

indenature



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latest news from indenature

INDENA AND SUPPORTIVE CARE: AN INDENA COMMITMENT

Antonella Riva and Paolo Morazzoni, Indena

Products of plant origin have always been a preferred option in the treatment of cancer and for fifteen years Indena has successfully conducted research into new anticancer drugs of natural origin. Potent anti-tubulin agents Paclitaxel and Docetaxel, natural molecules belonging to the class of taxanes and extracted from the yew tree (*Taxus baccata*), have gradually taken on a central role in cancer patient care. Furthermore, preclinical data on the molecule IDN 5404 have opened up good prospects for the therapeutic use of colchicines in oncology, as agents capable of destroying the tumor vascular system. Indeed this was presented to the 100th Congress of the American Association for Cancer Research. In addition to classical natural chemotherapy, other natural extracts have been investigated, this time from the perspective of primary chemo-prevention: an example of this is an initial pilot study on 25 patients which has suggested how the bilberry extract Mirtoselect® may help to prevent cancers in the gastrointestinal tract. The study, headed by Professor Andreas Gescher of Leicester University, was submitted to the 51st Annual Congress of the Italian Cancer Society. Besides their established use in cancer therapy and extensive research into primary chemo-prevention, a new frontier of "supportive care" is today opening up for natural products and in an even broader sense, the so-called "tertiary

chemo-prevention". "Supportive care" aims primarily to relieve symptoms and complications for patients diagnosed with cancer. Its main purpose is to prevent and modulate the unwelcome effects of antineoplastic drugs from the onset of therapy and throughout treatment. Even cancer drugs of the latest generation, in fact, although they are the result of a research process designed to target specific molecules, are not without side effects.

Secondly, supportive care aims to guarantee the patient, both during and following therapy, an overall improvement in quality of life that can range from pain control, modulation of appetite, to overcoming insomnia. It should be borne in mind that today, thanks to continuous research, 64% of cancer patients have a life expectancy of over 5 years. It has become necessary therefore to develop products which can be administered even over protracted periods of time and which are effective in alleviating problems associated with major aspects of daily life, such as fatigue or lack of sleep. Natural extracts, provided they are the result of high phytochemical standardization and used with adequate explanatory documentation, may prove to be an essential tool in supportive care.

Finally, considering the high survival rate of cancer patients, the international scientific community must increasingly turn their attention to so-called "tertiary chemo-prevention". Consequently, the focus will increasingly be on the identification of products able to prevent the risk of secondary events developing from anticancer therapies, recurrence of cancer in the long term or even the occurrence of a second primary tumor. In this area, the potential of natural products appears to be enormous.

Currently being planned and set up at a prestigious American institute, a clinical study will examine how Indena ginseng can be used in the treatment of fatigue in cancer patients.

Drawing on impressive research facilities and an extensive portfolio of natural extracts, Indena's specific commitment to oncology goes well beyond the areas of treatment and prevention, to encompass the very quality of life of cancer sufferers.

PHYTOSOME® ONLINE

Innovative phytosome technology patented by Indena enables more effective transport of the less bioavailable active principles, improving both cutaneous and intestinal absorption. Information relating to this new technology has now been made available online to meet industry needs. Visit www.phytosomes.info for clear explanation and documentation of the benefits of complexation of this active natural principle with phospholipids. The pages devoted to specific phytosomes such as Leucoselect®, Phytosome®, Siliphos®,

www.phytosomes.info homepage



or the more recent Meriva® and Virtiva®, detail the benefits of complexation over noncomplexed products, both in terms of efficacy and safety.

MORE PROTEINS, LESS SUGAR

Proteins contained in the seeds of leguminous plants are an important part of the protein intake from plant sources. In addition to their nutritional properties, studies are being made of their ability to modulate metabolic processes, with a possible effect in regulating blood sugar levels and control of body weight.

A fraction of a standardised extract of lupin enriched in conglutin-gamma produced interesting pharmacological results *in vivo* in the reduction of blood glucose, and the same glucose-lowering activity was demonstrated in a pilot clinical study versus placebo.

These encouraging findings were presented, with the publication of a poster entitled "Management of blood glucose levels by means of vegetable proteins", by Dr Paolo Morazzoni, Scientific Director of Indena, at the "6th World Congress on Prevention of Diabetes and Its Complications" held

last April in Dresden. The aim of this Congress was to collect and share the most innovative data on the diagnosis, treatment and prevention of diabetes in different populations. It provided an interesting platform for discussion and development in the prevention and management of diabetes.

Dresden, Frauenkirche



LEAVE THE CERTIFICATION TO INDENA

More and more Indena customers can now save on the time and resources it takes to submit processing and quality control documentation for their medicines. In April, Indena was granted Certificates of Suitability of the European Pharmacopoeia (CEP) for the dry extract of *Vaccinium myrtillus* L. (Myrtocyan®) and the dry hydroalcoholic extract of *Valeriana officinalis* L. (Valeroselect®). This follows in the wake of certificates obtained for natural and semi-synthesis Paclitaxel and Colchicine. Recognized in the EU, Australia, Canada and Switzerland, the certification is issued by the European Directorate for the Quality of Medicines (EDQM). This is the body that oversees the quality and compliance with the European Pharmacopoeia of substances used in medicines for human and veterinary use. As holder of the CEP, Indena is qualified to handle any changes in the production process directly with EDQM. And this means savings in product time-to-market for Indena customers.

Vaccinium myrtillus L.



NATURALLY SUSTAINABLE



Last March Indena obtained ISO14001 certification for its main Settala production site near Milan. The company's unceasing commitment to gradually reducing the carbon footprint of its production facilities has thus not only been recognised but also formalised.

Under the guidance of a specially formed committee, Indena has long implemented a whole raft of measures to monitor and improve the environmental sustainability of their premises. Particularly worthy of note are actions to reduce and recycle plant cooling water, save energy resources and cut down on the production of waste.

Care for the environment, not only as a resource to be safeguarded, but also as a crucial engine for development, has always guided Indena thinking and our studies of the natural world, of which biodiversity is one of the principal treasures and our source of inspiration.

A sustainable approach is not only a natural choice for Indena but our very calling.

MERIVA®

BIOAVAILABLE CURCUMIN

MERIVA®: FROM CURRY TO THE CLINIC

Turmeric (*Curcuma longa* L.) is the most important spice in Indian cuisine. Also known as Indian saffron, turmeric is one of the main ingredients of curry and is used by traditional Indian medicine for its anti-inflammatory properties. The yellow pigment (curcumin) has been examined in more than 2,500 pre-clinical studies to reveal its interesting potential in the treatment of various diseases, especially those involving inflammation. Any clinical development to date, however, has been hindered by its low solubility in water, chemical instability at intestinal pH values and its very low oral bioavailability. To counteract these limitations, Indena has developed and patented a compound of curcumin and phosphatidylcholine. Compared to unformulated curcumin, Meriva® guarantees greater stability and better oral absorption.

A new study undertaken by Italian researchers at the University of Chieti-Pescara, Indena and the University of Eastern Piedmont in Novara and published by Panminerva Medica has

demonstrated the effectiveness of Meriva® in relieving pain and increasing joint mobility in patients with osteoarthritis, the most common form of arthritic disease. Administered as a dietary supplement in association with the “best available treatments” prescribed by doctors, Meriva® has proven to be clinically effective. The gastro-protective properties of curcumin improved the pharmacological treatment of osteoarticular disease, significantly improving patients’ quality of life and reducing costs. The result obtained was attributed to its formulation with phospholipids using Phytosome® technology.

This is the first time that curcumin has proven clinically active at lower realistic doses. The dosage of turmeric used in the study (200 mg of curcumin/day) was in fact only slightly higher than the doses taken in an Indian diet rich in curry, where the ingredient is primarily consumed in an oily medium that aids the absorption of compounds such as curcumin which are insoluble in water.

ZANTHALENE® - A NOVEL INSTANT LIFTING AGENT

Sichuan pepper from China is obtained by grinding the seedpods of *Zanthoxylum bungeanum* (Maxim). The spice is widely used and valued in oriental gastronomy for its ability to evoke a tingling sensation, and gives the effect of a mild electric shock followed by a kind of numbness. Exciting new cosmetic properties have been found in Zanthalene®. This is the CO₂ extract from the Chinese plant rich in alpha-sanshools, molecules which are responsible for the activity of inhibition in synaptic transmission.

Already widely documented in several clinical studies as an anti-itch agent, it has recently been evaluated for its effectiveness in humans as an instant lifting agent.

Compared with an extract containing spilanthol able to produce a similar sensation on the skin, two different concentrations of Zanthalene® were tested around the eyes of 21 volunteers. The results showed its effectiveness in reducing the average roughness of the area

of application after only 30 minutes at a concentration of 1%. Starting out from a definition of the action mechanism, Indena research has thus identified a new application for an active substance already documented for

a different activity, thereby demonstrating that a rigorous scientific approach can often lead to exciting results. The novel application has recently been patented (WO 2010/094477).

Zanthoxylum bungeanum (Maxim) fruit husks



AMERICA FROM NORTH TO SOUTH

Rio de Janeiro, Brazil



From the cold reaches of Canada to the pampas of Argentina, the biodiversity of Mexico and the rhythms of Brazil, Indena's partners came from all over the Americas to meet last September in Rio de Janeiro during the first Regional Meeting of the Americas. The Sugarloaf Mountain provided the backdrop for this valuable opportunity for participants to exchange their ideas in

the exciting Brazilian surroundings. The two Americas, two continents so vast and diverse, represent both an exciting marketing challenge for Indena as well as a source of inspiration for new products. The meeting fulfilled its goal in increasing awareness of Indena products and fostered an atmosphere where partners were able to network and interesting ideas could emerge.

LEARNING WITH INDENA

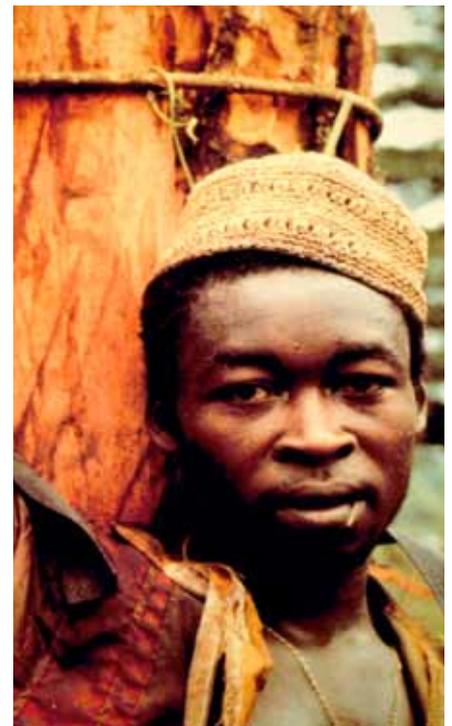
Indena has always made an active contribution to spreading knowledge in the field of phytotherapy, knowledge that is based on nearly 90 years of history, studies and discoveries. Through its strong links with academia and leading research centers, Indena experts are often invited to share their knowledge and participate in seminars, workshops and give university lectures. Over the past year, a number of postgraduate students of Phytotherapy from Italian universities and on other specialist courses have drawn on this expertise. These include the Universities of Milan, Rome (La Sapienza), Trieste and Siena. And not only does Indena go to university, universities often visit the Indena research center in Settala. Over the last twelve months, nearly 200 university students from both Italy and abroad have been taken on the journey which starts out with the identification of plant material and leads to the production of standardized extracts with all their beneficial effects for human health. A fascinating and stimulating experience for young people some of whom may well be called upon to devote their enthusiasm and creativity to future developments in this field.

PRUNUS AFRICANA: INDENA SUPPORTS SUSTAINABLE MANAGEMENT IN CAMEROON

The business of Indena is inextricably tied to nature and as a resource for our research biodiversity is priceless. Respect for the environment and sustainability are thus natural choices.

Unsurprisingly therefore, Indena has given its backing to "Non-detriment Findings for *Prunus africana* (Hook.f.) Kalkman in Cameroon". The project is sponsored by the International Tropical Timber Organisation (ITTO), an intergovernmental body that promotes the conservation and sustainable management of tropical forest resources. Fruit of a program of cooperation between ITTO and CITES (the Convention on International Trade in Endangered Species of Wild Fauna and Flora), the project was set up to provide thorough on-going monitoring of the status of the species in Cameroon, and to collect data on the biology, availability, management, use and trade of products derived from the *Prunus*. The CITES

officers in Cameroon will use the data to regulate the collection of *Prunus* tree bark and to ensure this natural resource is managed sustainably. *Prunus africana* is found in mountainous regions of Central and Southern Africa and Madagascar and may grow to a height of over 40 meters. The International Union for Conservation of Nature (IUCN) has classified this tall evergreen as a vulnerable species and placed it on their special Red List. As such it has been under the protection of CITES since 1993. Numerous clinical results have demonstrated the effectiveness of *Pygeum africanum* Hooker - the more popular name of *Prunus africana* - in reducing symptoms associated with benign prostatic hyperplasia in the early stages and prevent it spreading. This is confirmation indeed of the value of this ancient remedy, long used in the form of crushed bark by peoples in the Natal region of South Africa in the treatment of bladder disorders.



Prunus africana bark collector, Cameroon

CODEX HERBARUM

Members of the European Herb Growers Association (EUROPAM), who produce raw materials for use in medicinal and aromatic plants, met in Italy this year and resolved to introduce a European Codex Herbarum. The aim is to create a tool to provide technical and regulatory information about products of botanical origin in their different fields of application such as Health Foods, Cosmetics and Drug Manufacture. The Codex will include a comprehensive database of information on contaminants, testing procedures and legislation.

Botanists from Indena are members of the Association and have always worked very actively with EUROPAM to improve the quality of raw vegetal materials. They have contributed to the creation, development and dissemination of GACP guidelines (Good Agricultural and Collection Practices), which are now a requirement of the European Medicines Agency (EMA) for the production of Herbal Medicinal Products.

Dr Renato Iguera, Indena's Head of Botanical QC / QA has been part of EUROPAM for many years and is looking forward to applying his expertise to the production of a Codex Herbarum. The work should become a vademecum for the entire production chain, starting from the raw plant material, where quality is a primary and essential requirement.

OTANJOU-BI OMEDETOU GOZAIMASU! INDENA JAPAN!

Ten years ago Indena opened the doors of its Japanese headquarters in Tokyo. Since then Indena Japan, under the leadership of Susumu Kawada, has seen customer numbers grow year on year. It now supplies the Japanese market annually with over 35 tons of active ingredients destined for the pharmaceutical, cosmetics and food supplement industries, and ensures that Indena maintains a firm foothold in Asia.

SOLID PROGRESS MADE IN SETTALA



At work in the "Solids Department"

The Indena production plant in Settala has recently seen the inauguration of its new "Solids Department" designed to meet the quality specifications required by the standards of Good Manufacturing Practice. The new department covers a total surface area of 1,000 square meters and houses all the drying, grinding, mixing and packaging operations for solid materials. The buildings now contain dynamic dryers, grinding machinery, an atomiser, mixers, powder storage and handling equipment and packaging systems.

This is a multi-product facility and as such the manufacturing areas and material handling routes have been laid out to prevent any risk of cross-contamination between the different active ingredients, as required by the standards of Good Manufacturing Practices. Particular care

has been taken in the design of the production areas, both to ensure the optimal movement of staff and materials and to segregate the different manufacturing operations. For example, each machine or group of machines set up to process a given product is positioned in a dedicated environment and may not be used, even partially, for work on different products. Air quality in the plant and the conditioning system were also given great attention and engineered both to ensure compartmentalisation and to avoid any contamination risk. Meticulously studied in every detail, the new Indena "Solids Department" is a true example of manufacturing and technological excellence.

INDENA GAINS TGA APPROVAL FOR MANUFACTURING SITES

The Australian Therapeutic Goods Administration (TGA) is recognised as having some of the world's most stringent standards for herbal medicinal products.

TGA has adopted the PIC/S Guide for Good Manufacturing Practices for Medicinal Products and all medicinal products must be manufactured in accordance with this standard.

Indena has recently obtained TGA good manufacturing practices (GMP) certification for a number of their key production sites

including Milan, Palestro and Settala in Italy, and Tours in France.

This certification will help to streamline the strict supplier qualification requirements required in highly regulated markets such as Australia and throughout South East Asia. In addition to this there are significant benefits that can be leveraged in terms of reduced testing at the time of raw material receipt into customer's manufacturing facilities.

INDENA ON THE SPICE ROAD



Spices on display in the castle

Since the end of the 15th Century Padernello Castle has stood proud in the Po plain south of Brescia. This grand stately home, protected still by its moat, now plays host to cultural events such as conferences and exhibitions. This was the venue chosen by the Brescian provincial health authority for their exhibition "The Spice Road - People on the move", held in winter 2009. This was a multi-sensory journey following that taken of old by those spices, which could both set peoples apart as well as ring them together.

As they came into the castle from the winter mists, visitors were transported to a completely different dimension. Moving from one section to another of the exhibition, amid the exotic colours and aromas of the spice cones, they could watch a video

presentation on the story of spices through time; learn how they have been used in body care, the preparation of food, and indeed in the transition from magic to science, understanding the extent of their influence of spices on people's lives. Indena provided a specially produced video for the "Magic to Science" section, to explain how the use of spices, like other vegetal substances, has evolved and their importance today in pharmaceuticals, nutrition and cosmetics. In 2008 Indena contributed a chapter to the publication "Manuale di Spezieria", a handbook of spices, as part of this project designed to foster greater understanding and integration between eastern and western cultures.

A TRIBUTE TO YOSHIE

"Yoshie, our heartfelt gratitude for your passion, your expertise and your smile, which were so appreciated over the years you worked with us."

This is how we will remember Yoshie Katotomi, a prominent figure in Indena Japan. With her consummate professionalism, Yoshie represented a focal point for many of our customers in Japan. Passionate in her scientific research, to which she dedicated most of her life, she also chose to donate her body to science, to help the researchers of today and

tomorrow improve therapies for the treatment of breast cancer, a disease that cruelly was to take her away from us.

Even outside her working life, she was driven by her strong sense of responsibility and care for others. She combined her passion for skiing with voluntary work as a guide and instructor for blind and partially sighted skiers.

Yoshie will always be remembered with affection in Indena and we send our condolences to the Katotomi family.



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, health foods and cosmetics.

INDENA EVENTS CALENDAR

- **CPhI 2010** - Paris, France
5 - 7 October 2010
Paris Nord Villepinte
Stand 5M16 - Hall 5A
- **HI Japan 2010** - Tokyo, Japan
13 - 15 October 2010
Big Sight Exhibition Centre
Stand 2 - 249
- **Supply Side West 2010** - Las Vegas, USA
20 - 22 October 2010
The Venetian & Sands Expo
Stand 22071
- **NUCE 2010** - Milan, Italy
26 - 28 October 2010
Fieramilanocity
Stand F55 - Hall 1
- **In Cosmetics Asia 2010** - Bangkok, Thailand
2 - 4 November 2010
Bangkok BITEC
- **HI Europe 2010** - Madrid, Spain
16 - 18 November 2010
Feria de Madrid
Stand M28 - Hall 9
- **In-Cosmetics 2011** - Milan, Italy
29 - 31 March 2011
Fiera Milano, Rho
Stand Q39 - Hall 1
- **CPhI Japan 2011** - Tokyo, Japan
18 - 21 April 2011
Big Sight Exhibition Centre
- **Vitafoods 2011** - Geneva, Switzerland
10 - 12 May 2011
Palexpo Geneva
Stand 620
- **FCE Pharma 2011** - Saõ Paulo, Brazil
24 - 26 May 2011
Transamerica Expo Center
- **CPhI China 2011** - Pudong-Shanghai, China
21 - 23 June 2011
SNIEC - Shanghai New International Expo Center
- **Vitafoods Asia 2011** - Hong Kong
7 - 9 September 2011
Asia World Expo
- **CPhI Worldwide 2011** - Frankfurt, Germany
25 - 27 October 2011
Messe Frankfurt

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