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Endohealium™

Product Information

Endohealium™ Formula is designed to regenerate the endothelium, caused by the S-Spike protein damage found in the Covid virus and other inoculation-based sources. This phytotherapeutic extract formulation contains ***Citrus reticulata, Punica granatum, Pterocarpus marsupium, Petroselium crispum, Genista tinetoria, Polygonum cupidatum, Curcuma longa, Hibiscus sabdariffa and Cinnamomum verum.*** This is a synergistic herbal formula known to regenerate the endothelium.

Endothelial cells (ECs) line the inner wall of blood vessels and form a semipermeable barrier, which regulates the flux of fluid, proteins, and blood cells across the vascular wall into parenchymal tissue and maintains an antithrombotic and anti-inflammatory state of the microvascular bed. Endothelial injury leads to complications associated with inflammation, including increased vascular permeability, transmigration of inflammatory cells, exit of erythrocytes, tissue edema, and micro-thrombosis. Endothelial barrier dysfunction is a key initiating event of various vascular diseases, including atherosclerosis and in-stent restenosis. Evidence from humans and animals has demonstrated the central role of endothelial leakage in determining the outcome of vascular diseases.

After endothelial injury, the vascular repair process involves restoration of a functional endothelial monolayer (endothelial regeneration) and reestablishment of the endothelial junctions to reform a semipermeable barrier. The process of endothelial regeneration is thought to involve resident EC migration and proliferation and/or recruitment of circulating stem/endothelial progenitor cells (EPCs) that differentiate to ECs.

Citrus reticulata, Novel mechanisms for hesperetin action in endothelial cells inform effects of oral hesperidin treatment to improve endothelial dysfunction and reduce circulating markers of Hesperetin, and has vasculo-protective actions that may explain beneficial cardiovascular effects of citrus consumption.
Punica granatum, has several health benefits. Pomegranates can help prevent or treat various disease risk factors including high blood pressure, high cholesterol, oxidative stress, hyperglycemia, and inflammatory activities. Luteolinidin inhibits CD38 in vitro and that treatment of the ex vivo isolated heart results in increased postischemic salvage of NADP(H) and NAD(H) pools, and that this is directly correlated with improved vascular and cardiac contractile function.
Pterocarpus marsupium, the most common uses of pterocarpus in modern herbal medicine include to help support the body's natural ability to manage and regulate blood sugar levels. Pterostilbene is one the most active ingredients of pterocarpus extract for this purpose, and other significant components include epicatechin, marsupin and pterosupin. *Pterocarpus marsupium (*pterostilbene) helps in maintaining the blood glucose level by Nrf 2-mediated antioxidant mechanism and reducing oxidative damage to pancreas
Petroselium crispum, Apigenin is a flavonoid present in vegetables (parsley, celery, and onions), fruits (oranges), herbs (chamomile, thyme, oregano, and basil), and plant-based beverages (tea, beer, and wine) [14–16]. A previous study has shown that apigenin inhibits CD38, thus increasing NAD+ levels, and improving glucose and lipid homeostasis.
Genista tinetoria, inhibits the activity of Adenosine triphosphate (ATP) utilizing enzymes such as: tyrosine-specific protein kinases, topoisomerase II and enzymes involved in phosphatidylinositol turnover. It was found to induce apoptosis and differentiation in cancer cells, inhibit cell proliferation, modulate cell cycling, exert antioxidant effects, inhibit angiogenesis, and suppress osteoclast and lymphocyte functions.
Polygonum cupidatum, is a rich source of resveratrol. At nutritionally relevant concentrations, resveratrol inhibits NF-kappaB, which in turn attenuates tumor necrosis factor (TNF)-alpha–induced inflammation
Curcuma longa, *C. longa* contains multiple active components that exhibit antiinflammatory, antimicrobial, antioxidant, antifungal, antibacterial, antiviral, antiischemic, and antineoplastic properties.

Hibiscus sabdariffa, is known for its antibacterial, antifungal and anti-parasitic actions. It also significantly lowered serum cholesterol. Another scientific study also confirmed that ethanolic extract from the leaves of Hibiscus sabdariffa significantly exhibit hypo-lipidemic effect. The extract was also studied among subjects, some with and some without metabolic syndrome. Subjects with metabolic syndrome receiving the ethanolic extract had significantly reduced glucose, total cholesterol and low-density lipoprotein, while increasing high density lipoprotein. ***Cinnamomum verum,*** Cinnamon health benefits are attributed to its content of a few specific types of antioxidants, including polyphenols, phenolic acid and flavonoids.

Endohealium is uniquely extracted from select organic herbs, organic cane alcohol and deep ocean mineral water, as the extraction solvent. Utilizing advanced all-glass apparatus **Endohealium's** ingredients undergo hours of reflux extraction that applies heat and hydroalcohol to enhance the bioavailability of the resultant extraction.

- **Highly bio-available due to heat and hydro-alcohol reflux extraction**
- **Organic**, Non-GMO, Gluten free
- Extracted with **Maui-grown organic sugarcane alcohol** and deep ocean mineral water.

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Endothelial p110γPI3K Mediates Endothelial Regeneration and Vascular Repair Following Inflammatory Vascular Injury

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Abstract

Background—The integrity of endothelial monolayer is a *sine qua non* for vascular homeostasis and maintenance of tissue fluid balance. However, little is known about the signaling pathways regulating regeneration of the endothelial barrier following inflammatory vascular injury.

Methods and Results—Employing genetic and pharmacological approaches, we demonstrated that endothelial regeneration selectively requires activation of p110γPI3K signaling, which thereby mediates the expression of the endothelial reparative transcription factor FoxM1. We observed that FoxM1 induction in the pulmonary vasculature was inhibited in mice treated with p110γ-selective inhibitor and in *Pik3cg*$^{-/-}$ mice following LPS challenge. *Pik3cg*$^{-/-}$ mice exhibited persistent lung inflammation induced by sepsis and sustained increase in vascular permeability. Restoration of expression of either p110γ or FoxM1 in pulmonary endothelial cells of *Pik3cg*$^{-/-}$ mice restored endothelial regeneration and normalized the defective vascular repair program. We also observed diminished expression of p110γ in pulmonary vascular endothelial cells of ARDS patients, suggesting that impaired p110γ-FoxM1 vascular repair signaling pathway is a critical factor in persistent leaky lung microvessels and edema formation in the disease.

Conclusions—We identify p110γ as the critical mediator of endothelial regeneration and vascular repair following sepsis-induced inflammatory injury. Thus, activation of p110γ-FoxM1 endothelial regeneration may represent a novel strategy for the treatment of inflammatory vascular diseases.

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Citrus Polyphenol Hesperidin Stimulates Production of Nitric Oxide in Endothelial Cells while Improving Endothelial Function and Reducing Inflammatory Markers in Patients with Metabolic Syndrome

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Abstract

Context:

Hesperidin, a citrus flavonoid, and its metabolite hesperetin may have vascular actions relevant to their health benefits. Molecular and physiological mechanisms of hesperetin actions are unknown.

Objective:

We tested whether hesperetin stimulates production of nitric oxide (NO) from vascular endothelium and evaluated endothelial function in subjects with metabolic syndrome on oral hesperidin therapy.

Design, Setting, and Interventions:

Cellular mechanisms of action of hesperetin were evaluated in bovine aortic endothelial cells (BAEC) in primary culture. A randomized, placebo-controlled, double-blind, crossover trial examined whether oral hesperidin administration (500 mg once daily for 3 wk) improves endothelial function in individuals with metabolic syndrome (n = 24).

Main Outcome Measure:

We measured the difference in brachial artery flow-mediated dilation between placebo and hesperidin treatment periods.

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The study of aqueous extract of *Pterocarpus marsupium* Roxb. on cytokine TNF-α in type 2 diabetic rats

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Abstract

Objective:

This study was designed to investigate the effect of aqueous extract of *Pterocarpus marsupium* Roxb. on elevated inflammatory cytokine, tumor necrosis factor (TNF)-α in type 2 diabetic rats.

Materials and Methods:

Type 2 diabetes was induced by administering streptozotocin (90 mg/kg, i.p.) in a neonatal rat model. Aqueous extract of *P. marsupium* at a dose of 100 and 200 mg/kg was given orally to desired group of animals for a period of 4 weeks. After 4 weeks of drug treatment, parameters such as fasting blood glucose, postprandial blood glucose, and TNF-α in serum were analyzed.

Results:

Aqueous extract of *P. marsupium* at both doses, i.e., 100 and 200 mg/kg, decreased the fasting and postprandial blood glucose in type 2 diabetic rats. The 200 mg/kg had more pronounced effect on postprandial hyperglycemia. The drug also improved the body weight of diabetic animals. Cytokine TNF-α was found to be elevated in untreated diabetic rats due to chronic systemic inflammation. The aqueous extract at both doses significantly ($P < 0.001$) decreased the elevated TNF-α level in type 2 diabetic rats.

Conclusion:

Modulation of cytokine TNF-α by the rasayana drug *P. marsupium* is related with its potential anti-diabetic activity.

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Research Paper

CD38 inhibition by apigenin ameliorates mitochondrial oxidative stress through restoration of the intracellular NAD$^+$/NADH ratio and Sirt3 activity in renal tubular cells in diabetic rats

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ABSTRACT

Mitochondrial oxidative stress is a significant contributor to the pathogenesis of diabetic kidney disease (DKD). We previously showed that mitochondrial oxidative stress in the kidneys of Zucker diabetic fatty rats is associated with a decreased intracellular NAD$^+$/NADH ratio and NAD$^+$-dependent deacetylase Sirt3 activity, and increased expression of the NAD$^+$-degrading enzyme CD38. In this study, we used a CD38 inhibitor, apigenin, to investigate the role of CD38 in DKD. Apigenin significantly reduced renal injuries, including tubulointerstitial fibrosis, tubular cell damage, and pro-inflammatory gene expression in diabetic rats. In addition, apigenin down-regulated CD38 expression, and increased the intracellular NAD$^+$/NADH ratio and Sirt3-mediated mitochondrial antioxidative enzyme activity in the kidneys of diabetic rats. *In vitro*, inhibition of CD38 activity by apigenin or CD38 knockdown increased the NAD$^+$/NADH ratio and Sirt3 activity in renal proximal tubular HK-2 cells cultured under high-glucose conditions. Together, these results demonstrate that by inhibiting the Sirt3 activity and increasing mitochondrial oxidative stress in renal tubular cells, CD38 plays a crucial role in the pathogenesis of DKD.

INTRODUCTION

Diabetic kidney disease (DKD) is a serious diabetic microvascular complication and the leading cause of end-stage kidney disease (ESKD). Since in type 2 diabetic patients, the renal damage is induced by multiple metabolic risk factors, including hyperglycemia, hypertension, dyslipidemia, and over-nutrition/obesity, multifactorial management of all metabolic risk factors is recommended [1–3]. However, even when patients undergo the multifactorial management, the therapy is often insufficient to suppress the progression of DKD, and there is still a residual risk of progression to ESKD.

Renal tubular damage is closely associated with the pathogenesis of DKD, and is recognized as a "diabetic tubulopathy" [4, 5]. Since a large number of mitochondria reside in renal tubular cells to meet the high energy demand necessary for the reabsorption of nutrients, they are an important source of reactive oxygen species (ROS) in the kidney [6]. In the diabetic state, the mitochondrial function in tubular cells may be disrupted by increased energy demand due to the excessive reabsorption of glucose and sodium [7]. Therefore, protecting tubular cells against mitochondrial oxidative stress in diabetic kidneys might serve as a therapeutic strategy to preserve the renal function. Mitochondrial oxidative stress occurs due to the imbalance between