Attenutin™

Respiratory Support

What is Attenutin™?

Attenutin™ is a specially formulated, patent pending natural bioflavonoid composition clinically proven to support innate and adaptive immunity while supporting a healthy level of cytokines.* Attenutin™ has also been clinically proven to increase the levels of glutathione peroxidase (GSH-Px) highlighting its strong antioxidant activity.* Attenutin™ is composed of plant extracts standardized for specific bioflavonoids from two botanicals with a long history of safe human consumption for respiratory health, Scutellaria baicalensis and Acacia catechu (Senegalia catechu).

What Makes Attenutin™ Unique?

- Specially formulated, patent-pending natural bioflavonoid composition with long history of safe human consumption for supporting respiratory health*
- Suitable for short term usage in immune-stressing seasons*
- Clinically proven to support IgA & IgG antibodies production while supporting a healthy level of cytokines*
- Clinically proven to maintain enhanced healthy level of an antioxidation biomarker—glutathione peroxidase*
- Clinically proven to support mucosa of respiratory system for normal, healthy lung function*
- Scientific evidence showed to maintain healthy level of an alarmin protein HMGB1 and proven to support and protect the function of the respiratory system*

Plant Origin

Derived from roots of Scutellaria baicalensis and heartwood of *Acacia catechu*.

Applications

- Support innate and adaptive immunity*
- Support respiratory and lung function*
- Support phagocytosis activity of macrophage*
- Support mucosal immunity*
- Help regulate HMGB1 release*
- Provide strong antioxidant activity*

Formulation

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

Physical Properties

Greenish yellow to brown colored powder.

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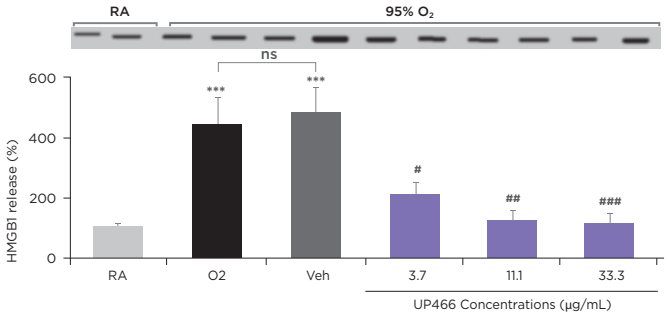
Mechanism of Action

The immune, respiratory support and antioxidation properties of Attenutin™ are derived from:

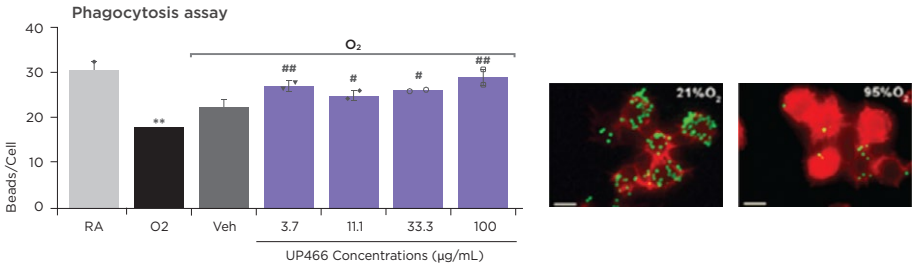
1. Regulation of a late stage alarmin, HMGB1

Fig. 1: Attenutin™ (coded UP446) Reduced HMGB1 release from immune cells (RAW 264.7) under oxidative stress



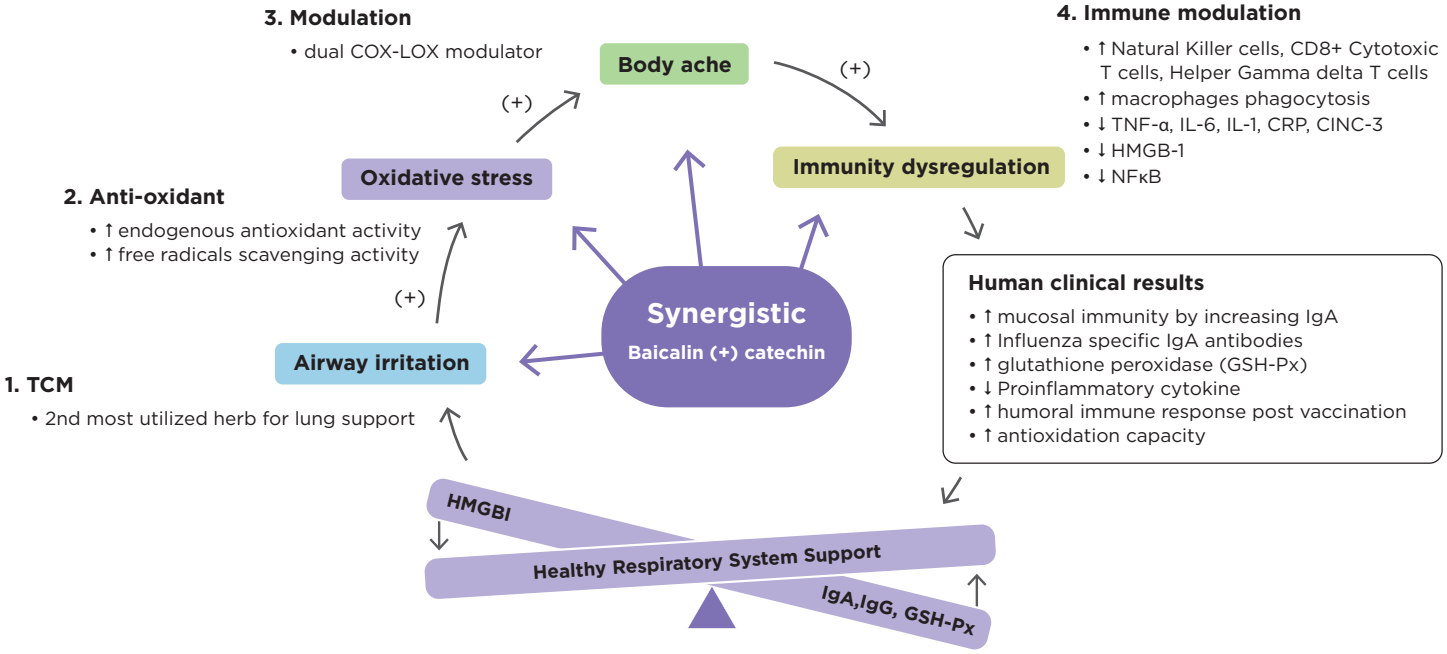
2. Increases phagocytic activity of macrophages

Fig. 2: Attenutin™ restored phagocytosis of immune cells (RAW 264.7) under oxidative stress



3. Attenutin™ maintains homeostasis of host defense mechanism

Fig. 3: Attenutin™ maintains homeostasis of host defense mechanism by a quadruple mechanism of actions



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

- Attenutin™ supported proper levels of HMGB1 release in hyperoxia induced oxidative stressed mouse model indicating its lung protection activity (Figure 4)
- Attenutin™ supported health of lungs (Figure 7) in LPS induced acute lung injury model with reduced key cytokines, chemokines (TNF-α, IL-6, IL-1, CRP, CINC-3) (Figure 5&6).
- Attenutin™ increased survival rate in hyperoxia induced oxidative stressed mouse model
- Attenutin™ decreased protein in the broncho-alveolar lavage in hyperoxia induced oxidative stressed mouse model highlighting its ability in support proper edema response in the lung
- Attenutin™ supported the body's natural response to the reduction of thymus size with age, which may affect the body's ability to mount an immune response (Figure 8)
- Attenutin™ supported significantly higher GSH-Px activity, indicating an increased capacity to neutralize free radicals (Figure 9)
- Attenutin™ supported a decrease in Advanced Glycation End products (AGEs) (Figure 10) indicating that Attenutin™ supplemented animals had lower levels of free radicals, specifically those that contributed to the aging phenotype of the D-Gal model.
- Attenutin™ supported increased CD49b+, NKp46+ Natural Killer cells, CD8+ Cytotoxic T cells, CD4+TCRγδ+ Helper Gamma delta T cells levels demonstrating that the bioflavonoid composition primes the inactivated immune system and causes expansion of immune cell populations, increasing immune "readiness" (Figure 11).

Fig. 4: Attenutin™ reduced HMGB1 in hyperoxia induced mouse model

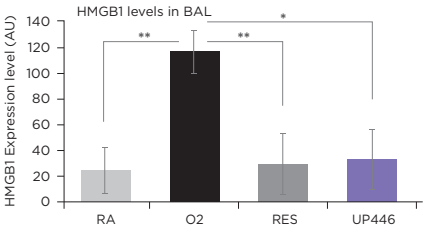
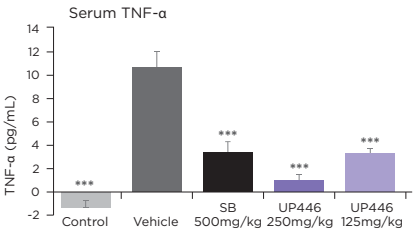
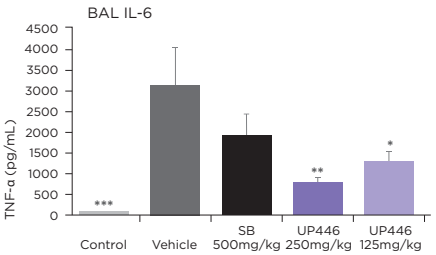


Fig. 5: Effect of Attenutin™ on serum TNF-α level.



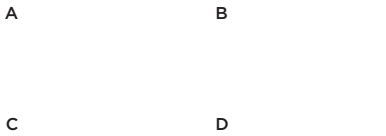
Data presented as Mean ± SE. n=10. ***P ≤ 0.0001.

Fig. 6: Effect of Attenutin™ on BAL IL-6 level.



Data presented as Mean ± SE. n=10. ***P ≤ 0.0001; **P ≤ 0.001; *P ≤ 0.05

Fig. 7: Attenutin™ supported lung tissue integrity



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

Fig. 8: Attenutin™ supported immune organ - thymus indices in an immune senescence model

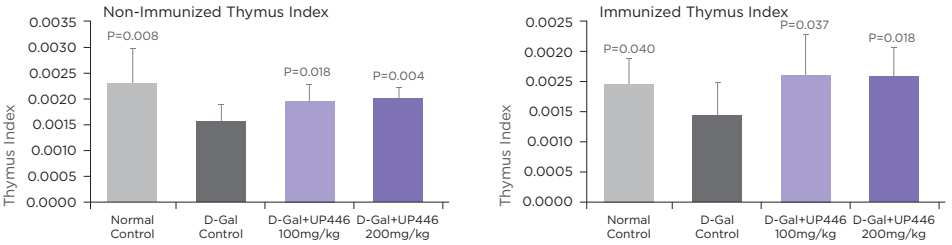


Fig. 9: Attenutin™ significant support in GSH-Px activity in immune senescence model

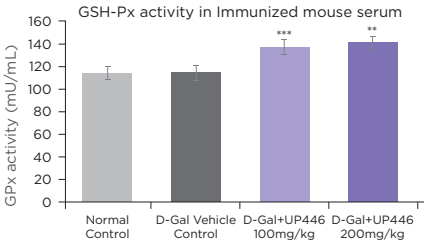


Fig. 10: Attenutin™ significantly decreased Advanced Glycation End products (AGEs) in immune senescence model

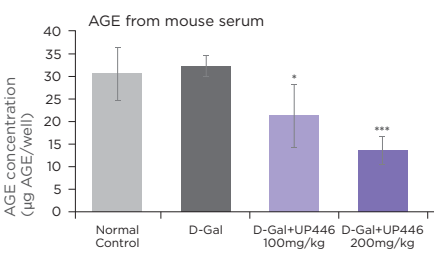
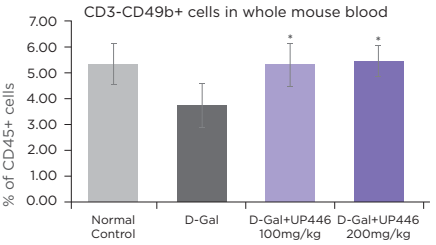


Fig. 11: Effect of Attenutin™ on CD3-CD49b+ cells in whole mouse blood



Clinical Data on Respiratory Support

- Supplementation with Attenutin™ was found to support increased total serum IgA concentrations (Figure 12) suggesting a more robust mucosal response to vaccination.
- Attenutin™ supplementation showed statistically significant increase in serum IgG and influenza B-specific IgG levels in the post-vaccination period indicating enhanced support of humoral protective immunity.
- Supplementation with Attenutin™ supported increased serum glutathione peroxidase (GSH-Px) levels (Figure 13) in the pre-and post-vaccination period highlighting improved antioxidation capacity of supplement.
- Attenutin™ supplementation produced statistically significant lower level of serum cytokine, IL-21.

Fig. 12: Attenutin™ significantly supported IgA mucosal immunity after immunization

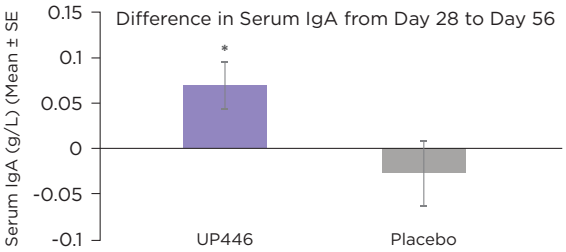
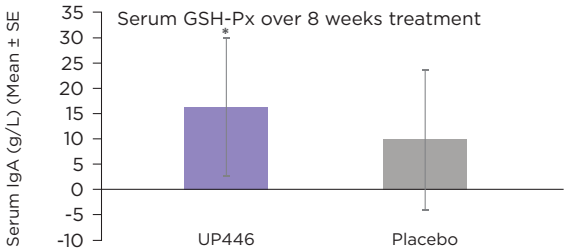


Fig. 13: Effect of Attenutin™ supplementation on serum GSH-Px from baseline and 8 weeks of supplementation.



***p<0.05 denotes significant increase in Attenutin™ group from D0 to D56**

The results of this randomized, triple-blind, placebo-controlled human clinical study indicated that oral supplementation with Attenutin™ 250 mg twice per day significantly supported the increase of total IgA concentrations in the post-vaccination period compared to placebo. IgA is the major immunoglobulin of healthy respiratory tract and is thought to be the most important immunoglobulin for mucosal defense. In this clinical study a total of 63.6% of participants in the Attenutin™ group had increases in IgA in the post-vaccination period, compared to only 37.5% in the placebo group. In addition, Attenutin™ supplementation supported the increased GSH-Px levels in the pre-vaccination and post vaccination period suggesting its benefit in mitigating general systemic oxidative stress.

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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.