

Marine Lipid Extract from the Green Lipped Mussel Oil **LYPRINOL®**

Introductory Information about

MARINE LIPIDS EXTRACTED FROM *Perna canaliculus*

LYPRINOL®



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1. What is Lyprinol®?

Lyprinol® is the registered name for a whole lipid extract, isolated from the New Zealand Greenshell™ Mussel, *Perna canaliculus*, containing a unique group of ETA's (Eicosatetraenoic Acids). Lyprinol® is a well documented, proven and researched success story for the treatment of inflammation.

The patented Lyprinol® Extract is sold throughout Asia, Australia, Holland, Israel, New Zealand, Scandinavia, Eastern Europe, UK, Canada, Ireland and USA. It is only sold in Soft Gel Capsules which are manufactured world wide by RP Scherer.

Lyprinol® has been developed and is manufactured 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 has been appointed by Pharmalink International to present and assist European companies with the marketing and 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 twenty years. Lyprinol® has been discovered and proven to be a natural, safe and effective inhibitor of the **lipxygenase pathways** in humans, one of the principal inflammation pathways in the human body.

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

One Lyprinol® Soft Gel Capsule containing 50mgs of this 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 and CNN Reports on the “Miracle from the Sea” have contributed to very profitable sales turnovers. The outstanding results from persons taking Lyprinol® formulated products has also contributed to exponentially increasing sales.



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2. Analytical Profile of Lyprinol®

Lyprinol® is a 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's, EPA's, DHA and others. It is several hundred times more powerful 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 are 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 n-3 or 18:4n-3)
 - 20:4 omega 3.

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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.

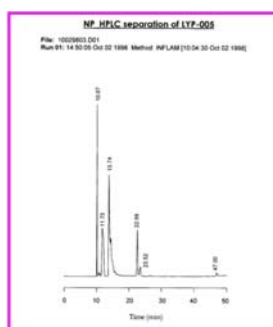
The percentage composition of the extracts analysed to date (12 analyses) is shown below:

<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)

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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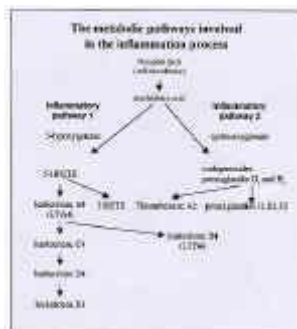
4. How it works

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 effect 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 4 is a potent chemotactic agent capable of attracting large numbers of leucocytes (white blood cells), to the site of the injury. While LTC 4, LTD 4, and LTE 4, which are metabolites of LTB 4, 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 one to two 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 (Eicosatetraenoic acid) - 50mg;
- Vitamin E (D-alpha-Tocopherol) as antioxidant - 0.225mg.

Capsule: Gelatin; Sorbitol syrup; Glycerin

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6. Research

Various studies have been conducted along with many publications. To name a few these are as follows;

1. A. Clinical Trial of Lyprinol® on Bronchial Asthma Patients. Asthma is an inflammatory disorder. In May, 1999 there was completed a study of the efficacy and safety of Lyprinol® in the treatment of patients with mild bronchial asthma by Dr. Alexander Yemelyanov, Professor of Hospital Therapeutic Clinic, Pavlov's St. Petersburg Medical University in St. Petersburg, Russia. Dr. Yemelyanov is very 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 have been posted at an Asthma Conference in Australia in September 2001 and has been submitted for full publication.
2. Clinical Trial of Immunomodulating Properties of Lyprinol®. Professor L.G. Rudenko, M.D., D.Sci., of the Institute of Experimental Medicine, Russian Academy of Medical Sciences, in St. Petersburg Russia, during May to October, 1999 to investigate the immunomodulating effects of Lyprinol®. Forty volunteers were administered a live influenza vaccine and half of these also took four Lyprinol® capsules per day for the first 28 days following receipt of the live influenza vaccine.

The results of the study were successful and showed that Lyprinol® (i) caused no suppression of the immune system and local immune responses, and (ii) enhanced the immune system's response to the live influenza vaccine by doubling the number of serum antibodies produced.

This is being submitted for publication in the Journal Infectious Diseases.

3. The Queen Elizabeth Hospital in Adelaide, Australia commenced in November the first human clinical trials on Lyprinol® for prostate cancer and breast cancer patients in an open clinical trial. This was done because of the proven linkage between the 5-lipoxygenase pathway in the proliferation of cancer and the 12-lipoxygenase pathway in the metastasis of cancer and Lyprinol®'s proven role in inhibiting these pathways safely and effectively in humans. The Hospital made a public announcement of its intention to conduct these trials on July 30, 1999. **The announcement made world wide headlines and was carried by CNN and BBC World television services.**
4. In 1980 a clinical trial was conducted at Glasgow's Homeopathic Hospital in Scotland by Drs. Robin and Sheila Gibson.

Groups from the Homeopathic Hospital and the Department of Surgery, Victoria Infirmary, Glasgow, Scotland, reported the results of a double-blind study involving 66 outpatients, 28 with rheumatoid arthritis and 38 with osteoarthritis. All had been scheduled for surgery to improve their joint conditions; all had failed to respond to conventional treatments.

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Patients were randomised into 2 groups. Group 1 received the mussel extract and group 2 a placebo (dried fish meal powder). Evaluation was done at day 90. Then all patients were given the mussel extract for 3 months.

Regular checks were done on joint stiffness, limbering up time, grip strength, articular index of joint tenderness, pain, functional efficiency, and time to walk 15 meters. Results showed that 68% of RA and 39% of OA patients experienced improvement. Ten percent of patients given the mussel extract experienced a transient aggravation of their symptoms. There were no side effects. The authors concluded: “The extract of New Zealand green-lipped mussel, *Perna canaliculus*, is an effective supplement or possible alternative to other therapies in the treatment of both rheumatoid arthritis and osteoarthritis. It reduces the amount of pain and stiffness, improves the patient’s ability to cope with life, and apparently enhances general health. Added to these benefits is the low incidence of side effects. It would therefore seem that the green-lipped mussel extract (Lyprinol®) could be of considerable value to patients suffering from these two chronic and disabling conditions.”

Gibson SLM. Gibson RG. The treatment of arthritis with a lipid extract of *Perna canaliculus*: a randomised trial. *Compl Ther Med* 1998;6:122-126.

5. Lyprinol® was tested and compared against forty over the counter remedies including three NSAID’s and was found to be superior to all of them. The research article (and an abstract of it) describing this comparison test is available in its entirety upon request. “Non-NSAID Over The Counter Remedies For Arthritis : Which Are The Good The Bad, the Indifference?” and “O.T.C. Remedies For Arthritis – Over The Counter (OTC) Oral Remedies for Arthritis and Rheumatism : How Effective Are They?” by Dr. M.W. Whitehouse, *et. al.* (Article published in the medical research journal Inflammopharmacology (1999).

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