for 100 g food)
Clove	314 446
Turmeric	159 277
Acai berries	102 700
Ginger powder	28 811
Goji berries	25 300
Ginger roots	14 840
Cucumber	114

▶ **The ORAC value of ECHINAN 4P is 124 865 µM Trolox for 100 g food.**

The whole clove obtained the highest ORAC index and the cucumber obtained the lowest of all the tested and analysed food. **ECHINAN 4P, just at 4% concentration of Echinacoside, showed impressive antioxidant properties.**

(Source: Nutrient Data Laboratory, Agriculture Research Service, US Department of Agriculture, Oxygen radical absorbance capacity (ORAC) of Selected Foods – 2007 – 2010).

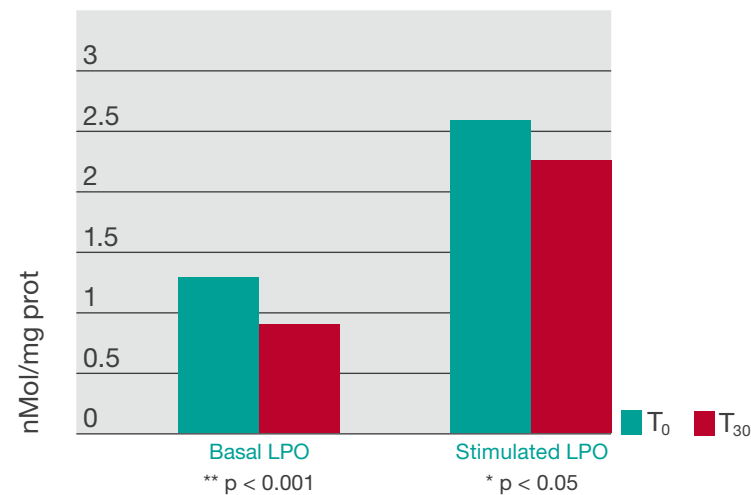
/ CLINICAL STUDY

EFFECTS OF ECHINAN 4P IN SPORTSMEN

In vitro and *in vivo* studies with ECHINAN 4P were carried out and the antioxidant properties of Echinacoside was demonstrated. Specifically, a clinical trial performed on sports practitioners, showed a clear protective action of Echinacoside against lipoperoxidation* related damages.

The open clinical trial was carried out on 19 healthy subjects, men and women, between age of 25 to 55 years old, practicing a regular physical activity (at least 3 times a week): 65 % marathon, 21 % gymnastics, 11 % volleyball and 5 % basketball. The subjects took a capsule a day measuring 65 mg of ECHINAN 4P for 30 days.

As a marker of the oxidative stress, in particular for the people practicing sports of endurance, the membrane lipoperoxidation* was measured at T₀ and at T₃₀, meaning respectively before the study start and at 30 days (study endpoint). Lipoperoxide levels were measured in basal condition and in stimulated condition, i.e. in a condition in which the decomposition of hydroperoxides, unstable intermediates of lipoperoxidation, was induced by adding a pro-oxidant agent.



The results, presented in the graphic below, indicate a significant difference before and after the consumption of ECHINAN 4P. Indeed, the level of lipoperoxidation* is significantly lower after the consumption of ECHINAN 4P, at rest and after physical activity. Therefore, *Echinacea Angustifolia* extract reduces the oxidative stress in sportsmen.



*what lipoperoxidation is!

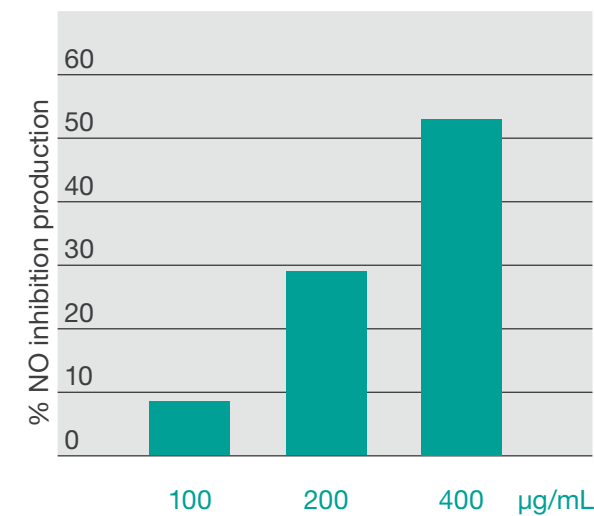
Oxygen (O₂) is essential for the living beings but it is also involved in the production of free radicals, thus causing an oxidative stress. During physical activity, there is a significant increase in oxygen consumption, and consequently, the production of free radicals is higher.

Free radicals bring about damages and alterations to the cell membrane lipids.

/ IMMUNE SYSTEM

The root of *Echinacea* is recognized for its stimulating properties on the immune system, as indicated by the monograph of the European Agency of the Medicine (EMA). Indeed, according to the agency and various scientific studies, the root of *Echinacea* provides:

- immunomodulatory activity: *Echinacea* facilitates the action of immune cells and makes them more effective at attacking pathogenic microorganisms. The plant increases the number and the activity of the immune system cells, specifically white blood cells and lymphocytes. It stimulates the activity of macrophages³ and induces cytotoxicity⁴. It allows the formation of cytokines (cells involved in the immune response).
- antimicrobial activity⁵
- anti-viral activity⁶: specifically, thanks to the presence of echinacoside
- antifungal activity⁷
- anti-inflammatory activity: it decreases the inflammatory occurrences



ANTI-INFLAMMATORY ACTIVITY

We established the anti-inflammatory activity of ECHINAN 4P by nitric oxide detection assay (NO). In this study, NO production is quantified through the detection of nitrite, NO²⁻, which is released by activated macrophages in the cell culture medium.

The results demonstrate an anti-inflammatory response of *Echinacea angustifolia*, which inhibits significantly the production of nitric oxide (NO) thus limiting the process of inflammation.



Echinacoside is an efficient helper during the cold season (winter). The extract contributes to the oral well-being. It is a true relief for the throat. ECHINAN 4P supports the immune system and the body's defense, especially at the level of the upper respiratory tract.

³ Luettig B, Steinmüller C, Gifford GE, Wagner H, Lohmann-Matthes ML. Macrophage activation by the polysaccharide arabinogalactan isolated from plant cell cultures of *Echinacea purpurea*. J Natl Cancer Inst. 1989 May 3; 81 (9): 669-75. PMID 2785214.

⁴ Stimpel M, Proksch A, Wagner H, Lohmann-Matthes ML. Macrophage activation and induction of macrophage cytotoxicity by purified polysaccharide fractions from the plant *Echinacea purpurea*. Infect Immun. 1984 Dec; 46 (3): 845-9. PMID 6389368.

⁵ Sharma S.M., Anderson M., Schoop S.R., Hudson J.B. Bactericidal and anti-inflammatory properties of a standardized *Echinacea* extract (Echinaforce®): Dual actions against respiratory bacteria. Phytomedicine 17 (2010): 563-568.

⁶ Hudson J, Vimalanathan S. *Echinacea* — A Source of Potent Antivirals for Respiratory Virus Infections. Pharmaceuticals. 2011; 4 (7): 1019-1031. doi: 10.3390/ph4071019.

⁷ Merali S Binns SE, Paulin-Levasseur M, Ficker C, Smith M, Baum BR, Brovelli E, Arnason JT (2003): Antifungal and anti-inflammatory activity of the genus *Echinacea* (Asteraceae). Pharm Biol 41: 412-420



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