Bio.Clear™ Endotox-LV

A botanical and nutrient blend to support the liver and LPS metabolism

Supporting LPS clearance

Bio.Clear™ Endotox-LV has been developed to encourage clearance of lipopolysaccharides (LPS) by supporting liver function, whilst also supporting bile production and flow.

Background

Lipopolysaccharides (LPS), also referred to as endotoxins, are large molecules that consist of a lipid and polysaccharide joined together. They are an important constituent of gram-negative bacteria and cyanobacteria cell walls, and are released in large numbers when the cell is broken down or the colony grows in large amounts [1].

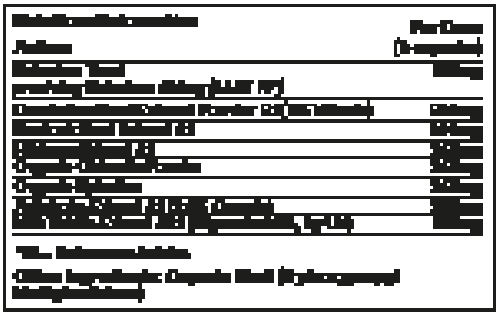
LPS bind to toll-like receptors, especially the toll-like receptor 4 (TLR-4). When bound to TLR-4 receptors, LPS induce the production of pro-inflammatory cytokines nitric oxide, and eicosanoids via tumour necrosis factor alpha (TNF-α) and interleukin beta (IL-β)[2]. TLR4 is found in many cell types, but especially in monocytes, dendritic cells, macrophages and B cells.

Small amounts of LPS are always present in the blood stream and play an important role in building our innate immunity [3]. In large quantities, LPS are so effective at inducing inflammation in the body, that they are often the basis of creating inflammatory models in research trials [4]. LPS exposure at its worst can lead to septicaemia, but they are also indicated as a driving factor in many other inflammatory disorders, such as metabolic syndrome, liver and renal diseases, chronic obstructive pulmonary disease, cardiovascular disease, autoimmunity and neurodegenerative disorders, amongst others [1,5–8].

LPS are treated as lipoproteins by the body, and are cleared primarily through the liver, where Kupffer cells and hepatocytes contribute the major effort [9,10]. People with liver pathology have been shown to have a higher amount of circulating LPS due to reduced liver functioning and increased intestinal permeability [6,11].

Supporting appropriate liver function, bile production and clearance is a way of supporting LPS clearance from the body and reducing related inflammation.

Bioactives



Hibiscus extract

Hibiscus sabdariffa has traditionally been used in India and Africa as a food and medicinal plant [12,13]. Traditionally it has been used for liver, kidney and cardiovascular disorders, urinary tract infections and as an antidote to food or chemical poisoning [12]. Hibiscus contains many phytochemicals, such as the flavanols delphinidin and cyanidin, hibiscitrin, gossypitrin and sabdaritrin, protocatechuic acid and arabinogalactans [13]. Protocatechuic acid has been shown to inhibit LPS-induced hepatic damage in rats, and reduce liver enzymes and inflammatory cytokines in an LPS model [14,15]. The polyphenols in hibiscus have been shown to have strong antioxidant and anti-inflammatory properties [14,16], and their pleiotropic effects may be useful in the metabolic condition that is associated with obesity [17].

A drink given to elderly subjects ameliorated LPS-induced renal

inflammation via downregulation of the pro-inflammatory cytokine network, and the NF-κB pathway. The drink also reduced the incidence of UTIs in residents with urinary catheters by 36% in long-term care facilities [18].

Hibiscus was used in this formula for its antioxidant, anti-inflammatory, hepatoprotective, and LPS-clearing abilities.

Burdock root extract

Arctium lappa is a large perennial herb that is traditionally used in Western, Native American and Chinese medicine. It is one of the constituents in the popular Essiac™ Tea, which is a popular formula used in people with cancer [19]. In folk medicine, burdock roots were popular remedies for hypertension, gout, hepatitis and other inflammatory disorders [20].

Burdock root has been shown to possess hepatoprotective [21], anti-inflammatory [22] and free radical scavenging activities in pharmacological and research trials [20,23]. These activities are attributed to the presence of caffeoylquinic acid derivatives, whilst the chemo-preventative effects are associated to lignans such as arctiin and arctigenin [24].

In a human clinical trial, osteoarthritis patients saw a significant decrease in IL-6, hsCRP and malondialdehyde (a marker of oxidative stress), while levels of serum total antioxidant capacity and activities of superoxide dismutase (SOD) were significantly increased, in comparison to controls, after three cups of burdock tea daily [25]. In a similar study of patients with osteoarthritis, cholesterol and lipoprotein levels improved, and blood pressure reduced [26]. In an inflammatory model of LPS-induced endotoxin shock, arctigenin was shown to ameliorate inflammation by regulating myeloid-derived suppressor cells (MDSCs), which are potent T cell suppressors [27]. Arctigenin also shows anti-inflammatory and antioxidative effects on LPS-induced acute lung injuries [28].

We chose to use burdock in this formula for its hepatoprotective, antioxidant, and its LPS induced inflammation modulating capacity.

Organic Spirulina and Chlorella

Spirulina *(Arthrospira platensis)* is a cyanobacterium alga with a high content of protein (up to 70%), vitamins, especially B12 and provitamin A (β-carotenes), and minerals, especially iron. It is also rich in phenolic acids, tocopherols and γ-linolenic acid [29]. Spirulina has been used as a food source in patients with allergic rhinitis, as an antioxidant and for its cholesterol lowering abilities [29].

Spirulina has been shown to have hepatoprotective and immune-enhancing properties, as well as modulating the gut microbiota – specifically reducing gram negative (LPS-containing) bacterial growth [30,31]. It is also able to reduce the pro-inflammatory effects of fatty liver disease [32]. In an LPS-induced model of inflammation, a maternal diet enriched with spirulina was shown to attenuate inflammatory markers in the pups [33,34]. Chlorella vulgaris, another microalgae used as a food source, has been shown to have similar anti-inflammatory properties to spirulina [35]. Chlorella has been shown to have an LPS-blocking effect at the TLR4, by competitively binding to the receptors, therefore helping to reduce the resultant inflammatory cascade [36]. Spirulina is thought to have a similar mechanism of action on LPS.

Milk thistle extract, Dandelion root extract and Artichoke extract

Traditionally, these botanicals have been used to support liver and bile function, as well as for their digestive capabilities. Milk thistle *(Silybum marianum)* is well-known for its hepatoprotective properties, especially conferred by the phytochemical silymarin and its metabolites [37]. Silymarin possesses hepatoprotective, antioxidant, anti-inflammatory, antifibrotic properties and attenuates the damage caused by LPS [38].

Artichoke *(Cynara scolymus)* is a common herbal medicine in Europe, traditionally used as a remedy to treat hepato-biliary disease and dyspepsia. It has been shown to possess antioxidant, choleretic, hepatoprotective, bile-enhancing and lipid-lowering effects, which corresponds with its historical use [39]. It has been shown to increase SOD, catalase, glutathione, and glutathione peroxidase levels in the liver, and decrease malondialdehyde levels in LPS-induced liver diseases [40].

Dandelion *(Taraxacum officinale)* is a well-known herb traditionally used for its choleretic, diuretic, antirheumatic, and anti-inflammatory properties. Studies have shown it to possess antioxidant, anti-diabetic and immune-modulating activities in response to LPS-induced conditions [41,42].

These hepatoprotective, choleretic, antioxidant and immunomodulatory herbs have been added to promote bile flow for LPS clearance, as well as being protective of LPS-induced inflammation.

Selenium

Selenium is an important micronutrient that is incorporated into selenoproteins, which have a wide range of pleiotropic effects, including antioxidant and anti-inflammatory, as well as involvement in thyroid metabolism. Selenium is an important co-factor of the antioxidant enzyme systems that protect the liver from reactive oxygen species (ROS), and support phase 1 and 2 detoxification pathways [43].

Selenium has been incorporated into this formula for its ability to support our own endogenous antioxidant systems that are involved in protection from LPS-induced ROS.

References

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