Andrographis for Immunity

From Ayurveda to Modern Science

AP-Bio™

natural™ REMEDIES

Immune Health at the Forefront

The human immune system has skyrocketed to the forefront of the global conversation as a result of the soon-to-be historic 2020 pandemic. The common shared concern is how to prevent getting and transmitting it; and looking into the future – how to transform the vaccination and response processes to ensure the next potential pandemic is quickly contained.

As is generally understood, there is no way to confidently and purely prevent any illness from occurring – however, there are successful means of reducing risk by bolstering immune function.

It is also widely known that the elderly and the very young (infants and toddlers) are the most susceptible to viral and bacterial assaults. According to the United Nations' 2015 World Population Aging report, by 2030, the global population aged 60 and over is expected to have grown by 56%. Products that support immune function for this population should perform very well in the marketplace. [1]

Each year, US Centers for Disease Control (CDC), noted that approximately 28% of all OTC medicine purchases are for cold and flu treatments. During a pandemic such as we have seen in 2020, this increases exponentially. In fact, because of the monumental 2020 pandemic, the desire to bolster immune support to ward off viruses will likely be a priority for global citizens for years to come.

The Global Immune Health Market

According to Nutrition Business Journal (NBJ), the growth of immune supplement sales is projected to leap above 25% this

Pre-Coronavirus sales of immune support supplements in the US grew 8.5% to reach $3.3 billion in 2019. Immune health will also fertilize sales of other supplement categories, and the overall growth potential for this year (2020) could be the highest in a decade, expected to surpass $50 billion.[2]

In this new age, consumers will be purchasing both symptom treatment (OTC medicines) as well as immune-health supplements to reduce incidence and intensity of viral infections. The field of opportunity to create successful, science-backed immune-support supplements has never been so fertile: by 2022, sales of immune-support supplements is expected to reach nearly $5 billion.

Global citizens are understanding the message that paying attention to their immune health will pay dividends in better and longer duration quality of life. The phrase, "life is too short" resonates now more than ever, and this energizes the desire to achieve and enjoy resistance to ailments that can temporarily put someone "out of order."

Respondents in a 2016 Harvard Opinion Research Program survey of 1,579 adults ranked immune health among the top-three reasons to research and buy supplements, over heart health/cholesterol, weight control, and digestive support. [3]

Sales of products claiming immune protection are up all over the world. In its report, "Immune Health Supplements Market: Global Industry Analysis and Forecast 2017-2025," Persistence Market Research had estimated the global immune-health supplement market at $14.4 billion in 2017, with a predicted CAGR of 7%, for an estimated increase to $25 billion by 2025 – this equates to 73.6% increase in eight years. [4]

Overall, seasonal flu outbreaks result in an average of $10.4 billion in direct costs of hospitalization and outpatient visits, according to the CDC. That total does not include indirect costs associated with lost productivity and worker absenteeism. According to the Bureau of Labor Statistics, employee absences on average are up an estimated 32% during the winter flu season compared with the rest of the year.

Colds are indeed common. According to the CDC, in the US, there are approximately 1 billion colds per year – the average American adult gets two to three colds each year, and children have more. The perennial challenge among all of us is to determine if any of the following common symptoms are a cold or flu, a virus or bacterial: cough, expectoration, nasal discharge, headache, sore throat, earache, fatigue, and or fever.

Although rhinovirus infections can occur anytime, they are more prevalent in the fall and spring; whereas, other types of colds and allergies seem to occur more often in the winter and early spring.[5] Even if one of those symptoms, such as a cough, runny nose or excessive tiredness appear, this means the immune system has, or has had, a weak moment.

Popular Solutions for Immune Health

When the first full-body sneeze occurs, when a fever ramps up, when the throat starts to "tickle," and when the voice begins to rasp, people tend to self-medicate with a variety of widely available products. And, as the global consumer demand for immune support (and cold/flu season safety) ramps up, there is a real need for more.

Consumers will turn to the conventional "cold and flu" aisle for symptomatic relief, often purchasing pain relievers such as ibuprofen or paracetamol, cough syrups such as dextromethorphan, decongestant nasal sprays and assorted other OTC formulas.

Increasingly, consumers are also looking to supplements to buttress their immune activity when it needs to fend off a virus. And given the current landscape that has been altered by the COVID-19 pandemic, the prevention mindset will drive millions of new consumers globally to the immune support category.

Vitamin C

is the "go to" natural immune booster for consumers worldwide. According to the aforementioned NBJ webinar, citing NetRush real-time statistics, 57% of Amazon's top 100 fastest-growing vitamin products are vitamin C.[2] Vitamin C is known to boost immunity by supporting epithelial barrier function against pathogens, increases phagocyte activity and boosts production of lymphocytes – both are immune cells that patrol, identify and neutralize harmful agents such as viruses. [6]

Zinc

typically taken as lozenges and effervescent powders (for beverages), is the top mineral for immunity and taken typically at the first symptom arises. One meta-analysis has concluded that between 80 and 92 mg per day of zinc can reduce common cold duration by up to 33%. [7]

Echinacea

is likely the top known "cold" herb, and meta-analyses show that the herb is more effective than a placebo in reducing common cold symptoms[8] as well as decreasing the risks of developing a cold by 58% and shortening the duration of a cold by 1.4 days. [9]

Olive Leaf

The extract of olive leaf contains a unique active compound, oleuropein as well as hydroxytyrosol, which have been stated by researchers to exert antioxidant, anti-inflammatory, antibacterial and anti-viral actions. One placebo-controlled study of high school athletes showed that those who consumed olive leaf extract had a significant 28% reduction in sick days stemming from upper respiratory illness. [10]

Black Elderberry

Native to Europe, the most common type is Sambucus nigra, also known as the European elderberry or black elder. Today, it is one of the most popular supplements to treat cold and flu symptoms.[35]

Clearly, any dietary supplements that act as immunomodulators (that modulates immunity and inflammation) in providing immune resistance or tolerance would be welcome. And although these popular solutions remain effective, there is always room for more solutions, especially now. And there is a botanical with historic use and clinical research for immune support – *Andrographis paniculata.*

Traditional Uses of Andrographis for Immunity

Almost every herb you are familiar with and that is commercially available has longstanding use among indigenous populations. Such an herb is *Andrographis paniculata.*

Andrographis paniculata Nees *(A. paniculata)* commonly known as Chiretta, King of Bitters or Kalmegh, is a standout medicinal botanical in the rich history of Ayurveda, a dominant worldwide system of healing that has its roots in India. [11]

In Ayurveda, *A. paniculata* has been consumed to reduce symptoms of upper respiratory tract infections and colds, as well as other infectious conditions. Later on, the botanical has been used in combination with antibiotics to control dysentery, a severe form of diarrhea.

Andrographis paniculata is widely used as a medicinal plant in South and Southeast Asia and is traditionally used for treating a variety of ailments. It was recommended in Charaka Samhita dating to 175 BC for treatment of jaundice along with other plants in multi plant preparations. [12]

The plant has been used to help recover from general fatigue after fever and dysentery. The juice of fresh leaves is an Ayurvedic remedy to relieve colic pain, loss of appetite, irregular stools and diarrhea.

In traditional Asian medicine, *A. paniculata* was popularly used as an immune health herb and has been known for its demonstrated use in fighting cold, flu and upper respiratory infections. [12]

Traditional Asian medicine systems recommends *A. paniculata* to rid the body of excess heat (fever) due to its "cold property" activity, which also helps the body rid itself of toxins. In other systems, *A. paniculata's* "blood purifying" abilities have made it a popular remedy for chronic seasonal fever and related symptoms.[13]

Pre-Clinical Research Supports Andrographis Use for Immunity

It's only natural that as research technology has evolved, the scientific community would focus on revealing how and why traditional medicinal uses of herbs such as Andrographis work to support desirable immune function.

Quality monographs on Andrographis are available in the United States Pharmacopoeia, European Pharmacopoeia and Indian Pharmacopoeia, among others, enabling herbal manufacturers to ensure the quality of Andrographis in their immune-support products.

Numerous studies have been conducted by researchers, especially in Asia, to validate anecdotal evidence of the medicinal properties exerted by *A. paniculata* mostly according to Ayurvedic practitioners. Phytochemical research has shown that *A. paniculata* contains diverse compounds including labdane diterpenoid lactones, flavonoids and other compounds. Andropholide has been identified as the most prominent diterpenoid lactone, and others include deoxyandrographolide and neoadnrographolide. [14, 15]

Herbal remedies featuring *A. paniculata* have been reported to hasten recovery from the common cold and increase the immune system's resistance to thwart cold episode onset; several earlier studies and a meta-analysis have validated these abilities. [16, 17, 18]

In one study, three isolated compounds from *A. paniculata* showed moderate, favorable increases in blood lymphocytes, a type of white blood cell that is fundamentally important in healthy immune function. [19]

When a rhinovirus penetrates the cells lining the nasopharynx (upper back of the throat), those infected cells release interleukin-8 (IL-8), which launches an inflammatory cascade that creates greater symptom intensity including sore throat.

One phytochemical study on *A. paniculata* demonstrated that dehydroandrographolide, andrographolide and neoandrographolide exhibited a strong anti-inflammatory effect by inhibiting expression of pro-inflammatory compounds and that andrographolide, seemingly the most potent active compound in the plant, may also influence down-expression of genes involved in inflammatory cascade. [20]

Clinical Evidence Validates Andrographis for Immune Health

One randomized, double-blind placebo-controlled study tested the use of a 1200 mg Andrographis extract for five days in 158 adults experiencing a cold.

The andrographis supplementation showed significant improvement of all cold symptoms from the beginning of day 2 compared to placebo.[21]

A randomized, double-blind study examined the use of Andrographis in 152 adults who had pharyngotonsillitis, a throat infection. The volunteers were given a standard medication (paracetamol) or 3 g or 6 g *Andrographis paniculata* daily for a week. The high dose (6 g) group had similar relief of fever and sore throat as the paracetamol group.[22]

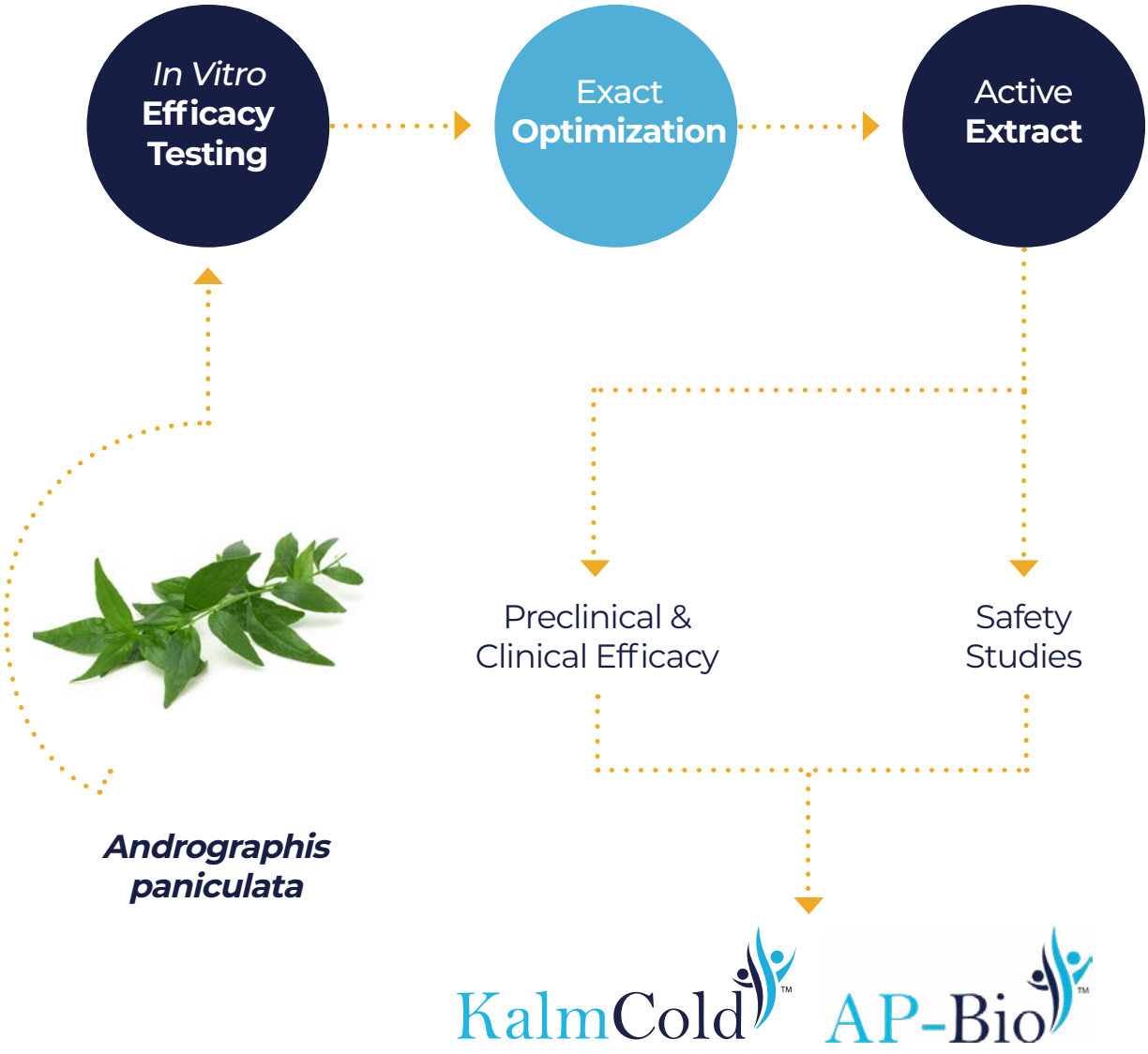
A meta-analysis of both English and Chinese databases included 33 RCTs totaling 7,175 adults and children, concluded that improved cough and sore throat compared to placebo, and had a statistically significant effect in improvement of overall symptoms of acute upper respiratory tract infections. [23]

Development of AP-Bio®

A unique, effective and safe *Andrographis paniculata* for the worldwide immune support marketplace is AP-Bio®, also known as KalmCold® in the EU markets. AP-Bio® is standardized to 7 phytoconstituents: andrographolide,isoandrographolide, neoandrographolide, 14-deoxy-11, 12-didehydroandrographolide, andrograpanin, skullcapflavone-I and 7-O-methylwogonin. It is also standardized to 30% andrographolide, the prime active constituent.[24]

After the herb is cultivated, harvested, and sent through a battery of tests for identity/authentication and other quality control assays, it goes through an extract optimization process that produces and protects the seven key actives.

The final extract that is AP-Bio® has also been subjected to preclinical and clinical efficacy studies, which have all shown potent, reliable and attractive immune-support benefit, especially in individuals who reported experiencing symptoms of common cold generated by a lowered immune response.



AP-Bio® Strengthens Immune Response

A randomized, double blind placebo controlled clinical study was conducted to evaluate the efficacy of AP-Bio® in 223 volunteers (men and women aged 18 to 60) with uncomplicated upper respiratory tract infection (URTI). The assessment involved quantification of symptom scores by Visual Analogue Scale. Nine self-evaluated symptoms of cough, expectoration, nasal discharge, headache, fever, sore throat, earache, malaise/fatigue and sleep disturbance were scored. The participants were randomized to consume either 200 mg per day of AP-Bio® (also known as KalmCold®) for five days.

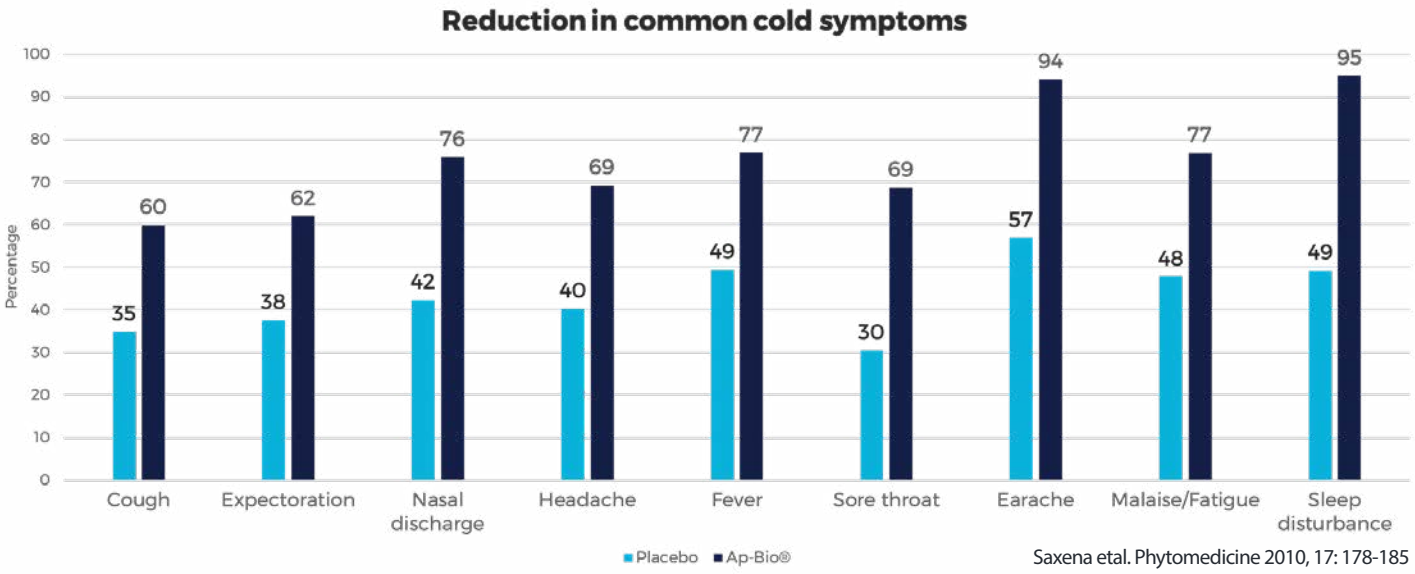
In both groups, mean scores of all symptoms showed a downward trend from day 1 to day 3 -- but from day 3 to day 5 most of the symptoms in placebo treated group either remained unchanged (cough, headache and earache) or became aggravated (sore throat and sleep disturbance), while in the AP-Bio® group all symptoms (except earache) showed a marked downward trend.

The comparison of overall efficacy of AP-Bio® over placebo was found to be significant -- 2.1 times (52.7%) higher than placebo. The conclusion of this study was that AP-Bio® was effective in reducing symptoms of upper respiratory tract infection.[25]

A smaller portion of each group had aggravated (most intense) symptoms at day 5. In the placebo group, 14 participants (13%) still had aggravated symptoms, compared to 1 (0.9%) in the AP-Bio® group; also at the study's conclusion, symptoms of 3 in the placebo group (2.8%) remained unchanged, compared to 1 in the AP-Bio® group (0.9%). [26]

Condition	Subjects with symptoms of common cold
Dose	200 mg per day
Participants	223 adults (Age: 18-60 years)
Duration	5 days
Evaluation	Day 1, Day 3, and Day 5 (using Visual Analogue Scale)
Outcome	AP-Bio® showed 2 times efficacy as compared to placebo and was well tolerated

Results - Randomized double blind placebo controlled clinical study of AP-Bio®



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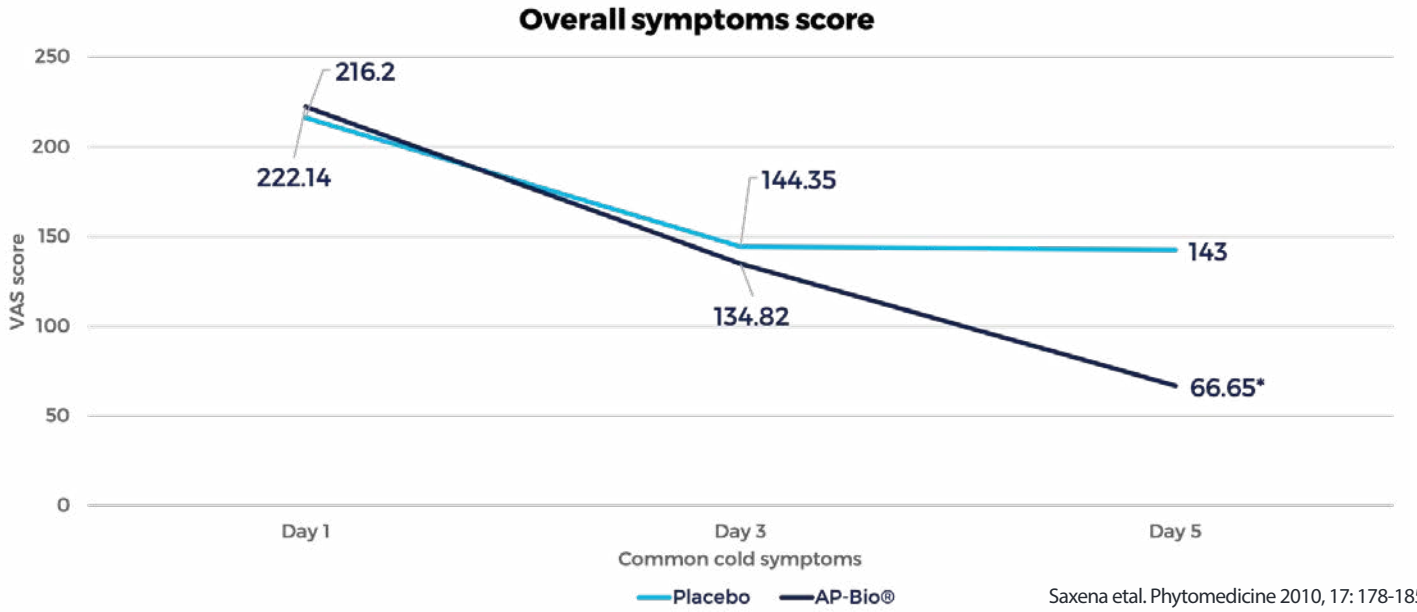

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How AP-Bio® Supports Immune Function?

AP-Bio® has been shown to stimulate phagocytosis, an activity of the immune system whereby phagocytes (immune cells) engulf and ingest invading or irrelevant matter.

In a study of mice injected with carbon, researchers found that those subjects given AP-Bio® at a dose of 41 mg per kg of body weight for seven days exhibited significantly improved clearance of the carbon compared to carbon injected mice that were not given AP-Bio®.[29]

AP-Bio® also has a positive impact on natural killer (NK) cell efficiency. NK cells are lymphocytes that are one of the first responders on the scene of a virus attack; NK cells provide rapid responses to virus-infected cells, acting about three days after infection. To evaluate AP-Bio®'s role in NK activity, mice were fed 41 mg per kg of body weight of the herb for 10 days. Their NK cells' activity was accelerated versus the NK cells of mice in the control group.[30]

Earlier research has shown that the primary mechanisms of action of *A. paniculata* are attributed to the ability of its signature component – andrographolide – to inhibit an inflammatory cascade; for example, its ability to reduce neutrophil adhesion and transmigration by suppressing the number and density of macrophage-1.[27]

Andrographolide is also a potent immunostimulatory. One study found that it, along with *A. paniculata* constituents 14-deoxyandrographolide and 14-deoxy-11,12 didehydroandrographolide showed enhanced proliferation and interleukin-2 (IL-2) induction in human peripheral blood lymphocytes. [28]

How AP-Bio® Supports Inflammation Management?

The immune system is not isolated – it affects and is impacted by inflammatory response.

Overall, inflammation is a physiological response to tissue damage and is accompanied by a characteristic series of localized events. Inflammation most commonly occurs when microbes have overcome the non-specific defense mechanisms. Its purpose is protective -- to isolate, neutralize and remove both the causative agent (bacteria, viruses, etc.) and the damaged tissue so that healing can take place.

In individuals who have weakened immunity, the process of isolating, inactivating and removing the infectious agent and the damaged tissue becomes compromised, leading to symptoms of inflammation like pain, swelling or fever.

One mouse study using *Andrographis paniculata* extract not only inhibited species of free radicals (eg, superoxide, hydroxyl radicals, etc.), it also was able to inhibit carrageenan-induced inflammation. [31]

One study examined the effects of AP-Bio® on inhibition of inflammatory mediators including lipopolysaccharide-induced nitric oxide, prostaglandin E2, interleukin-1beta, and interleukin-6, among others. It was found that this extract of *Andrographis paniculata* showed significant anti-inflammatory and anti-allergic properties. The researchers suggested that the findings may serve as a platform for development of ingestible solutions to manage inflammation. [32]

In a follow-up study, the authors validated the control of inflammatory compounds via contact with the constituents of AP-Bio® *A. paniculata*, as well as revealed more actions. Specifically, the researchers observed that lipolysaccharide-stimulated interleukin-1 beta production was inhibited by andrographolide, isoandrographolide and 7-O-methylwogonin while lipolysaccharide-stimulated interleukin-1 production was inhibited by andrographolide, isoandrographolide and skullcapflavone-I. The different AP-Bio® *A. paniculata* constituents worked on different pro-inflammatory compounds, however, isoandrographolide and andrographolide were equally adept at inhibiting both. [33]

AP-Bio® possibly acts by inhibiting the release of inflammatory mediators viz., LTB4, PGE2, TXB2, IL-6, IL-1B, and nitric oxide.

Safety of AP-Bio®

Andrographis paniculata has been used traditionally and conventionally without any known toxicity. The available human studies on *A. paniculata* have not indicated any serious adverse effects.[18]

A genotoxicity study was performed on AP-Bio®. The results in three *in vitro* tests demonstrated that AP-Bio® did not damage DNA, and therefore is deemed non-genotoxic. In addition, an acute oral toxicity test showed that AP-Bio® was safe after oral administration as a single dose to Wistar rats up to 5000 mg/kg body weight.[34]

Sustainability of AP-Bio®

The process of cultivating *Andrographis paniculata* for AP-Bio® has always been one that keeps renewability of resources – including human – at the forefront to sustain quality yields. We minimize our carbon footprint by cultivating mostly with non-fossil fuels and without machinery that uses the fossil fuels. We reuse the water used for growing the botanical crop.

During manufacturing/processing, the majority of the power utilized is from hydro and solar energy sources. All the effluents from manufacturing facility are disposed responsibly as per statutory norms. We are an ISO14001-certified (environmental management) organization, and our manufacturing facility is surrounded by trees to provide a green belt.

Why Choose AP-Bio®?

AP Bio® is clinically shown to support immunity at 200 mg per day; this low dose allows for flexibility in formulation. It is relied upon for many brand marketers, their retailers and their consumers. More than 800 million doses have been consumed worldwide. Consumers will appreciate its clean label attributes – USP compliant for pesticide residue and heavy metals, non-irradiated, NON-GMO Project-verified, and is certified both Kosher and Halal.

AP-Bio® is manufactured under strict global guidelines of safety and quality control. Its manufacturer, Natural Remedies, has achieved ISO 22000, ISO 9001and OHSAS 18001 certification from Bureau Veritas, is NSF GMP-certified, USFDA inspected.

In Conclusion

Each year going forward, the world will look at winter immunity in a very different way – characterized and anchored by proactivity. This is where dietary supplements that have science, sustainability and integrity will make a positive impact.

AP-Bio® taken daily at only 200 mg can help people across the globe to build up resistance and enjoy the benefits of a robust, high-functioning immune system. And because it has been shown to help assuage common mild upper respiratory infection symptoms, it can be a useful natural, safe solution by itself or as a complex formula.

AP-Bio™

natural™ REMEDIES

About Natural Remedies

Natural Remedies is a global research-driven botanical healthcare company whose core competency lies in manufacturing standardized herbal extracts. Its branded products are clinically substantiated, scientifically validated innovations. Known as a leader in scientifically based botanical extracts, Natural Remedies has contributed to various international pharmacopoeia, including over 100 monographs internationally and over 220 phyto-compounds isolated for global reference standards. Our vision is to harness nature and apply science for health and happiness.

Want to Learn More?

hhp@naturalremedy.com

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