

More Than Twenty Years of Research on Lyprinol™

The 1970's

Lyprinol™ and its antecedent product, stabilised green lipped mussel powder, have been the subject of more than twenty years of scientific and medical research in Australia and other countries.

During the 1970's McFarlane Laboratories Pty. Ltd., which later became part of the MacLab Group of Companies in Melbourne, was established to distribute Seatone (encapsulated freeze-dried green lipped mussel powder) in Australia.

Researchers had conducted a number of initial clinical studies of green lipped mussel powder for arthritis in the 1970's. However, the majority of these studies proved unsatisfactory. In 1978 a husband and wife doctor team, the Drs. R.G. and S.L.M. Gibson, conducted an outstandingly positive study in Glasgow, Scotland at two major public hospitals, the results of which were published in a peer reviewed journal in 1980:

- Gibson RG, Gibson S, Conway V, Chappel D. *Perna canaliculus* in the treatment of arthritis. *Practitioner* 1980; 224: 955-960.

The 1980's

In the early 1980's MacFarlane became concerned over criticism which had been voiced by certain medical and scientific commentators challenging the value of freeze dried New Zealand green lipped mussel powder for the treatment of arthritis.

RMIT University, Melbourne Research

In 1982, following discussions with RMIT University in Melbourne, McFarlane Laboratories decided to fund research in the Natural Products Chemistry Unit of RMIT's Department of Applied Biology. The challenge for RMIT was to seek and identify the active component or components which was believed to exist in the N.Z. green lipped mussel. This work was planned to cover an initial two year period but has continued to this day.

Shizuoka University, Japan Research

In 1983, the research team at RMIT was joined by a Japanese research group headed by Professor Takuo Kosuge, head of the Shizuoka College of Pharmacy at Shizuoka University, Japan and one of Japan's most respected research chemists.

In early 1984 Professor Kosuge determined that there was a major problem with the mussel powder produced by McFarlane in that it was found to be extremely unstable and lacking in potency due to rapid oxygen degradation (oxidation). Professor Kosuge determined that unless some method could be developed to stabilise the mussel powder and prevent its oxidation, it would be of little or no value for use as a serious natural treatment for arthritis, which was the commercial aim of McFarlane.

After testing all known anti-oxidants without success, Professor Kosuge turned to research that he had conducted twenty years earlier on a traditional method used by Japanese fisherman to preserve their stored fish for future consumption. Professor Kosuge postulated that the answer to the problem of rapid oxidation of green lipped mussel powder might lie in his earlier research into this traditional method. Indeed,

such proved to be the case. As a result of this work McFarlane patented and developed a natural stabilisation process for green lipped mussel powder which prevented its oxidation and allowed it to be studied by researchers without degrading in potency.

This work occurred at the time that McFarlane's Australia assumed control of the Auckland processing plant of McFarlane New Zealand.

McFarlane Australia (MacLab) realised that a totally new approach to the manufacture of mussel extract was required. Accordingly, a decision was taken to sell its shareholding in the New Zealand company to its UK partners and to establish a totally new manufacturing plant to incorporate its newly patented process. It took many years to implement this decision but the MacLab plant located in Nelson, New Zealand is now considered to be a GMP state-of-the-art processing facility.

RMIT University Research

In the 1980's, after the Japanese research group had completed its research on the stabilisation of green lipped mussel powder, research activity on this substance continued at RMIT University.

The RMIT University research team was headed by Professor Robert Borland and was supported by Associate Professor Theo Macrides, a graduate of Oxford University, and Professor Andrew Sinclair, Professor of Food Sciences, who is considered one of the world's foremost experts in lipids.

During this time the Australian government supported research on stabilised green lipped mussel powder through various grants. Research into stabilised green lipped mussel powder became a joint RMIT/McFarlane project with McFarlane providing the industry partner funding.

The 1990's

The Queen Elizabeth Hospital, Adelaide Research

In the early 1990s the RMIT group approached Dr. Henry Betts, who is the Principal Scientist of the Rheumatology Research Laboratory at The Queen Elizabeth Hospital in Adelaide, South Australia.

Dr. Betts had perfected a technique for testing anti-inflammatory compounds in an *in vitro* system. The RMIT/ McFarlane group asked Dr. Betts if he would agree to test various fractions extracted from the New Zealand green lipped mussel.

It was through this research that Dr. Betts developed a strong interest in the mussel's non-polar lipid fractions which were later named Lyprinol™ by the MacLab Group.

The University of Queensland, Brisbane Research

Once the active fractions of the green lipped mussel had been identified, it was decided that animal studies should be conducted to test safety and efficacy. The research team was fortunate when Dr. Michael Whitehouse of the Department of Medicine, The University of Queensland in Brisbane, an internationally recognised expert in the testing of anti-inflammatory compounds, agreed to become involved.

Dr. Whitehouse achieved a First in Chemistry at Oxford University at 22, a Masters in Organic Chemistry at 23, a Doctorate in Biochemistry at 25, and was a Fellow of the Royal Institute of Chemistry by the time he was 32. He was also Professor of Pharmacology at the University of California at Los Angeles (UCLA) and now, at 68, is a world authority on arthritis and Honorary Research Consultant at the Department of Medicine, The University of Queensland.

Dr. Whitehouse readily agreed to become involved in researching the anti-inflammatory properties of stabilised green lipped mussel powder. Dr. Whitehouse had conducted work previously into the anti-inflammatory properties of green lipped mussel powder. Dr. Whitehouse approached the project as a sceptic as he had previously tested the unstabilised mussel powder in his animal models with poor results.

Over several years Dr. Whitehouse has exhaustively tested Lyprinol and has presented his findings in several papers at international symposiums around the world. These include several published articles: Anti Inflammatory Activity of a Lipid Fraction (**Lyprinol**) from the New Zealand Green Lipped Mussel, *Inflammopharmacology*, 1997; 5: pp. 237-246; and Whitehouse MW, Roberts MS, Brooks PM. Over-the-counter oral remedies for arthritis and rheumatism: How effective are they? *Inflammopharmacology* 7, 80-105, 1999.

Dr. Whitehouse has stated that Lyprinol™ represents a quantum leap forward in nutritional therapeutics whilst at the same time condemning the inferior quality of other non-stabilised mussel powder products produced in New Zealand.

Dr. Henry Betts Discovers Lyprinol™'s Effect on the Lipoxygenase Inflammation Pathway

During Dr Betts' testing of Lyprinol™, he discovered that the lipids were potent 5-lipoxygenase inhibitors. The 5-lipoxygenase pathway is a principal pathway of inflammation in the human body. Dr. Betts advised his findings to Professor Robert Borland, a Fellow of the Royal College of Pathologists and a Fellow of Darwin College, Cambridge University and at the time the Dean of Biomedical Science at RMIT University. This discovery opened up the possibility of testing and using Lyprinol™ for the treatment of various chronic inflammatory disorders such as arthritis, asthma, inflammatory bowel diseases, psoriasis and other disorders in which the lipoxygenase inflammation pathway is involved.

Pavlov Medical University, St. Petersburg, Russia Research on Lyprinol™ and Asthma

As a result of this discovery, Professor Borland approached Professor A. Emelyanov, Chief Respiratory Physician at the Department of Allergy and Lung Disease, Pavlov Medical University, St. Petersburg, Russia, to investigate the efficacy of Lyprinol™ for the treatment of mild to moderate asthma patients. A clinical trial was conducted on 40 patients in a double-blind placebo-controlled study. The results were significant as each patient experienced a noticeable effect in the reduction of his rescue and preventative medication. Both Professor Emelyanov and his collaborator, Professor Peter J. Barnes of the Department of Thoracic Medicine, National Heart and Lung Institute in London, are eminent researchers in respiratory medicine. Professor Barnes, a world acclaimed expert in the field of asthma, has published over 800 peer reviewed articles. Professor Emelyanov is a respiratory physician who has been responsible for testing many new asthma drugs introduced by large pharmaceutical companies.

Their research study of the use of Lyprinol™ for mild to moderate asthma sufferers, "Treatment of asthma with lipid extract of New Zealand green-lipped mussel: a randomized clinical trial," was published in the European Respiratory Journal, Vol. 20, Issue 3 - 2002.

These same medical researchers expect to conduct a further extension of this clinical study on the treatment of Lyprinol™ for moderate to severe asthma patients commencing in November, 2002.

Prince Alfred Hospital, Queensland Research on Lyprinol™ and Asthma

In June, 2002, the Prince Alfred Hospital in Queensland announced on Channel 9 Television News that Professor Mitchell of the Asthma Foundation in Queensland had commenced a clinical trial to study Lyprinol™'s sparing effect with steroids in treating moderate to severe asthma cases. This study has now been completed and the results will be released shortly.

Pharmalink International Limited Purchase of Lyprinol™

In 1999 Pharmalink International Limited (Pharmalink) purchased the Lyprinol™ patents, trademarks, technical know-how and other intellectual property from the MacLab Group in Australia. This purchase allowed the MacLab Group to focus on green lipped mussel production and freeze drying. Pharmalink became the owner of Lyprinol™ and concentrated its activities on the world wide marketing and distribution of Lyprinol™.

The Institute of Experimental Medicine, St. Petersburg, Russia Research on the Immune Stimulating Effects of Lyprinol™

During the intense media interest arising in August, 1998 as result of the announcement made by The Queen Elizabeth Hospital, a New Zealand based research scientist suggested that, since Lyprinol™ was an anti-inflammatory compound, it might suppress or weaken the immune system and therefore could lead to an increase in colds and other diseases. Pharmalink's scientists repudiated this claim based on reports from thousands of patients who appeared to be healthier, not less healthy, from their use of Lyprinol™. Nevertheless, Pharmalink decided to conduct a clinical study in this area in order to refute the thesis of suppression of the immune system. A team led by Professor Larisa Rudenko, Department of Virology, Institute of Experimental Medicine, St. Petersburg, Russia, conducted a double-blind, placebo-controlled clinical study which showed that Lyprinol did not suppress the immune system at all but actually boosted the effectivity of the body's response to an oral flu vaccine used in the study by more than 100%. For these reasons, the researchers concluded that Lyprinol™ possessed significant prolonged immunostimulating effects on post-vaccination antibody and cell mediated immune responses to a vaccination of live influenza. The researchers showed that the treatment of Lyprinol™ produced no side effects and did not lead to any suppression of systemic or local immunity nor did it alter total or differential white blood counts.

The results of this clinical study, which completely refuted the concern expressed by the New Zealand based research scientist, have been submitted recently for publication to the peer reviewed medical journal, *Vaccine*.

Glasgow Homeopathic Hospital, Scotland Research on Lyprinol and Osteo-Arthritis and Rheumatoid Arthritis

Later in 1998 Drs. S.L.M. Gibson and R.G. Gibson published the results of a double-blind randomised 3-month study of patients with Osteo-Arthritis ("OA"), so-called "wear and tear arthritis," or Rheumatoid Arthritis ("RA"), an auto-immune disorder. Sixty patients were enrolled in a parallel comparison study and for a further 3-month period using the lipid extract (Lyprinol™) for all patients. The clinical study was conducted at the Outpatient Department of the Glasgow Homeopathic Hospital, Scotland. The patients on Lyprinol™ received 210mg per day.

The results were impressive: 76% of RA and 70% of OA patients benefited. Measures of AI, LUT, and FI were significantly improved within 3 months. This research paper was titled, "The treatment of arthritis with a lipid extract of *Perna canaliculus*". Gibson S.L.M., Gibson R.G. The treatment of arthritis with a lipid extract of *Perna canaliculus*: a randomised trial. Complementary Therapeutic Medicine 1998; 6:122-126.

Dr. Neils H. P. Hertz, M.D., Copenhagen, Denmark On-Going Research on Osteo-Arthritis

An ongoing study is being conducted by Dr. Niels H.P. Hertz, MD, in Copenhagen, Denmark. This study includes 13 patients with longstanding Osteo-Arthritis in one or both knees and/or hips. Twelve of 13 patients have reported a dramatic 50% reduction of pain (VA), and 50% an improvement at day 21-28. The same results were confirmed at day 42-56.

Hong Kong Institution FDA-Approved Clinical Facility On-Going Clinical Study of Lyprinol For Osteo-Arthritis

There is ongoing a double-blind placebo-controlled clinical study at the Hong Kong University which is a U.S. FDA approved clinical study center using an FDA clinical protocol for the study of Lyprinol™ for arthritis of the knee and hip. The study involves 90 patients and is due for completion in January 2003.

Other Research Studies of Lyprinol™

Other research studies completed on Lyprinol™ are:

- Hooper S. The effect of marine oils on markers of thrombosis in the blood of healthy females. Oct 1998, Thesis, BSc (Hon), Royal Melbourne Institute of Technology, Melbourne, Victoria, AU.
- Sinclair A.J., Murphy K., Li D. Marine lipids: Overview, new insights and lipid composition of Lyprinol. *Allergy & Immunology*: 32, 261-271, 2000.
- Halpern, G.M. "Anti-inflammatory Effects of a Stabilized Lipid Extract of *Perna canaliculus* (Lyprinol)." *Allergie & Immunologie* 32(2000)272-78.
- Halpern, G. Lyprinol: a natural solution for arthritis and other inflammatory disorders. Avery Press (member of Penguin Putnam Inc), 2001, New York.