

## THE POWER OF PHOSPHOLIPIDS

Naturopathic support for optimal cellular function

Cell membranes are dynamic, complex structures that are exquisitely sensitive and reactive to environmental changes and disparate signals from within and outside cells. They are formed from a double layer of special fats – phospholipids – along with proteins and other lipids including cholesterol. They play a critical role in fluid movement around and within cells, as well as electrolyte and pH balance. Membrane lipid bilayers also surround the internal cellular organelles including the mitochondria, which have indisputable roles in fuel metabolism and energy (ATP) production.

A biological maxim states “structure subserves function” placing the utmost importance in ensuring the structure of cell membranes is addressed as part of any naturopathic programme. This can be achieved by supplying phospholipids through the diet and also from high quality phospholipid powder supplements.

Mitochondrial membranes are particularly susceptible to damage, in part due to the high levels of harmful free radicals that are produced by the ATP producing pathways that line the inner mitochondrial membrane, which in turn damage cardiolipin – a lipid found almost exclusively in the mitochondrial inner membranes. If there is insufficient cellular antioxidant systems response or simply an overproduction of reactive oxidative molecules then these free radical species can damage the delicate mitochondrial inner membrane ultimately leading to their functional decline and eventual degradation via programmed cell death. Free radicals leaked from damaged and permeable mitochondria also cause oxidative damage to other cellular constituents.

It's now understood that compromised mitochondrial cell structures can be an underlying mechanism for a myriad of pathological conditions linked to injury, disease, inflammation and ageing. Conditions include chronic fatigue syndrome (CFS), chemotherapy induced fatigue,

fibromyalgia, Lyme's disease, as well as chronic inflammatory intestinal diseases, Alzheimer's disease, Parkinson's disease, auto-immunity, migraine headaches and Autistic Spectrum Disorders (ASD) and others.<sup>1</sup> This is not surprising as ATP production is fundamental to cellular function and therefore life!

We will now go on to explore the implications for cell and mitochondrial membrane damage and naturopathic approaches for supporting cell membrane structure as outlined using phospholipid preparations in the well studied Membrane Lipid Replacement (MLR) model.



## WHAT ARE PHOSPHOLIPIDS?

Glycerophospholipids, a group of phospholipids, form major components of all biological cell membranes. The different types of glycerophospholipids are essential for optimal cellular function; they provide structure and integrity to cell membranes, as well as playing a role in intracellular pathways and cell-cell communications.<sup>2</sup>

Glycerophospholipids, along with other components, form both the extracellular membranes that encapsulate the cell contents and the membranes that surround internal organelles such as the energy (ATP) generating mitochondria and the nucleus, which contains the genetic material (DNA) of the cell.

There are several major groups of phospholipids including:

- Phosphatidyl choline (PC)
- Phosphatidyl serine (PS)
- Phosphatidyl ethanolamine (PE)
- Phosphatidyl inositol (PI)
- Phosphatidyl glycerol (PG)

PC and PE are the most abundant membrane matrix phospholipids found on the outer side of cell membranes. PC usually accounts for greater than 50% of the phospholipids in

cellular membranes.<sup>3</sup> PS and PI are more readily found on the inner side of the membrane. PG is a precursor for cardiolipin; a lipid found almost exclusively in the mitochondrial inner membranes. The structure and function of the mitochondrial membrane envelope is vital for the function of aerobic respiration pathways producing ATP.<sup>4</sup> The phospholipid ratios in different membranes therefore have profound consequences for membrane properties, function, activities and organisation.<sup>5,6</sup>

Glycerophospholipids are synthesised within cells but are also acquired from dietary sources to ensure a ready supply for cell membrane requirements. There is also a rich history of using high quality phospholipid supplements in the Membrane Lipid Replacement (MLR) model to modify cellular and intracellular membranes in order to improve mitochondrial function and reduce fatigue<sup>7</sup>, more of which we will discuss later in this newsletter.

## CELL MEMBRANE STRUCTURE

The cell membrane lipid bilayer has been extensively studied and it's now known that the phospholipid components form an integral part of the structure, as discovered and described in the Fluid Mosaic Model.<sup>8</sup> Phospholipids in a healthy cell membrane provide a scaffold like structure that is more fluid rather than rigid in nature. These physicochemical properties allow movement of nutrients, electrolytes, proteins and other molecules back and forth across the cell membrane helping to maintain fluid movement and cellular pH, as well as playing an important role in signalling between cells.

## CELL MEMBRANE DAMAGE

External and internal cell membranes are complex structures that are susceptible to damage by a number of factors with acute, but also more problematically, long-term consequences (Table 1). Particularly notable is the link between stress and cell membrane damage; research shows that chronic production of adrenaline and cortisol arising from adverse states of stress can influence the cell membrane metabolism.<sup>9</sup>

**TABLE 1: CAUSES OF CELL MEMBRANE DAMAGE**

<b>Lifestyle; smoking, e.g. cyanides from tobacco smoke, stress</b>
<b>Environmental toxins</b>
<b>Poor diet; alcohol, e.g. sulfites from red wine, vitamin and mineral deficiencies, low intake of dietary phospholipids</b>
<b>Medications</b>
<b>Disease</b>
<b>Ageing</b>
<b>Increased exposure/ reduced buffering capacity of free radicals produced from cellular metabolism</b>

## MITOCHONDRIAL MEMBRANE DAMAGE

There are many clinical manifestations arising from cell membrane damage with fatigue being one of the most notable.<sup>9</sup> This can be attributed to a number of connected reasons including damage to mitochondrial membranes. However, simply supplying increased amounts of metabolic fuel through the diet, such as in the form of carbohydrates, in order to boost cellular energy production can actually cause further damage and harm.<sup>10,11</sup> What is more worrying is that once mitochondrial membrane damage is initiated (Table 1), mitochondrial dysfunction becomes a self-perpetuating vicious cycle. Our state of health is therefore connected by the very state of the cell/mitochondrial membrane.

Cardiolipin is a specialist lipid located in the mitochondrial inner membrane. It is synthesised inside the mitochondria from two PG molecules and is functionally required for activity of the electron transport system and production of ATP. Mitochondrial membranes are, by virtue of their close proximity to the site of energy generation, exposed to high levels of free radicals produced from ATP-producing pathways and are susceptible to oxidative damage resulting in membrane permeability and "leakage" of the harmful free radicals into the cell. If left unchecked, free radicals can cause great levels of damage to the mitochondria and other cell structures located in their immediate vicinity, resulting in altered cellular metabolism, inflammation and even premature initiation of cell death or conversely the prevention of appropriate mitochondrial removal. This is especially pertinent as a typical 21st century sedentary lifestyle favours chronic metabolic oversupply of nutrients promoting damage to mitochondrial membranes and the induction of what is known as 'sterile inflammation'.<sup>12,13,14</sup>

Mitochondrial impairment and membrane damage has been linked to injury, disease, and inflammation and ageing encompassing a wide range of conditions such as chronic fatigue syndrome (CFS), chemotherapy induced fatigue, fibromyalgia, Lyme's disease, as well as chronic inflammatory intestinal diseases, Alzheimer's disease, Parkinson's disease, auto-immunity, migraine headaches and Autistic Spectrum Disorders (ASD).<sup>1</sup>

## MEMBRANE REPAIR

Our bodies have a sophisticated system to replace the damaged membrane components, especially the oxidation-sensitive membrane phospholipids in the mitochondria. This system depends on the ingestion (from diet and supplements) and transport of undamaged/unoxidised membrane phospholipids and their precursors to each of our cells.

Dietary and supplementary phospholipids are very efficiently absorbed across the brush border as micelles from the small intestines<sup>15</sup>, and eventually released into the lymphatic or circulatory systems where they pass through the liver and around the body bound to plasma carrier proteins or lipoproteins.<sup>16</sup>

Once inside the cells, phospholipids diffuse or are carried by special lipid transport proteins to their site of action, such as the mitochondrial membranes, where they can replace the damaged membrane components. The damaged parts of the membranes are further degraded and removed from our cells or reutilised to extend the functional life of associated mitochondria in a process known as fission/fusion.

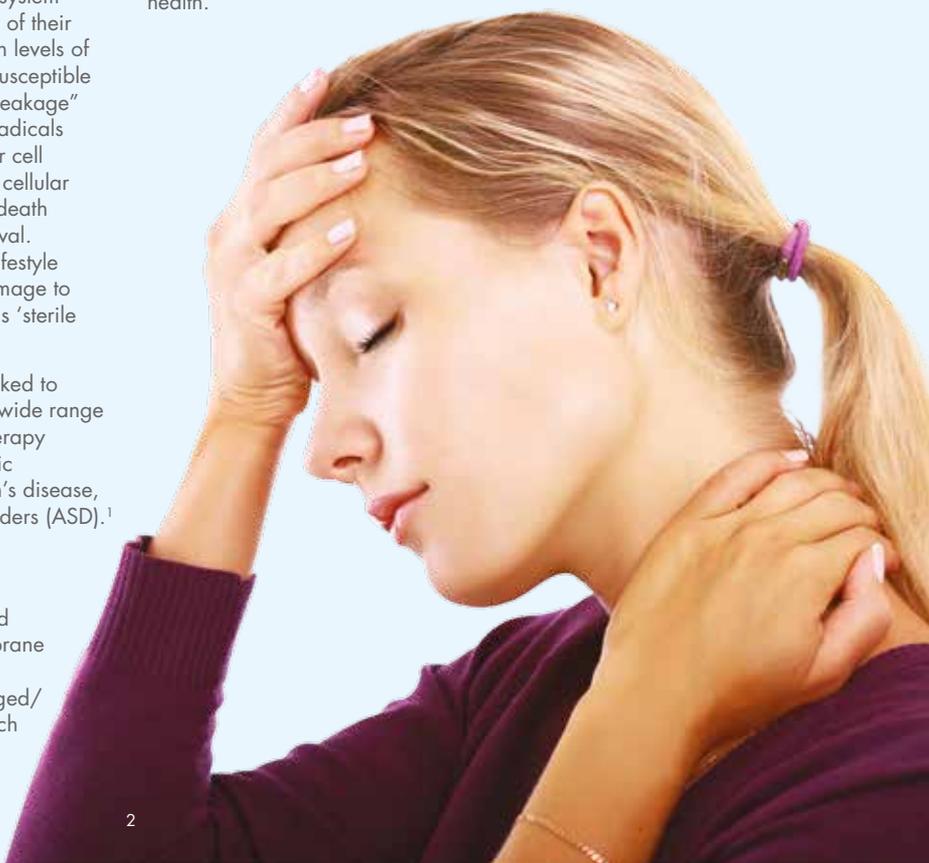
## PHOSPHOLIPIDS IN THE DIET

Phospholipids are some of the most plentiful substances in the body so there needs to be a ready supply of good quality and different types. The body can synthesise phospholipids endogenously, as well as make use of dietary sources found in egg yolks, milk, fish, turkey, liver, chicken and beef. Some plants sources also provide phospholipids including legumes and cabbage. However, 15kg soya beans would have to be consumed to deliver around 1.8g of membrane phospholipids – not a practical or an appealing thought!<sup>17</sup> An average but balanced diet may provide around 2-8g phospholipids per day.<sup>18</sup>

The need for a daily supply of quality phospholipids and their component parts often means supplementation with high quality phospholipid powders is required to support a variety of health outcomes, especially when managing fatigue related complaints. The end result is to supplement sufficient daily phospholipids, of the right quality and ratio, to transform cellular membranes throughout the body so that enzymes, receptors, and other components of the cell membrane are more active and membranes are less permeable, less deformable and have greater functionality.<sup>19</sup> When the correct mix of phospholipids are used this has a clinically relevant effect on energy production, and inflammation associated symptoms.

## MEMBRANE LIPID REPLACEMENT (MLR) MODEL

The Membrane Lipid Replacement (MLR) support model employs NT Factor<sup>®</sup>, a stable non-GM soya lecithin powder with patented, specialised phospholipid blend, to target mitochondrial inner membranes and facilitate cardiolipin repair. In particular, NT Factor<sup>®</sup> can facilitate a quantifiable reduction in fatigue where damaged membranes are responsible. This specialised mix of phospholipids can therefore be implemented as part of a successful naturopathic approach to restore membrane structure and functionality in people in which fatigue is a component of their deleterious health.



## NT FACTOR® CLINICAL TRIALS

Mitochondria cannot be synthesised de novo inside cells so the effective control of mitochondrial biogenesis and turnover becomes critical in the maintenance of ATP production, and therefore reduction and management of fatigue.<sup>20</sup> NT Factor® is a patented blend of phospholipids including PG, which is a precursor for the mitochondria membrane phospholipid cardiolipin.<sup>21</sup> Clinical trials and research shows the varied and wide-reaching benefits of this specialist phospholipid powder formulation, due, in part, to its affinity for mitochondrial membrane support.<sup>18</sup> NT Factor® is suitable for vegans and well tolerated for both short and long-term use and can therefore be used as part of a naturopathic programme to support mitochondrial function.

There are extensive clinical trials of MLR using NT Factor® powder, as described below:

Clinical Use of NT Factor®	Study & Clinical Trial Results
Reduced fatigue associated with ageing and chronic disease (including Chronic Fatigue Syndrome, fibromyalgia and Lyme's Disease)	Reduces lipid peroxidation - positively affects mitochondrial cell membrane lipids damaged by oxidative stress within 12 weeks <sup>22,23</sup>
Reduced fatigue associated with cancer and chemotherapy treatment,	Reduces lipid peroxidation - positively affects mitochondrial cell membrane lipids damaged by oxidative stress <sup>20</sup>
Reduced adverse affects of chemotherapy (e.g. nausea, skin changes, digestive dysfunction)	81% patients on NT Factor with vitamin and mineral formulation reported overall quality of life parameters <sup>26</sup>
Restoration of mitochondrial function in aged subjects	Studies show that mitochondrial function can be returned in older adults to levels similar to that found in young adults <sup>27</sup>
Metabolism modifications (weight management)	Positively modifies body mass and appetite restraint by reducing cravings for sweets and fats <sup>28</sup>
Improved cardiovascular blood markers and cholesterol lowering	35 individuals of average age 60.7 years saw improved cardiovascular blood marker levels including homocysteine when taken in conjunction with B vitamins. Sequesters cholesterol and oxidised glycerolphospholipids into lipid droplets for their eventual removal via the GI system <sup>29</sup>
Reduces inflammation and oxidative stress associated with changes in ageing, degenerative and metabolic diseases	Associated with mitochondrial and cellular support <sup>1</sup> which may be supportive in cardiovascular disease (e.g. hypertension, atherosclerosis, coronary heart disease), neurodegenerative disease (e.g. Alzheimer's disease), chronic respiratory disease, diabetes and autoimmune diseases
May help restore gut function and eubiosis	MLR along with diet can help reduce gastrointestinal related sterile inflammation and restore gut bacteria balance <sup>20</sup>
Improves mental clarity	29 subjects reported perceived improvements in cognition function, mental clarity and focus <sup>30</sup>



NT Factor® in powder form can be easily mixed into fresh juices or smoothies to successfully restore mitochondrial function and primarily reducing fatigue.<sup>20</sup>

## NT FACTOR® IN NATUROPATHIC NUTRITION PROGRAMMES

Other nutrients, such as magnesium (in bioavailable organic citrate form), antioxidants and CoEnzyme Q10 can be supplemented alongside NT Factor® and a naturopathic diet to support cellular function and energy production.<sup>31</sup>

Additional improvements to mitochondrial function have also been observed in diets that involve caloric restriction, such as fasting for 16h (e.g. eating between hours of 11am - 6pm) or intermittent fasting, as well as addressing factors that can contribute to membrane and mitochondrial damage such as toxins and dysbiosis.<sup>9</sup>

# NT FACTOR® RECIPES

## ANTIOXIDANT SMOOTHIE

### INGREDIENTS

- ½ avocado
- 50g blueberries
- Juice from ½ a lime
- 1 cup almond milk
- ½ cup water
- ¼ tsp NT Factor® powder
- ½ tsp raw honey to taste

### HOW TO MAKE

Add all ingredients to a blender and process on high speed for 20-30 seconds. Add more water or additional almond milk to achieve desired consistency.

## POWER PORRIDGE

### INGREDIENTS

- ½ cup organic porridge oats
- 2tbsp sunflower seeds
- 1tbsp ground linseed
- 1 cup water or almond milk
- ¼ tsp high NT Factor® powder
- ¼ cup stewed apples or mixed berries
- ½ tsp ground cinnamon

### HOW TO MAKE

Soak the porridge oats, sunflower seeds and ground linseeds for 2-8h (e.g. overnight) in the water or almond milk. Add more water/almond milk to get desired consistency then stir in NT Factor® powder. Add stewed apples and cinnamon topping.



**i** Should you need a more detailed approach, or should you have any questions or concerns that are not addressed in this article, you are always welcome to contact our nutritional advice team on 0845 603 5675 (9.00am – 5.00pm Monday – Friday).

Alternatively if you would like a more personalised approach, addressing dietary recommendations, lifestyle changes etc., we would suggest you consider consulting a qualified nutrition adviser or therapist, which you can do by either asking us for details of your local practitioners, or contacting the Federation of Nutritional Therapy Practitioners on 0870 312 0042 or by emailing them at [admin@fntp.org.uk](mailto:admin@fntp.org.uk).

For more information visit the website at: [www.fntp.org.uk](http://www.fntp.org.uk)

This newsletter was co-written with and for Nutrigold by Dr Elisabeth Philipps DPhil, a highly qualified and practicing Natural Nutritional Therapist and a member of the Federation of Nutritional Therapists.

To find out more please visit [www.hartwellnutrition.co.uk](http://www.hartwellnutrition.co.uk).

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