

## **RISK OF HEART DISEASE REDUCED IN SMOKERS BY GRAPE SEEDS**

*An Italian study on Indena's Leucoselect™ Phytosome® extract was published in the recent October edition of the journal Metabolism*

*Milan, 28th November 2003* – The botanical grape seed extract *Leucoselect™ Phytosome®*, produced in the form of a bioavailable complex by the Italian company Indena, could prove to be an efficient means of preventing cardiovascular problems, especially for people with a high risk factor. These are the results of an Italian study published by the prestigious international journal *Metabolism* in its October number. A team of researchers from the Universities of Chieti, Ferrara, and Milan, together with Indena, has shown that the botanical ingredient studied and marketed by the Italian company, a world leader in the production of raw botanical materials, protects easily oxidised low-density lipoproteins (LDL) under oxidation stress as observed in heavy smokers. This oxidation, if not combated, causes the formation of plaques that are the main symptom of atherosclerosis, a fairly common ailment mainly affecting people in their fifties.

The clinical study, scrupulously conducted against placebo using the cross over, double-blind, randomised method, involved 24 healthy individuals over the age of 50 for 14 weeks. All those taking part were regular smokers of more than ten cigarettes per day, and during the first stage of four weeks, one group was given a daily dose of 150 mg of *Leucoselect™ Phytosome®* and the other group given 150 mg of a placebo. After a three-week "wash-out period", the second four-week stage followed during which the groups received the opposite treatment.

By means of a series of analyses to check the fatty component of the blood, made before and after the end of each phase of study, the researchers found that "treatment with *Leucoselect™ Phytosome®*, compared with the placebo, induced a 20% reduction of the lipidic peroxidation, with a significant 15% increase of LDL resistance to oxidating stress", as explained by Professor Roberto Maffei Facino, in charge of this study at Milan University. At the same time, an increase in the overall plasmatic anti-oxidant capacity was observed which confirms that the product is easily assimilated. Responsible for this proven activity on LDLs are the procyanidins, a family of molecules belonging to the class of flavonoids. Present in large quantities in grape seeds, procyanidins act as a powerful defence mechanism against free radicals and for a long time have been recognised as mainly responsible for the beneficial effects of red wine.

Indena Scientific Director, Paolo Morazzoni, praised the very positive results given by the extract: "We are talking of a highly standardised complex made up of procyanidins and phospholipids derived from soy, which is more bioavailable than procyanidins alone. Indena is committed to offering valid scientific knowledge concerning all products of natural origin still officially considered to be "border line". With studies and research conducted with about forty national and international centres, for more than eighty years Indena has been promoting a serious understanding of the therapeutic benefits of Phytotherapy.

### **LEUCOSELECT™ PHYTOSOME®**

*Leucoselect™ Phytosome®* is a complex containing a standardised extract based on procyanidins obtained from grape seeds and phospholipids from soy beans, which facilitate assimilation in the organism. Indena produces the ingredient as a raw material which is then sold to pharmaceutical or food companies who market the product under other brands. Depending on varying national regulations, the products may be registered as drugs in some countries and food supplements in others.

[www.indena.com/pdf/leucoselect.pdf](http://www.indena.com/pdf/leucoselect.pdf)

<sup>1</sup> Effect of a Standardized Grape Seed Extract on Low-Density Lipoprotein Susceptibility to Oxidation in Heavy Smokers. Vigna, G.B. ; Costantini F. ; Aldini, G. ; Carini, M. ; Catapano, A. ; Schena, F. ; Tangerini, A. ; Zanca, R. ; Bombardelli, E. ; Morazzoni, P. ; Mezzetti, A. ; Fellin, R. ; Maffei Facino, R. *Metabolism*; 52; 1250-1257 ; 2003.

<sup>2</sup> The study was conducted thanks to the collaboration of the Department of Clinical and Experimental Medicine at the University of Ferrara, the Department of Medicine and Sciences of Ageing at the University of Chieti, the Institute of Pharmaceutical Chemistry and Toxicology and the Department of Pharmacological Sciences at the University of Milan, and the Indena company.

## **ITALIAN RESEARCH CONFIRMS THAT A NEW BOTANICAL ANTITUMOR MOLECULE IS READY FOR TOXICOLOGICAL AND CLINICAL DEVELOPMENT**

*During the international symposium on "Novel Approaches for the Discovery of Anticancer Agents" in Freiburg, the Milan National Tumor Institute presents its studies on Indena's IDN5390 molecule*

*Milan, 19 June 2003* - Italian research is at the core of development of new chemotherapy treatment for fighting cancer. A study presented yesterday by Graziella Pratesi, a researcher at the Istituto Nazionale

dei Tumori in Milan, reaffirmed interest in IDN5390, a promising molecule derived from the precious Yew tree, which has been identified by the Italian company Indena.

Evidence in favor of IDN530 was reiterated during the international symposium on "Novel Approaches for the Discovery of Anticancer Agents" , organized in Freiburg by the Central European Society for Anticancer Drug Research (CESAR) and the Freiburg University Tumor Biology Center. The studies presented were all conducted in close cooperation with the Italian company Indena, world leader in the research and production of active principles and ingredients of botanical origin, for use in the pharmaceutical industry.

Researcher Graziella Pratesi explains that "The conclusion of the pre-clinical phase is encouraging for the development of a new type of drug. This active principle of vegetable origin could allow more tolerable, less invasive and more efficient chemotherapy treatment. Compared to chemotherapy used at present, IDN5390 is administered orally and for longer and more regular periods, thus increasing the efficacy of the treatment which has proved to be well tolerated".

Taxanes represent an important class of anticancer drugs in tumor growth inhibition treatment, requiring the use of cytotoxic drugs that inhibit the expansion of cancer cells and kill them by interfering with their capacity to divide and replicate. They have a proven clinical outcome on solid tumors such as in ovarian cancer, lung and breast cancers. Paclitaxel and docetaxel are currently the most widely used taxanes. IDN 5390 was selected as an anti-angiogenetic agent for its marked efficacy in inhibiting the migration of endothelial cells on which there is a low cytotoxic effect. IDN 5390 has proved to be very effective and well tolerated when administered orally for longer and more regular periods.

In vivo tests on IDN5390 involved the administration of doses of up to 4.5 g (a quantity 20 times more than the maximum dose of paclitaxel), which, during the 9 weeks of treatment, gave no evidence of toxicity. Metronomic treatment using IDN 5390, at a rate of 1 or 2 daily doses for a prolonged period, proved to be efficient against a wide range of human tumors transplanted *in vivo*, but also for tumors resisting treatment with paclitaxel, which is still the most common taxane used in chemotherapy. Finally, the antitumor effects of IDN 5390 can be compared to the optimal effects of paclitaxel, but in some types of tumor such as ovarian carcinoma, resistant to both paclitaxel and cisplatin, IDN 5390 clearly has an important antitumor effect.

These studies are a further expression of the success of Indena Research in the panorama of antitumor drugs derived from the Yew tree. Given the industrial-scale production of paclitaxel, of which Indena is the biggest manufacturer at world level, and the licensing agreement with Bayer for the new antitumoral IDN 5109/BAY 59-8862, now in an advanced stage of clinical development, new roads are opening to research, demonstrating the potentiality of phytochemicals in the development of new drugs

## NOTES TO EDITORS

### PACLITAXEL

Paclitaxel is an anticancer agents obtained from plants. It is a diterpene pseudoalkaloid derived from *Taxus baccata* L. Paclitaxel has been shown to display significant activity against a number of tumours, such as cancer of the ovary, breast, lung and prostate, and against melanoma. Paclitaxel blocks cell replication thanks to its capacity to stabilise the microtubules, thereby inhibiting the depolymerisation of tubulin. In this way cell loses spatial and temporal control of assembling and disassembling the microtubules and can no longer divide. Microtubules are an integral component of eukariotic cells and are implicated in a variety of cellular functions.

Indena is the major paclitaxel producer worldwide.

<sup>1</sup> IDN 5390: an oral taxane candidate for protracted treatment schedule.

<sup>2</sup> Novel Approaches for the Discovery of Anticancer Agents (18 - 21 June '03) at the Tumor Biology Center, University of Freiburg, Germany.