Membrane Lipid Replacement—a functional approach to repairing cellular membranes, reducing symptoms, and restoring function

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ABSTRACT

Membrane Lipid Replacement (MLR) uses natural, protected membrane lipid supplements to safely replace damaged, oxidized lipids in cellular membranes in order to restore membrane function, decrease various symptoms and improve health. Membrane injury occurs in essentially all chronic and acute medical conditions as well as in normal aging and development. The repair of damaged cellular membranes, and the removal of impaired membrane lipids and other toxic molecules from cells, are essential to recovery and health. Clinical studies have demonstrated the advantages of MLR in restoring membrane and organelle function and reducing fatigue, pain and other symptoms in chronic illnesses and aging patients. MLR has also been used in in vitro studies to demonstrate its ability to increase cell motility and resistance to oxidative damage. It also has the ability to enhance the bioavailability of other nutrients and their transport across intestinal epithelial cell barriers.

Keywords: membrane phospholipids, lipid transport, lipid oxidation, mitochondrial function, fatigue, pain, chronic disease symptoms, aging
INTRODUCTION

Membrane Lipid Replacement (MLR), the use of all-natural, protected, plant-sourced oral membrane lipid supplements to safely replace damaged, oxidized lipids in cellular membranes, can restore membrane and organelle function, decrease chronic symptoms, and improve health outcomes \[1-5\]. MLR supplements fit the definition of functional foods and contain mixtures of cell membrane glycerolphospholipids, fatty acids, and other lipids that are protected by fructooligosaccharides and antioxidants \[1-3\]. Once ingested, the MLR phospholipids are transported to tissues and cells where these MLR lipids can replace and remove damaged intracellular and cellular membrane lipids as well as other hydrophobic toxic molecules from cells and tissues \[3,5,6\].

Membrane injury, caused mainly by free radical oxidative damage, occurs in essentially all chronic and acute medical conditions, including cancers, degenerative diseases, environmental exposures, and in normal processes, such as aging and development \[4-7\]. After ingestion, the protected MLR glycerolphospholipids and other lipids are dispersed, absorbed, and internalized in the small intestines, where they can be subsequently transferred, exchanged or partitioned into circulating lipoproteins, liposomes, micelles, and membranes of circulating cells and other lipid carriers. They are then transported in the lymphatics and blood circulation to tissue and cellular sites where they are taken in by cells using various transport mechanisms. Once inside cells, the MLR glycerolphospholipids and other lipids are conveyed by concentration-dependent partitioning into various intracellular membranes mediated by lipid carriers, lipid globules, liposomes, chylomicrons, or by direct intracellular membrane-membrane interactions \[2,3,5\]. The entire process appears to be driven by ‘bulk flow’ or ‘mass action’ principles, where surplus concentrations of replacement lipids can stimulate the natural exchange and removal of damaged membrane lipids. The replacement lipids can
undergo further enzymatic alterations at their ultimate cellular membrane sites to reflect the lipid compositions at these sites [2,5,8].

**CLINICAL STUDIES**

Human studies have demonstrated the advantages of MLR in restoring membrane and organelle function, reducing fatigue, pain, and other symptoms in chronic illness and aging [1-7]. For example, the use of MLR supplementation to improve age-related symptoms in middle-aged, pre- and post-menopausal women was investigated in a randomized, double-blind, placebo-controlled study [9]. The study subjects, post-menopausal women, complained of fatigue but were otherwise relatively healthy. The participants in this clinical trial were given MLR with NTFactor Lipids or placebo for 4 or 8 weeks, and fatigue, vigor, mood, and various menopause symptoms were monitored. The women that received 1.2 g per day NTFactor Lipids showed greater reductions in fatigue compared to placebo, and there were significant improvements in patient vigor. Sleep, confusion, anger, and menopausal symptoms were evaluated using Quality of Life instruments and showed improvements in the MLR group. Cardiovascular parameters were also examined, and in the MLR group there were reductions in diastolic blood pressure and improvements in cardio-ankle vascular index [9].

A recent use of MLR in environmental illnesses was initiated for chemically exposed war veterans [6,10]. Many veterans of the first Gulf War returned and slowly displayed multiple signs and symptoms related to their deployment and environmental exposures. The multisymptom chronic illnesses associated with this war have been called Gulf War Illness(es) (GWI) [11,12]. Some GWI patients appear to have their illnesses linked to chemical exposures, such as oil spills and fires, smoke from military operations, chemicals on clothing, and exposures to pesticides, chemoprophylactic agents (pyridostigmine bromide), chemical weapons, and other possible chemicals [13,14].

We first initiated case studies on veterans of the Gulf War that reported a variety of signs and symptoms that were related to their chemical exposures. These case studies indicated that MLR could improve clinical status by reducing symptoms, such as fatigue, pain, and other symptoms [10]. Next, a clinical study was initiated using oral NTFactor Lipids (6 g per day) to see if veterans’ self-reported multiple symptom severities improved with time while on the oral MLR supplement. In this study there were gradual and significant reductions in symptom severities related to fatigue, pain, musculoskeletal, nasopharyngeal, breathing, vision, sleep, balance, gastrointestinal symptoms, chemical sensitivities, and other symptom categories during the 6-month study [6].

Other examples of the use of MLR in various health and clinical conditions are listed in Table 1. What is notable about the potential uses of MLR in humans is that these conditions span multiple situations, from common conditions like obesity and aging to various degenerative and metabolic diseases and cancers. What is clear from these studies is that MLR can also be a useful addition to conventional medical treatments for a number of
commonly found illnesses and conditions to repair damaged cellular membranes and in the process reduce the severities of a variety of chronic signs and symptoms as well improve general health [1-5].

**Table 1.** Current and potential uses of oral MLR supplements and revised suggested daily dose levels.

<table>
<thead>
<tr>
<th>Use/condition</th>
<th>Age</th>
<th>MLR type</th>
<th>NTFL dose$^b$</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>aged senior</td>
<td>NTFactor/L$^c$</td>
<td>2-3</td>
<td>Nicolson et al. [4]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Aged senior</td>
<td>NTFactor/L</td>
<td>4</td>
<td>Agadjanyan et al. [15]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>CFS/ME adult/teen</td>
<td>NTFactor/L</td>
<td>4</td>
<td>Nicolson &amp; Ellithorpe [16]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>CFS/ME adult</td>
<td>ATP Fuel</td>
<td>4</td>
<td>Nicolson et al. [17]</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Chronic fatigue adult</td>
<td>ATP360</td>
<td>N/A$^d$</td>
<td>Hamilton &amp; Jensen [18]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Fibromyalgia adult</td>
<td>NTFactor/L</td>
<td>4</td>
<td>Nicolson et al. [19]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Menopause senior</td>
<td>NTFactor/L</td>
<td>2</td>
<td>Hirose et al. [9]</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Obesity, fatigue adult</td>
<td>NTFactor</td>
<td>2</td>
<td>Ellithorpe et al. [20]</td>
</tr>
<tr>
<td>Brain health</td>
<td>Neurodegen. dis. adult</td>
<td>NTFactor/L</td>
<td>4</td>
<td>Nicolson et al. [21]</td>
</tr>
<tr>
<td>CD health</td>
<td>CD risk/CD dis. adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Ellithorpe et al. [22]</td>
</tr>
<tr>
<td>Metabolic health</td>
<td>MetSyn/diabetes adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Nicolson [23]</td>
</tr>
<tr>
<td>Metabolic health</td>
<td>Diabetes adult</td>
<td>ATP Fuel</td>
<td>3-4</td>
<td>Nicolson et al. [17]</td>
</tr>
<tr>
<td>Neurobehavior</td>
<td>Autism Spectrum dis. child</td>
<td>NTFactor/L</td>
<td>1-3</td>
<td>Nicolson et al. [3]</td>
</tr>
<tr>
<td>Infections</td>
<td>Lyme/mycoplasma adult</td>
<td>ATP Fuel</td>
<td>4</td>
<td>Nicolson et al. [24]</td>
</tr>
<tr>
<td>Fertility</td>
<td>Fertility Diseases adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Ferreira et al. [25]</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Cancer adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Nicolson [26]</td>
</tr>
<tr>
<td>Anemia</td>
<td>Anemia adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Nicolson et al. [3]</td>
</tr>
<tr>
<td>Injury</td>
<td>Spinal injury adult</td>
<td>NTFactor/L</td>
<td>3-4</td>
<td>Ellithorpe et al. [12,123]</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>Rheumatoid arthritis adult</td>
<td>ATP Fuel</td>
<td>4</td>
<td>Nicolson et al. [12,123]</td>
</tr>
<tr>
<td>General health</td>
<td>Pregnancy adult</td>
<td>NTFactor/L</td>
<td>2-3</td>
<td>Ellithorpe et al. [27]</td>
</tr>
<tr>
<td>Chemical detox</td>
<td>GW Illnesses adult</td>
<td>NTFactor/L</td>
<td>6</td>
<td>Nicolson &amp; Breeding [6,10]</td>
</tr>
</tbody>
</table>

$^a$Modified from Nicolson et al. [5]. Abbreviations: CD, cardiovascular disease; CFS/ME, chronic fatigue syndrome/myalgic encephalomyelitis; GW, Gulf War; MetSyn, metabolic disease/syndrome; MLR, Membrane Lipid Replacement; N/A, not applicable; NTFL, NTFactor Lipids;

$^b$Suggested revised dose range in grams per day based on NTFactor Lipids$^a$

$^c$NTFactor$^®$ or NTFactor Lipids$^®$

$^d$Not Available
OTHER STUDIES
MLR lipids have been used to demonstrate the role of membrane integrity in maintaining cellular function. For example, NTFactor Lipids® can repair mitochondrial membranes and restore mitochondrial function in human cells [15]. MLR has also been used to repair spermatozoa membranes and increase the motility of sperm and resistance to oxidative damage [25,28].

Finally, MLR can improve the transport and bioavailability of nutrients not associated with MLR ingredients. Using an intestinal epithelial bioabsorption tissue culture model based on the transport of nutrients across a monolayer of human intestinal Caco-2 cells, NTFactor Lipids® was found to increase the transport and bioavailability of three test nutrients (coenzyme Q10, curcumin and quercetin) [29]. Therefore, in addition to its own abilities to improve health outcomes, MLR has the potential to improve the bioavailability and properties of various other nutrients that could also be beneficial to health [29].

CONCLUSION
Clinical trials have shown the efficacy and usefulness of MLR supplements in reducing symptoms associated with loss of mitochondrial and other cellular functions and improving the quality of life in patients with a variety of chronic illnesses and normal age-related loss of function. Recent efforts have focused on the effects of MLR supplements on reducing pain, gastrointestinal and other symptoms as well as age-related functional loss. MLR can also improve the bioavailability of certain nutrients and improve membrane function and cellular properties, such as cell motility [25,28].

List of Abbreviations: GWI, Gulf War Illnesses; MLR, Membrane Lipid Replacement

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