



Attenutin™ is a natural, proprietary bioflavonoid composition, clinically proven to support the respiratory system and a healthy lung function. Attenutin™ is composed by two specific bioflavonoids, *Scutellaria baicalensis* and *Acacia catechu*, with long history of safety.



PRODUCT PROFILE SHEET

What makes Attenutin™ unique?

Attenutin™ is composed of plant extracts standardized to specific bioflavonoids from two botanicals with a long history of safe human consumption for respiratory health support, *Scutellaria baicalensis* and *Acacia catechu* (*Senegalia catechu*).

Scientific research on Attenutin™ demonstrates its ability to increase the levels of glutathione peroxidase (GSH-Px) and highlights its strong antioxidant activity. Glutathione peroxidase is an antioxidant enzyme with the capacity to scavenge free radicals. This in turn helps to prevent lipid peroxidation and maintain intracellular homeostasis as well as redox balance. Cellular redox homeostasis is an essential and dynamic process that ensures the balance between reducing and oxidizing reactions within cells and regulates the excess of biological responses and events. Therefore and based on scientific research, Attenutin™ acts to support the respiratory system by assisting the IgA & IgG antibodies production, enhancing healthy levels of the antioxidation biomarker glutathione peroxidase and maintaining healthy levels of the alarmin protein HMGB1.

The discovery

The main constituent of Attenutin™, *Scutellaria baicalensis*, has been used in TCM preparations for respiratory health for centuries.¹⁻² Prolonged exposure to oxidative stress from environmental air pollution and/or lung injury can cause impaired innate immunity by increasing HMGB1 level leading to a reduced macrophage function.³

These effects will cause a compromised host defence mechanism subjecting the host unable to clear invading pathogens in the lungs. Recently, Unigen did a series of in-vitro and in-vivo studies and determined HMGB1 as the main target for its efficacy for lung protection and respiratory health support. HMGB1 (high mobility group box 1) is known to activate an exponential inflammatory response and serve as an alarmin

mediating various cellular responses including chemotactic cells movement and release of proinflammatory cytokines through activation of NF-kB.⁴⁻⁶

Thus, reducing the levels of HMGB1 in the airways and/or blocking their activities, could provide important immune and respiratory protective strategies. Besides its strong anti-oxidation property, in multiple studies, Attenutin™ was found to modulate the immune system, reduce HMGB1 release, and balance cytokine response to prevent respiratory and lung tissue damages. These results were also supported by triple blind human clinical trial.

Product Advantages

- ✓ **Unique Plant-based composition**
Specially formulated natural bioflavonoids
- ✓ **Natural option for short term usage in immune-stressing seasons**
- ✓ **Scientific Evidence**
Supporting healthy respiratory and lung function and strong antioxidant activity
- ✓ **Discovered through screening of the unique Unigen's PhytoLogix® library**
Validated for its function clinically
- ✓ **Safe**
Long history of safe human consumption plus extensive safety studies

Research

Pre-clinical Studies

Unigen has carried out multiple scientifically sound preclinical in vivo and in vitro assays to evaluate the MOA and activity of Attenutin™ and found:

- Reduced HMGB1 release from immune cells under oxidative stress and restored phagocytosis.
- Supported proper levels of HMGB1 release in hyperoxia induced oxidative stressed mice.
- Supported health of lungs in LPS induced acute inflammatory lung injury of mice with reduced key cytokines, chemokines (TNF- α , IL-6, IL-1, CRP, CINC-3).
- Increased survival rate in hyperoxia induced oxidative stressed mouse model.
- Decreased protein in the broncho-alveolar lavage in hyperoxia induced oxidative stressed mouse model.
- Supported the body's natural response to maintain thymus size with age.
- Supported significantly higher GSH-Px activity.
- Supported a decrease in Advanced Glycation End products (AGEs).
- Supported increased innate and adaptive immune cells such as CD49b+, NKp46+ Natural Killer cells, CD8+ Cytotoxic T cells, CD4+TCR γ δ + Helper Gamma delta T cells levels.



Human Clinical Study on Respiratory Support

A clinical study was conducted comparing daily Attenutin™ supplementation (one 250 mg capsule in the morning and one 250 mg capsule in the evening) to placebo.

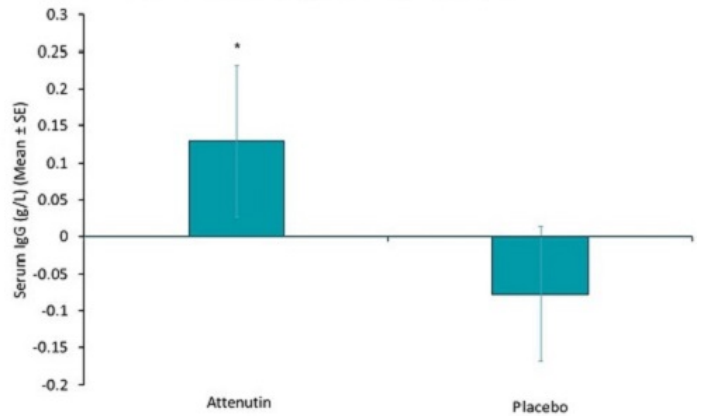
The study participants (25 per arm), who were between 40 and 80 years of age, consumed the test compounds for 28 days before administration of the quadrivalent influenza vaccine.

The study participants then continued supplementation for another 28 days after vaccination. Study lasted a total of 56 days.

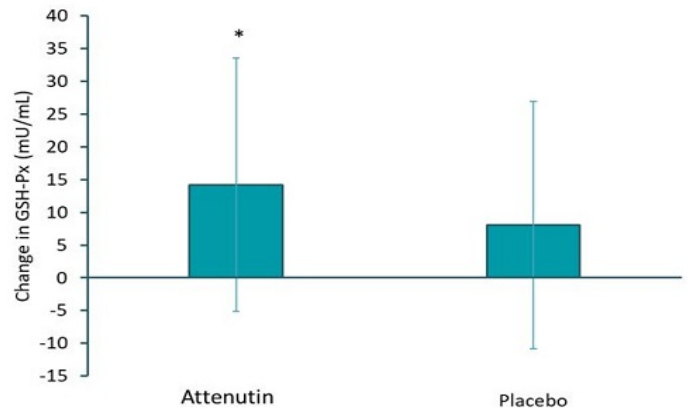
Blood samples were taken at day 0, day 28, and day 56 and were tested for differences in immune cell populations, antibodies, and antioxidation markers, among other parameters. Safety outcomes, such as liver enzyme levels and other blood chemistry markers were measured, and adverse events were recorded.⁷

Study results:

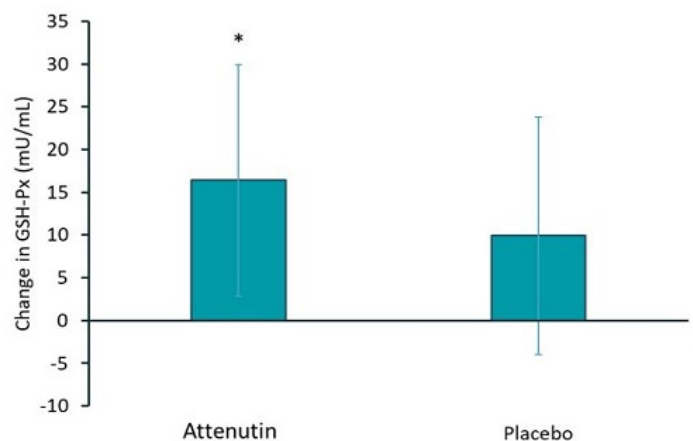
- Supplementation with Attenutin™ was found to support increased total serum IgA concentrations suggesting a more robust humoral response to vaccination.
- Attenutin™ supplementation showed statistically significant increase in IgG levels in the post-vaccination period indicating enhanced support of humoral protective immunity.
- Supplementation with Attenutin™ supported increased serum glutathione peroxidase (GSH-Px) levels in the pre-and post-vaccination period highlighting improved antioxidation capacity of supplement.



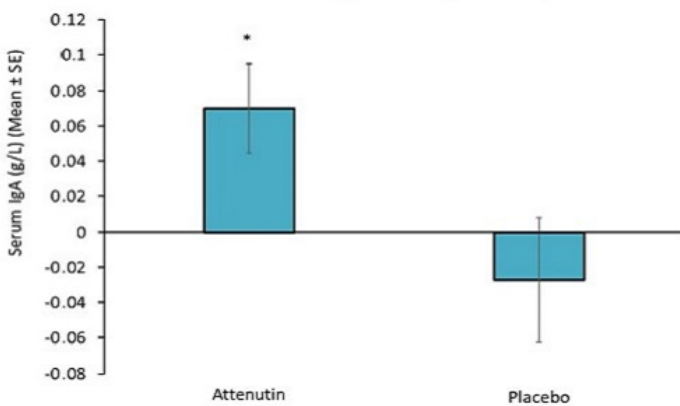
Graphic 2: Attenutin™ significantly supported IgG, humoral immunity after immunization



Graphic 3: Effect of Attenutin™ supplementation on serum GSH-Px after 4 weeks



Graphic 4: Effect of Attenutin™ supplementation on serum GSH-Px after 8 weeks



Graphic 1: Attenutin™ significantly supported IgA mucosal immunity after immunization



New Pre-Clinical Study on HMGB1 and Lung Inflammation

HMGB1 is among the key inflammatory mediators up regulated at the time of chronic exposure to pollution. Extracellular HMGB1 accumulation in the airways and the lung plays a significant role in the pathogenesis of inflammatory lung injury.

In a new published (September 2023) pre-clinical study, Attenutin™ was evaluated for its efficacy in attenuating acute inflammatory lung injury and sepsis. For this study mice models of disorders and oxidative stressed innate immune cells were utilized.⁸

Results showed statistically significant decreases in mortality (50%), proinflammatory cytokines (TNF-, IL-1, IL-6) and chemokines (CINC-3) in serum and bronchoalveolar lavage fluid (BALF). An increased bacterial clearance from airways and lungs; reduced airway total protein and decreased extracellular HMGB1 were observed in-vivo.

Furthermore, a statistically significant 75.9% reduction in the level of extracellular HMGB1 and an increase in phagocytosis were observed in cultured macrophages.

The results of this pre-clinical study strongly suggest that Attenutin™ could be indicated for oxidative-stress-induced lung damage protection, possibly through attenuation of increased extracellular HMGB1 accumulation.

Reducing the level of extracellular HMGB1 induced by oxidative stress and/or respiratory tract infection may have a significant impact on protecting the lungs from injury and preserving normal physiological respiratory tract functions.

In summary:

- Attenutin™ is clinically proven to support IgA & IgG antibodies production while supporting a healthy level of cytokines.
- According to research, Attenutin™ maintains enhanced healthy levels of the antioxidation biomarker - glutathione peroxidase.
- Scientific evidence shows its role in supporting mucosa immunity in the respiratory system for normal, healthy lung function.
- Scientific evidence shows its ability to maintain healthy levels of HMGB1, to support and protect the function of the respiratory system.

Potential Benefits for Sport Nutrition

We have described how research supports Attenutin™'s ability to reduce increased HMGB1 accumulation. It is known that neutralisation of HMGB1 and therefore inflammatory responses, may prevent muscle loss and damage.

Based on this, Attenutin™ may also offer potential benefits for athletes and people practicing sports regularly.

Product Safety

Acute toxicity, repeated chronic toxicity, pharmacological safety, reproductive and developmental toxicity, and genotoxicity in in vivo safety studies have demonstrated the safety of Attenutin™. Furthermore, extensive human clinical safety studies were conducted on Attenutin™ composition at multiple dose levels and durations.

Product Range

Ingredient	Active Content	Grade	Mesh Size
Attenutin	Min 60% Baicalin Min 10% Catechins	Powder	NLT 80% thru 80 mesh

Product Pack Size

25kg is the standard pack size for Attenutin™.

Product Applications

Attenutin™ is mainly used in capsules and tablets, but can also be used in liquid applications. We suggest you use flavouring (i.e berry) which will cover the slightly bitter taste when formulating liquid applications.

Product Dosage

According to clinical evidence the recommended daily dosage of Attenutin™ is 500 mg/day administered in two 250mg dosages am/pm.

The Phytologix® Technology Platform



Attenutin™'s unique formulations are discovered and developed through Unigen's proprietary Phytologix® Technology Platform. This proprietary informatics database contains comprehensive botanical profiles on over 12,000 plants and data on more than 15,000 extracts and 300,000 HTP fractions. Unigen scientists used these profiles to identify plants whose actives delivered the most effective health benefits.

About

UNiGEN

Unigen focus on identifying and studying the unique bioactive natural products of medicinal botanicals and then developing them into research-driven, proprietary standardized extracts for use in nutraceutical, cosmetic, and pharmaceutical finished products.



References

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