

Active Ingredients from Natural Origin



Phytotherapy is an equally **ancient and modern** science. The study of the medicinal properties of plants dates back to the dawn of our species but is also the **basis of modern pharmacology**. The approach to plants has become **increasingly scientific** in time - from a **traditionally known** use research has begun to try to identify the **active ingredients** present in plants and find how they work.

Many are the examples of active ingredients from vegetable origin that are still of primary importance today; morphine, taxol and

colchicine are only a few of the plant-derived molecules for pharmaceutical use. Only in a few cases, however, may a botanical derivative be present as a pure isolated molecule or as a **complex of molecules**, whose activities can be recognised only if they are **considered as a whole**.

Reproducibility of the safety and efficacy data of a botanical derivative can be guaranteed in time only if the derivative has been **standardised**, that is, it must be **reproducible** and always the same in its whole and not only in its marker or recognised active ingredient.

Quality

Indena 30: Quality Controls

ORIGIN MAKES THE DIFFERENCE

Quality of the starting botanical material is a prerequisite to obtain **first-rate vegetable extracts**.

The choice of suppliers and cultivations, as well as control of the soil, harvesting period and ways and drug storage,

are fundamental parameters for a good start: biomass also undergoes botanical, chemical, microbiological controls, together with the verification of the absence of any polluting agents, before it is processed for extraction.

PROCESSING: RIGOROUS CONTROLS

The whole manufacturing process is monitored through **rigorous observation of the GMP** (Good Manufacturing Practices) standards with well-defined procedures and verification analysis in the most important manufacturing stages.

Every parameter and critical point is described exhaustively and submitted to double check in a **Master Batch Record**. Controls are performed from the first grinding stages to plant cleansing standardisation.

FINAL ANALYSES: CONTROL AND THEN CONTROL AGAIN

Finally the extract is submitted to **final analyses** that guarantee product conformity to specifications. To do this, Indena has adopted the most **advanced technologies** and sophisticated analytical instruments. State-of-the-art reference standards are employed.

More than 30 controls are performed from the starting material to the finished product: the quality of our products is monitored during all of the manufacturing process stages in full compliance with the most **rigorous controls of the production system**.

Cosmeceutic active ingredients

Escin β -sitosterol phytosome[®]

The **therapeutic benefits** of escin are supported by a large number of scientific studies demonstrating its **antiedematous, vasoconstrictive and stimulating effects on blood circulation**.^{1,2}

The development of the escin β -sitosterol phytosome[®] complex improves its **tolerability**, skin absorption and, consequently, **efficacy**.

18 β -glycyrrhetic acid phytosome[®]

18 β -glycyrrhetic acid phytosome[®], which is derived from glycyrrhizic acid obtained from liquorice, has marked **anti-inflammatory properties** comparable, when applied topically, only to those of hydrocortisone.

The phytosomal form of the compound ensures **greater tolerability and bioavailability** of the active ingredient and a **longer-lasting action**.

Ginkgo biloba dimeric phytosome[®]

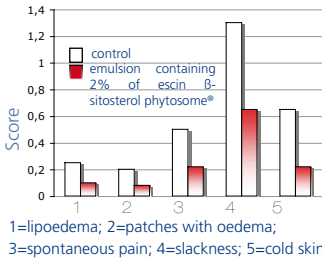
The Ginkgo biloba dimeric phytosome[®] extract **enhances capillary performance** by acting on vessel kinetics. **It improves vessel elasticity** thus favouring **skin microcirculation**. This is the reason why it is indicated to **maintain correct capillary activity**. The phytosomal extract form improves its absorption and efficacy.

Zanthalene[®]

Zanthalene[®] is an extract obtained from *Zanthoxylum alatum* Maxim., a plant native to China. The pharmacological research has clarified its mechanism of action: Zanthalene[®] blocks sodium channels and exerts a **soothing action** on the skin and mucosae by reducing transmission of the impulse that brings pain and hitch.

Escin β -sitosterol phytosome®:

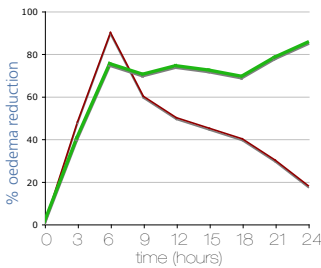
antiedematous



43 female volunteers suffering from venous stasis and cellulitis were treated with an emulsion containing 2% escin β -sitosterol phytosome®.³ The product was applied once a day for 30 days. Among the many parameters examined by the investigators, in particular, the **improvement of lipoeidema and patches** with oedema suggests that its active ingredient possesses a marked antiedemagenous activity.

18 β -glycyrrhetic acid phytosome®:

anti-inflammatory



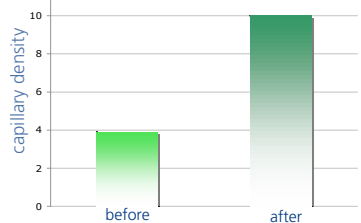
The antiinflammatory and antiedemagenous effects of the 18 β -glycyrrhetic acid phytosome® were assessed in the experimental model of Croton oil-induced oedema reduction. At the same dose (0.16 μ M), the action of the 18 β -glycyrrhetic acid phytosome® was found to be greater and to last longer than that of 18 β -glycyrrhetic acid alone. This means that the complex with the phytosome® not only **increases the active ingredient tolerability** and absorption, but also **improves its efficacy**.

Ginkgo biloba dimeric phytosome®:

microcirculation improver

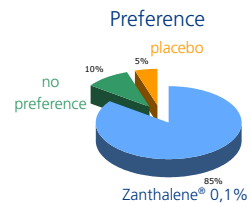
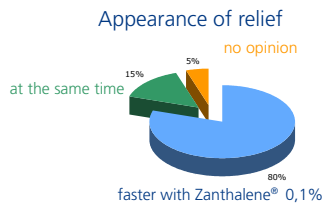
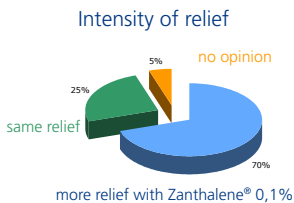
Effect on capillary density induced by *Ginkgo biloba* dimeric phytosome®

35 volunteers were treated with an emulsion containing 3% Ginkgo biloba dimers phytosome® to assess its vasokinetic properties.⁴ **Capillary density** and **blood flow rate** were assessed prior to, and after 45 minutes from, application. Both parameters **increased** in a statistically significant manner, thus confirming its **vasokinetic activity**.



Zanthalene®:

soothing and anti-reddening



The soothing efficacy of Zanthalene® 0.1% was demonstrated in a lotion applied to the scalp of a group of women following hair dyeing. Most of them reported a **feeling of relief**, and the **skin** even looked **less irritated**.⁵

Technology: phytosome®

improves bioavailability of the active ingredient

What is a phytosome®?

A phytosome® is a **complex** of a natural active ingredient and a phospholipid.

What is the use of phytosomes?

Phytosomes are used to improve bioavailability of active ingredients. Active components with too high polarity⁶ cannot overcome the lipid barrier of the skin or alimentary canal and, therefore, cannot be absorbed. Phytosomes help to **reduce polarity of active substances**, thus making them more easily absorbable. In other words, phytosomes are an **innovative transportation system** for poorly bioavailable active ingredients.

What are the advantages of phytosomes?

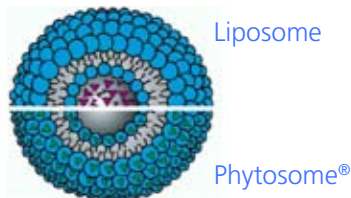
They **improve skin absorption** and, consequently, **bioavailability of active ingredients**.⁷

In both oral and topical tests,⁸ phytosomes demonstrated a **higher biological activity** compared to an equal amount of the active ingredient or extract not made into a complex with a phytosome®.

What is the difference between phytosome® and liposome?

Phytosomes are structures in which the active ingredient is anchored to the polar head of the del phospholipid and becomes an **integral part of the micellar membrane**, unlike liposomes, in which the active ingredient is generally contained inside the micelle structure consisting of phospholipids.

- ▲ Active ingredient
- Phospholipid
- Complex





Indena S.p.A. is the **world's leading company** in the identification, development and production of **plant-derived active ingredients** that find use in the pharmaceutical, food and cosmetic industries. The fundamental element of Indena's success is the research work, including: screening of medicinal plants that ethno-pharmacologic studies have identified as having promising characteristics, the identification of **new active ingredients** and the definition of advanced extraction and purification systems for industrial application. Supported by **over 80 years' experience** in the botanical field, Indena carry on phytochemical research on their products directly in their Research Centre in Settala (MI), while they resort to the collaboration of the most prestigious universities and private research institutes in the world for biological safety and efficacy verifications to clinical phase I studies. The Company has applied for, and registered, **over 150 patents** and boasts about **700 scientific publications**.

Indena employs a **staff of over 700**, including some 10% working fulltime in research operations. In addition to the management and production seat in Milan, the Company is present all over the world with **5 production sites and 5 branch offices**. Their experts constantly communicate and interact with the most important International Regulatory Authorities like WHO, EMEA and ESCOP, and collaborate with leading pharmacopoeias.



Indena S.p.A.
Viale Ortles, 12
20139 Milano
www.indena.com