AN INTEGRATIVE TREATMENT APPROACH TO CASTRATION-RESISTANT PROSTATE CANCER

An Integrative Treatment Approach to Castration-Resistant Prostate Cancer

Ben L. Pfeifer, M.D., Ph.D.
Professor and Director for Research and Development
Aeskulap International, Lucerne, Switzerland

Aeskulap International is combining conventional and complementary oncological treatments to create effective therapies for patients with metastatic and castration-resistant prostate cancer. This integrative approach includes: basic complementary treatment measures, such as dietary- and life style changes, specific physical therapy and exercise programmes, psycho-oncology measures, hyperthermia- and fever therapies, detoxifying treatments, enzyme therapy and specifically designed medical treatments utilizing various plant derived preparations (phytotherapy).

In Western Europe prostate cancer is the most frequent malignant tumour type in man. Standard hormone-ablation therapies for men with recurring cancer after radical prostatectomy and / or radiation therapy often achieve only a short-term control of tumour growth. Due to clonal selection of hormone independent cancer cells, the so called castration-resistant (formerly called hormone-refractory) stage of the disease develops in many of these patients. At this stage, therapeutic options are limited to "watch and wait" strategy, second-line hormonal therapies, or eventually chemotherapy which often causes significant side effects without truly extending the patient's life.

Since each patient with advanced, metastatic and castration-resistant prostate cancer is different and also responds different to treatment, even if PSA levels and disease history might be similar, Aeskulap International offers tailor-made treatments including a supportive phytotherapy protocol for each individual patient. Depending on specific patient data, a special combination of phytotherapy compounds is chosen from the following product list for treatment: Prostasol, Curcumin combi extra forte, BioBran, IMUPROS, Modified Citrus Pectin, Indole-3-Carbinol, Imusan, *Convolvulus arvensis* extract, and Artemisinin. In situations with very high PSA levels, aggressive tumour histology, and failing second line hormonal treatment (for example: Arbiraterone - Zytiga and MDV 3100), we also prescribe Aeskulap-Sitosterol-Mix, a tailor-made compound that greatly improves the efficacy of our phytotherapy protocol.

The following provides a short summary on the above mentioned substances used in our treatment protocols; a more detailed information sheet for each substance as well as specific details about our treatment protocol can be requested from our office under: service@aeskulap-international.org or by phone: +41418290436 or +491636913909.

Prostasol contains various plant extracts, all known to support prostate health. The combination of Bio-Curcumax – a highly bio-available form of curcuma, Linumlife – a flaxseed extract rich in lignans, and Resveratrol – a strong anti-oxidant derived from grape seeds provides anti-inflammatory, anti-oxidative and anti-cancer properties.

Curcumin combi extra forte is a combination formula with extracts from Turmeric root and Piperin from black pepper. It has powerful anti-oxidative, anti-inflammatory and anti-tumour activities. Curcuma extracts are utilized worldwide in treatment protocols for

patients with cancer. Their beneficial effects have been described in more than 3000 studies.

BioBran is a processed rice bran polysaccharide containing Arabinoxylan as a major component which has a powerful immune-modulatory effect. In particular, it increases the number and function of T- cells, B-cells and NK cells. BioBran also enhances apoptosis of cancer cells directly. The substance is non-toxic, and it is easily absorbed after oral intake. The effectiveness of BioBran has been documented in experimental and clinical studies published in peer-reviewed journals. At Aeskulap Hospital in Switzerland, BioBran is considered an important component of integrative tumour therapy for patients with prostate cancer and cancer in general.

IMUPROS is an orthomolecular combination formula, containing selenium, zinc and calcium, the vitamins C, D and E, as well as genistein, lycopene and epigallocatechin gallate; it provides the vitamins, minerals, and other vital substances necessary to maintain a healthy function of the prostate gland.

Modified Citrus Pectin is a complex water soluble, indigestible polysaccharide obtained from the peel and pulp of citrus fruits and modified by means of high pH and temperature treatment, to affect numerous rate-limiting steps in cancer metastasis. The anti-adhesive properties of MCP help to reduce the metastatic potential of cancer cells. MCP also exerts powerful apoptotic signals forcing in particular metastatic cancer cells to initiate cell death programs in multiple human malignancies.

Indole-3-Carbinol is a special formula combining plant-derived substances from the Indol / Carbinol group with Resveratrol. This combination helps to maintain normal cellular function and cell division, provides protection from free oxygen radicals, and modulates the estrogen metabolism. It is used in the adjuvant treatment of breast-, cervical-, and prostate cancer. It is effective in hormone-sensitive as well as hormone-independent variants of breast- and prostate cancer.

Imusan is an extract mixture of fifteen mostly Chinese herbs with proven efficacy against various cancer cell lines and stimulatory effects on natural killer cells. Imusan is boosting natural defence mechanisms of the immune system and it supports proper immune function in the fight against cancer.

Convolvulus arvensis extracts contain various proteoglycanes with significant anti-angiogenesis effect which reduces the blood supply to primary tumour as well as metastatic lesions helping to slow down cancer growth.

Artemisinin is a secondary plant compound extracted from "*Artemisia annua*". It is used worldwide for treatment of multi-resistant strains of Malaria. Besides Artemisinin, several flavones and other active biologic substances have been isolated from "*Artemisia annua*" - all demonstrating significant effects against various cancer cells.

Over the last 15 years, more than 10,000 men have used our phytotherapy protocols for treatment of their prostate cancer. Most of these men had reached the castration-resistant stage of the disease and were metastatic when they entered our treatment protocols. There was clinical benefit from our integrative treatment approach in about 2/3 of all men treated with our phytotherapy protocols. This benefit was measured in reduction of PSA levels of more than 50%, reduction of pain from metastases, and improvement in quality of live as well as prolongation of time to disease progression.

Currently, a surprisingly large number of men with initially far progressed metastatic prostate cancer (bone, lung, lymph nodes) in the castration-resistant stage of the disease are alive on our treatment protocol, surviving significantly longer than expected by their primary care physicians.

Effectiveness and side effects of our phytotherapy protocols for advanced, metastatic and castration-resistant prostate cancer were evaluated in two prospective and two retrospective clinical studies with a total of 684 patients.

The first prospective study goes back to the year 2000. Sixteen men were treated over a period of six months for their hormone-refractory prostate cancer receiving the a standard dose of 2.9 g of the Prostasol-like precursor compound, PC-SPES. The results of this study were published in the year 2000 in the British Journal of Urology. The second prospective study followed in 2005, and here, 174 patients were treated over a period of 12 months with a much more complex phytotherapy protocol, consisting of the four 'core compounds', Prostasol, Curcumin, IMUPROS and BioBran. The patients in this study received individual dosages of the respective core compounds, which were adjusted on a monthly basis according to clinical assessments as well as laboratory data of the patients, including PSA levels. In special situations, this protocol was extended by the additional use of MCP, Artemisinin, and I3C. Efficacy and side effect profile of this treatment protocol were evaluated with regular laboratory testing, a 'quality of life' questionnaire, and with repeated CT-, bone scan- and MRI examinations to estimate tumour volume. Patient data was collected prior, during and at the end of the six and twelve months study periods, respectively.

Significant PSA declines were observed in these studies in about two thirds (68%) of the patients on the protocol. Reduction of tumour volume was seen in about half of the patients, and 65% of patients reported improvement in their quality of life, in particular a reduction of pain. Side effects, such as soreness of breast nipples (~35%), decline in libido and erectile function (~30%), slight anaemia (~15%) and dyspepsia (~5% mostly in the first two treatment weeks) were reported; these reversed and vanished when patients came off the treatment protocol. Thrombotic events and/or pulmonary embolism were recorded in less than 1% of the patients whereby the causative connection to the treatment protocol was unclear.

The retrospective studies from 2011 and 2013 did confirm the positive clinical responses with regards to tumour growth control and improvement of quality of life as seen in the earlier prospective studies. Clinical data of the last 14 years of a total of 494 patients were collected and evaluated. To date 106 of these men (about 21%) have died due to disease progression; the remaining 388 patients are alive and continue to enjoy the positive effects of our treatment programme, which provided disease- and symptom control for them, lasting on average for 4.7 years. Remarkably, 28 of these patients with castration-resistant and metastatic disease are alive now for more than 10 years (8 of them even 14 years) – and this with a well-controlled tumour and good quality of life.

Our experience shows that an integrative treatment approach utilising a complex basic oncology treatment programme in combination with specific phytotherapeutic protocols can significantly improve clinical outcome and quality of life for many prostate cancer patients, even with advanced disease stages.

ProstaSol™

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 12th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to ProstaSol™ produced by medpro Holland B.V. This combination product is produced in Holland as a food supplement, but has been effectively used as a natural remedy in the complementary medicinal treatment of patients with prostate carcinoma.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- ProstaSol contains only the components listed on the label and no synthetic additives.
- ProstaSol is used parallel to conventional treatments (for example, as a complementary medicine in conjunction with radical operations or radiation) and on its own in the "castration-resistant" stage of prostate cancer.
- ProstaSol is often used in combination with Curcumin and Biobran by doctors within our network in preparation for a prostate biopsy to prevent micro-metastasis due to potential spread of cancer cells.
- ProstaSol, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in the treatment of patients with prostate cancer, there are several clinical pilot studies and retrospective investigations as to the effectiveness of ProstaSol which have made it rather popular with patients and their urologists or oncologists.

If you decide to include ProstaSol as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

ProstaSol™

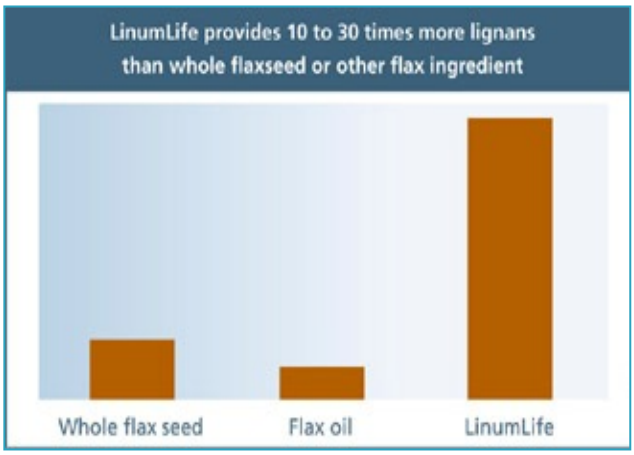
ProstaSol contains the following ingredients:
LinumLife (Lignane from flax seeds), Regrestrol (various sitosterols), Biocurcumin BCM-95® (good bioavailable curcuminoids), and saw palmetto extract *(Serenoa repens)*, Ginseng, *(Panax ginseng)*, Baikal Skullcap *(Scutellaria baicalensis)*, the African prune tree *(Pygeum africanum)*, Reishi *(Ganoderma Lucidum)* and Japanese knotweed *(Polygonum cuspidatum)*, which is the best natural source of resveratrol and quercetin.

In the Netherlands, ProstaSol is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals. ProstaSol is often used by urologists and oncologists as a complementary oncological treatment for patients who have prostate cancer.

The following are some clinically proven effects of individual ingredients:

LinumLife (Lignane from flax seed)

LinumLife is a standardized extract from flax seeds with a high concentration of so-called lignans - secondary plant matter with a phyto-oestrogenic effect. Additionally, lignans have a significant antioxidant effect and generally serve to keep cells healthy while also preventing cancer. A 2004 scientific report from the Cancer Institute in Heidelberg recommended using flax seed oil and flax seeds in the prevention of breast and colon cancer. Lignans also have a positive effect on benign prostate enlargement; they reduce the size of the prostate gland. The lignans in LinumLife are clinically tested, safe, and easily tolerated.



Regrestrol (Sitosterol-Mix)

Regrestrol-complex contains four different sterols: *Beta-Sitosterol, Campesterol, Stigmasterol* and *Brassicasterol*. Sterol and Sterolin are actually plant fats that can be found in very high concentration in many nuts and seeds. Sterol and Sterolin are known for their healing properties in conjunction with prostate illnesses. European researchers confirmed in the renowned magazine "The Lancet" that plant-based sterols and sterolins effectively fight prostate illnesses.

For over twenty years, urologists have been successfully using sterols and sterolins instead of chemical preparations. Additional clinical studies have shown that sterols and sterolins have important inflammation-reducing properties and thus work as a prophylactic in conjunction with inflammation, diabetes, and cancer. These substances contain considerable adaptogenic properties, modulate the immune system, and protect healthy cells from being attacked by our immune system.

Due to this last characteristic, sterol and steroline also help with auto-immune illnesses, which also plays a role in the development of prostate conditions. In a random, placebo-controlled study of 177 patients with enlarged prostate glands, the effectiveness and safety of Beta-Sitosterol was tested and found to be sound. The results from patients receiving treatment with Beta-Sitosterol were much better than those of the control group, which received a placebo. Prostate illnesses declined greatly, and quality of life improved significantly.

Researchers at the University of Buffalo in the USA have concluded that sterols slow down the growth of prostate, breast, and colon cancers. In this study, the results of which were presented to the annual conference of American Research Biologists, phytosterol (Beta-Sitosterol) decreased the number of cancer cells by 60% in a lab test. It is also known that Beta-Sitosterol causes testosterone levels to sink, and decreases the activity of certain enzymes which convert this hormone into a biologically active form. The researchers also discovered that Beta-Sitosterol stimulates intercellular signal mechanisms and hinders uncontrolled cell splitting.

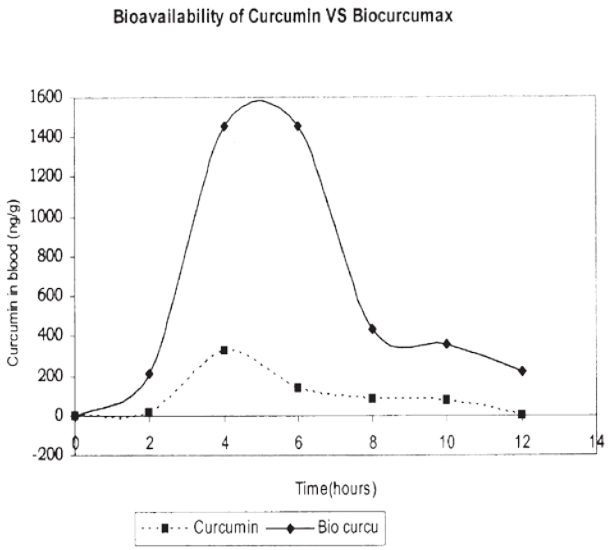
Biocurcumin BCM95®

Curcuma root and powder

Biocurcumin BCM95 is a patented extract made from turmeric, which possesses a number of biological effects, such as antioxidants, anti-inflammatory, antibacterial, and anti-rheumatic effects and a significant anti-cancer effect. In contrast to normal turmeric extract, Biocurcumin BCM95 possesses an extremely high bioavailability (about seven times as great). That means that an oral dosage of only 250 mg of Biocurcumin BCM95 produces approximately the same blood-drug level as a dosage of 1,500 mg of normal turmeric extract, or about 37,500 mg of simple Curcumin Powder. Therefore, taking Biocurcumin BCM95 quickly delivers a therapeutic concentration of curcuminoids into the blood stream.

The BCM95 Complex positively distinguishes itself with the following properties:

- 100% natural turmeric extract *(Curcuma longa)* without added artificial ingredients
- clinical studies show that BCM95 Extract has a bioavailability that is seven to eight times better than other Curcumin extracts
- much smaller dosages are required to achieve the same effect of conventional curcumin extracts
- has a powerful antioxidant effect
- has extremely good anti-inflammatory properties



From a medical standpoint, the antioxidant, anti-carcinogenic, and the inflammatory reducing properties of the turmeric extract are of particular interest. These properties are used in the treatment of various diseases, such as intestinal, lung, and liver diseases, and with inflammatory diseases, Alzheimer's, heart attacks, and cancer illnesses. Clinical tests and studies conducted on animals confirm in particular the cancer-reducing properties in the treatment of stomach, intestinal, liver, and skin cancer. Even advanced metastasis development can be considerably reduced through the use of Curcumin.

Saw palmetto *(Serenoa Repens)*

The healing property of the lipophilic extract of the fruit of the saw palmetto (*Serenoa repens*) in conjunction with prostate illnesses has long been known. Randomized double-blind studies have shown that saw palmetto extract is effective with benign prostate enlargement at a dose of 320 mg per day and that it greatly improves urinary and bladder function. The maximum, as well as the average urinary flow rate improved upon taking this extract. In comparison to the usual synthetic substances containing finasteride, saw palmetto has at least the same effectiveness with fewer side effects, is better tolerated, and the treatment is also much more cost-effective. Saw palmetto research has concentrated on its application in prostate treatment. Aside from positive effects on benign prostate issues, saw palmetto also has a proven effect in conjunction with prostate cancer. It hinders, for instance, cell proliferation in prostate cancer tissue and supports the normal programmed cell death (apoptosis) of cancer cells.


Saw palmetto

Ginseng


Ginseng Root

Recently ginsenosid and saponin, the pharmacological properties in ginseng root, have been used in Europe, although the healing properties of the ginseng root in conjunction with numerous diseases have been long known primarily in China and other Asiatic countries.
The substance saponin in particular inhibits breast and prostate cancer cells, in prostate carcinoma, it suppresses the PSA value. It also has a positive influence on androgen receptors and on the enzyme 5-alpha-reductase. Ginsenoid supports normal programmed cell death (apoptosis) in prostate cells and reduces the activity of so-called Bcl-2 genes, which make cells invincible,

thereby causing and supporting cancer. Moreover, ginsenosid restricts the process of metastasis and decreases the development of cancer cells in other tissues. Lastly, ginsenosid inhibits new growth of blood vessels, which leads to growth retardation of primary tumours and of metastasis (anti-angiogenic effect).

Recent research results have shown that ginseng has a preventative effect on various kinds of cancer.

Ginsenoside has a significant anti-inflammatory effect in addition to its cancer-inhibiting effect and thus also fights illnesses characterized by inflammation (for example, rheumatism or diabetes mellitus).

Baikal Skullcap *(Scutellaria baicalensis)*

Baikal Skullcap

Extract from the *Scutellaria baicalensis* contains the flavonoid baicalin, which causes programmed cell death (apoptosis) in DU-145 prostate cancer even in very low concentration. That is why researchers at the molecular biological centre at Valhalla University in New York were able to show in studies on prostate cancer cell cultures that scutellaria extract causes a reduction of about 65% in cancer cell growth and curbs PSA production in these cells. Baicalin reduces growth not only in prostate cancer cells, but also in other types of cancer, such as lung cancer and brain tumours. Russian researchers have been able to prove that baicalin has a positive effect on blood pressure in patients with tumour anaemia and also minimizes the side effects of chemotherapy.

African prune tree *(Pygeum africanum, Prunus africana)*

Pygeum africanum

Pygeum extract comes from the bark of a plum tree native to Africa. Since the sixties, this extract has been used successfully in the treatment of bladder and prostate problems, especially in therapy addressing benign prostatic hyperplasia. At this time, for instance, pygeum is the most important substance in the treatment of benign prostatic hyperplasia. Its effects have been proven in double-blind studies. Taking standardized pygeum extract reduces the enzyme activity of the so-called 5-alpha-reductase and inhibits inflammation so that a noticeable improvement in water solubility is perceptible. In the objective measurement of urine emission, there is improved urine flow. A multicentre study at the University of Bratislava has shown that daily intake of 100 mg of pygeum (over the course of about two months) increased quality of life and greatly improved the amount of urine per excretion. So far, research has shown no side effects from pygeum.

Reishi *(Ganoderma lucidum)*

Reishi mushrooms have been used for over 4000 years in Chinese medicine. The ingredients within the fruit bodies of the mushroom, such as Triterpenoide, a sterole, manitol, coumarin, and various polysaccharides, are used medicinally. Furthermore, the mushrooms contain various trace elements, such as zinc, germanium, manganese, iron, copper, and even calcium. Recent research results show that reishi mushroom extract strengthens the immune system and also demonstrates immune modulating properties. The reishi has proven itself particularly useful in the treatment of prostate illnesses, since it inhibits prostate inflammation, thereby working against prostatitis. It also suppresses cell adhesion and cell migration in prostate cancer, thereby reducing tumour migration.

Reishi Colony

Japanese knotweed *(Polygonum cuspidatum)*

Japanese knotweed *(Polygonum cuspidatum)* is one of the best natural sources of resveratrol, a phytoalexin that has antioxidant, anti-inflammatory, and anti-cancer properties and which belongs to the category of polyphenols. Diverse clinical studies and animal tests with resveratrol demonstrate the positive effects of this substance on cancer, autoimmune diseases, arteriosclerosis, Alzheimer's, cardiovascular diseases, and arthritis, among other illnesses.

Japanese knotweed

Polyphenols are also known for their high redox potential, which makes them ideal radical inhibitors. Like coenzyme Q10, resveratrol is purported to directly seal over the mitochondria of the so-called proton leak and to neutralize reactive oxygen-based free radicals. Moreover, it has the capacity to stimulate a number of the body's own different antioxidant enzyme systems (for example, the superoxide dismutase and some catalases). In addition, resveratrol prevents lipid peroxidation, namely the oxidation of LDL-Cholesterol, which in its oxidized form can be stored in the vascular wall and prepare the way for the development of arteriosclerosis. Resveratrol prevents this process and therefore works against the calcification of the blood vessels. Moreover, a significant neuron-protective effect is attributed to resveratrol, so that it is hoped that it can also one day be used in the treatment of Alzheimer patients.

The positive effects of resveratrol in conjunction with various disease patterns can also be partially explained by its significant anti-inflammatory effects. This allows resveratrol to reduce two enzyme systems in the body, namely the Cyclooxygenase 2 and the intricate nitrogen monoxide synthetase, both of which play an essential role in inflammatory reaction. A number of studies have shown over the course of the last few years that chronic inflammations in particular are extremely important for the pathogenesis of many diseases, from the development of arteriosclerosis, to neuronal degeneration, to the formation of cancer. As early as the 90‘s, it was demonstrated that resveratrol possesses an anti-cancer effect at all three levels of the disease: it prevents cancer, reduces the growth of cancer, and reduces metastasis. These effects of resveratrol are based upon the ability to send the already existing cancer cells into the programmed cell death (apoptosis), to increase the effective-

ness of the toxic cellular effects of conventional chemotherapy or radiation, and to counteract therapy resistance.

Quercetin is a flavonoid extracted from the so called secondary plant matter of *Polygonum cuspidatum*. This substance has impressive anti-oxidant, anti-inflammatory, and immune-modulatory effects and regulates the cell cycle. Quercetin is virtually non-toxic when taken orally or intravenously. Studies from the famous Mayo Clinic and the Dana Farber Cancer Institute at Harvard University in the USA have shown that Quercetin blocks the growth of androgen-sensitive and hormone-resistant prostate cancer cells, making them sensitive to heat; the substance is therefore suitable to support hyperthermia treatments. Quercetin is not only applicable as a treatment and prevention substance in prostate cancer, however. It is also applicable in conjunction with breast cancer, colon cancer, lung cancer, and several other types of cancer.

Curcumin combi extra forte™

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 12th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to Curcumin combi extra forte ™ produced by medpro Holland B.V. This combination product is produced in Holland as a food supplement, but also serves as an effective natural remedy in complementary oncological treatment of patients who have prostate cancer. As such, it has become an important part of our treatment protocol.

Our doctors and researchers have tested this product both in the laboratory, as well as clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- Curcumin combi extra forte contains only the components listed on the label and not a single synthetic additive.
- Curcumin combi extra forte can be used in conjunction with conventional treatments for prostate inflammation and in complementary oncological prostate cancer therapy (for example, as concurrent medicine with radical operation, together with chemotherapy, and after radiation treatment).
- Curcumin combi extra forte is an integral part of the treatment of hormone-refractory (castration-resistant) prostate cancer within the scope of the so-called Pfeifer Protocol. (see: http://www.clearfeed.com/pfeifer/prostate-cancer.html)
- Curcumin combi extra forte is also used in combination with ProstaSol and Biobran by doctors within our network to prevent micro-metastasis due to possible spreading of cancer cells that may result from prostate biopsy or transurethral resection of the prostate (TURP).
- Curcumin combi extra forte, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in treatment of patients with prostate diseases, there are well-founded studies in the medical literature as to the effectiveness of Curcumin extracts in connection with cancer patients. In addition, there are clinical pilot studies on Biocurcumin BCM95® Extract, which is a component of Curcumin combi extra forte, have already been published and may be obtained from us upon request.

If you decide to include Curcumin combi extra forte as a complementary oncologic treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your doctor team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

Curcumin combi extra forte™

Curcumin combi extra forte contains the following ingredients: Biocurcumin Complex - BCM95® (high-quality bio-available curcuminoids) and Polygonum cuspidatum (root extract with 50% resveratrol, pterostilbene and quercetin).

In the Netherlands, Curcumin combi extra forte is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals. Curcumin combi extra forte is often used by cancer patients and by patients with chronic degenerative and inflammatory diseases.

Some clinically proven effects of individual ingredients follow:

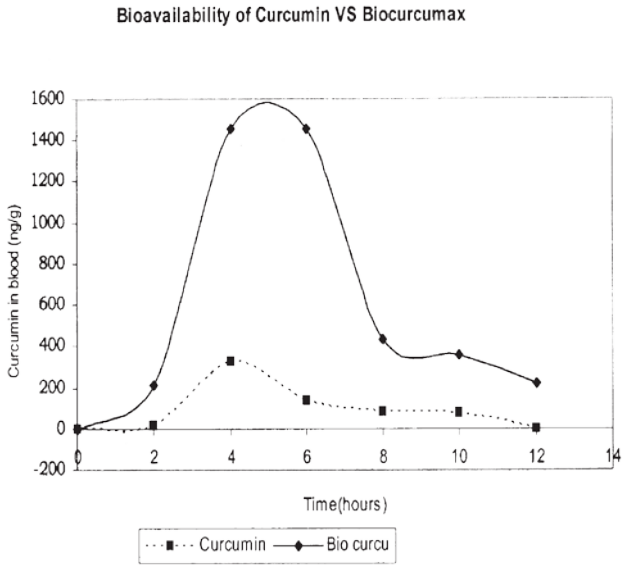
Biocurcumin BCM95®

Curcuma root and powder

Biocurcumin BCM95 is a patented extract made from turmeric, which possesses a number of biological attributes, such as antioxidant, anti-inflammatory, antibacterial, and anti-rheumatic effects, as well as a significant anti-cancer effect. In contrast to normal turmeric extract, Biocurcumin BCM95 possesses an extremely high bioavailability (about seven times as great). That means that an oral dosage of only 250 mg of Biocurcumin BCM95 achieve approximately the same blood-drug level as a dosage of 1,500 mg of normal turmeric extract, or about 37,500 mg of simple Curcumin Powder. Therefore, taking Biocurcumin BCM95 quickly delivers a therapeutic concentration of curcuminoids into the blood stream.

The BCM95 Complex distinguishes itself with the following positive properties:

- 100% natural turmeric extract *(Curcuma longa)* without added artificial ingredients
- clinical studies show that BCM95 Extract has a bioavailability that is 7-8 times higher than other curcumin extracts
- much smaller dosages than conventional curcumin extracts achieve the same effect
- has a powerful antioxidant effect
- has extremely good anti-inflammatory properties



From a medical standpoint, the antioxidant, anticarcinogenic, and inflammatory reducing properties of the turmeric extract are of particular interest. These properties are used in the treatment of various diseases, such as intestinal, lung, and liver diseases, and with inflammatory diseases, Alzheimer's, heart attacks, and cancer illnesses. Clinical tests and studies conducted on animals confirm in particular the cancer-reducing property in the treatment of stomach, intestinal, liver, and skin cancer. Using curcumin can considerably reduce even advanced metastasis development.

Japanese knotweed *(Polygonum cuspidatum)*

Japanese knotweed *(Polygonum cuspidatum)* is one of the best natural sources of resveratrol, a phytoalexin that has antioxidant, anti-inflammatory, and anti-cancer properties and which belongs to the category of polyphenols. Diverse clinical studies and animal tests with resveratrol demonstrate the positive effects of this substance on Alzheimer's, arthritic cancer, autoimmune diseases, arteriosclerosis, and cardiovascular diseases, among other illnesses. Polyphenols are also known for their high redox potential, which makes them ideal free-radical inceptors.


Polygonum cuspidatum

It is said that resveratrol, like coenzyme Q10, directly seals the mitochondrial membrane of the so-called proton leaks and neutralizes reactive oxygen-based free radicals. Moreover, resveratrol has the capacity to stimulate the body's own various antioxidant enzyme systems (for example, the superoxide dismutase and its own catalases). In addition, resveratrol prevents lipid peroxidation, namely the oxidation of LDL cholesterol, which in its oxidized form can be stored in the vascular wall and prepare the way for the development of arteriosclerosis. Resveratrol prevents this process and therefore counteracts the calcification of the blood vessels. Moreover, a significant neuron-protective effect is attributed to resveratrol, so that it is hoped that it can also one day be used in the treatment of Alzheimer patients.

The positive effects of resveratrol on the most diverse disorders can also be partially explained by its significant anti-inflammatory effects. This allows resveratrol to reduce two enzyme systems in the body at the same time, namely the Cyclooxygenase 2 and the intricate nitrogen monoxide synthetase, both of which play an essential role in inflammatory reaction. In the last few years, a number of studies have shown that in particular chronic inflammation is extremely important for the pathogenesis of many diseases, from the development of arteriosclerosis to neuronal degeneration to the formation of cancer. As early as in the 90's, it was demonstrated that resveratrol possesses an anti-cancer effect at all three levels of the disease: it prevents cancer, reduces its growth, and reduces

metastasis. These effects of resveratrol are based upon the ability to send the already existing cancer cells into programmed cell death (apoptosis) and to increase the effectiveness of the toxic cellular effects of conventional chemotherapy or radiation. These characteristics could increase the effectiveness of such treatments and counteract therapy resistance, which is often observed.

Quercetin is also extracted from the so-called secondary plant matter of *Polygonum cuspidatum*. This substance has impressive antioxidant, anti-inflammatory, and immune-modulatory effects and regulates the cell cycle. Quercetin is virtually non-toxic when taken orally or intravenously. Studies from the famous Mayo Clinic and the Dana Farber Cancer Institute at Harvard University in the USA have shown that Quercetin blocks the growth of androgen-sensitive and hormone-resistant prostate cancer cells, making them sensitive to heat; the substance is therefore suitable to support hyperthermia treatments. Quercetin is, however, not only applicable as a treatment and prevention substance in prostate cancer. It is also applicable in conjunction with breast cancer, colon cancer, lung cancer, and several other types of cancer.

BioBran®

(A product of Daiwa Pharmaceutical Co., Ltd.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to BioBran® (MGN-3) produced by DAIWA Pharmaceutical Ltd., Tokyo, Japan. This nutraceutical is produced as a food supplement and has been effectively used as a natural remedy in complementary medicinal treatment of patients with prostate- and other cancer entities.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- BioBran contains only the components listed on the label and no synthetic additives.
- BioBran can be used in conjunction with conventional treatments for prostate cancer, for example, in the perioperative setting with radical prostatectomy, or in the recovery period after radiation treatment and during and after chemotherapy.
- BioBran is an integral part of our treatment program for prevention and treatment of prostate- and other cancer entities.
- BioBran is also used in combination with Curcumin combi extra forte, IMUPROS, and ProstaSol by doctors within our network to prevent micro-metastasis due to the possible spreading of cancer cells following prostate biopsy (tissue removal from the prostate) or transurethral resection of the prostate (TURP).
- BioBran, used at the suggested dosage, causes no side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in treatment of patients with prostate cancer, there are well-founded preclinical studies, as well as some clinical studies evaluating the effectiveness of BioBran with regard to immune system support and its direct anti-cancer effect.

If you decide to include BIOBRAN as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors with any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

BioBran®

BioBran MGN–3 was developed ten years ago by Hiroaki Maeda, Director of Research and Development of Daiwa Pharmaceutical Co., Ltd in Tokyo, Japan. Maeda was primarily interested in finding solutions for human health and agriculture using natural phytonutrients. In the late eighties, Maeda focused on polysaccharides, which have been known to strengthen the immune system. In collaboration with Daiwa Pharmaceutical and led by Yasuo Ninomiya and Mamdooh Ghoneum, Professor of Immunology at Drew University of Medicine and Science in Los Angeles, Maeda developed complex short-chain polysaccharides (mainly arabinoxylan and other hemicelluloses) which he later named BioBran MGN-3. Small doses of this food-based mixture have been clinically proven to enhance immune response when ingested in vitamin form. The supplement is made by breaking down rice bran with enzymes from the shitake mushroom.

What is BioBran MGN-3 Arabinoxylan?

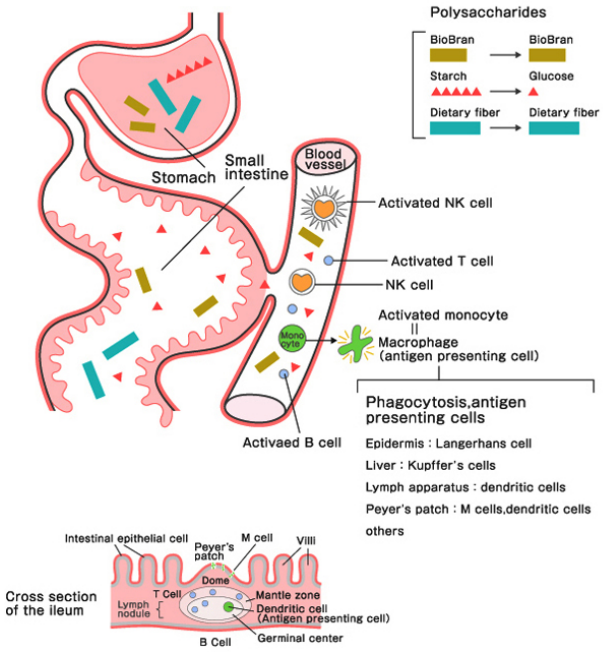
Certain large polysaccharide molecules – complex carbohydrates such as plant fibre – can stimulate the immune system. Research has shown that fibre in general can lower cholesterol, improve carbohydrate metabolism and reduce intestinal toxicity. While rice bran in general is known for its antiviral properties, certain mushroom fibres in particular have been known to enhance immune response. Unfortunately, plant fibres are largely indigestible, so these immune-enhancing benefits remain unutilised as the fibre simply passes through and out the body. However, once these very long polysaccharide molecules (specifically from rice bran) are broken down into much smaller particles called hemicelluloses – the most effective of which are known as arabinoxylan compounds – the advantages not only vastly increase, it also has an immediate effect on the body's immune system. This is because the fibre now has a small enough molecular weight that it can be absorbed undigested into the bloodstream via the small intestines.

The leading manufacturer of this type of hemicellulose food supplement is Daiwa Pharmaceutical in Japan. They use a unique and patented process in which rice bran is broken down and partially hydrolysed using shitake mushroom enzymes (lentius edodes mycelia extract) to create a unique and natural mixture of hemicelluloses, the principle ingredient of which is the arabinoxylan compound or b-1, 4 xylophyronase hemicellulose. Although shitake mushroom enzymes are used in the process, no quantifiable amount of the mushroom can be found in the final product, so most people with mushroom intolerances do not experience an allergic reaction.

The resulting mixture of hemicelluloses from this process was generically called BioBran MGN-3. The three letters refer to the scientists that developed, researched and financed it: Maeda, Ghoneum and Ninomiya. It is also referred to as BioBran MGN-3 arabinoxylan compound because arabinoxylan is one of its main ingredients. As it is a mixture of natural ingredients (hemicelluloses), BioBran MGN-3 is categorized as a food supplement or 'functional food'. Due to this array of natural ingredients, it is much easier for the body to absorb than single substances like conventional medicines. More importantly, this is thought to account for its lack of unwanted side-effects.

What is the effect on the body?

BioBran MGN-3 arabinoxylan can strengthen a weak immune more powerfully and safely than any other natural or synthetic product. Professor Ghoneum, Head of Immunology Research at Drew University of Medicine and Science, states that BioBran MGN-3 is actually the most potent immunnomodulator he has researched. Although no one knows exactly how it works, it is thought to enhance the production of natural cytokines in the body (substances such as interferons, interleukins and tumour necrosis factors). These not only help by directly destroying rogue cells and viruses, they also kick-start the immune system by increasing lymphocyte activity – B cells, T cells and particularly NK (natural killer) cells. B cells produce antibodies while T cells and NK cells float through the body destroying virally or bacterially infected cells and cancer cells. In its lifespan, one NK cell can kill up to 27 cancer cells by attaching itself to them and injecting them with deadly chemical granules which destroy the abnormal cell in less than 5 minutes.



The immune system

The immune system is a collective army consisting of a trillion white blood cells, bone marrow, antibodies, cytokines and the thymus gland that help identify and destroy the millions of microbes (bacteria, viruses, parasites and fungi) that penetrate our body each day, as well as the thousands of our own cells that have become genetically abnormal or cancerous. The immune system is considered just as complex as the nervous system: it can produce a matching antibody for each of the millions of different infectious agents as well as remember how to reproduce those decades later.

When the body is under a great deal of stress or in a diseased state, the immune system can become overloaded and the activity of these protector cells can slow down. This is often compounded by medical treatments – such as chemotherapy in the case of cancer – which further weakens the immune system. A weakened immune system is less capable of preventing cancerous cells and infections from attacking and spreading throughout the body.

It is very important to optimise the immune system and NK cell activity during disease prevention and treatment. As these cells comprise 15% of the body's white blood cells, they are considered the 'elite troops' of the immune system and any rise in activity will greatly increase the chances of a rapid recovery. This is also why research on immunnomodulators often focus on this single parameter of NK cell activity – it is easy to measure in a laboratory using a 51 Cr-release assay and it gives a good indication or 'snap shot' of the overall health and strength of the immune system. Most research into BioBran MGN-3 therefore involves extensive testing on NK cell activity. BioBran MGN-3 intrigues physicians around the whole world because it not only stimulates NK cell activity with more than 300%, but also T cell and B cell activity with 250% and 200% respectively, without toxicity or other adverse side effects (unlike the synthetic cytokines currently being used by oncologists, such as interleukin-2 and other (toxic) substances).

Research has shown that, provided BioBran MGN-3 is regularly included in a healthy daily diet, stimulation of the immune system does not need to decrease over time. This lack of hypo-responsiveness with prolonged use is exceptionally rare in immunomodulatory substances and means that BioBran MGN-3 will remain effective with long-term use. NK cell activity usually peaks around 1 to 2 months on a high dose, after which it can be maintained at an adjusted dosage.

The ability to enhance the immune system makes BioBran MGN-3 an important food supplement in a variety of situations. Please note that most of the research has been conducted in relation to cancer and that more research must be conducted on viral infections, bacterial infections and diabetes.

General health maintenance

Even in healthy people, BioBran MGN-3 can strengthen the immune system by stimulating white blood cell activity, which in turn increases immunity and the body's ability to fight infections and abnormal cells before they have a chance to spread.

Cancer

BioBran MGN-3 increases survival chances by stimulating the activity of NK cells and promoting the rejection of abnormal cells. It also enhances quality of life for those on chemotherapy and hormone therapy due to its ability to alleviate the side effects of medications used during these treatments (e.g. as nausea or hair loss). Cancers of the blood, such as leukaemia or multiple myeloma, show the best benefits and good results have also been seen in other forms of cancer such as lymphoma, ovarian, prostate and breast cancer.

It is important to note that MGN-3 is best used in combination with conventional cancer treatments such as chemotherapy or surgery. These treatments drastically reduce the number of cancer cells in the body while BioBran MGN-3 helps the body destroy or manage the rest. Most of the research into the benefits of BioBran MGN-3 arabinoxylan on cancer has been conducted in conjunction with conventional cancer treatments.

Viral Infections

BioBran MGN-3 has the ability to improve the immunological parameters in patients with HIV, AIDS and Hepatitis B and C (Interferon-Gamma production, GOT, GPT and Gamma GPT). Laboratory research has revealed that it can inhibit the replication of the HIV virus without toxicity. Once again, BioBran MGN-3 must be used in conjunction with conventional therapies.

Bacterial Infections

For bacterial infections such as colds, fevers and food poisoning, BioBran MGN-3 can help strengthen the immune system when used together with conventional treatments. BioBran MGN-3 has been proven to fight bacterial infections by stimulating the immune system.

Diabetes

BioBran MGN-3 has the ability to lower blood sugar levels, although it is not a replacement for insulin or glucose monitoring. Further research is certainly needed in this area.

Is all this supported by clinical trials?

Unlike other natural supplements, extensive clinical research has been done on MGN-3 arabinoxylan – including human trials – the results of which have been published in leading medical journals. The research took place at UCLA/DREW University in the United States and various universities and medical research institutes in Japan, including Chiba University, Kobe Women's College, Jichi Medical School, Nippon University, Kyushu University, Nagoya University, Kyoto University, Toyama Medical University and Kawasaki Medical University.

The main researcher of BioBran MGN-3 is and remains Dr Mamdooh Ghoneum, a professor at the Department of Immunology at Drew University of Medicine and Science in the United States. The doctor is now an internationally renowned authority in the field of cancer immunology therapy received a PhD from the University of Tokyo in radioimmunology and completed his postdoctoral work in immunology at UCLA. Over the past twenty years he has researched various substances that can enhance the immune system, but says that BioBran MGN-3 is the most effective immune complex he has ever tested. He was so impressed with the results that he devoted all of his research efforts to treatments using this compound.

Although research on the immune response to BioBran MGN-3 arabinoxylan has been positive for diseases ranging from cancer and diabetes to viral infections such as AIDS and Hepatitis B and C, there is clearly a need for larger scale clinical in vitro research, including double-blind trials, to determine exactly how an increase in immune response (particularly NK cell activity) can be translated into clear recovery and survival statistics for the aforementioned disease. More tests are being planned around whole world and any new results will appear in the news section.

Does BioBran MGN-3 have any toxicity or side-effects?

No. BioBran MGN-3 arabinoxylan is a natural product with no adverse or toxic side-effects; this has been verified by blood tests and research into liver and kidney function in people that have taken high doses of this substance over several months.

Although mushroom enzymes are used during production, no mushroom content can be found in the final product, which means that most people with a mushroom allergy can take this supplement without experiencing an allergic reaction. This substance has been authorized by the Japanese Health Food and Nutrition Food Association and has passed a strict evaluation under the supervision of the Ministry of Health and Welfare.

How much BioBran MGN-3 should I take and when?

Because the body does not build up resistance to BioBran MGN-3 over time, this food supplement can be taken safely and effectively for a prolonged period.

Most research into BioBran MGN-3 was conducted using 30to 45mg/kg/day in separate doses taken with meals and can ultimately be maintained at a dose of 15mg/kg/day. Dr Ghoneum recommends a dosage of at least 500mg per day to maintain good health. For diabetes, hepatitis B, hepatitis C and other infections he recommends a dose of 1000mg per day. For cancer and AIDS he recommends 3grams per day for one month and then 1gram per day. BioBran must always be taken after meals (preferably 30 minutes later) while larger daily intakes must be divided into three portions and taken after breakfast, lunch and dinner. If the person taking the supplement is very ill, the dose can be maintained at 3 grams per day for an extended period.

In order to maintain good health, we always recommend you inform your doctor that you are taking this supplement so he or she can integrate it into your treatment plan. As previously mentioned, BioBran MGN-3 is very effective for late-stage cancers when used in conjunction with conventional treatments such as surgery and/or chemotherapy (during which most of the tumour was removed) while increased NK cell activity maintains the rest.

IMUPROS™

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to IMUPROS™ produced by medpro Holland B.V. This combination product is manufactured in Holland as a food supplement, and is a natural remedy primarily for maintaining prostate health and can be used as a complementary medicinal preventative for hyperplasia of the prostate and prostate cancer.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- IMUPROS contains only the components listed on the label and no synthetic additives.
- IMUPROS can be used as a preventative against prostate diseases and in the treatment of prostatitis and prostate cancer.
- IMUPROS, in combination with ProstaSol, Biobran, and Curcumin combi extra forte, is also used by doctors in our network in the prevention of micro-metastasis due to potential spread of cancer cells during biopsies (removal of tissue) and in conjunction with the transurethral resection of the prostate (TURP).
- IMUPROS, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

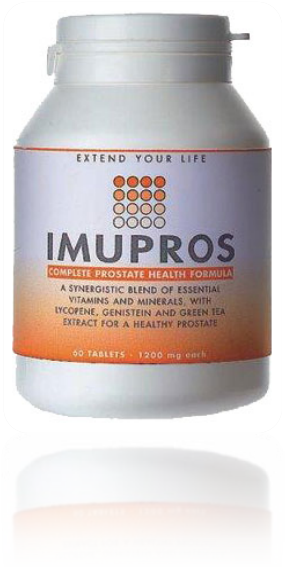
Although there are no so-called placebo-controlled, double-blind studies in conjunction with this product and its application in treatment of patients with prostate diseases (incidentally, this is often the case with nutritional supplements, as such studies are unnecessary and frequently impossible), there are well-founded studies as to the effectiveness of IMUPROS in connection with prostate diseases, including two clinical studies wherein IMUPROS was used to treat patients with prostate cancer in combination with ProstaSol, Biobran, and Curcumin. These studies show a PSA reduction, a decrease in joint pain, and an inhibition and reduction of tumor volume in patients with prostate cancer at the stage of castration resistance.

If you decide to include IMUPROS as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449



IMUPROS™ is an orthomolecular combination product consisting of various extracts from various homoeopathic plants and of select vitamins and minerals, so that the individual ingredients all come exclusively from natural sources. The product helps maintain good prostate and bladder function and prevents prostate and bladder diseases.

One tablet of IMUPROS (1200 mg) contains the following ingredients:

- Green tea extract (a source of epigallocatechin gallate)
- Soy extract (a source of genistein)
- Soy extract (a source of genistein)
- Tomato extract (a source of lycopene) C, E, D and the minerals calcium, selenium, and zinc

In the Netherlands, IMUPROS is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals.

A specific production process makes certain that the individual ingredients in the tablets do not chemically react with one another. The individual ingredients are packed in various "time release" vessels and are released at different times into the gastro-intestinal system. In this way the release of individual ingredients into the bloodstream is optimized and the so-called bioavailability is improved. Another advantage of the product that is also worth mentioning is that it enables a drastic reduction in the daily dosage of tablets or capsules for the prevention and complementary treatment of prostate diseases. Whereas the ingredients outlined above formerly had to be individually taken in the form of 20-30 tablets or capsules daily, IMUPROS provides a similar effect in the easy, tolerable form of only three tablets per day.

IMUPROS is frequently used by patients with prostate diseases (prostatitis, hyperplasia of the prostate, and prostate cancer), as a general complementary medicinal measure, and as supplementary therapy alongside conventional treatment.

The following are some clinically proven effects of individual ingredients:

The pharmacological effectiveness of the individual ingredients in IMUPROS is widely known. In what follows, the scientifically proven effects of these individual ingredients will be addressed: tocopherolsuccinat (vitamin E), cholecalciferol (vitamin D), ascorbic acid (vitamin C), calcium, zinc, selenium (sodium selenite), genistein, lycopene, and epigallocatechin gallate:

<u>Vitamin E:</u>
This fat-soluble chemical substance helps to prevent prostate cancer. A very well-known study from Finland conducted by Heinonen et al. (J Nat'l Cancer Inst., 1998) shows that taking vitamin E reduces the frequency of prostate cancer by about 32% and the fatality rate due to prostate cancer to about 41%. In another study conducted by Fleschner et al. (J Urol, 1999), it was made clear that the growth rate of prostate cancer in animals was reduced by vitamin E. This very exciting finding as to the effectiveness of vitamin E in the context of prostate cancer has encouraged researchers around the world to look for more evidence of the protective effect of this vitamin. In the meantime, it is certainly to be recommended that both at-risk men and patients with prostate cancer should increase their daily intake of vitamin E so that they can take advantage of the preventative effect of this vitamin. Currently the recommended daily allowance is somewhere between 400 and 1,000 IU of so-called tocopherole. IMUPROS delivers between 500 and 1,000 IU of natural vitamin E in the recommended daily dosage of 3-6 tablets.

Vitamin D:

Epidemiological studies have shown that vitamin D (cholecalciferol) plays a very important role in the prevention of prostate cancer. In the USA, for example, it was noticed that the frequency of prostate cancer in the northern states was much higher than it was down south. Epidemiologists wondered why. Dr. Gary Schwartz of the University of Miami researched the connection between prostate cancer frequency and the amount of ultraviolet light (Ann Epidemiol 1997), or sunshine, the men in the different regions received. The result was baffling: the mortality rate due to prostate cancer was the highest in the places where the sun shone the least. We know today that small amounts of ultraviolet rays reduce the amount of our own body's' vitamin D synthesis of 7-dehydrocholesterol. The result is that less vitamin D reaches the liver and kidneys, where the active form of the vitamin, namely dihydroxycholecalciferol, is made. The consequence is less active vitamin D on hand, which it seems to play a role in the development of prostate cancer. Dr. Feldman of Stanford University and Dr. Miller of the University of Colorado have researched this connection in more depth and have shown that vitamin D can attach itself to certain protein receptors in prostate cells, reducing cell division and thereby decreasing the growth of both benign and malignant prostate tissue. Subsequently Dr. Feldman, along with Gross et al. (J Urol, 1998) and Koike et al. (Porc Annu Meet Am Assoc Cancer res, 1997) have been able to demonstrate in research on patients that 1.25 dihydroxycholecalciferol and newer vitamin E analogues (such as Rocaltrol) effectively reduce the growth of prostate cancer.

Vitamin C:

This vitamin is known for its significant antioxidant effects, which are best used in conjunction with vitamin E. It is generally recommended that 1,000 mg vitamin C be taken after eating in order to suppress the peroxide formation that arises from burning fat. Vitamin C reduces the mortality rate in coronary vascular diseases and prolongs life expectancy in patients with coronary sclerosis (British Medical Journal, 1997). Taking more than 500 mg of vitamin c per day is also known to reduce the risk of bladder cancer by about 60% and can significantly reduce the risk of breast cancer. An experimental study (Cancer Letters, 1997) shows that the life expectancy of animals with malignant tumors is significantly extended with vitamin C supplementation, and complete tumor retrogression occurred in 16.8% of the animals. The recommended daily dosage of IMURPOS follows the RDA of these studies, delivering 750 mg of vitamin C for men who want to prevent prostate cancer and 1,500 mg for men who have prostate cancer.

Calcium:

Calcium absorption must be taken into consideration with vitamin D. Excessive calcium intake (>2,000 mg per day) reduces the conversion of vitamin D into the biologically active 1.25 dihydroxycholecalciferol. Therefore, excessive calcium intake can cancel out the preventative effects of vitamin D on prostate cancer. A very expensive study conducted at Harvard University (Health Professionals Follow-up Study), which is universally recognized, even shows that calcium intake of more than 2,000 mg per day can increase the risk of prostate cancer. As with just about every scientific claim, there are varying opinions as to whether an increase in calcium intake leads to prostate cancer. Dr. Richard Hayes of the National Cancer Institute, for instance, saw no effect of calcium intake on the progression of prostate cancer in his study. Everyone agrees, however, that most men do not get enough calcium. The RDA is somewhere around 1,000 mg for healthy men between 19-25 years old. IMUPROS contains about 470 mg of calcium in the RDA for men with prostate cancer and is therefore far from the critical dosage per day.

Zinc:

This trace element supports a whole range of immune functions and a deficiency in zinc can potentially increase susceptibility to cancer in general. Zinc is necessary for the normal function of many enzymes, especially those which have an antioxidant effect. When zinc levels drop in the blood stream, the NK cells, T helper cells, and immune system macrophages are suppressed. Feng et al. have been able to show (Mol Urol, 2000), that high intracellular zinc levels can cause apoptosis in

prostate cancer cells. Liang et al. (Prostate, 1999), and Iguchi et al. (Eur J Biochem, 1998) have furthermore shown that zinc can inhibit cancer cell growth in the prostate by influencing the cell cycle, and that on top of this, tumor progression and metastasis go hand-in-hand with a drop in the ability to retain zinc in prostate cells. IMUPROS contains 50 mg of zinc and ensures the necessary amount of this trace element.

Selenium:

This mineral is just as effective at preventing prostate cancer as vitamin E is. In the globally recognized study conducted by Dr. Larry Clark (Br J Urol, 1998) of the University of Arizona, USA, research was conducted to see whether selenium had a preventative effect against skin cancer. 1,300 men took part in the study. Half of them received 200 micrograms of selenium per day, while the other half received a placebo. The study was conducted over the course of eight years. At the end of the study, Dr. Clark concluded that selenium had no preventative effect on skin cancer, which is widespread in Arizona. He did, however, discover that the men in the group which took selenium had a 50% reduction in the occurrence of prostate cancer. Moreover, the occurrence of lung and gastrointestinal cancers were also about half as great in the group which took selenium. Dr. Willett of Harvard University (J Natl. Cancer Inst, 1998) studied the amount of selenium in the bloodstream of a group of men and concluded that lower selenium levels were connected to a higher risk of prostate cancer. This study is also supported by Dr. Giovannucci (Lancet, 1998). More recently, the world-famous National Cancer Institute (NCI) in the USA has organized a study which examines the preventative effects of selenium and vitamin E on prostate cancer in 32,000 men. We do not yet know exactly how selenium prevents prostate cancer. A useful hypothesis is the proven effect of selenium on the enzyme glutathione peroxidase. Selenium activates this enzyme, which possesses a very strong antioxidant property. Selenium is to be found in various cereals and garlic, especially when these are grown in selenium-rich soil. However, it is often not enough for prostate cancer patients to get selenium from food sources. As a preventative measure for prostate cancer and as a complementary medicine in the treatment of prostate cancer, the daily dosage should be somewhere between 400 and 800 micrograms.

Genistein:

This is a plant source of estrogen, an especially high concentration of which is found in soy and which is well known for its anti-osteoporosis and antioxidant effects. As an isoflavone, genistein also possesses the ability to help reduce cholesterol and is used as a preventative measure against cancers which are connected to hormones, such as breast cancer, cancer of the endometrium (innermost layer of the uterus), and prostate cancer. Higher doses reduce the growth of hormonal-dependent cancer types and is cytotoxic (destroys cancer cells). These properties were what caused the National Cancer Institute in the USA to systematically research whether genistein could be used to fight cancer. A comparison of the amount of soy used in Japan with that of a Western diet reveals that the Japanese consume about 50 mg genistein per day, whereas the amount in Western diets is a meager 2 mg per day. Epidemiological research agrees that this lower daily intake of phytoestrogen from the soy plant is one of the main reasons that the frequency of breast and prostate cancers is 20 times as high in Western Europe. In studies using cell cultures of human prostate cancer, Geller et al. (Prostate, 1998) showed that genistein suppresses the enzyme tyrosine kinase. This enzyme normally serves to increase growth of prostate cancer cells. Further biological effects of genistein have been seen in animal tests. From these it has been shown that genistein also possesses significant anti-angiogenesis properties, that is, it can prevent the development of new vessels in tumor tissue, thereby in effect starving it. IMUPROS contains 150 mg of genistein in the RDA for men with prostate cancer. The preventative dosage of IMUPROS delivers about 75 mg of genistein per day, which is a little more than that contained in Asian diets.

Lycopene:

This carotenoid (which gives tomatoes their red pigment) has extremely strong antioxidant and anticancer properties. Dr. Giovannucci of Harvard University is purportedly the founder of lycopene

research in conjunction with prostate cancer. He conducted a large study on 47,894 men which looked at the connection between the intake of various carotenoids and retinol and the risk of getting prostate cancer (J Natl Cancer Inst, 1995). He concluded that lycopene intake sinks the risk. Men who consumed tomatoes and tomato products a number of times during the course of a week had a 41% lower risk of getting prostate cancer. More recent research even shows that lycopene can also be used therapeutically. Lycopene, it would seem, is the most dominant carotenoid in the blood and is not converted into vitamin A. It makes up about 50% of all the carotenoids in the blood and the highest concentration seems to be in the prostate, since a slightly higher level is detectable there than in blood. Recently Kucuk et al. (Urology, 2001) published findings that, in men with localized prostate cancer, the intake of 30 mg of lycopene per day just prior to a radical operation significantly reduces PSA before the operation starts and the malignancy of the tumor tissue in the removed prostate is lower. IMUPROS contains 30 mg of lycopene as a therapeutic dosage for patients who already have prostate cancer. It is recommended that about 15 mg of IMUPROS lycopene be taken per day for prevention.

Epigallocatechin gallate:

This highly effective antioxidant is a polyphenol (also known as catechin) which comes from green tea (*camellia sinensis*). Epigallocatechin gallate (EGKG) is the most important of the four catechins in green tea for patients with prostate cancer. EGKG inhibits the enzyme urokinase (Jankun et al.; Nature, 1997), which is found in many kinds of human cancers and which assists in the process of metastasis. Urokinase triggers the basement membrane of cell connections and thereby enables the infiltration of cancer cells into foreign tissues, thus causing metastasis (Ennis et al.; Proc Annu Meet Am Cancer Res, 1997). EGKG is also an excellent inhibitor of 5-alpha-reductase, the enzyme which causes the conversion of testosterone into biologically active dihydrotestosterone, thereby opportunely intervening in the androgen regulation of prostate cells. Consumption of green tea is widespread in Japan and China, but not so much in the West. A therapeutic dose of IMUPROS delivers 350 mg of EGKG per day, which amounts to about 30 cups of green tea.

Summary:

IMUPROS is an orthomolecular combination product made from various medicinal plants and of select vitamins, minerals, and trace elements which help maintain healthy prostate function and prevent prostate diseases.

IMUPROS has the following effects:

- Neutralizes free radicals by way of an antioxidant effect on prostate tissue
- Optimizes cellular renewal, reduces inflammation and risk of prostate infection, and improves urinary flow in old age
- Prevents hyperplasia of the prostate and development of cancer in the prostate gland
- Strengthens the immune system (cellular resistance)

The RDA should be somewhere between 1-3 tablets. Side effects are not expected to occur at this dosage. If needed, the dosage may be increased for a short period of time.

Aeskulap-Modified-Citrus-Pectin (AMCP)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to Aeskulap-Modified-Citrus-Pectin (AMCP) produced by Aeskulap-International AG's compounding contract pharmacy in Switzerland. This commercially available supplement has been shown to inhibit cancer cell metastasis, lower cholesterol, and remove toxic metals from the human body.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- Aeskulap-Modified-Citrus-Pectin contains only components as listed on the label.
- Aeskulap-Modified-Citrus-Pectin can be used in conjunction with conventional treatments for cancer, for example in the perioperative setting with radical oncological surgery, prior, during and after radiation treatment, and with chemotherapy.
- Aeskulap-Modified-Citrus-Pectin is an integral part of our treatment program for metastatic breast- and prostate cancer. In this setting, the doctors of our network combine AMCP with ProstaSol, Indole-3-Carbinol, Curcumin combi extra forte, IMUPROS, IMUSAN and BioBran for added benefit.
- Aeskulap-Modified-Citrus-Pectin, used at the prescribed dosage, is usually well tolerated.

Although there are no so-called placebo controlled, double-blind studies for this product and its application in the treatment of patients with breast- and prostate cancer, there are well-founded preclinical studies, as well as clinical studies with modified citrus pectin demonstrating the effectiveness of this compound in reducing metastases.

If you decide to include Aeskulap-Modified-Citrus-Pectin as a complementary oncological treatment, you may want to take advantage of our Aeskulap Patient Care Service and consult our expert doctors with any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne,
Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

Aeskulap-Modified-Citrus-Pectin (AMCP)

Aeskulap-Modified-Citrus-Pectin (AMCP) contains fractionated, heat- and pH modified pectin, a complex polysaccharide obtained from the peel and pulp of citrus fruits. AMCP is rich in galactoside residues, in particular β-galactose, known to have strong affinity for certain types of cancer cells.

The galactoside-containing carbohydrate side chains of AMCP can mimic or compete with natural ligand(s) of the so called tumour galactoside-binding protein, galectin-3, found on cancer cells, affecting cellular interactions relevant for metastasis.

AMCP also exerts immune stimulating effects in humans, increasing the activities of cytotoxic T cells, B cells and NK cells.

In search of naturally occurring substances useful in the treatment of cancer metastasis, modified citrus pectin (MCP) has emerged as a promising anti-metastatic drug candidate. MCP has been found to be effective in vitro and in vivo against various cancer entities, such as prostate- and breast carcinoma, melanoma, colon carcinoma, multiple myeloma, and hemangiosarcoma.

Prostate Cancer

Dr Pienta and his group were the first to examine MCP's effectiveness against prostate cancer and its metastasis. They used a Dunning rat model. The animals were injected with prostate cancer cell lines and given drinking water which contained various MCP concentrations. While this oral administration of MCP did not affect primary tumour growth, it significantly reduced metastases when compared with the control animals. Later, Dr Strum and his colleagues examined the effect of MCP on prostate specific antigen (PSA) doubling time in seven prostate cancer patients administering MCP orally at a dosage of 15 grams per day. PSA doubling time reflects the speed of cancer growth, and in four of the seven patients PSA doubling time exhibited more than 30% lengthening, which represents a decrease in the cancer growth rate.

Breast Cancer

As seen with prostate cancer and other cancer entities, research demonstrates that metastases of breast cancer cell lines also require adhesion and aggregation of the metastatic cancer cells to tissue endothelium to facilitate invasion of other tissue. The anti-adhesive efficacy of modified citrus pectin was examined in an in-vitro model utilizing breast carcinoma cell lines T-47D and MCF-7. The adhesion of these malignant cells to blood vessel endothelia was markedly blocked by MCP, thus inhibiting the metastatic process. In a more recent human study, the galectin-3 expression was examined in 27 patients suffering from invasive breast cancer. This study revealed that more aggressive histologic grades of breast cancer exhibited decreased galectin-3 expression, likely reflecting increased cancer cell motility and metastatic potential.

Melanoma

Dr Platt and Dr Raz examined the process of metastasis in a B16-F1 tumour model in mice. This melanoma of this cell line is highly aggressive and causes reliably metastases in the test mouse. Using this system, they determined that MCP significantly decreased tumour metastases to the lung. In comparison to regular citrus pectin, the administration of MCP resulted in a more than 90% decrease in tumour metastases.

Safety and Side Effects

Because MCP is a soluble fibre, oral administration of modified citrus pectin is unlikely to result in any gastric intolerance, even at higher doses. No adverse reactions of MCP have been recorded in the scientific literature. As with any dietary fibre at high doses, MCP may result in mild cases of loose stool, which is usually self-limiting and does not warrant discontinuation of treatment.

Indol-3-Carbinol

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to Indol-3-Carbinol™ produced by medpro Holland B.V. This combination product is produced in Holland as a food supplement and has been effectively used as a natural remedy in the complementary medicinal treatment of patients with breast, cervical, and prostate cancers.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- Indol-3-Carbinol contains only the components listed on the label and no synthetic additives.
- Indol-3-Carbinol can be used either parallel to conventional breast- and prostate cancer treatments, or as a complementary oncological therapy for these diseases (for example, as co-medication with radical operations, parallel to radiation, and during and after chemotherapy).
- Indol-3-Carbinol is an integral part of our treatment program for secondary prevention of breast cancer relapse, whether or not the primary tumour was hormonally dependent.
- In combination with Curcumin combi extra forte and BioBran, Indol-3-Carbinol is also used by doctors in our network in the prevention of micro-metastasis due to potential spread of cancer cells during biopsies (removal of tissue) of breast- and prostate tumours.
- Indol-3-Carbinol, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in treatment of patients with breast and prostate cancers, there are well-founded pre-clinical studies, as well as one clinical study, as to the effectiveness of Indol-3-Carbinol. These studies show a significant reduction in the growth of hormone-dependent and hormone-independent cancer cells in the laboratory, as well as positive clinical results of Indol-3-Carbinol in patients with breast-, cervical- and prostate cancer.

If you decide to include Indol-3-Carbinol as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

Indol-3-Carbinol

Indol-3-Carbinol contains the following ingredients:
Indol-3-carbinol, a plant-based substance from the indole group, is extracted from a number of cruciferous plants, including resveratrol and quercetin, a polyphenol and flavonoid, extracted from Japanese knotweed (*Polygonum cuspidatum).*

In the Netherlands, Indol-3-Carbinol is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals. Indol-3-Carbinol is often used by patients who have breast cancer and by patients who have cervical cancer. It is also used as complementary therapy for prostate cancer.

The following are some clinically proven effects of individual ingredients:

Indol-3-Carbinol (I-3-C) is extracted from various cruciferous vegetables such as cauliflower, kale, Brussels sprouts, and broccoli; resveratrol and quercetin are best obtained from grapes or Japanese knotweed *(polygonum cuspidatum).* The effective combination of these two substances helps maintain healthy cellular function.

Only a third of all breast cancer cases are oestrogen-receptor positive, and only about half of those respond to the oestrogen-blocking tamoxifen and Even if the patient responds initially, a tamoxifen resistance eventually develops. Two thirds of all breast cancer cases can't even be treated with tamoxifen to start with. In such cases, the current preferred treatment is broad-spectrum chemotherapy. Although this toxic therapy is often effective, it involves many side effects which influence the patient's quality of life and which make expensive follow-up treatments necessary. I-3-C does not have this disadvantage and works with tamoxifen and chemotherapy synergistically – which makes it particularly suited for complementary therapy with breast cancer.

I-3-C and its metabolite diindolylmethane (also called DIM) are especially popular due to their antioxidant, detoxifying, and oestrogen-modulatory effect and their capacity to inhibit pathological cell growth. Nascent research results show that I-3-C and DIM work synergistically so that, for example, growth of breast, prostate, and cervical cancer cells slow down or stop entirely. I-3-C also slows down a gene associated with cancer which encodes for an important enzyme called Cdk6-Kinase. DIM can't do this.

I-3-C also prevents the proliferation of breast cancer cells which are not oestrogen dependent. Here is a significant advantage over the conventionally used tamoxifen in cancer therapy, which can be effective only in cases of breast cancer which are oestrogen dependent. Researchers at the University of Los Angeles have shown that I-C-3 reduced the growth of oestrogen receptors in positive breast cancer cells by about 90%, whereas tamoxifen only reduced it by about 60%.

Italian researchers have recently created a synthetic product from I-C-3 that has twice as strong an effect on oestrogen-receptor-negative breast cancer cells. Just as with I-C-3, it also inhibits the same enzyme (Cdk6 Kinase). The researchers believe that the tetramer they developed can be further developed into a medication. Initial results show that normal cells are not influenced by this substance.

Japanese knotweed *(Polygonum cuspidatum)*

Resveratrol is advantageously obtained from Japanese knotweed *(Polygonum cuspidatum)*, which is considered to be one of the best natural sources of this phytoalexin, which has become famous in medicine for its antioxidant, anti-inflammatory, and anti-carcinogenic properties. Diverse lab tests and animal experiments with resveratrol show the positive effects of this substance on cancer, autoimmune disorders, arteriosclerosis, Alzheimer's, cardiac diseases, and arthritis.

Polygonum cuspidatum

Polyphenols are also known for their high redox potential, which makes them ideal radical inhibitors. Just like coenzyme Q10, resveratrol is purported to directly seal over the mitochondria of the so-called proton leak and to neutralize reactive oxygen-based free radicals. Moreover, it has the capacity to stimulate a number of the body's own different antioxidant enzyme systems (for example, the superoxide dismutase and some catalases). In addition, resveratrol prevents lipid peroxidation, namely the oxidation of LDL-Cholesterol, which in its oxidized form can be stored in the vascular wall and prepare the way for the development of arteriosclerosis. Resveratrol prevents this process and therefore counteracts the calcification of the blood vessels.

Moreover, a significant neuron-protective effect is attributed to resveratrol, so that it is hoped that it can one day be used in the treatment of Alzheimer patients.

The positive effects of resveratrol on the most diverse disorders can also be at least partially explained by its pronounced anti-inflammatory effects. The is allows resveratrol to inhibit two enzyme systems in the body at the same time, namely the Cyclooxygenase 2 and the intricate nitrogen monoxide synthetase, both of which play an essential role in inflammatory reaction. A number of studies have shown in the last few years that chronic inflammations in particular are extremely important for the pathogenesis of many diseases, from the development of arteriosclerosis to neuron degeneration to the formation of cancer. As early as in the 90‘s, it was demonstrated that resveratrol possesses an anti-cancer effect at all three levels of the disease: it prevents cancer, reduces its growth, and reduces metastasis. These effects of resveratrol are based upon the ability to send the already existing cancer cells into programmed cell death (apoptosis) and to increase the effectiveness of the toxic cellular effects of conventional chemotherapy or radiation. These charac-

teristics could increase the effectiveness of such treatments and counteract therapy resistance, which was often observed.

Quercetin is also extracted from the so-called secondary plant matter (flavonoid) *Polygonum cuspidatum*. This substance has impressive antioxidant, anti-inflammatory, and immune-modulatory effects and regulates the cell cycle. Quercetin is virtually non-toxic when taken orally or intravenously. Studies from the famous Mayo Clinic and the Dana Farber Cancer Institute at Harvard University in the USA have shown that Quercetin blocks the growth of androgen-sensitive and hormone-resistant prostate cancer cells, making them sensitive to heat; the substance is therefore suitable to support hyperthermia treatments. Quercetin is, however, not only applicable as a treatment and prevention substance in prostate cancer. It is also applicable in conjunction with breast cancer, colon cancer, lung cancer, and several other types of cancer.

Summary:

I-C-3 is used in the prevention of breast cancer, colon cancer, and other types of cancer. The National Institute of Health in the USA has identified I-C-3 as a potential preventative for various kinds of cancer and is making efforts to clinically prove this hypothesis.

I-C-3 is suitable for complementary oncological treatment of cervical, breast, and prostate cancers.

I-C-3 is also suitable in the treatment of fibromyalgia, with larynx tumours, and in respiratory areas (laryngeal and respiratory papillomatoses) and systemic lupus erythematosus (SLE).

Additionally, a few doctors use I-C-3 to balance hormone levels, to detoxify the liver and gastrointestinal tract, and to support the immune system.

IMUSAN™

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to IMUSAN™ produced by medpro Holland B.V. This combination product is manufactured in Holland as a food supplement and has been effectively used as a natural remedy in the complementary medicinal treatment of patients with malignant diseases and immunity deficiencies.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- IMUSAN contains only the components listed on the label and no synthetic additives.
- IMUSAN can be used in conjunction with conventional treatments for cancer, or alone when oncological therapy fails or is not tolerated. It can also be used as a general immunity booster (for instance, as concurrent medicine with radical operations, chemotherapy, post radiation).
- IMUSAN, in combination with Biobran, is also used by doctors in our network in the prevention of micro-metastasis due to potential spread of cancer cells during biopsies (removal of tissue from cancerous tumours).
- IMUSAN, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its clinical application in cancer patients, there are well-founded pre-clinical studies, as well as one clinical study, as to the effectiveness of IMUSAN. These studies show a significant reduction in the growth of various cancers, both in the laboratory and in clinical practice.

If you decide to include IMUSAN as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

IMUSAN™

IMUSAN™ is a purely plant-based product created from various Asian and European medicinal plants. It is produced according to traditional Chinese medicine. It contains the following medicinal plants:

Agrimony *(Agrimonia pilosa);* Round-leaved Winter-green *(Pyrola rotun-difolia);* Corydalis rhizome *(Corydalis yanhusuo)*; Reishi *(Ganoderma Lucidum);* Red Spider Lily *(Lycoris radiata);* Patrinia *(Patrinia heterophylla);* Stephania herb *(Stephania sinica);* Rabdosia (*Rabdosia rubescens);* Desert broomrape *(Cistanche deserticola);* Ginseng *(Panax ginseng);* Shiny-leaf prickly-ash *(Zanthoxylum nitidum)* and Liquorice *(Glycyrrhiza glabra).*

In the Netherlands, IMUSAN is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals. Due to its various biological properties, IMUSAN is often used by patients who have general immunity deficiencies or cancer. It is also used on its own as a complementary oncological measure and in complementary therapy before, during, and after toxic procedures such as chemotherapy and radiation.

The following are some clinically proven effects of individual ingredients:

Agrimonia pilosa

Hairy Agrimony *(Agrimonia pilosa)* belongs to a plant genus which is a subfamily of the rosoideae within the rose family (Rosaceae). The agrimony species is widespread in Europe and Asia and reaches as far as Sri Lanka and Java. A few types are also found in North America and Mexico. As a medicinal plant, *Agrimonia pilosa* has been well-known for an especially long time for its inflammation-reducing properties. Alcoholic extracts of the plant can also quickly reduce the strongest inflammation reaction. Extracts from the stem and leaves also have analgesic, antibacterial, and antipyretic effects.

Agrimonia pilosa is therefore used frequently in cases of abdominal pain, sore throat, and headaches. Extracts from the leaves have a high amount of agrimony, which increases heart function, decreases blood sugar levels, and increases blood pressure. The leaves of the plant are also rich in vitamin K, which is why *Agrimonia pilosa* is also used to support thrombus formation and haemostasis. Root extracts from the plant work as an astringent and diuretic and are used in the treatment of colds, tuberculosis, and diarrhoea.

Round-leaved wintergreen (Pyrola rotundifolia) is a plant from the subfamily of the wintergreen and monotropa hypopitys plants (Monotropoideae) in the heather family (Ericaceae). The leaves of this medicinal plant have anti-rheumatic, antiseptic, antispasmodic, astringent, cardiotonic, contraceptive, diuretic, sedative, and tonic effects.

Pyrola rotundifolia

Water extracts are used locally for skin diseases, but also gurgled in conjunction with throat conditions, as well as with ulcers in the mouth.

The extracts are also suitable for use in conjunction with treatments for carbuncles and painful swelling. Water extracts are also used to rinse inflamed eyes. The extract can be used internally to treat epilepsy and other illnesses of the central nervous system. *Pyrola rotundifolia* contains arbutin, a diuretic that possesses an antibacterial effect, which can be of use with urinary tract infections.

Corydalis rhizome *(Corydalis yanhusuo)*

Extracts of ***Corydalis yanhusuo; (Chinese name: Yan Hu Shuo)*** have been used for many centuries in traditional Chinese medicine. Alternative medicine has shown that various parts of the plant can have a positive effect on very different illnesses. For instance, some of these extracts are purported to have properties which improve blood and which ease almost every kind of pain, including cramps (spasms). Corydalis is therefore frequently used in the treatment of menstrual cramps and the pain they cause. It is also applicable for use with general stomach aches. The plant, and in particular the root extracts, contain various effective protoberberine type 1 and 2 alkaloids (for instance, coptisine, corydaline, palmatine), which are responsible for the analgesic, antispasmodic, and sedative effects. Furthermore, substances extracted from Corydalis are significantly anti-carcinogenic and have the capacity to minimize coughing, raise cardiac output, and inhibit high blood pressure.

Corydalis rhizome

As a result of the positive sedative effects of the aporphin-alkaloid "bulbocapnin", corydalis extract is also used in traditional Chinese medicine for the treatment of cramps such as muscle tremor and vestibular nystagmus. So it follows that patients who have Parkinson's and Meniere's diseases should also benefit from treatment using corydalis extract. Many studies are currently underway which look at the application of corydalis in conjunction with cancers, menstruation pain, high blood pressure, cramps, and as a natural painkiller.

Reishi *(Ganoderma lucidum)*

The reishi or lingzhi mushroom has been used for over 4,000 years in Chinese medicine. The ingredients within the fruit bodies of the mushroom, such as triterpenoids, sterols and various polysaccharides such as mannitol and coumarin are used in medicine. Furthermore, the mushrooms contain various trace elements, such as zinc, germanium, manganese, iron, copper, and even calcium. Recent research results show that reishi mushroom extract strengthens the immune system and also demonstrates immune modulating properties. The reishi has proven itself particularly useful in the treatment of prostate illnesses, since it inhibits prostate inflammation, thereby counteracting prostatitis. It also suppresses cell adhesion and cell migration in prostate cancer, thereby reducing tumour migration.

Reishi Colony

Individual reishi mushrooms

Red spider lily *(Lycoris radiata)*

Lycoris radiata

Lycoris radiata, also known as "red spider lily," belongs to the onion and tuber family, the amaryllidaceae. The plants get to be about 10 to 30 cm tall and are cultivated mostly in central and south Japan. Extracts of the tuber root are used in the treatment of swelling, ulcers, and nervous disorders in children. Contained within the flowers are two alkaloids which have an emetic and expectorant effect. Extracts from the shrubs are often used as an antidote to poison in traditional Chinese medicine. The flowers can also be made into a paste which can be applied to burns and open wounds. The anti-carcinogenic effect of the extract of lycoris radiata is due to various alkaloids, such as dehydrolycorine, bulbispermine, methylen-dioxylhomolycorine-N-oxide and dihydromethyl-hydroxy-phenanthridine, which have a very potent cytostatic and cytotoxic effect on different cancer cell cultures. Some of the alkaloids also have significant anti-malaria effects.

Patrinia *(Patrinia heterophylla)*

For hundreds of years, *patrinia heterophylla* has been used in traditional Chinese medicine for the treatment of menstrual pains, ulcer formation, liver inflammations (hepatitis), tonsillitis, and a few other medical problems. Recent research results have shown that extracts from this medicinal plant have very high anti-carcinogenic effects.

Patrinia heterophylla

Various triterpenes have been identified in Patrinia heterophylla as being the primary substances possessing an anti-carcinogenic effect. Also extracted from Patrinia heterophylla is an additional substance called isocoumarin glycosides, which demonstrates a significant capacity to fight cancer cells in the uterus. Various proteins and polysaccharides from this medicinal plant have been isolated which intervene in energy metabolism and in the signal transduction of cancer cells, reduce oxidative stress, and can trigger apoptosis (programmed cell death).

Stephania herb *(Stephania sinica)*

Stephania sinica belongs to the moon seed family (*menispermaceae*), which is native to Southeast Asia, Africa, and Australia. Stephania (*menispermaceae*) is widespread and has been used in folk medicine for centuries to counteract various illnesses, such as asthma, tuberculosis, diarrhoea, diabetes mellitus, malaria, and cancer.

Stephania sinica

More than 150 alkaloids, flavourings, lignans, steroids, terpenoids, and coumarin have been isolated in the stephania sinica herb. Many of these substances have biological activity. Anti-malaria, antiviral, antibacterial, anti-inflammatory, anti-pain, immune-modulatory, and anti-carcinogenic effects have all been attributed to it. That is why it is known that dehydrocrebanine and crebanine, two of the isolated ingredients in stephania sinica, have a significant inhibitory effect in the growth of stomach carcinoma cells, leukaemia cells, and liver cancer cells.

Rabdosia *(Rabdosia rubescens)*

The two most important properties of this fast-growing, terpenoid-rich labiate are oridonin and rubescensin A and B, both of which are known for their cancer-inhibiting effects. Extracts made from the entire plant improve digestion, soothe inflammation, and are used primarily in China in the prevention of breast cancer and prostate carcinoma. Laboratory results show that the positive effects on breast and prostate cancer are not due to a hormonal effect, but rather to the direct influence of the cell cycle and apoptosis (direction of programmed cell death).

Rabdosia rubescens

Recent studies have also shown that oridonin inhibits the growth of primary bone cancers (multiple myeloma) and various types of leukaemia by initiating apoptosis. The anti-carcinogenic effect of oridonin is also free of side effects, since healthy cells are not influenced. *Rabdosia rubescens* also reduces the blood supply to transplanted breast tumours and thereby inhibits the growth of those tumours. In prostate cancer, the effects of *Rabdosia rubescens* also inhibit the development of so-called androgen independent cancer cells, which almost always develop after prolonged anti-hormonal treatment. In this way, the effectiveness of conventional anti-hormonal therapy for prostate cancer is extended by way of *Rabdosia rubescens*. A study using 115 patients with inoperable oesophageal cancer showed that patients who received *Rabdosia Rubescens* in conjunction with conventional therapy had a survival rate three times as high as patients in the comparison group, who only received chemotherapy.

Desert broomrape *(Cistanche deserticola)*

Desert broomrape (Chinese name: "Rou Cong Rong") is an albino parasitic plant that has been used as a tonic in traditional Chinese and Japanese medicine for about 1800 years. Modern pharmacological research has shown that *cistanche deserticola* possesses a broad spectrum of biological properties. That is why it is known to have significant hormone-regulatory, immune-modulatory, neuron-protective, anti-oxidant, anti-apoptotic, anti-inflammatory, and anti-nociceptive effects. Furthermore, extracts of cistanche counteract exhaustion and promote bone growth. The so-called phenylethanoids glycoside, acteoside, echinacoside and cistanoside in *cistanche deserticola* seem to be responsible for these effects.

Cistanche deserticola

Various animal experiments have shown that a polysaccharide from *cistanche deserticola* has immune modulatory effects which increase the phagozytose capacity of macrophages, thereby strengthening cellular defence. It has also been shown that acteoside from cistanche significantly increases the ability to swim in mice without causing muscular damage and without piling on lactate in muscles. *Cistanche deserticola* extracts appear to improve the muscles' ability to store energy. The same extract has also been observed to improve both learning and memory capacity in test animals, which also increases the growth of nerve tissue.

Although most of the pharmacological effects of cistanche extract have only been confirmed in lab and animal experiments, this medicinal plant is highly desirable and has been placed on the list of endangered species.

Ginseng *(Panax ginseng)*

Recently ginsenosid and saponin, the pharmacological properties in ginseng root, have been used in Europe, although the healing properties of the ginseng root in conjunction with numerous diseases have been long known primarily in China and other Asiatic countries. The substance saponin in particular inhibits prostate cancer cells and suppresses increase in the PSA value. It also has a positive influence on androgen receptors and on the enzyme 5-alpha-reduktase.

Ginseng Root

Ginsenoid supports normal programmed cell death (apoptosis) in prostate cells and reduces the activity of so-called Bcl-2 genes, which make cells invincible thereby causing and supporting cancer. Moreover, ginsenosid restricts the process of metastasis, decreases the development of cancer cells in other tissues, and possesses an anti-angiogenic effect which reduces new vessel formation in metastases and primary tumours, thereby restricting the blood flow to tumour tissue ("starvation of the tumour"). Recent research results have shown that ginseng also has a preventative effect against various kinds of cancer and ginsenoside has a significant anti-inflammatory effect in addition to its cancer-inhibiting effect.

Shiny-leaf prickly-ash *(Zanthoxylum nitidum)*

Zanthoxylum nitidum is a flowering plant in the citrus family, which primarily grows in Southeast Asia and northern Australia. The Chinese name is "liang mian zhen". Almost all zanthoxylum species are used medicinally. In India zanthoxylum is used, for example, to counteract toothache and fever and to fight coughing, vomiting, and diarrhoea. In China, individual zanthoxylum species are also used to fight pain, as well as to treat stomach ailments and cancers. Nitidine, a substance in shiny-leaf prickly-ash, has been identified as effective in fighting cancer. Additionally, this substance has also been used effectively in conjunction with AIDS and malaria agents. Particular plant extracts from zanthoxylum also have antibacterial effects.

Zanthoxylum nitidum

Liquorice *(Glycyrrhiza glabra)*

Liquorice extracts contain various saponins of glycyrretic acids, which function as expectorants and mucolytic agents and possess antibacterial and antimicrobial properties.

Glycyrrhiza glabra

It has also been experimentally and clinically shown that extracts from liquorice have anti-inflammatory, cramp-suppressive, and antiviral effects. An American study published in the “Journal of Clinical Investigation” has additionally shown that the glycyrretic acids in liquorice can prevent cancer by inhibiting an enzyme that is needed for cancer growth. Liquorice is used as an alternative treatment for sore throats, bronchitis, and stomach aches and for viral infections and cancer.

Summary:

IMUSAN is a purely biological product made from extracts of various medicinal plants which have had the following effects on patients with general immunity deficiencies and various kinds of cancers:

- Strengthening of the immune system (cellular resistance)
- Inhibition of cancer growth by strengthening normal programmed cell death (apoptosis) and direct cytotoxic properties
- Neutralizes free radicals by way of an antioxidant effect
- Antiviral activity
- Anti-inflammatory property
- Pain-reduction property

The recommended daily allowance (RDA) should be between 2-3 capsules and can be increased as needed. Side effects are not expected at this dosage.

Aeskulap-
Convolvulus arvensis-Extract
(ACAE)

(A phytotherapeutic prescription compound)

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to Aeskulap-*Convolvulus arvensis*-Extract (ACAE) produced by Aeskulap-International AG's compounding contract pharmacy in Switzerland. This commercially available supplement has been shown to inhibit the growth of a primary cancer and metastases.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- Aeskulap-*Convolvulus arvensis*-Extract contains only components as listed on the label.
- Aeskulap-*Convolvulus arvensis*-Extract can be used in conjunction with conventional treatments for primary cancer and metastatic disease.
- *Aeskulap-Convolvulus arvensis-Extract* is an integral part of our treatment program for metastatic breast- and prostate cancer. In this setting, the doctors of our network combine ACAE with Indole-3-Carbinol, ProstaSol, Curcumin combi extra forte, IMUPROS, and BIOBRAN for added benefit.
- Aeskulap-*Convolvulus arvensis*-Extract, used at the prescribed dosage, is well tolerated.

Although there are no so-called placebo controlled, double-blind studies for this product and its application in the treatment of patients with breast- and prostate cancer, there are well-founded preclinical studies with proteoglycans extracted from *Convolvulus arvensis*, as well as clinical observations and case studies demonstrating clinical effectiveness of this compound.

If you decide to include Aeskulap-*Convolvulus arvensis*-Extract as a complementary oncological treatment, you may want to take advantage of our Aeskulap Patient Care Service and consult our expert doctors with any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne,
Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

Aeskulap-Convolvulus arvensis-Extract (ACAE)

Aeskulap-Convolvulus arvensis-Extract (AMCP) contains a proprietary extract of the common bindweed, comprised of various proteoglycan molecules. The extract significantly inhibits the growth of abnormal cells and new blood vessels. It also has a distinct immune-stimulatory effect.

Since Dr. Folkman hypothesized that controlling angiogenesis could be a feasible anti-tumor strategy, clinical oncology has seen an ever growing interest in angiogenesis inhibitors as anti-tumor agents. Because of anecdotal reports of clinical benefit for cancer patients after consumption of an extract of the common bindweed (*Convolvulus arvensis*), AIDAN corporation first tested extracts of this plant for anti-angiogenesis and immune stimulating effects. Their initial research work best summarizes the biological properties of this extract as well as its clinical potential and possible side effect profile.

With permission of AIDAN Products LLC, we have provided a copy of their initial research paper following here:

ANTI-ANGIOGENIC, ANTI-TUMOR AND IMMUNOSTIMULATORY EFFECTS OF A NON-TOXIC PLANT EXTRACT (PGM)

Authors: Riordan NH, Meng X, Riordan HD.

ABSTRACT

Recruitment of new blood vessels plays a crucial role in tumor survival and growth. Several agents that act as angiogenesis inhibitors are currently being investigated as anti-tumor agents. Proteoglycan extract (PGM) was tested for anti-angiogenic, immunostimulatory, and anti-neoplastic activity. PGM is a non-toxic extract of the ubiquitous plant, Convolvulus arvensis. In the chicken egg chorioallantoic membrane assay PGM inhibited new blood vessel growth in a dose-dependent manner. Results were 18, 55, and 73% inhibition at concentrations of 50, 100, and 200 mcg, respectively. PGM significantly inhibited tumor growth in the mouse fibrosarcoma (S-180 Kun Ming 3-4 week old mixed male/female, 10 animals per group, 250-1000 mcg daily doses for 14 days), and mouse Lewis lung carcinoma (C57, 6 week old mixed male/female, 10 animals per group, 250-1000 mcg daily doses for 14 days) models. Inhibition (54-77% inhibition by weight compared to controls, up to 96.8% by cellular composition) occurred regardless of route of administration: intravenous; intraperitoneal; subcutaneous; and oral. PGM induced lymphocyte growth in a dose dependent manner. The ability of PGM-treated phagocytes to phagocytose yeast cells was 85% greater than controls. We conclude that PGM is a potent angiogenesis inhibitor that has immunostimulatory activity in vitro and anti-tumor activity in vivo and that PGM should be studied further as an anti-neoplastic agent.

BACKGROUND

Every aspect of tumor growth requires vascular growth.[1] In 1971 Folkman hypothesized that controlling angiogenesis could be a feasible anti-tumor strategy.[2] Recently the description of angiostatin and endostatin has resulted in increased interest in angiogenesis inhibitors as anti-tumor agents.[3-6] Because of an anecdotal report of complete remission in a case of human ovarian carcinoma after consumption of an extract of the ubiquitous plant Convolvulus arvensis, we tested extracts of this plant for anti-angiogenesis and immune stimulating effects. Convolvulus arvensis is well known to contain toxic alkaloids. Therefore, in this study we examined a high molecular weight water extract of the plant that does not

contain appreciable concentrations of alkaloids, which are depleted in the manufacturing process. The extract is primarily comprised of proteoglycan molecules and is herein referred to as PGM. In this study PGM was tested for angiogenesis inhibition on the chicken egg chorioallantoic membrane, for immune stimulating activity on human lymphocyte proliferation and human phagocyte activity, and for antitumor activity in mouse fibrosarcoma and mouse Lewis lung carcinoma models.

MATERIALS AND METHODS / PGM PRODUCTION

The aerial portions of Convolvulus arvensis were collected from land on which no pesticides or herbicides have been used for >15 years. The fresh raw material (194.25 grams) was blended for 5 minutes with 1250 ml deionized water H_2O (6.44 ml/g) in a commercial blender. The mixture was then boiled for 30 minutes and allowed to cool. The boiled mixture was then filtered with a 100 micron sieve. The filtrate was centrifuged at 11,300 g for 15 min., at 4°C. The supernatant was then filtered sequentially through a 1.5 11m fiber glass filter and a 1.2 11m nylon filter. This filtrate was subsequently passed through a 30 kd YM-30 (Amicon) membrane. The retentate of that filtration is referred to as PGM.

CHICKEN EGG CHORIOALLANTOIC MEMBRANE ASSAY

1 day old fertilized chicken eggs (Groves Farms, McPherson, Kansas) were incubated for 10 days at 37°C. A 1 cm^2 side window was cut in the egg shell to expose the chorio-allantoic membrane (CAM). A 3mm-diameter methylcellulose disc impregnated with either Heparin 10 µg (as an angiogenesis inducer), or Heparin 10 µg plus the agent was placed onto each of the CAMs. Six eggs were used for the control group and six for each of the treatment groups. The eggs were incubated for four more days, at which time the egg shell surrounding the window was peeled back, and 2-3 mL of dairy cream was injected under the CAM as a contrast agent. Each CAM was photographed, and scored for angiogenesis using a scale from 0 (no angiogenesis) to 4+ (highest concentration of new capillary growth).

MOUSE SARCOMA MODEL / SUBCUTANEOUS

Mixed gender Kun Ming mice 3-4 week of age, weighing 20-22 grams were bred and housed at Beijing Hepatitis Institute, Beijing, China. 0.2 mL of phosphate buffered saline (PBS) solution containing 8X105 S-180 murine sarcoma cells were injected subcutaneously in the left groin of each animal. The mice were randomly assigned to groups of 10. After 24 hours, either 0.1 mL of normal saline as a control, or 0.1 mL containing 500 µg of PGM dissolved in normal saline was injected subcutaneously in the right groin of each animal. The animals received treatment daily for 14 days, at which point the experiment was terminated. On days 9 and 14 two diameters of the subcutaneous tumors were measured by callipers. On day 14, the animals were sacrificed and tumors were resected and weighed.

INTRAVENOUS AND INTRAPERITONEAL AND ORAL

Studies were conducted as above except for route of administration and dosage. For the oral study, dosages of 125, 250, 500, and 1000 mcg were used.

MOUSE LEWIS LUNG CARCINOMA MODEL

Mixed gender C57 mice 6-8 week of age, weighing 20-22 grams were bred and housed at Beijing Hepatitis Institute, Beijing, China. 0.2 mL of PBS solution containing 1 X 10^5 Lewis lung carcinoma cells were injected subcutaneously in the left groin of each animal. The mice were randomly assigned to groups of 10. After 24 hours, either 0.1 mL of normal saline as a control, or 0.1 mL containing between 250 and 1000 µg of PGM dissolved in normal saline was injected subcutaneously in the right groin of each animal. The animals received treatment for 21 days, at which point the

experiment was terminated. On day 21, the animals were sacrificed, and the tumors were resected and weighed.

LYMPHOCYTE PROLIFERATION

Human lymphocytes were harvested using venepuncture, and subsequently isolated by use of a centrifuged density gradient. They were then incubated in a commercial lymphocyte culture medium (1 x 10^6 cells per ml) with and without added PGM (AIM V, containing interleukin 2 and 2 mercamptoethanol) in an atmosphere containing 95% air, 5% carbon dioxide, at 37°C, for 3 days. The lymphocytes were then counted using a Coulter Epics XL flow cytometer. A per cent increase in lymphocyte growth was obtained according to the following equation:

Lymphocyte growth increase (%) = (Average number of lymphocytes of test group/Average number of lymphocytes of control group X 100) -100

PHAGOCYTIC ACTIVITY

Two buffy-coat samples were prepared by centrifuging tubes containing anti- coagulated human blood from two subjects. The samples were then divided in two. To one buffy-coat from each subject, 2 micrograms PGM were added. One buffy-coat from each subject served as control. All samples were incubated for 5 hours. Then 30 milligrams of freshly rehydrated baker's yeast was added to all samples. After one hour, a stock 2x solution of acridine orange stain was added to each sample. An aliquot of each sample was then placed on a microscope slide. The percentage of phagocytes (monocytes and polymorphonuclear cells) containing intracellular baker's yeast from each sample was counted using a fluorescence microscope and recorded.

RESULTS / CHICKEN EGG CHORIOALLANTOIC MEMBRANE ASSAY

Angiogenesis was inhibited in a dose dependent manner by PGM. The results are summarized in Table 1. Images of two chorioallantoic membranes are shown in Figures 1 (control) and 2 (200 mcg/egg PGM).

TABLE 1

200 mcg/egg	100 mcg/egg	50 mcg/egg
73% p .0001	55% p .001	18%

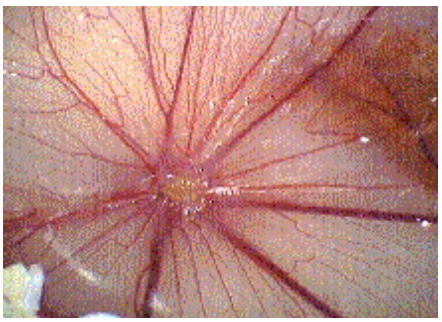
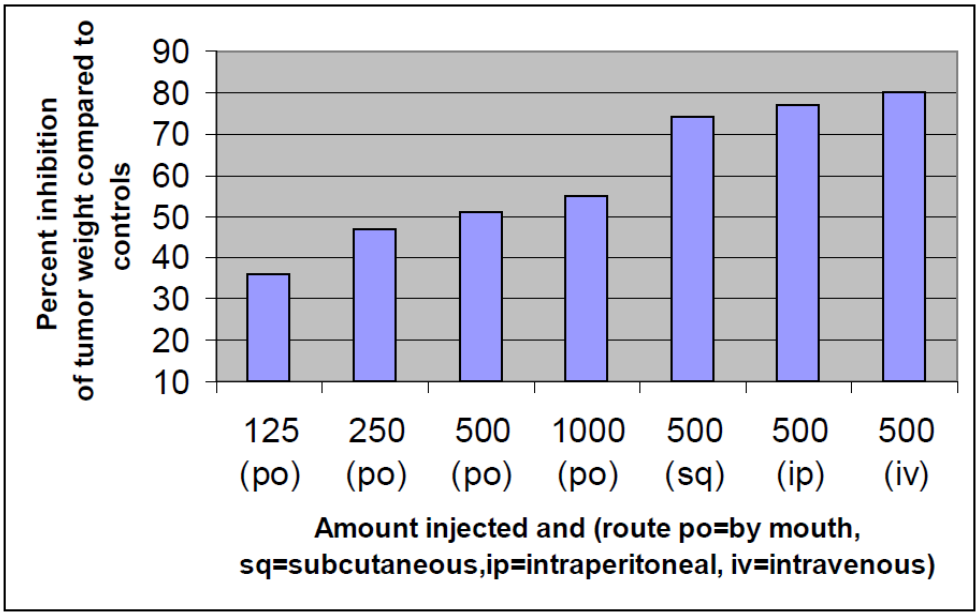


Fig. 1 Heparin control +3.5

Fig. 2 PGM 200ug/CAM +0.5

MOUSE SARCOMA MODEL

Figure 3 summarizes data for subcutaneous intravenous and intraperitoneal and oral PGM in the S-180 tumor model. Orally, PGM inhibited tumor growth in a dose dependent manner that did not achieve the same inhibition as the injected routes even at a higher dose (1000 mg/injection). p .01 for all subsets.



MOUSE LEWIS LUNG CARCINOMA MODEL

PGM inhibited tumor growth in the Lewis lung carcinoma model by 62% at the highest concentration injected, 1000mcg/day (p .001).

LYMPHOCYTE PROLIFERATION

Lymphocytes proliferated in a dose-dependent manner to the PGM. The results are summarized in Table 2.

Table 2

Conc. (mcg/ml)	0	.8	4	20	100
% increase lymphocytes	0	12	35	20	46

PHAGOCYTIC ACTIVITY

An average increase of 85% in the percentage of phagocytes containing intracellular baker's yeast was seen in the treated samples compared to the controls.

DISCUSSION

Data were presented demonstrating that an extract of the plant Convolvulus arvensis has potent angiogenesis inhibiting- and immune-stimulating qualities. This extract also demonstrated anti-tumor effects in two mouse tumor models. The anti- angiogenesis mechanism of action of this extract has not been elucidated. This extract should be studied further to elucidate its anti-tumor effects and mechanisms of action.

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Artemisinin

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please, find enclosed product information pertaining to Artemisinin produced by medpro Holland B.V. in the Netherlands. This product is manufactured as a food supplement, and it contains 1000mg Chinese Wormwood extract per capsule.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- ARTEMISININ contains only the components listed on the label and no synthetic additives.
- ARTEMISININ can be used in combination with standard treatment methods for a variety of cancer entities, including breast-, prostate-, lung-, pancreas-, brain- and intestinal cancers.
- ARTEMISININ, in combination with ProstaSol, BioBran, and Curcumin combi extra forte, is used by the doctors in our network in the treatment of metastatic and castration-resistant prostate cancer, as well as to protect against micro-metastasis due to spread of cancer cells during biopsy and / or transurethral resection of the prostate (TURP).
- ARTEMISININ, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in treatment of patients with cancerous diseases, there are several well-designed laboratory- and animal studies as to the effectiveness of ARTEMISININ in connection with cancer in general, and prostate cancer in particular. There also is one observational investigation of the effects of ARTEMISININ in the treatment of hormone-sensitive and hormone-refractory prostate cancer patients, demonstrating a PSA-reducing effect and amelioration of metastatic pain.

If you decide to include ARTEMISININ as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors about any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne,
Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

ARTEMISININ™ is an extract of *Artemisia annua*, a plant that is also called Chinese Wormwood. Artemisinin was discovered as the active component of *Artemisia annua* in the early 1970s, and the leaf flavonoids from this plant, contained in many traditional Chinese herbal preparations, have shown a wide variety of biological activities against malaria and cancer.

In the Netherlands, ARTEMISININ is prepared as food supplement; however, the manufacturing process follows international standards for the production of pharmaceuticals.

ARTEMISININ is frequently used by patients with parasitic infections; in particular Malaria. The anti-Malaria efficacy of artemisinin has been recognized by the WHO and is reflected in the recommended use of artemisinin and its semi-synthetic analogs, such as dihydroartemisinin, artemether, arteether, and artesunate for otherwise treatment-resistant strains of Malaria. In the last decade, however, more and more scientific work has shown that artemisinin exerts also very potent anti-cancer effects. Today, many cancer patients utilize artemisinin in combination with their conventional therapy for added benefit in their fight against cancer.

Recently, it also has been suggested that artemisinin and its semi-synthetic analogs might become even more effective in the treatment of parasitic diseases (such as malaria) and cancer, if simultaneously administered with flavonoids. The flavonoids present in *Artemisia annua* leaves have been linked to suppression of CYP450 enzymes responsible for altering the absorption and metabolism of artemisinin in the body, but also have been linked to a beneficial immune-modulatory activity in subjects afflicted with parasitic and chronic diseases. The pleiotropic response towards artemisinin in cancer cells includes growth inhibition by cell cycle arrest, stimulation of apoptosis, inhibition of angiogenesis, disruption of cell migration, and modulation of nuclear receptor responsiveness.

Artemisinin also contains an endoperoxide moiety that reacts with intracellular iron to form cytotoxic free radicals. Cancer cells are known to contain a significantly higher free iron concentration than normal cells (almost factor of 1000), and it has been shown that artemisinin and its analogs exert a selective stimulation of apoptosis in many cancer cell lines. Cancer cells express a high concentration of transferrin receptors on their cell surface that facilitate uptake of the iron-carrying protein transferrin from the plasma via endocytosis. By tagging artemisinin to transferrin, artemisinin will be selectively picked up and concentrated in cancer cells and both, artemisinin and iron, would be transported into the cell in one package. Once such artemisinin-tagged transferrin molecule is endocytosed, iron will be released within the cancer cell and react with artemisinin moieties tagged to transferrin. The free radicals that are formed in that process can kill the cancer cell. Presently, potent and target-selective artemisinin-compounds are being developed, including artemisinin dimers and trimers, artemisinin hybrids, and artemisinin compounds that are bound to molecules involved in the intracellular iron-delivery mechanism. All these compounds are promising and potent anticancer compounds that probably have significantly less side effect than traditional chemotherapeutic agents.

Moreover, artemisinin has significant anti-angiogenic, anti-inflammatory, and anti-metastatic effects. Therefore artemisinin compounds are attractive cancer chemotherapeutic drug candidates, however, artemisinin and its analogs have short plasma half-lives, and require high dosages and frequent administration to be effective for cancer treatment.

ARTEMISININ is a very promising anti-cancer drug candidate. It is well tolerated, and in doses up to 50mg per kg body weight, practically without side effects. However, it has a short half-life and its bioavailability reduces rather quickly when taken orally due to reduced absorption through the intestinal wall. Nevertheless, given within the frame work of a suitable treatment protocol, artemisinin can provide significant benefits to cancer patients.

ARTEMISININ has the following effects:

- It creates selective cytotoxic effects in various cancer cells due to free radical generation (cancer cell time bomb) when reacting with the high iron concentration found in cancer cells.
- It causes a dose- and time-dependent G1 cell cycle arrest in various cancer cells which is not depending on its ability to create free radical toxicity.
- It causes dose- and time dependent cell cycle arrest (G1 phase) in androgen-responsive as well as in androgen-unresponsive prostate cancer cell cultures.
- It has significant anti-angiogenic effects in animal models with transplanted cancers, including prostate cancer; it reduces primary tumor growth and growth of metastases.

PROSTECTAN™

(A product of medpro Holland B.V.)

Product information

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to PROSTECTAN™ produced by medpro Holland B.V. This combination extract is produced in Holland as a food supplement and has been effectively used as a natural remedy in the complementary medicinal treatment of patients with prostate illnesses.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- PROSTECTAN contains only the components listed on the label and no synthetic additives.
- PROSTECTAN can be used in conjunction with conventional treatments for inflammation and benign enlargement of the prostate gland, as well as in complementary oncological prostate cancer therapy (for example, as concurrent medicine with radical operation, or parallel to radiation treatment and during and after chemotherapy).
- PROSTECTAN is an integral part of our treatment program for secondary prevention of prostate illnesses.
- PROSTECTAN is also used in combination with Curcumin combi extra forte, IMUPROS, and BioBran by doctors within our network to prevent micro-metastasis due to the possible spreading of cancer cells from prostate biopsy or trans-urethral resection of the prostate.
- PROSTECTAN, used at the suggested dosage, causes no clinically significant side effects and is generally well tolerated.

Although there are no so-called placebo controlled, double-blind studies in conjunction with this product and its application in treatment of patients with prostate illnesses, there is one clinical pilot study on the application of PROSTECTAN in patients with biochemical relapse after radical prostatectomy was concluded in 2012. It could be shown that PROSTECTAN had a very positive effect on the patients' PSA-doubling time, which was prolonged by almost 130%, associated with significant inhibition of tumour growth.

If you decide to include PROSTECTAN as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors with any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

PROSTECTAN™

PROSTECTAN™ contains the following plant-based extracts: Reishi *(Ganoderma lucidum)*, Saw palmetto *(Serenoa repens)*, liquorice *(Glycyrrhiza glabra)*, Baikal Skullcap *(Scutellaria baicalensis)*, Ginseng *(Panax ginseng)*, Woad *(Isatis tinctoria)*, chrysanthemum *(Dendranthema morifolium)*, Rabdosia *(Rabdosia rubescens),* and Biocurcumin complex „BCM95“ with various, with high-quality, bioavailable curcuminoids and LinumLife (Lignane from flax seeds).

In the Netherlands, PROSTECTAN is prepared as a food supplement; however, the manufacturing process follows international regulations for the production of pharmaceuticals. PROSTECTAN is frequently used by patients who have chronic prostatitis, with prostatic hyperplasia (benign enlargement of the prostate gland), and in complementary therapy of prostate cancer.

The following are some clinically proven effects of individual ingredients:

Reishi *(Ganoderma lucidum)*

Reishi Colony

Individual reishi mushrooms

The reishi or lingzhi mushroom has been used for over 400 years in Chinese medicine. The ingredients within the fruit bodies of the mushroom, such as triterpenoide, sterols and various poly-saccharides such as mannitol and coumarin are used in medicine. Furthermore, the mushrooms contain various trace elements, such as zinc, germanium, manganese, iron, copper, and even calcium. Recent research results show that reishi mushroom extract strengthens the immune system and also demonstrates immune modulating properties. The reishi has proven itself particularly useful in the treatment of prostate illnesses, since it inhibits prostate inflammation, thereby counteracting prostatitis. It also suppresses cell adhesion and cell migration in prostate cancer, thereby reducing tumour migration.

Saw palmetto *(Serenoa Repens)*

Saw palmetto

The healing properties of the lipophilic extract of the fruit from the saw palmetto (*Serenoa repens*) in the treatment of prostate illnesses have long been known. Randomized double-blind studies have shown that saw palmetto extract is effective with benign prostate enlargement at a dose of 320 mg per day and that it greatly improves urinary and bladder function. The maximum, as well as the average urinary flow rate improved upon taking this extract.

In comparison to the usual synthetic substances containing finasteride, saw palmetto has at least the same effectiveness with fewer side effects, is better tolerated, and the treatment is also much more cost-effective. Saw palmetto research has concentrated on its application in prostate treatment. Aside from positive effects on benign prostate issues, saw palmetto also has a proven effect in the treatment of prostate cancer. It hinders, for instance, cell proliferation in prostate cancer tissue and supports the normal programmed cell death (apoptosis) of cancer cells.

Liquorice *(Glycyrrhiza glabra)*

Liquorice extracts contain various saponins of glycyrretic acids, which function as expectorants and mucolytic agents, as well as possessing antibacterial and antimicrobial properties.

Glycyrrhiza glabra

Experimentally and clinically, it is also known that extracts from liquorice have anti-inflammatory, cramp-suppressive, and antiviral effects. An American study published in the “Journal of Clinical Investigation”, has also shown that the glycyrretic acids in liquorice can prevent cancer by inhibiting an enzyme that is needed for cancer growth. Liquorice is used as an alternative treatment for sore throats, bronchitis, and stomach aches, as well as for viral infections and cancer.

Scutellaria Baicalensis *(Baikal Skullcap)*

Baikal Skullcap

Extract from *Scutellaria Baicalensis* contains the flavonoid baicalin, which causes programmed cell death (apoptosis) in DU-145 prostate cancer even in very low concentration. That is why researchers at the molecular biological centre at Valhalla University in New York were able to show in studies on prostate cancer cell cultures that scutellaria extract causes a reduction in cancer cell growth by about 60% and curbs PSA production in these cells.
Baicalin hinders cell growth in many other types of tumours as well. These include lung and colorectal cancers and brain tumours. Under the influence of the flavonoid baicalin, cell division is inhibited and normal programmed cell death (apoptosis) is supported.

Russian researchers have been able to prove that baicalin has a positive effect on blood renewal, improving blood flow in bone marrow in patients with tumour-induced anaemia and also minimizes the side effects of chemotherapy.

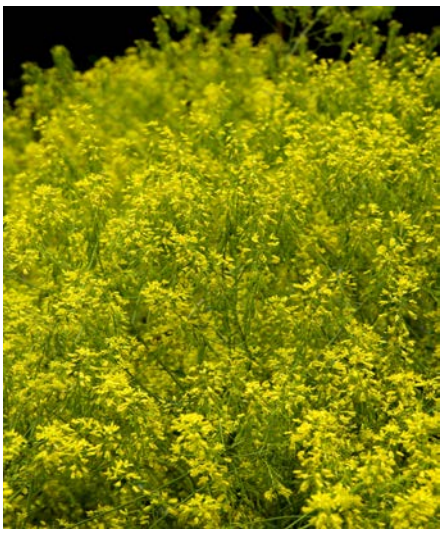
Ginseng *(Panax ginseng)*

Ginseng Root

Recently ginsenoside and saponin, the pharmacological effects in ginseng root, have been used in Europe, although the healing properties of the ginseng root in the treatment of numerous diseases have been long known primarily in China and other Asiatic countries. The substance saponin in particular inhibits prostate cancer cells and suppresses increase in PSA value. It also has a positive influence on androgen receptors and on the enzyme 5-alpha-reductase.

Ginsenoside supports normal programmed cell death (apoptosis) in prostate cells and reduces the activity of so-called Bcl-2 genes, which make cells invincible, thereby causing and supporting cancer. Moreover, ginsenoside restricts the process of metastasis, decreases the development of cancer cells in other tissues, and possesses an anti-angiogenic effect which reduces new vessel formation in metastases and primary tumours, thereby restricting the blood flow to tumour tissue ("starvation of the tumour"). Recent research results have shown that ginseng also has a preventative effect against various kinds of cancer and ginsenoside has a significant anti-inflammatory effect in addition to its cancer-inhibiting effect.

Woad *(Isatis tinctoria or indigotica)*



Isatis tinctoria

Woad is a biennial plant in the mustard family. The roots and parts of the trunk have been used for hundreds of years in traditional Chinese medicine for patients with a variety of tumours.

Isatis indigotica has tumour-active substances in all parts of the plant. One of these substances is indirubin, which inhibits an important cell cycle enzyme in the tumour cell, namely, the so-called “cyclin”-dependent kinase, and in so doing, significantly reduces the growth of breast and prostate cancer cells, for instance.

The aqueous extract of parts of the plant are purported to help hinder tumour development and proliferation. Mild side effects, such as rare allergic reactions and light dizziness, occur with very high doses.

Rabdosia *(Rabdosia rubescens)*

The two most important properties of this quickly growing, terpenoid-rich labiate are oridonin and rubescensin a and b, both of which are known for their cancer-inhibiting effects. Extracts made from the entire plant improve digestion, soothe inflammation, and are used primarily in China in the prevention of breast cancer and prostate carcinoma.

Rabdosia rubescens

Laboratory results show that the positive effects on breast and prostate cancer do not occur due to a hormonal effect, but rather by way of direct influence of the cell cycle and apoptosis (direction of programmed cell death).

Recent studies have also shown that oridonin inhibits the growth of primary bone cancers (multiple myeloma), as well as various types of leukaemia by initiating apoptosis. The anti-carcinogenic effect of oridonin is also free of side effects, since healthy cells are not influenced. *Rabdosia rubescens* also reduces the blood supply to transplanted breast tumours and thereby inhibits the growth of those tumours. In prostate cancer, the effects of *Rabdosia rubescens* also inhibit the development of so-called "androgen independent cancer cells", which almost always develop after prolonged anti-hormonal treatment. In this way, the effectiveness of conventional anti-hormonal therapy for prostate cancer is extended by way of *Rabdosia rubescens*. A study using 115 patients with inoperable oesophageal cancer showed that patients who received *Rabdosia Rubescens* in conjunction with conventional therapy had a survival rate three times that of patients in the control group, who only received chemotherapy.

Chrysanthemum *(Dendranthema morifolium)*

Extract from the chrysanthemum flower *(Dendranthema morifolium)* contains triterpentriole and triterpentriole. In a study at the National Cancer Institute (NCI) in the USA, it was shown that one of these substances, namely arnidiol, was extremely effective in fighting 58 of 60 kinds of cancer cells. The substance killed these cancer cells in the lab within a short amount of time and thereby also showed an "additive effect" in combination with *Rabdosia rubescens*.

Dendranthema morifolium

In traditional Chinese medicine, the healing properties of chrysanthemum flowers have been known for a few thousand years. In this tradition the extract of chrysanthemum flower leaves are purported to improve eyesight, eliminate headaches, and have calming, antibacterial, anti-fungal, and anti-inflammatory properties. The coronary arteries are also purportedly enlarged by chrysanthemum extract, which improves overall cardiovascular function.

Biocurcumin BCM95®

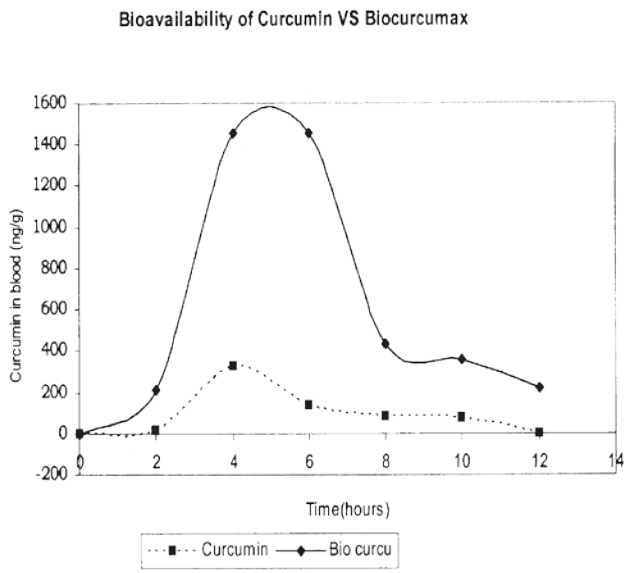
Curcuma root and powder

Biocurcumin BCM95 is a patented extract made from turmeric, which possesses a number of biological effects, such as anti-oxidant, anti-inflammatory, antibacterial, and anti-rheumatic effects. Additionally, this curcumin extract has a significant anti-carcinogenic effect which acts on many different kinds of tumours.

Biocurcumin BCM95 has 7-8 times better bioavailability than other Curcumin extracts. That means that with an oral dosage of only 250 mg of Biocurcumin BCM95, approximately the same blood-drug level is achieved as in a dosage of 1,500 mg of normal turmeric extract, or about 37,500 mg of simple Curcumin Powder. Therefore, taking Biocurcumin BCM95 quickly delivers a therapeutic concentration of curcuminoids into the blood stream.

The BCM95 Complex positively distinguishes itself with the following properties:

- 100% natural turmeric extract *(Curcuma longa)* without added artificial ingredients
- clinical studies show that BCM95 Extract has a 7-8 times better bioavailability than other Curcumin extracts
- achieves the same effect as that produced by high doses of conventional curcumin extracts with much smaller doses
- has a powerful antioxidant effect
- has extremely good anti-inflammatory properties



From a medical standpoint, the antioxidant, anti-carcinogenic, and inflammatory-reducing properties of turmeric extract are of particular interest. These properties are used in the treatment of various diseases, such as intestinal, lung, and liver diseases, as well as with inflammatory diseases, Alzheimer's, heart attack, and cancer illnesses. Clinical tests and studies conducted on animals confirm in particular the cancer-reducing property in the treatment of stomach, intestinal, liver, and skin cancer. Even advanced metastasis development can be considerably reduced by using curcumin.

LinumLife (Lignans from flax seed)

LinumLife is a standardized extract from flax seeds with a high concentration of so-called lignans – secondary plant compound with a phyto-oestrogenic effect. The lignans have a pharmaceutical rather than a nutritional effect, characterized by powerful antioxidants- and a low oestrogenic activity, which serve to keep cells healthy while also preventing cancer.

A scientific report from the Cancer Institute in Heidelberg from 2004 recommended using flax seed oil and flax seeds in the prevention of breast and colon cancer. Lignans also have a positive effect on benign prostate enlargement reducing the size of the prostate gland.

LinumLife is clinically tested, safe, and well tolerated.

Aeskulap-Sitosterol-Mix

(A phytotherapeutic prescription compound)

Aeskulap international

Lucerne, June 28th, 2013

Dear Colleagues,
Dear Patient,

Please find enclosed product information pertaining to Aeskulap-Sitosterol-Mix produced by Aeskulap-International AG's compounding contract pharmacy in Switzerland. This phytotherapy drug is individually prescribed for each patient and manufactured as so-called "Magistral-Rezeptur" (prescription magistralis) for the treatment of prostate cancer.

Our doctors and researchers have tested this product both in the laboratory and clinically. We will gladly provide you with the results of these independent tests upon request. The most significant results follow here in brief:

- Aeskulap-Sitosterol-Mix contains only components as prescribed by a physician.
- Aeskulap-Sitosterol-Mix can be used in conjunction with conventional treatments for prostate cancer, for example, in the perioperative setting with radical prostatectomy or prior, during and after radiation and chemotherapy.
- Aeskulap-Sitosterol-Mix is an integral part of our treatment program for treatment of prostate cancer, even in the so-called castration-resistant stage.
- Aeskulap-Sitosterol-Mix is used in combination with ProstaSol, Curcumin combi extra forte, IMUPROS, and BioBran by doctors within our network to treat prostate cancer of all stages, in particular also metastatic and castration-resistant variants of the disease.
- Aeskulap-Sitosterol-Mix, used at the prescribed dosage, is usually well tolerated. Nevertheless, about 25-30% of treated patients may notice some breast nipple soreness and slight breast enlargement. Impairment of libido and erectile function, and some stool softening has also been reported. All side effects are reversible upon dose reduction and discontinuation of treatment.

Although there are no so-called placebo controlled, double-blind studies for this product and its application in the treatment of patients with prostate cancer, there are well-founded preclinical studies, as well as two retrospective clinical studies evaluating the effectiveness of Aeskulap-Sitosterol-Mix in prostate cancer.

If you decide to include Aeskulap-Sitosterol-Mix as a complementary oncological treatment, you should inform your doctor. You may also take advantage of our Aeskulap Patient Care Service and consult our expert doctors with any special medicinal questions you might have.

Whatever you decide, we wish you much success with your treatment and all the best!

Your medical team at Aeskulap International

Grendel 2, 6004 Lucerne, Switzerland
info@aeskulap-international.org
Phone: +41 41 417 4448
Fax: +41 41 417 4449

Aeskulap International Medical Services AG
Grendel 2
6004 Lucerne, Switzerland

Phone: +49 163 691 3909
Fax: +49 221 222 1866
service@aeskulap-international.org