Symetrian™

Support Immune Homeostasis

What is Symetrian™?

Symetrian™ is a standardized, patent pending, Aloe-based composition for a healthy immune homeostasis.* It is clinically proven to promote rapid immune cell activation and production of circulating TCRγδ+ Gamma delta T cells, suggestive of its heightened immune surveillance at portals of entry, providing immediate immune response.* Symetrian™ has also been clinically proven to increase the levels of glutathione peroxidase (GSH-Px) highlighting its strong antioxidant activity.* Symetrian™ is composed of plant extracts standardized for specific polysaccharides and polyphenols from three botanicals with a long history of safe human consumption for immune support, ***Aloe barbadensis*** (Aloe vera), ***Poria cocos*** and Rosemary (***Rosmarinus oicinalis***).

What Makes Symetrian™ Unique?

- Standardized, patent-pending, novel Aloe-based composition with long history of safe human consumption for immune support*
- Suitable as a long-term daily supplement for all populations.
- Extensive scientific evidence including two randomized, double-blind placebo-controlled, IRB approved clinical studies
- Clinically proven to support maintenance of healthy immunity homeostasis*
- Clinically proven to support cellular and humoral immunity by increasing TCRγδ+ Gamma delta T cells and IgG antibodies*
- Clinically proven to support healthy inflammatory response by maintaining healthy cytokine levels and cytokine responses*
- Clinically proven to support strong antioxidant activity*
- Clinically proven to support rapid immune activation and response*
- Clinically proven to activate Natural killer cells and Gamma delta T cells within hours*

Plant Origin

Derived from ***Aloe vera*** leaf gel powder, ***Poria cocos*** sclerotium extract and Rosemary leaf extract.

Applications

- Maintenance of immunity homeostasis*
- Provide heightened mucosal immunity at the portal of entry for increased immune surveillance and/or a robust response*
- Promote innate and adaptive immunity*
- Provide strong antioxidant activity*

Formulation

Can be used as an active agent alone or formulated with other cold/flu agents in tablets, capsules, gummi, gels, liquids, powders, bars and other delivery systems.

Physical Properties

Brown colored powder easily suspended in water.

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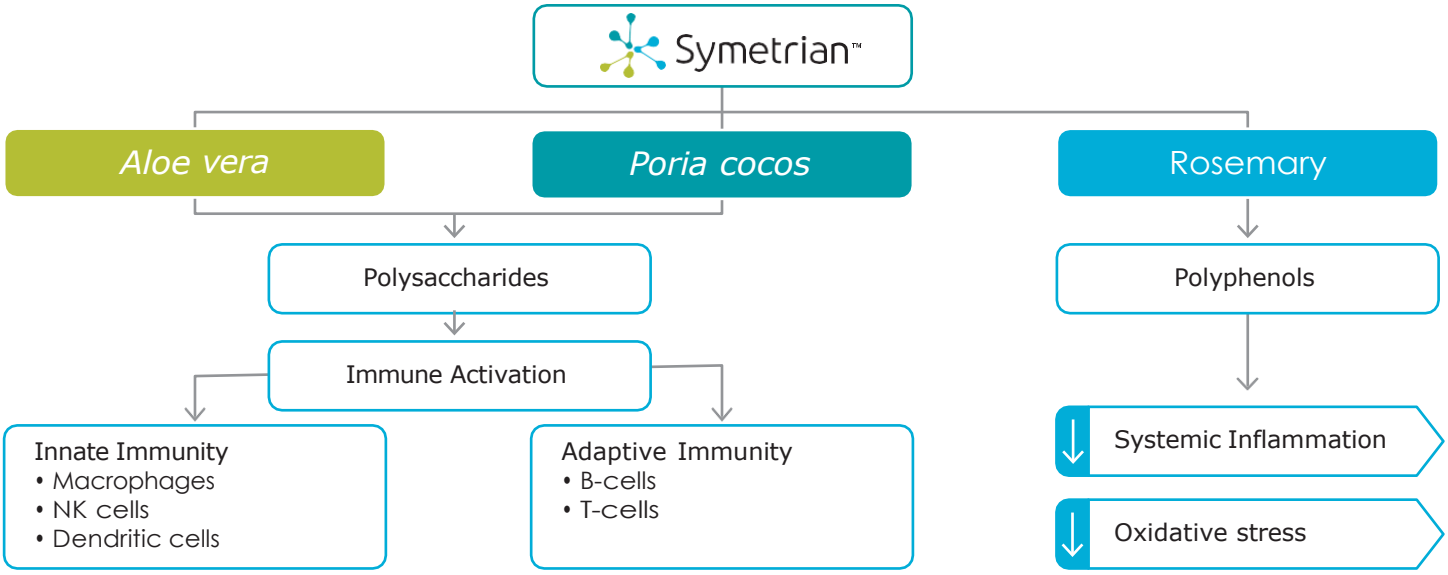
Mechanism of Action

Immune homeostasis and/or immune stimulation and modulation of Symetrian is derived from:

1. Stimulation of innate immunity
2. Enhancement of adaptive immunity
3. Suppression of systematic inflammation and oxidative stress

Fig. 1: Immune homeostasis effect of Symetrian™



Pre-Clinical Data on Acute Lung Injury and Oxidative Stress-Induced Immune Senescence

- Symetrian™ protected animals from Lipopolysaccharide (LPS)-induced sepsis (Figure 2)
- Symetrian™ supported health of lungs (Figure 3) in LPS-induced acute lung model, with reduction of key cytokines, chemokines (TNF-α, IL-6, IL-1, CRP, CINC-3)
- Symetrian™ increased survival rate in hyperoxia-induced oxidative stress mouse model (Figure 4)
- Symetrian™ decreased bacterial load in the broncho-alveolar lavage in hyperoxia-induced oxidative stress mouse model, highlighting its ability in clearing airway bacteria in the lung (Figure 5)
- Symetrian™ supported the body's natural response to protect thymus against oxidative stress-induced immune senescence, which may affect the body's ability to mount an immune response (Figure 6)
- Symetrian™ supported increased SOD activity and increased anti-oxidative protein NRF2, indicating an increased capacity to neutralize free radicals (Figure 7 & 8)
- Symetrian™ supported increased CD3+ T-cells, CD4+ helper T-cell, CD8+ Cytotoxic T cells, NKp46+ Natural Killer cells, CD4+TCRγδ+ Gamma delta T cell levels, IgA, demonstrating that the composition primes the immune system and causes expansion of innate and adaptive immune cell populations (Figure 9)

Fig. 2: Synergistic effects of Symetrian™ (UP360) and its individual components in reducing mortality rate

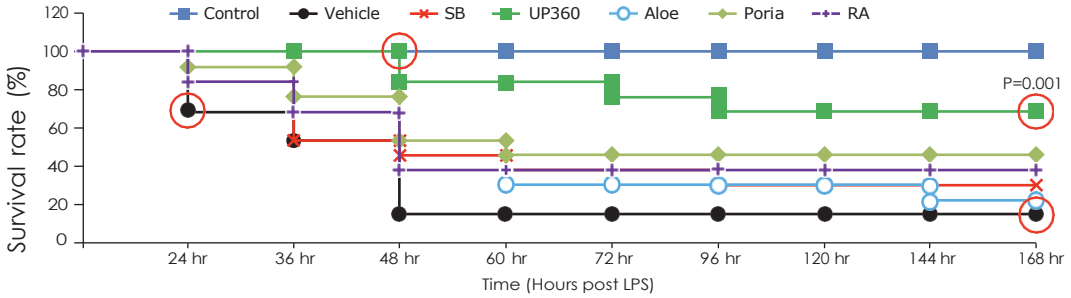
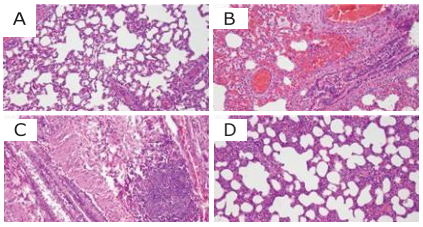


Fig. 3: H&E stain of lung tissue from LPS induced rats supplemented with Symetrian™ (UP360) at 500 mg/kg.



A=normal control, B= Vehicle control, C= Sodium Butyrate, D= UP360 (500 mg/kg). Magnification 100x.

Fig. 4: Mortality rate of mice exposed to hyperoxia conditions and infected with *P. aeruginosa.*

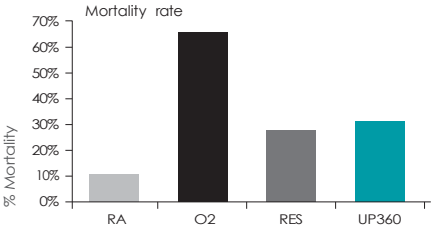
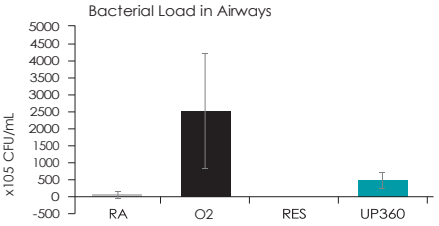


Fig. 5: Bacterial loads in the bronchial alveolar lavage fluid from *P. aeruginosa*-infected mice.



RA= room air control, O2= hyperoxia condition, RES= Resveratrol in hyperoxic condition, D= Symetrian™ (UP360) (500 mg/kg) in hyperoxia condition

Fig. 6: Thymus indices from immune senescent mice supplemented with Symetrian™ (UP360)

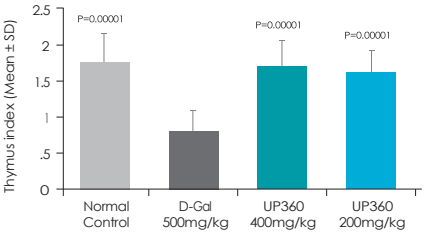


Fig. 7: Serum SOD enzyme (U/mL) from immune senescent mice supplemented with Symetrian™ (UP360)

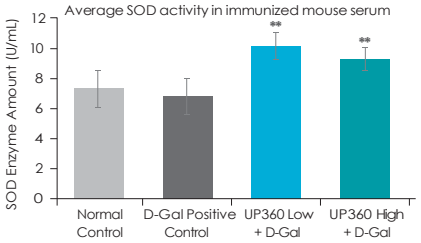


Fig. 8: Relative Nrf2 protein from immune senescent mice and Symetrian™ (UP360)-supplemented mouse spleens

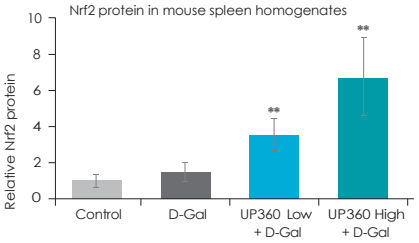
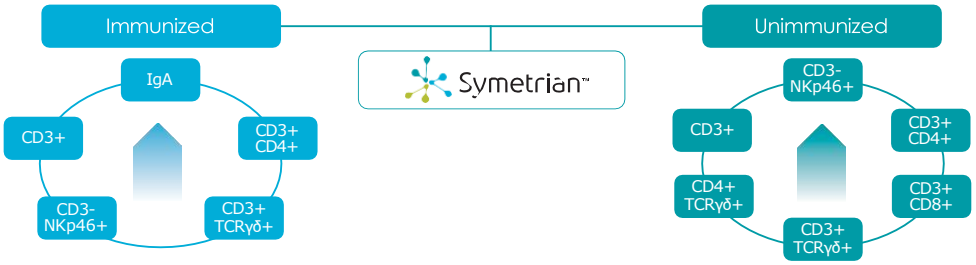


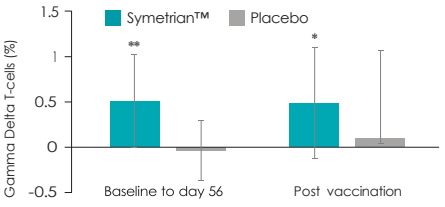
Fig. 9: Summary of innate and adaptive immunity markers stimulated by Symetrian™ in the immune senescent mouse model



Clinical Data on Immune Support

- Supplementation with Symetrian™ 500 mg twice per day was found to increase expansion of Gamma Delta (γδ) T Cells (Figure 10) suggesting a more robust cellular response highlighting its primarily role in first line of defense and immune surveillance
- Symetrian™ supplementation showed statistically significant increase in influenza B-specific IgG levels, in the post-vaccination period indicating enhanced support of humoral protective immunity
- Supplementation with Symetrian™ supported increased serum glutathione peroxidase (GSH-Px) levels highlighting improved antioxidation capacity
- Symetrian™ supplementation produced statistically significant increase in the level of serum IL-1RA, indicating its property maintaining healthy cytokine response

Fig. 10: Differences in γδ T-cells population

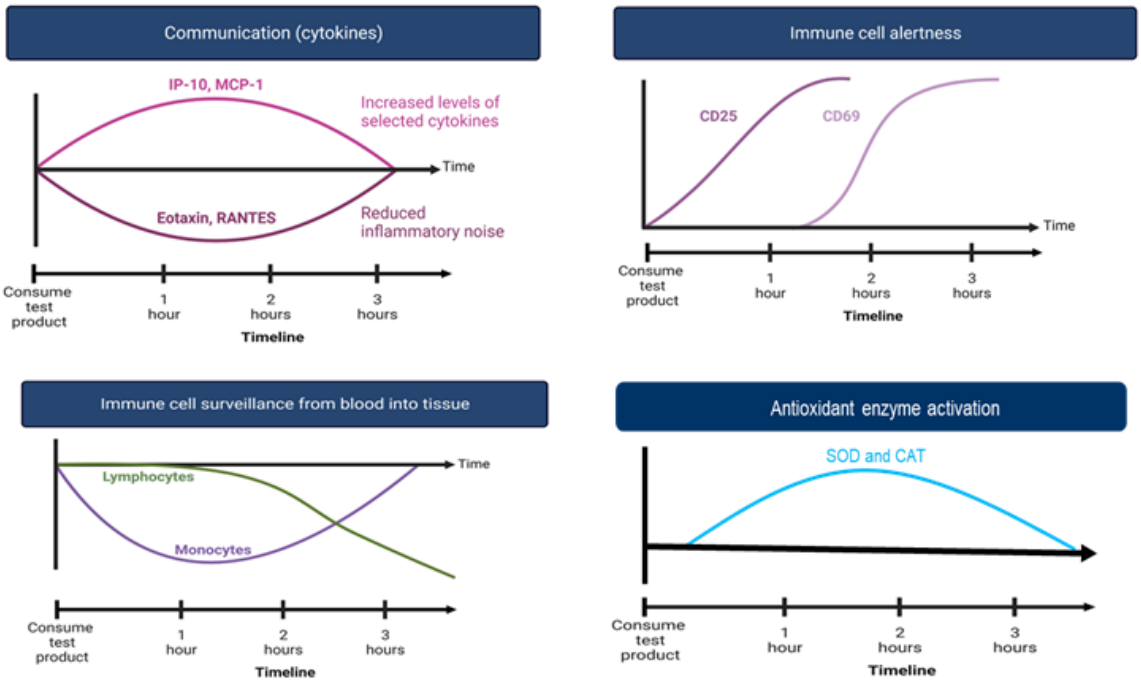


The results of this randomized, triple-blind, placebo-controlled study indicated that supplementation with Symetrian™ at 500 mg twice per day significantly supported heightened immune surveillance as a result of expansion of the Gamma delta T-cells compared to placebo. Through the course of the supplementation, subjects who were given Symetrian™ showed a gradual increase in the level of these T cells, moving from day 28 to day 56, where Symetrian™ showed 21.5% and 24.5% increase in the percent of TCRγδ+ cells populations at days 28 and 56 post supplementation, respectively. In contrast, the placebo group showed decreases in this cell population at the same time frame where 10.5% and 5.6% reduction in the percent of TCRγδ+ cells were observed at days 28 and 56 post supplementation, respectively. Compared to placebo, subjects who received Symetrian™ showed 23.5% and 38.9% increases in the percent of TCRγδ+ cells populations at days 28 and 56 post supplementation, respectively.

Clinical Data on Rapid Immune Modulation

- Supplementation with Symetrian™ at 500 mg single oral dose showed rapid immune activation and proliferation in a randomized double-blind placebo controlled cross over human clinical study
- Supplementation with Symetrian™ showed progressive activation in the numbers of lymphocytes (NKT cells, NK cells; cytotoxic T cells, γδT cells) over a 3-hour period in the blood where the percent changes were found statistically significant against placebo
- Supplementation with Symetrian™ increased activation markers (CD25, CD69 and CD56) on innate and adaptive immune cell populations (monocytes, NK cells, NKT cells, and γδT cells) as early as 1 hour post 500 mg oral supplementation. The CD25 increase after 1 hour and 2 hours was statistically significant for the NKT cells and γδT cells, respectively

Fig. 11: Rapid activation and proliferation of first line of defense by Symetrian™



Collectively, rapid activation of NKT cells and γδ+ T cells, expansion of γδ+ T cell, monocyte and lymphocyte populations for immediate mucosal response and immune surveillance, increased Influenza B-specific IgG antibodies for boosted immune response, augmented GSH-Px activity for a better equipped antioxidation capacity and enhanced healthy cytokine responses as a result of increased level of IL1-RA, suggest the beneficial use of Symetrian™ for a healthy immune support and balanced response for immune homeostasis.

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*These statements have not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease. These statements are presented for informational purposes only and are not intended to be presented to final consumers.