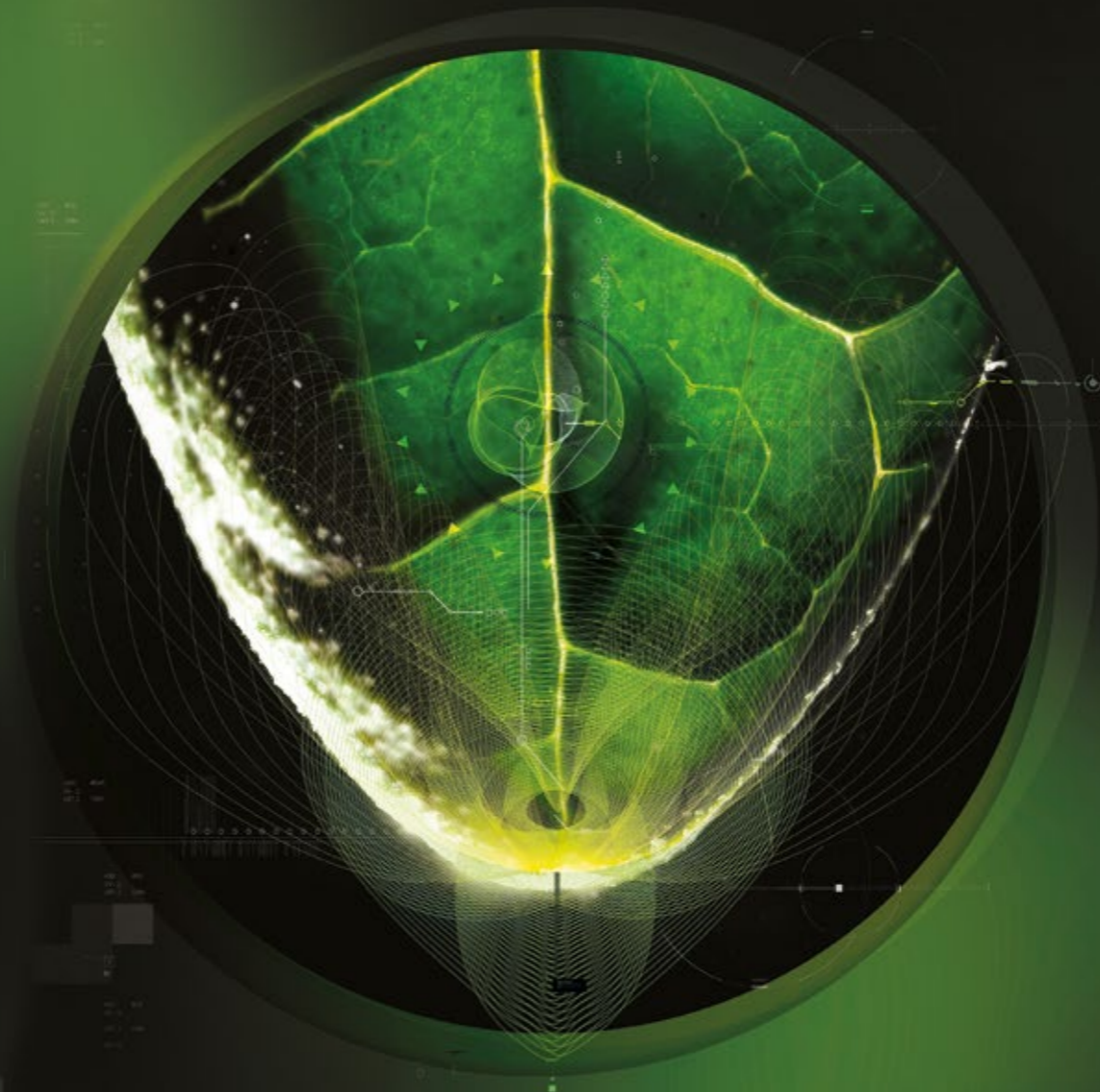


**FOLLOW THE PLANTS**  
+100 YEARS OF BOTANICAL EXCELLENCE



 **indena**<sup>®</sup> 100+  
YEARS  
SCIENCE IS OUR NATURE. SINCE 1921



## OUR MISSION

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At Indena we believe that an in-depth knowledge in active ingredients derived from medicinal plants and the search for excellence at all times are crucial commitments to serving our customers in pharmaceuticals and health-foods.

Research and production technologies are the main focus of our mission and the way we create a “value difference” for our partners.

And we’ve got more than a century of experience to prove it.



## MILESTONES IN THE HISTORY OF INDENA

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The origins of the company date back to 1921, when Carlo Boccaccio Inverni began producing extracts from medicinal plants for pharmacists and the emerging Italian pharmaceutical industry. When Biagio Alberto Della Beffa joined as partner and Managing Director, the firm became a joint-stock company, trading under the name of Dott. Inverni & Della Beffa S.p.A.

During the 1950s, Biagio Alberto's son Luigi Della Beffa added to the existing business a new pharmaceutical division (Inverni della Beffa S.p.A.) to manufacture and market finished dosage forms from botanical derivatives.

In 1969, a new site for the production of extracts and pure molecules, together with a pivotal research and development centre, was set up in Settala, near Milan.

In the early 1980s, the botanical derivatives business was reorganised as a new company, Indena S.p.A.

In the 1990s Indena, already present worldwide with a commercial and cultivation network, opened new production plants, notably in France and India, and additional commercial branches.

Throughout its long history, Indena has specialised in the identification, development and production of plant derived purified extracts and pharmaceutical active principles including flavonoids, glycosides, aminoacids, alkaloids and their semi-synthetic derivatives.



## FACTS & FIGURES

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**960** employees

**5** international branches

**4** production sites worldwide

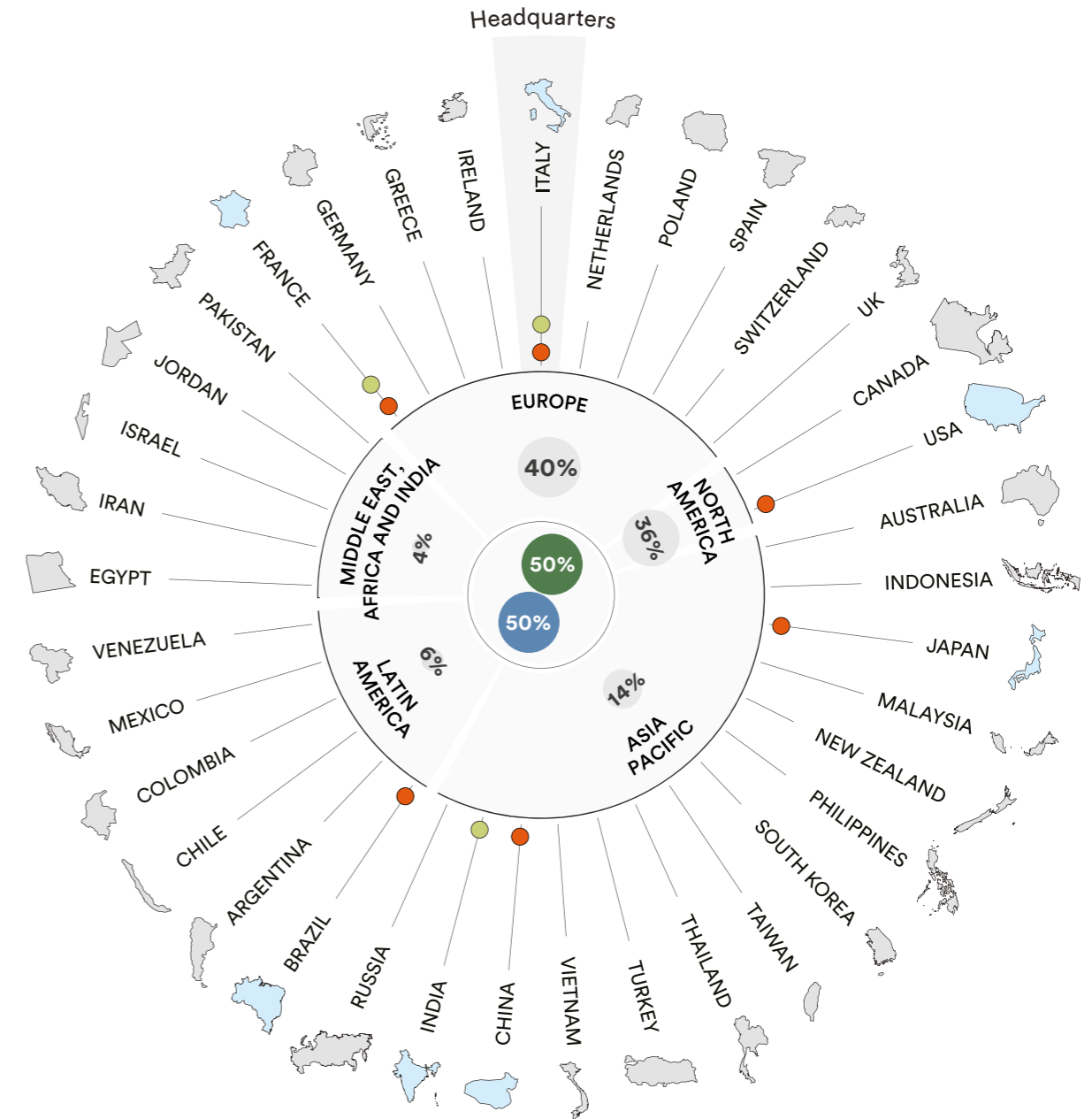
sales in more than **80** countries

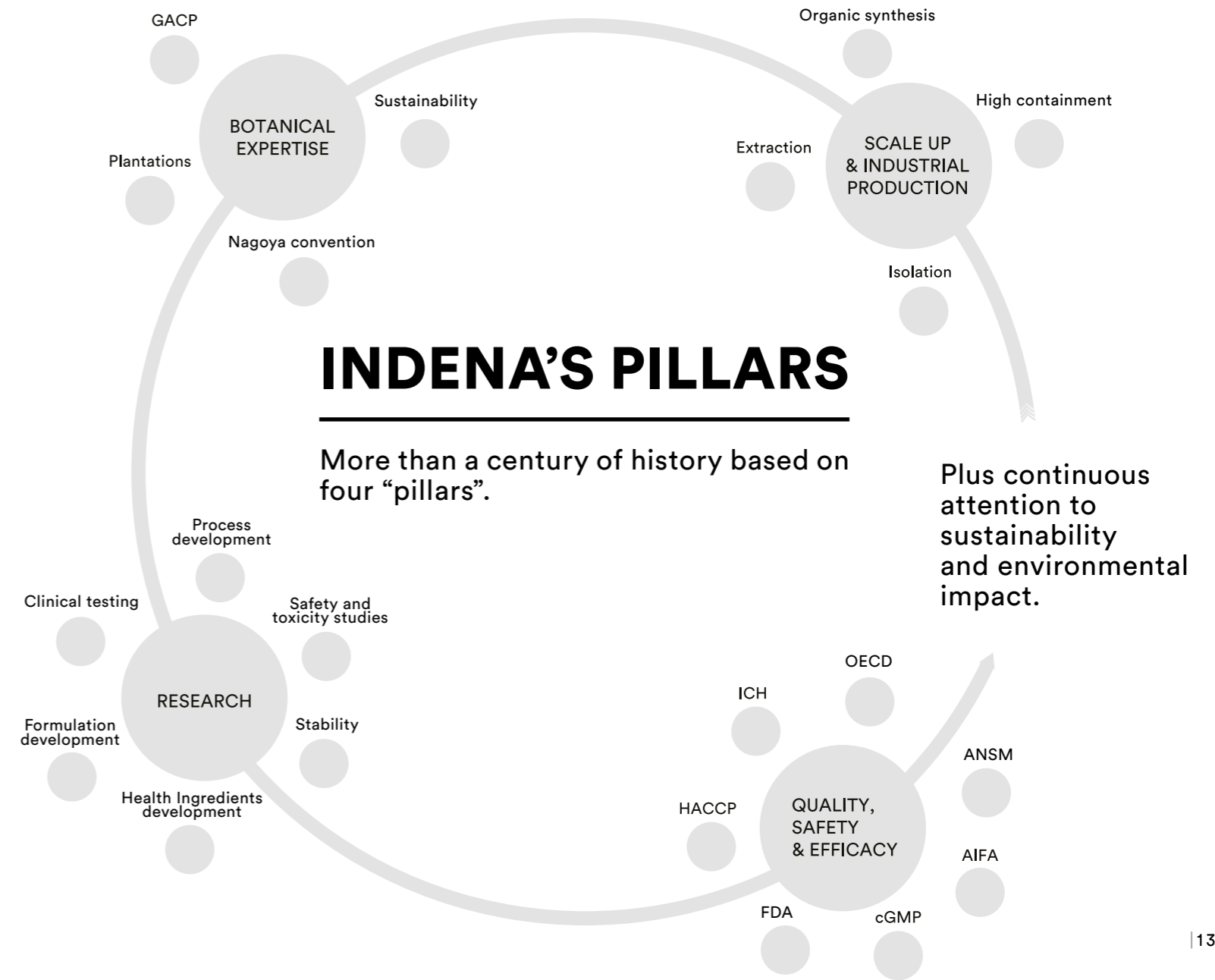
more than **100** primary patents

# THE INDENA MARKET

BUSINESS SECTORS ● Pharmaceutical ● Health-food

ORGANISATION ● direct presence ● sales organisation ● production







## A RESEARCH BASED COMPANY

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At Indena, we have always been inspired by a rigorous scientific approach in our research.

In PROCESS RESEARCH, original advanced industrial production processes are designed and engineered for work on existing or new molecules, as well as for the development of new APIs and HPAPIs.

In PRODUCT RESEARCH we focus on active ingredients for the health and nutrition market, supporting them with safety and efficacy data and applying innovative delivery technologies as needed.



## **BOTANICAL SOURCES**

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In addition to traditional gathering of wild plants, Indena has established a worldwide network of plantations to provide high quality vegetal raw material.

Internationally recognised botanical experts monitor more than 3,000 hectares of Good Agricultural and Collection Practices (GACP) compliant plantations, which today account for more than 60% of the vegetal raw material we use.

We pursue the highest botanical standards with maximum respect for the environment and biodiversity.

To achieve well-identified and consistently high-quality vegetal raw material, we use micropropagation and traditional plant breeding, but never GMO.





# INDENA PRODUCTION

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Advanced, highly flexible and environment-friendly state-of-the-art technology is used throughout the Indena manufacturing cycle.

Indena's facilities incorporate separate authorised areas for handling pharma and food grade natural derivatives, where the Quality System ensures compliance with cGMP and Hazard Analysis and Critical Control Points (HACCP) guidelines.

With more than 100 DMFs, Indena's pharmaceutical products meet US-FDA and EU requirements, and two production sites are accredited by Japanese authorities.

Health-food pre-mixed preparation.

Fermentation production capabilities.

Spray drying capabilities from organic solvents on different scales, developed in decades of operations.



## MAIN PRODUCTION EQUIPMENTS AT OUR SITES

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- Grinding apparatus (hammer- and knife-grinders) | plant material grinding
- Percolators (static and dynamic) | plant material extraction
- Reactors | reaction, crystallisation, concentration
- Concentrators (thin-film concentrators) | solvent evaporation
- Liquid-liquid extractors | selective extraction, purification process
- Columns for chromatography | concentration, purification, isolation
- Centrifuges, filter-press | solid-liquid separation
- Driers (tray driers, driers with stirring, microwave) | drying
- Spray dryers | Spray drying
- Mills and sieves | milling and sieving of powders
- Mixers | blending of powders, standardisation



# PROCESS DESIGN FOR HIGH-CONTAINMENT SYNTHESIS

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## PROCESS DEVELOPMENT & SCALING-UP CAPABILITIES:

- Process design for High Potency Compounds synthesis
- Route optimisation (statistical Design Of Experiment) and scale-up
- Preparation of small scale material, from grams to kilograms
- cGMP manufacturing of APIs for clinical trials

## ANALYTICAL & PRECLINICAL SUPPORT:

- Related substances and secondary metabolites identification
- Support to process development
- IPC and release analysis for GMP production
- Solid state characterization and polymorphism screening for IP protection
- Investigational and regulatory stability studies
- Collaboration with the most important international analytical organizations (EP and USP, AOAC) to promote analytical methods innovation

## PRODUCTION SCALE CAPABILITIES:

- First purification of cytotoxic APIs
- Final purification and drying of cytotoxic APIs
- Semi-and-total-synthesis of HPAPIs
- Availability of industrial suites (equipped with 20 linear meter glove boxes)
- Availability of 2 kilolabs (LK1 and LK2) for clinical and smaller scale commercial supplies of HPAPIs with OEL 20 ng/m<sup>3</sup>
- Lab, pilot and industrial scale multipurpose fermentation plants
- Intermediate and large scale spray dryers, both working with class 2 organic solvents, also in the presence of excipients/co-polymers (for drug product intermediates)



# INDENA QUALITY

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## 1\_ Quality of the raw material:

- identification of the plant through specific protocol and analyses, such as botanical checks, chromatographic profiles, or DNA analysis;
- purification of the botanical extract: if the plant contains toxic, allergenic or unwanted substances, it is important to remove these components and obtain an extract deemed purified;
- standardization combines different lots to ensure that the botanical extract always has the same composition of constituents.

## 2\_ Control of the supply chain:

- suppliers are accredited on the basis of rigorous criteria of quality, sustainability and traceability;
- GAPC guidelines for good agricultural and collection practices are implemented in the supply chain;
- the need for high quality raw materials is reconciled with the principles of biodiversity and sustainability indicated by international conventions and standards such as the Convention on Biological Diversity (CBD);
- the entire supply chain is under continuous control from cultivation to the delivery of the raw material to the production sites.

## 3\_ Quality of the manufacturing processes:

- technologically advanced and safe production plants for both raw materials and operators;
- process compliant with production standards and regulations such as Good Manufacturing Practices (GMP) and the Hazard Analysis Critical Control Points manual (HACCP);
- use of high-quality, precisely defined excipients to optimize the effectiveness of the active ingredient;
- meticulous inspection of the finished product.



## **SUSTAINABILITY & THE ENVIRONMENT**

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Nature has always been for Indena both a source of inspiration and an essential resource. We have always been conscious of how important it is to preserve and regenerate the natural balance of every living source and for this we strictly follow laws, guidelines, procedures and programs with the aim of guaranteeing the safety of employees, safeguarding environment and biodiversity. These aims lie at the heart of the projects undertaken within the Sustainable Sourcing Program and dedicated to the communities involved in the collection of the many species that Indena markets. Indena is committed to driving progress towards the UN's Sustainable Development Goals, aiming at putting sustainability first – from raw materials sourcing to production and marketing – with a focus on environmental impact, use of renewable energies and building a more circular economy. The ever increasing effort to reduce the environmental impact of production sites has led to significant results in its main facilities, all certified ISO 14001 and ISO 45001.



# ACTIVE PHARMACEUTICAL INGREDIENTS

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Isolated or semisynthetic pure products and extracts are produced in compliance with cGMP and supported by CTD-DMFs.

Among our main products:

## PACLITAXEL

*Taxus media* Rehder - Root, leaf and twig -  $\geq 97.0\%$   $\leq 102.0\%$  by HPLC - Anticancer

## 10-DAB III

*Taxus baccata* L. - Twig and leaf -  $\geq 96.0\%$  by HPLC - Chemical intermediate

## THIocolchicoside

*Gloriosa superba* L. - Seed -  $\geq 98.0\%$   $\leq 102.0\%$  by potentiometry - Muscle relaxant

## COLCHICINE

*Gloriosa superba* L. - Seed -  $\geq 97.0\%$   $\leq 102.0\%$  by potentiometry - Antigout

## DOCETAXEL

*Taxus baccata* L. - Twig and leaf -  $\geq 97.0\%$   $\leq 102.0\%$  by HPLC - Anticancer

## MYRTOCYAN®

*Vaccinium myrtillus* L. - Fresh frozen fruit -  $\geq 32.4\%$   $\leq 39.6\%$  of anthocyanins, 1.0% anthocyanidins by HPLC - Capillarotropic

## ESCIN

*Aesculus hippocastanum* L. - Seed -  $\geq 97.0\%$   $\leq 103.0\%$  by potentiometry - Antioedema

## GINKGO BILOBA

*Ginkgo biloba* L. - Leaf -  $\geq 22.0\%$   $\leq 27.0\%$  of flavonoids,  $\geq 2.6\%$   $\leq 3.2\%$  of bilobalide,  $\geq 2.8\%$   $\leq 3.4\%$  of ginkgolides A,B,C,  $\leq 5$  ppm of ginkgolic acids by HPLC - Blood circulation improver



# HEALTH - FOOD INGREDIENTS

Indena leverages its solid pharmaceutical background for the health-food field, developing biologically active ingredients for supplements, functional, medical and baby food products for more than 40 years. These include:

## BEANBLOCK®

*Phaseolus vulgaris* L. - Common bean -  $\geq 6.0\%$  as alpha amylase inhibitor by HPLC - 1,100 U/mg of alpha amylase inhibiting activity,  $\geq 10,000 \leq 30,000$  HAU/g of hemagglutinating activity by spectroph./enzym. - Appetite regulator, Healthy blood sugar metabolism

## GREENSELECT®

*Camellia sinensis* (L.) O. Kuntze - Young leaf -  $\geq 60.0\%$  of total polyphenols,  $\geq 40.0\%$  of (-)-epigallocatechin-3-O-gallate,

## LEUCOSELECT®

*Vitis vinifera* L. - Seed -  $\geq 95.0\% \leq 105.0\%$  of proanthocyanidins by GPC -  $\geq 13.0\% \leq 19.0\%$  of catechin and epicatechin by HPLC - Antioxidant activity, Circulatory health

## MIRTOSELECT®

*Vaccinium myrtillus* L. - Fresh frozen fruit -  $\geq 36.0\%$  of anthocyanins by HPLC -  $\geq 25.0\%$  of anthocyanins as anthocyanidins by spectrophotometry - Eye health, Circulatory health, Antioxidant activity

## MITIDOL®

*Zingiber officinale* Roscoe - rhizome + *Acmella oleracea* L. - flowers -  $\geq 2.4 \leq 3.9\%$  total gingerols and shogaols -  $\geq 0.30 \leq 0.60\%$  spilanthol by HPLC - Natural ache relief

## OPEXTAN®

*Olea europaea* L. - Fruit -  $\geq 10.0\%$  of total polyphenols by spectrophotometry -  $\geq 2.0\% \leq 3.5\%$  of verbascoside,  $\geq 4.5\%$  of hydroxytyrosol and its derivatives by HPLC - Antioxidant activity, Healthy skin, Healthy cardiovascular function

## PRODIGEST®

*Cynara cardunculus* L. + *Zingiber officinale* Roscoe - Artichoke extract -  $\geq 28.0 \leq 34.0\%$  by HPLC Ginger extract -  $\geq 6.0\% \leq 7.0\%$  by HPLC - Digestive health

Indena standardised extracts have full chemical characterisation backed by QUALITY, SAFETY AND EFFICACY TESTS.



# ENHANCING THE POWER OF PHYTONUTRIENTS

## PHYTOSOME® The Delivery System

OVER 4 BILLION SERVINGS  
DELIVERED GLOBALLY\*

# HEALTH - FOOD INGREDIENTS

## PHYTOSOME®

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Phytosome® – a proprietary **MULTITALENTED** technology platform developed by Indena - is the breakthrough 100% food-grade delivery system that optimizes the botanical performance, benefits and power.

### CASPEROME®

*Boswellia serrata* Roxb. ex Colebr. - Resin - ≥25.0% of boswellic acids by HPLC - For healthy inflammatory response

### RELISSA™

Melissa Phytosome® *Melissa officinalis* L. 17-23% of lemon balm by HPLC - Calming action, Healthy sleep, Relaxation

### GREENSELECT®

*Camellia sinensis* (L.) O. Kuntze - Young leaf - ≥19.0% ≤25.0% of polyphenols expressed as (-)-epigallocatechin-3-O-gallate, ≥13.0% of (-)-epigallocatechin-3-O-gallate, ≤0.1% of caffeine by HPLC - Antioxidant activity, Weight loss agent

### MERIVA®

*Curcuma longa* L. - Rhizome - ≥18.0% ≤22.0% of curcuminoids by HPLC - Joint health, For healthy inflammatory response

### QUERCEFIT™

*Sophora japonica* L. – Flowers - ≥34.0% ≤42.0% of quercetin by HPLC - Sports nutrition, allergy seasons' discomforts control, antioxidant activity

### SILIPHOS®

*Silybum marianum* (L.) Gaertn. - Fruit - ≥29.7% ≤36.3% of silybin by HPLC - Healthy liver

### UBIQSOME®

CoQ10 Phytosome® - 18-22% of coenzyme Q10 by HPLC - Cellular energy

### VAZGUARD™

*Citrus bergamia* Risso & Poit. - Fruit juice - ≥11.0% ≤19.0% of total flavanols by HPLC - Cardiovascular health





# FLAVOURS

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Botanical extracts with organoleptic properties

## AMMONIUM GLYCYRRHIZATE

*Glycyrrhiza glabra* L. - Root |  $\geq 98.0\%$   $\leq 102.0\%$  of monoammonium glycyrrhizate

## ANISE

*Illicium verum* Hooker fil. - Fruit |  $\geq 0.5\%$  of anethole by GC

## CHAMOMILE

*Matricaria recutita* L. - Flowering head |  $\geq 1.2\%$  of total apigenin by HPLC

## GINSENG 1/2/10%

*Panax ginseng* C.A. Meyer - Root | 1.0, 2.0, 10% of total ginsenosides and malonyl-ginsenosides calculated on the dried substance by colorimetry

## GRAPE SEED

*Vitis vinifera* L. - Seed |  $\geq 95.0\%$  of proanthocyanidins by spectrophotometry,  $\geq 5.0\%$   $\leq 15.0\%$  of catechin and epicatechin by HPLC

## GUARANA

*Paullinia cupana* H.B. et K. - Seed | 12% of total alkaloids by HPLC

## LEMON BALM

*Melissa officinalis* L. - Flowering head |  $\geq 10\%$  of hydroxycinnamic derivatives calculated as rosmarinic acid

## OPLODEX™

*Quercus* spp. Wood - *Camellia sinensis* (L.) O. Kuntze Leaf - *Vitis vinifera* L. Seed | Balanced and synergistic combination of polyphenolic botanical extracts

## QUASSELECT®

*Quassia amara* L. Wood |  $\geq 53.0\%$   $\leq 57.0\%$  as sum of quassin and neoquassin by HPLC



# CDMO

## CONTRACT DEVELOPMENT AND MANUFACTURING ORGANIZATION

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### CUSTOM SERVICES

With a century long experience and continuous technological expansion, Indena has focused on Contract Development and Manufacturing services for its partners, supporting product development from clinical trials to large scale commercial manufacturing.

Indena's R&D center is in Italy, while the production units are in Italy (Settala and Palestro), France and India and incorporate separate authorised areas for handling pharma and food grade natural derivatives, and the Quality System ensures compliance with cGMP and Hazard Analysis and Critical Control Points (HACCP) guidelines.

### CYTOTOXICS AND HPAPIs

Indena HPAPIs contract manufacturing services include a full range of dedicated development and manufacturing solutions such as fermentation, extraction, isolation, purification, synthetic modifications and total synthesis for active pharmaceutical ingredients on a wide range of scales.

This facility incorporates appropriate room pressurization, airlocks, ventilation and isolators to properly handle highly potent solids and liquids down to 20 ng/m<sup>3</sup> OEL (SafeBridge® Class 4). Settala site is regularly inspected by the main Regulatory Authorities.



## DISSEMINATING KNOWLEDGE ON MEDICINAL PLANTS

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Indena acts to foster interest in medicinal plants and natural products:

- By founding *Fitoterapia*, a Journal published since 1924 and today recognised as a premier source for research on medicinal plants (2012 Impact Factor: 2.231, currently distributed by Elsevier)
- By publishing monographs and books on medicinal plants
- By sponsoring Masters and specialist schools in phytotherapy
- By offering scholarship grants to young researchers



# THE INDENA ORGANISATION

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## HEADQUARTERS

Indena S.p.A. | Milan | Italy

## RESEARCH CENTRE

Indena S.p.A. | Settala (MI) | Italy

## INTERNATIONAL BRANCHES

Indena Biotechnology (Shanghai) Co., Ltd. | China

Indena Brasil Ltda | São Paulo | Brazil

Indena Japan Co., Ltd. | Tokyo | Japan

Indena S.A.S. | Paris | France

Indena USA Inc. | Seattle | WA | USA

# THE INDENA PRODUCTION SITES

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Indena S.p.A. | Settala (MI) | Italy

Bernett S.r.l. | Palestro (PV) | Italy

Indena S.A.S. | Tours | France

Indena India Pvt. Ltd. | Bangalore | India



Indena S.p.A. | Settala (MI) | Italy



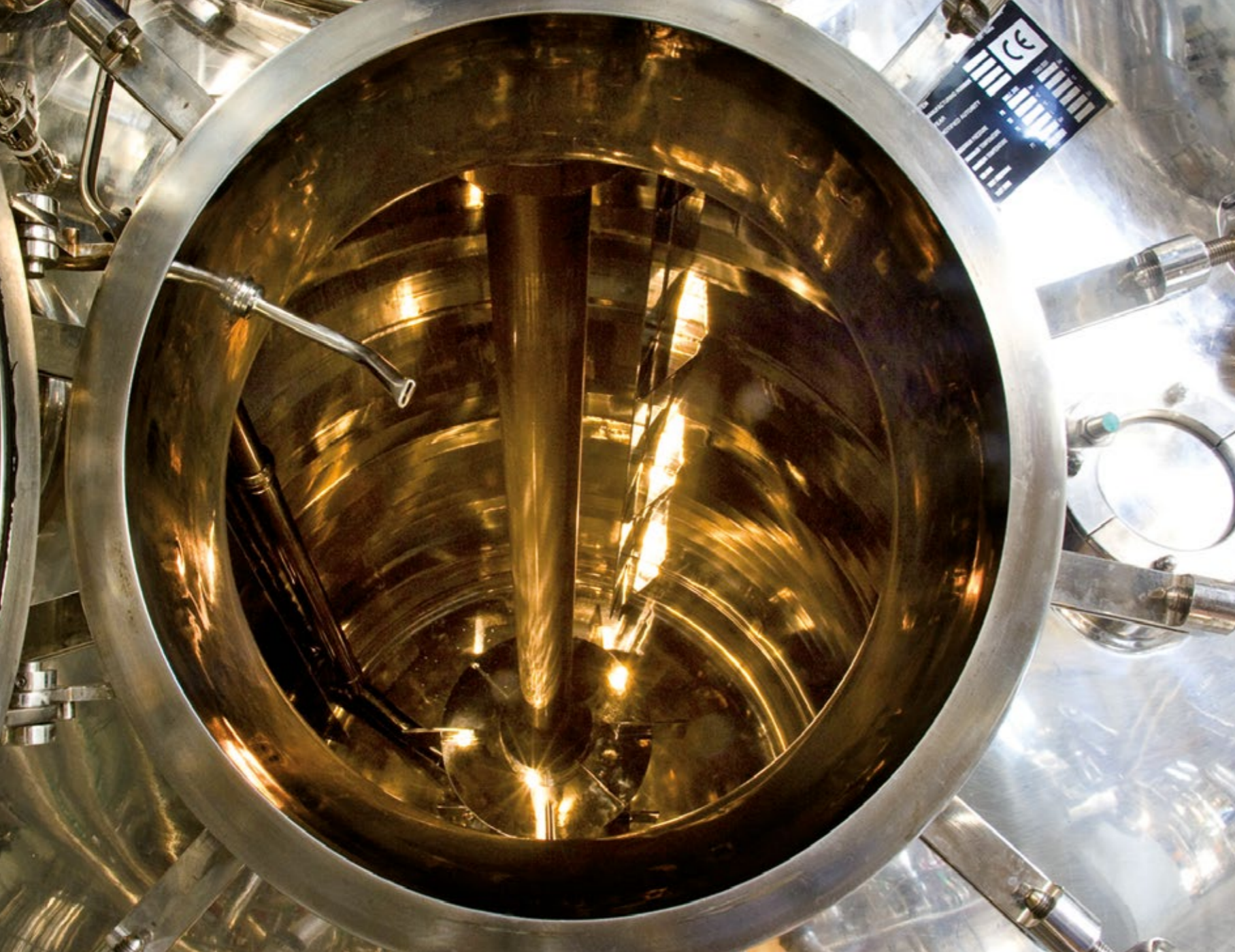
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Indena S.A.S. | Tours | France



Indena India Pvt. Ltd. | Bangalore | India



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EXCELLENCE  
QUALITY**

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