

**CO2 Marine Lipid Extract from Green Lipped Mussel Oil**  
**LYPRINOL™**

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**Introductory Information about**

**MARINE LIPIDS  
EXTRACTED FROM**  
*Perna canaliculus*

**LYPRINOL™**



# CO2 Marine Lipid Extract from Green Lipped Mussel Oil LYPRINOL™

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Our best advocates are our customers who regain mobility.

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### 1. What is Lyprinol™ ?

Lyprinol™ is the registered trade mark for a lipid extract, isolated from the New Zealand Greenshell™ Mussel, *Perna canaliculus*, containing a unique group of polyunsaturated fatty acids including ETA (Eicosatetraenoic Acid). Lyprinol™ is a well documented, proven and researched success story for the treatment of inflammation.

The patented Lyprinol Extract is sold throughout Asia, Australia, New Zealand, Scandinavia, Europe, UK, Canada, Ireland and USA. It is sold in Soft Gel Capsules manufactured worldwide by GMP certified encapsulators.

Lyprinol® was developed and patented by Mac Lab in Nelson, NZ, in the heart of the Greenshell™ Mussel growing area. It is marketed and distributed internationally by Pharmalink International Ltd. In Europe, RP Scherer Germany is the exclusive encapsulator. Lyprinol® Capsules are sold through Tony Jacobs, Managing Director of Pharmalink Services Europe GmbH. He is a company director and has been appointed by Pharmalink International to present and assist European companies with the marketing and supply logistics.

Lyprinol® is a unique synergistically linked group of six marine fatty acids extracted from the “**stabilized**” freeze dried mussel powder of New Zealand’s Greenshell™ Mussel, *Perna canaliculus*. Greenshell™ Mussel is often also referred to as the Green-Lipped Mussel.

Scientists in Australia, New Zealand, Europe and Japan have studied Lyprinol® for more than thirty years. Lyprinol® has been proven to be a natural, safe and effective inhibitor of the human **lipoxigenase pathways**, one of the principal inflammation pathways in the human body.

Lyprinol™ has been used successfully for the treatment of **Osteoarthritis, Rheumatoid Arthritis and Asthma** and is being studied for its effectiveness against other inflammatory diseases such as **Crohn’s disease, Ulcerative Colitis, Lupus and Psoriasis**. Importantly, Lyprinol®, as a natural food extract, causes no gastrointestinal toxicity or other side effects.

**One Lyprinol® Soft Gel Capsule containing 50mgs of unique highly concentrated and stabilized extract oil, has the equivalent active ingredient of over 40 x 500 mgs capsules of stabilised Greenshell™ Mussel Powder.**

BBC, CNBC and CNN Reports on the “Miracle from the Sea” have contributed to the growing consumer brand recognition. The benefits noted by Users of Lyprinol™ has led to unusually strong repurchase, further contributing to sales growth and success.



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### 2. Analytical Profile of Lyprinol®

**Lyprinol™ is unique marine lipid oil extracted from the “stabilised” freeze dried flesh of New Zealand's Green Lipped Mussel, *Perna canaliculus*. It is a unique and synergistically linked group of six marine lipid groups including omega-3 PUFA's, ETA, EPA, DHA, DPA, OTA and others. Studies confirm that it has several hundred times more anti inflammatory inhibition than MaxEPA and fish oil, evening primrose oil and flax oil. Lyprinol® has been proven to inhibit the lipoxygenase pathways in the human body with no side effects at all.**

Lyprinol® is quite different in structure compared to other marine oils in both the bonding of the omega fatty acids and of course its efficacy. Following is a description of Lyprinol® provided to us by Andrew Sinclair, Professor of Food Science at Australia's RMIT.

1. Lyprinol® is an orange to dark orange viscous liquid obtained by the supercritical carbon dioxide extraction of the New Zealand Green Lipped Mussel. Lyprinol® is a mixture of five main lipid classes. The minimum amounts of these different lipids in Lyprinol® is as follows :
  - sterol esters (5%),
  - triacylglycerol (10%),
  - free fatty acids (10%),
  - sterols (2%),
  - polar lipids including monoacyl- and diacyl-glycerols (1%).
2. There about approximately 8-10 different marine sterols in the sterol ester and sterol fraction. The main sterols are (each representing at least 10% of the total sterols present).
  - cholesterol,
  - brassicasterol,
  - 24-methylenecholesterol
  - 22-cis-dehydrocholesterol
3. Lyprinol® contains more than 30 different fatty acids which are mixtures of saturated, monounsaturated and polyunsaturated fatty acids. The main fatty acids are (each representing at least 10% of total fatty acids).
  - palmitic acid
  - palmitoleic acid,
  - eicosapentaenoic acid and
  - docosahexaenoic acid
4. Lyprinol® is a source of long chain omega 3 polyunsaturated fatty acids, essential for health in humans. The two main omega 3 PUFA present in Lyprinol® are
  - eicosapentaenoic acid (20 carbons and 5 double bonds, shorthand = 20:5 omega 3)
  - docosahexaenoic acid (22: 6 omega 3).
5. Lyprinol® contains several other fatty acids which belong to the omega 3 PUFA family. These fatty acids all have four double bonds and have carbon chain lengths of 18 and 20 carbon atoms, respectively; thus they are described as
  - 18:4 omega 3 (18:4 v3 or 18:4n-3) (Octadecatetraenoic Acid, OTA)
  - 20:4 omega 3.(Eicosatetraenoic Acid, ETA)

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A possible **monograph** for Lyprinol® would be “an orange to dark orange viscous oil containing free fatty acids and sterol esters rich in palmitic acid, palmitoleic acid, eicosapentaenoic acid and docosahexaenoic acid and sterols rich in cholesterol, brassicasterol, 24-methylenecholesterol and 22-cis-dehydrocholesterol”.

The lipids and fatty acids in Lyprinol® are common constituents of the human diet, particularly for people consuming fish, shell fish and marine molluscs. These foods have been consumed by humans throughout the course of human evolution.

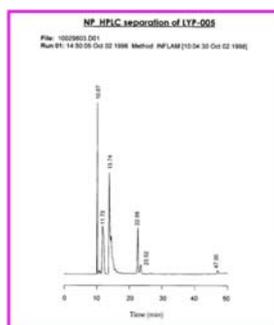
The percentage composition of the extracts analysed to date (12 analyses) is shown below:

<u>Fraction</u>	<u>Mean</u> (range)
SE	9 (8-11)
TAG	69 (60-80)
FFA	11 (6-14)
DAG	6 (4-9)
S	3 (2-4)
MAG	1 (1-2)
PL	0.7 (0.5-0.8)

SE = sterol esters, TAG = triglycerides, FFA = free fatty acids, S = sterols, MAG = monoglycerides, PL = phospholipids.

Main peaks from the GLC profiles are shown below, with the data expressed as percent of total fatty acids:

<u>Peak</u>	<u>Retention Time</u>	<u>Mean</u>
Myristic (14:0)	13.3 mins	5 (4-6)
Palmitic (16:0)	17:0	17 (15-18)
Palmitoleic (16:1)	17.7	10 (8-11)
Stearic (18:0)	20.1	2 (2-3)
Oleic acid (18:1)	20.7	2 (2-3)
Octadecamonoenoic (18:1)	20.8	2 (2-3)
Linoleic (18:2)	21.6	1.5 (1.3-1.7)
Linolenic (18:3)	22.8	1.6 (1.2-1.8)
Octadecatetraenoic (18:4)	23.4	3 (2-4)
Eicosapentaenoic (20:5)	27.5	18 (16-20)
Docosahexaenoic (22:6)	33.1	15 (13-17)



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### 3. Comparison with other Products

*In vivo* studies undertaken at The University of Queensland tested the anti-arthritic properties of **Lyprinol™**.

Using the standard model for evaluating the potency of anti-arthritic drugs, **Lyprinol™** was measured against its ability to reduce the swelling which occurs in adjuvant induced poly arthritis in rats. Inflammopharmacology.

The results were dramatic, with **Lyprinol™** reducing joint swelling by 93% compared with untreated controls.

Following these outstanding findings The University of Queensland scientists set out to compare **Lyprinol™** with two widely used anti-arthritic drugs, namely Indomethacin & Ibuprofen.

When given orally at the same dose rate (5mg/kg body wt./day) **Lyprinol™** outperformed the drugs Indomethacin & Ibuprofen by a factor of 2:1. This was a staggeringly successful outcome for **Lyprinol™**.

More recently a double blind clinical trial conducted at the West Glasgow Hospital University NHS Trust involving 60 patients, 30 of whom had classical rheumatoid arthritis and 30 with clinical & radiological evidence of osteoarthritis, showed outstanding results.

Both rheumatoid and osteoarthritis patients showed a significant improvement with 76.7% of the rheumatoid and 70% of the osteoarthritic patients benefiting from the trial. If the drop-outs are excluded, then 79% of rheumatoid patients and 80% of osteoarthritic patients benefited.

\* The results from this paper have been published in the journal "Complementary Therapies in Medicine". (Sept. 1998). Further human clinical trials have confirmed these findings.

**Lyprinol™** was compared with Flax Oil, Evening Primrose Oil, Salmon Oil and Max EPA (fish oil) in the adjuvant induced poly arthritis test system. Studies Whitehouse - Inflammopharmacology 1+2

On a dosage per body weight basis **Lyprinol™** is:

- 100 times more potent than Max EPA
- 125 times more potent than Green lipped mussel powder
- 175 times more potent than Evening Primrose Oil
- 175 times more potent than Salmon Oil
- 200 times more potent than Flax Oil in controlling the joint swelling associated with arthritis.



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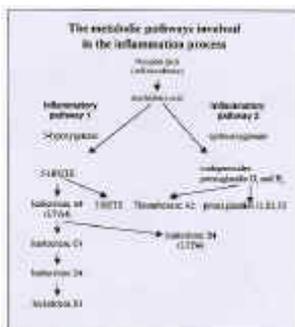
### 4. How it works

The process of inflammation is highly complex and is defined as the body's reaction to physical, chemical or biological injury which, in a normal healthy individual, results in the localisation of the problem and regeneration or repair of the damaged tissue. Unfortunately, inflammatory response is not always beneficial to the individual.

A prime example is that of osteoarthritis, an inflammatory disease which can affect all the bone joints of the human body but primarily affects the "wear and tear" joints of the feet, knees, hands, hips, shoulders, elbows and back which have usually had the effects of many years of work and sometimes injury.

In certain circumstances, the process itself can cause damage and injury. The auto-immune disease, rheumatoid arthritis, where the body attacks itself, and the hypersensitive states leading to asthma and anaphylactic shock, are examples of uncontrolled inflammatory responses.

Initiation and control of the inflammatory process is complex and governed by an array of biomolecular mechanisms. One important pro-inflammatory mechanism is closely associated with cell-membrane bound arachidonic acid, which becomes converted into other compounds in the body which are potent inflammation-supporting substances.



This occurs by two major pathways in our metabolism:

The 5-lipoxygenase pathway leading to the formation of leukotrienes, and

The cyclo-oxygenase pathway which leads to the formation of prostaglandins and thromboxanes

Many of the products of these pathways have potent inflammation-supporting properties. For instance, LTB<sub>4</sub> is a potent chemotactic agent capable of attracting large numbers of leucocytes (white blood cells), to the site of the injury. While LTC<sub>4</sub>, LTD<sub>4</sub>, and LTE<sub>4</sub>, which are metabolites of LTB<sub>4</sub>, are potent bronchoconstricting agents and were formerly identified as SRS-A's (slow reacting substance of anaphylaxis), a key factor in anaphylactic shock.

Currently used anti-inflammatory drugs function mainly by inhibiting the cyclo-oxygenase pathway. In view of the important functions of the inflammatory process ascribed to the lipoxygenase pathway, there has been considerable scientific effort to develop a 5-lipoxygenase pathway inhibitor over the past decade.

Lyprinol™ has been discovered and proven to be a natural, safe and effective inhibitor of the **lipoxygenase pathways** in humans, one of the principal inflammation pathways in the human body.

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### 5. Doseage

Most people should begin with two capsules twice a day for three to four weeks or until desired results are felt.

Some may try three times a day during this period.

Thereafter, decrease your dosage to one or two capsules once or twice a day as desired



The daily level needed to obtain maximum effect can vary for each individual. If your body requires less, temporary initial irritation of symptoms may occur with too high a dosage. If this occurs, simply decrease the amount taken. Some individuals with serious needs may not receive maximum benefit from Lyprinol™ for four weeks, so it is important to not discontinue too soon.

*Capsules should be consumed with or after meals with water.*

#### ***Ingredients per capsule:***

- Natural mono-unsaturated Olive oil - 100mg;
- Lyprinol™ GLM pat.lipids - 50mg;
- Vitamin E (D-alpha-Tocepherol) as antioxidant - 0.225mg.

***Capsule:*** Gelatin; Sorbitol syrup; Glycerin



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### 6. Research

Only Lyprinol™ has been validated as safe and without side effects with 30 years of research. The areas of research cover inflammatory conditions under the headings of Asthma, Rheumatoid Arthritis and Osteoarthritis, Inflammatory Scientific Research, Pain Control, Inflammatory Bowel Disease and Sports Medicine.

#### **Asthma Research**

In 1999, Pharmalink International Ltd commissioned a Lyprinol™ Clinical Trial of Lyprinol™ on Bronchial Asthma Patients. Dr. Alexander Yemelyanov, Professor of Hospital Therapeutic Clinic, Pavlov's St. Petersburg Medical University in St. Petersburg, Russia conducted the study. Dr. Yemelyanov is experienced in testing new asthma drugs for AstraZeneca and Rhone Poulenc. Forty asthma patients, male and female, were enrolled in a double-blind randomised placebo-controlled study. The study concluded that Lyprinol™ showed beneficial effects on clinical symptoms, peak expiratory flow rate and concentration of hydrogen peroxide in exhaled air condensate in mild asthma patients. The study results were posted at an Asthma Conference in Australia in September 2001 and have been peer reviewed and published in the European Respiratory Journal, 20, (2002). Further human trials on Asthma are being conducted.

#### **Rheumatoid and Osteo Arthritis Research**

After more than thirty years of research, clinical trials have shown that Lyprinol is more effective in reducing arthritic pain and inflammation than other remedies. Additional clinical trials have demonstrated that Lyprinol can outperform proprietary pharmaceutical NSAIDs as well as remedies such as the traditional fish and plant oils containing omega-3 and omega-6 fatty acids. Here is a selection of studies.

The first notable research on mussel extract was conducted at the Homeopathic Hospital and the Department of Surgery, Victoria Infirmary, Glasgow, Scotland by Drs Robin and Sheila Gibson and published in 1980. Results showed that 68% of RA and 39% of OA patients experienced some improvement. Difficulties with duplication of results led us to understand the need to identify and "stabilise" the active components. The company Maclab Ltd spent the next 10 years researching the active components. The stabilisation process was patented and the product containing the active ingredient, "Lyprinol™" was trade marked and finally commercialised in 1994. In 1998, the Gibsons again tested the new stabilised extract called Lyprinol™ and noted that it could be of considerable value to patients suffering from these two chronic and disabling conditions.

Printed in Complementary Therapy Med ;6:122-126 1998. The treatment of arthritis with a lipid extract of Perna canaliculus: a randomised trial.

From 1997 to 2003, Dr Michael Whitehouse from the University of Queensland, Australia, published and researched inflammatory processes and products.

Dr. Whitehouse and his colleagues compared Lyprinol to forty over-the-counter remedies, including three NSAIDs, and found it to be superior to all of them.  
Printed for Inflammopharmacology 7, (1999).

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In 2000, Dr. Michael Whitehouse of the University of Queensland, Australia, compared Celebrex and Vioxx, two COX-2 inhibitors, with Lyprinol and also with Anaprox, an NSAID (naproxen) in clinical use since 1972, in laboratory rats. At a dosage rate of 15 mg/kg of body weight/day, Celebrex and Lyprinol protected against experimentally induced arthritic inflammation in the rats about equally (78% reduction in inflammation). Vioxx did not reduce inflammation until the dosage was raised significantly, and then it reduced inflammation only minimally. Anaprox appeared to score well, reducing inflammation by over 80%. However, it also created the largest number of gastric side effects. The other agents did not produce any gastric disturbance. Dr. Whitehouse concluded that the Lyprinol™ was as effective as Celebrex and had no adverse side effects.

Dr. Whitehouse also compared the effectiveness of Lyprinol™ with that of the prescription drug indomethacin. He showed that, with a dosage of 5 mg/kg of body weight, the oil extract was 97% effective in reducing swelling. In comparison, indomethacin, which is toxic at this dosage, was only 83% effective.

Printed in the Inflammation Revolution, Square One Publishers, (2005)

Dr Chak Sing Lau at the Queen Mary Hospital of the University of Hong Kong, 2004, organized a double-blind study conducted at the Queen Mary Hospital of the University of Hong Kong. He compared the effects of Lyprinol vs. placebo on the signs and symptoms and quality of life in patients with osteoarthritis of the knee. Eighty patients with knee OA were randomized to receive either Lyprinol or placebo for six months. All were allowed paracetamol/acetaminophen (Tylenol) rescue treatment to control pain during the study and were reviewed regularly for assessment of arthritis and safety evaluation. Assessment of each patient's OA included the use of a standard 100 mm visual analog scale (VAS) to allow the patient to "quantify" his/her pain, patient's and physician's global assessment of OA, a validated Chinese version of a specific knee score (COKS), a validated Chinese version of a score addressing the impact of arthritis (CAIMS2-SF), and two laboratory common tests—erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), both considered as valid markers of active inflammation.

Improvement in almost all of the arthritis assessment variables was observed in both groups of patients, emphasizing the need for placebo-controlled studies; the placebo effect may be important and may lead to false, optimistic conclusions. However, there was a significantly greater improvement in the perception of pain (VAS) and patient's global assessment of OA in those who took the mussel lipid oil when compared to those who had received the placebo; this significant difference persisted even after adjusting for the amount of paracetamol/acetaminophen (Tylenol) consumed to control the pain. This was observed from week four, confirming the slow effect of the lipid oil. Patients who took Lyprinol but not placebo also had improved scores in the CAIMS2-SF physical and psychological domains from week four, meaning an improved quality of life. The mussel oil extract was safe and well tolerated by all patients.

Printed in Progress and Nutrition Journal, 6, (2004)

Dr. Se-Haeng Cho of Yonsei Medical Clinic, in Seoul, Korea, organized a multicenter two-month clinical trial with a total of eight specialized clinics. Sixty patients with symptomatic, painful OA of the knee and hip were included to receive mussel oil (Lyprinol) at a dose of two capsules twice daily. The physicians analyzed the following: pain according to VAS; an

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international index designed by Dr. Michel Lequesne (Lequesne index); global assessment by the patient and by the physician; and adverse effects. The treatment with Lyprinol led to significant improvement of the signs and symptoms of OA as determined by all efficacy measurements. After the four- and eight-week treatment periods, 53% and 80%, respectively, of patients experienced significant pain relief and improvement of joint function. There were no reported adverse effects attributable to the green-lipped mussel oil. • In Germany, a group of physicians studied the efficacy and tolerability of a combination of the green-lipped mussel lipid oil and high concentrations of the fish oils EPA and DHA in patients with rheumatoid arthritis (RA). This twelve-week study was conducted on 50 adults, both men and women. A total of 34 patients required drug therapy before and during the study. But by the end of the study, 21 (62%) were able to reduce their dosage and, more importantly, 13 were able to terminate all medications. At week twelve, 38% were symptom free, and the number of patients complaining of severe pain decreased significantly from 60% (at the beginning of the study) to 25% at the completion of the trial. That special combination of the lipid extract of the green-lipped mussels and selected omega-3 fatty acids was very well tolerated, with just one episode of transient mild nausea.

Printed in *Allergie & Immunologie*, 35(2003)

Jorg Gruenwald in Berlin, Germany 2004, organized a group of physicians to study the efficacy and tolerability of a combination of the green-lipped mussel lipid oil and high concentrations of the fish oils EPA and DHA in patients with rheumatoid arthritis (RA). This twelve-week study was conducted on 50 adults, both men and women. A total of 34 patients required drug therapy before and during the study. But by the end of the study, 21 (62%) were able to reduce their dosage and, more importantly, 13 were able to terminate all medications. At week twelve, 38% were symptom free, and the number of patients complaining of severe pain decreased significantly from 60% (at the beginning of the study) to 25% at the completion of the trial. That special combination of the lipid extract of the green-lipped mussels and selected omega-3 fatty acids was very well tolerated, with just one episode of transient mild nausea.

Printed in *Advances in Therapy*, 21 (2004)

### **Anti inflammatory Scientific Research**

Dr Theo Maccrides led a team of researchers at Melbourne RMIT University from 2005 to 2008 and published in consecutive issues of the journal *Comparative Biochemistry and Physiology*. Part B, looked at both commercial Lyprinol and super-critical carbon dioxide (CO<sub>2</sub>) extracts from the mussel, on both COX and leukotriene levels in vitro. The Lyprinol™ commercial extract exhibited strong inhibition of COX-1 and COX-2, wrote the researchers, with the free fatty acid and triglyceride fractions identified as the active anti-inflammatory compounds. Hydrolysis of the extracts using potassium hydroxide or protease enzymes increased COX inhibition by up to ten-fold said the researchers. "These results support the use of the commercial mussel extracts, in particular Lyprinol, as an alternative for conventional [non-steroidal anti-inflammatory drugs] NSAIDs and fish oil treatment in the relief of the symptoms of arthritis," concluded the researchers.

The second study extracted and isolated the free fatty acid fraction from the mussel and identified novel omega 3 polyunsaturated fatty acids ( $\omega$ -3 PUFA), thought to originate from the algae and other micro organisms unique to New Zealand waters. The researchers identified the most bioactive fractions as C18:4, C19:4, C20:4, and C21:5. "The C20:4 was the predominant PUFA in the extract, and was a structural isomer of arachidonic acid (AA),"

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wrote the researchers. "The novel compounds may be biologically significant as [antiinflammatory] AI agents, as a result of their in vitro inhibition of lipoxygenase products of the AA pathway." The prostaglandins derived from omega-3 fatty acids are said to be anti-inflammatory, while prostaglandins derived from omega-6 fatty acids, like AA, are proposed to be pro-inflammatory."The inflammatory precursor AA is an ω-6 PUFA of 20 carbons in length and has 4 unsaturated double bonds (positions 5, 8, 11 and 14) with each double bond being separated by one methylene group," explained the researchers. They confirmed the presence in the mussel oil extract of unusually bonded and structured free fatty acids that affected the COX and LOX pathways directly and safely.

Printed in Comparative biochemistry and physiology part B: biochemistry and molecular biology (published August 2007)

### **Pain Relief**

In 2006, Pharmalink International Ltd, commissioned Dr Samuel Lo at the Hong Kong Polytechnic University, to investigate if there were protein expressions related to pain and inflammation reacting to the intake of Lyprinol. Two separate trials and reports were published in eCam in 2007 and 2008. Dr Georges Halpern then summarized the research and explained the mode of action of Lyprinol in relation to cytokine pain control and published the molecular chemistry science explaining why Lyprinol reduces pain.

Printed in Progress and Nutrition, 10, 2008

### **Inflammatory Bowel Disease**

In 2004, Danik Tenikoff and Karen Murphy, at the University of Adelaide, Australia, commenced investigation of induced inflammatory bowel disease (IBD) in rats. In summary, they found that Lyprinol has the potential to reduce the severity and onset of IBD. The indices of colitis compared with fish oil indicate that Lyprinol may have provided the potential to be more beneficial for treatment of colonic inflammation than fish oil. Further human clinical studies were recommended. These further studies are currently under way.

Printed in Journal of Gastroenterology, 40, (2005)

### **Sports Medicine**

In 2008, Andreas Rehn (Nutritionist) Germany, tested the lung capacity of aged 35+ Marathon Runners with and without Lyprinol intake. They found an improved lung intake and general improvement in recovery and muscle soreness.

This was then repeated by Professor Dr Baum at the Cologne Sports Institute with young professional cyclists who did not have inflammatory symptoms. No changes were shown due to Lyprinol intake. Thus confirming that Lyprinol is not a performance booster and cannot be classified as a drug in the sporting fraternity.

Further research is currently being undertaken on the benefits of Lyprinol intake for sports people with age related, injury related or asthma related inflammatory conditions.

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### 8. Internet Information

See

[www.lyprinol.com](http://www.lyprinol.com)   [www.lyprinol-sport.com](http://www.lyprinol-sport.com)   [www.lyprinol.de](http://www.lyprinol.de)

### 9. Company Information and Contact

Pharmalink International Limited, is the owner of the patents, trade marks and intellectual property associated with Lyprinol™. This is a privately listed company with over 1000 shareholders.

Robert Myer,	Chairman and Managing Director
John Waitzer	Director, responsible for Sales and Marketing
Nardo Leviste	Director, responsible for Accounting and Administration
Dennis Goquingco	Director, responsible for Financial Administration
Tony Jacobs	Director, responsible for European Business
Gloria Eleazar	Macau Sales Office Manager
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