Muscadine Grape (*Vitis rotundifolia*): An Emerging Superfruit for Immune Protection

The Original American Grapes: The Hero Polyphenol Antioxidants

Researchers around the world have been looking at benefits and potential uses of grape compounds for health and anti-aging since at least the 1970’s.

Commonly known grape compounds like resveratrol and grape seed extracts have been researched for combating viruses and bacteria, often through their broad impact on antioxidant mechanisms, but also by blocking replication of RNA and DNA of pathogenic microorganisms.

Resveratrol, quercetin, and other polyphenol antioxidants are found naturally in high concentration in muscadine grapes. These compounds are researched to be the future of immune superfoods.

Immune Regulation is Top of Mind in 2020

Recent worldwide health concerns regarding contagious viruses has become an area of interest among everyone, not just health enthusiasts.

Nature has provided many unique compounds to be used to enhance health, and there are some shown to support immune function and modulate the immune stress response.

So what really happens when a person is exposed to an infection? To keep it simple, the body’s numerous and various immune cells start waking up and increase signaling to each other to mobilize, like an army. These cells may lead to inflammation in certain tissues or organs, and then increase production of a certain type of immune cell called cytokines. These increased cytokines lead to mucus production, which in a very strong immune response can go into overdrive and hinder lung function.

Ideally, when exposed to infection some of the best ways to block progression is to:

- Prevent pathogen adhesion and infection
- Prevent pathogen replication
- Prevent inflammatory response
- Prevent cytokine overproduction/mucus overproduction
Polyphenols: Plant-based Immune Regulators

Polyphenols, one of many categories of natural substances, exhibit a range of biological activities. Polyphenols promote immunity to foreign pathogens in various ways.

Immune cells express multiple types of polyphenol receptors that recognize and allow cellular uptake of polyphenols. This uptake activates signaling pathways, triggering an immune regulation response. Some polyphenols can induce epigenetic changes in cells. Dietary interventions that involve polyphenols may modulate immune responses by affecting epigenetic mechanisms, such as regulatory DNA methylation, histone modification, and microRNA-mediated posttranscriptional repression that alter the expression of genes encoding key immune factors. As a result, polyphenols can be used to regulate innate and adaptive immunity, intestinal mucosal immune responses, and immune resistance to allergens.

Clues on Immune Support come from Muscadine Antioxidant Activity in the Body

Muscadines’ whole-food synergy was confirmed when studies found it may stimulate both types of antioxidant defenses in the body -- exogenous and endogenous. (Most antioxidants only support a limited number of antioxidant pathways). Supporting both antioxidant pathways means that the immune system is better equipped to defend your body against invaders.

Recent studies show that muscadines are more effective at quenching free radicals, compared to isolated immune-supporting antioxidants like vitamin C and quercetin.

Resveratrol: A Most Intriguing Immune Regulating Polyphenol

Stilbenes like resveratrol in muscadine exhibit extraordinary potential for immune support.

For example, resveratrol is potentially beneficial for supporting both innate and adaptive immunity. Resveratrol has been shown to directly target central cellular components of innate and adaptive immunity like macrophages, lymphocytes, and dendritic cells.

In animal experiments, resveratrol exerts an immunomodulatory effect by decreasing the expression of the activating receptors CD28 and CD80 on immune cells and increasing the production of the immunosuppressive cytokine IL-10.

Research has found resveratrol to be safe and without side effects, unlike many immune drugs.

Muscadine Supports Healthy Immune Defense on Mitochondrial Level

Muscadine grape polyphenols, including resveratrol and quercetin, are found to impact genetic regulation of the body's own antioxidant and immune defenses, compared to antioxidants in conventional grapes.

Muscadine is one of the few fruits found to exert a balancing (or homeostatic) effect that starts in the engines of your cells – in the mitochondria. In particular, resveratrol which is abundant in muscadine is known to reduce oxidative stress and stimulate mitochondrial function through SIRT1 (sirtuin) activity. Sirtuins are proteins in cells that help to increase the longevity of mitochondria and cells, and increasing their levels in the body is thought to increase lifespan.

Numerous studies suggest muscadine’s potential to support cellular function that can translate into benefits for cardiovascular health, brain function, digestion, immunity, men's health and liver detoxification.
The antioxidants in muscadines are also studied to improve physical and cognitive performance in younger people. For example, muscadine antioxidants are associated with an improved rate of recovery from inflammation from physical exertion.

Recent research has shown how powerful muscadines are, as one of the most potent and diverse antioxidants found in fruits. Hence it’s nickname as the “Superfruit of the South”.

Stilbenes such as resveratrol are thought to enhance the function of mitochondria, the powerhouses of our cells. A 2019 study found that muscadine fruit extract enhances mitochondrial function and cellular bioenergetics in heart cells when they are stressed.

Another recent study found that multiple types of muscadine grapes consistently produce four major stilbenoids such as t-piceid, t-resveratrol, ε-viniferins, and t-pterostilbene, which are considered natural resveratrol analogs. Studies suggest that the entire spectrum of stilbenes in resveratrol may be more potent than resveratrol alone.

**Muscadine and Elderberry: Dark Berries Researched For Immune Health**

Both muscadine and elderberry contain a high amount of polyphenols associated with immune support, and extract from both fruits are shown to exhibit similar activity in the body.

Muscadines are one of the most highly researched fruits native to the United States. In fact, more than 100 preclinical and clinical studies have been published on muscadine. And there are thousands more studies that have verified the bioactivity and health benefits of the antioxidant compounds in muscadine.

Muscadine fruit powder is a whole-food source of nutrients including a diverse polyphenolic combination; muscadine contains resveratrol, oligomeric proanthocyanidins, catechins and ellagitannins. This diversity of polyphenols is distinct from elderberry, which contains mostly anthocyanins and flavonoids as predominant classes of polyphenols.

There are various sources of dark berries. The nutrients from muscadine grapes are in food-bound form, which generally means they’re bioavailable and better absorbed into cells.

![Antioxidant Composition of Muscadine and Red Grape](image)

Above: Antioxidant concentration of Muscadine versus red grape (units in ppm). Muscadine contains higher levels of several classes of antioxidant polyphenols, including resveratrol, quercetin, catechins, and oligomeric proanthocyanidins.

**There’s A Few Differences Between Grapes and Elderberries**
Elderberries are associated with immune support, because they have been traditionally used in Europe, and elderberries are a dark berry with polyphenols.

Muscadines share many of the same characteristics of elderberry. Although it is difficult to compare different sources of grapes and berries directly, each one stands on its own scientific research.

But there are some key differences that can be considered based on the scientific studies on both berries:

**Muscadines Are Higher in Polyphenols Than Elderberry**

A review of testing data on elderberry and muscadine revealed that muscadine is up to 3 times richer in polyphenols compared to elderberry (see chart below).

As a result, muscadine could exert a greater effect than elderberry for immune support.

**Muscadine and Elderberry Exhibit Similar Antiviral Activity**

In one head-to-head study in cells comparing muscadine and elderberry, muscadine phenolics acted in a similar manner similar elderberry. In a test the H1N1 virus and this effect can be observed without direct contact between extract and virus.

The polyphenol-preparation from Muscadine grape was tested in a blend with chemically pure resveratrol. The blend containing Muscadine polyphenols reduced the inflammatory response to a test meal, in part via the induction of genes involved in production of antioxidant enzymes.

These include genes, such as Nrf-2, that regulate the expression of antioxidant proteins that protect against immune challenges, oxidative stress and inflammation.
1. Effect of Muscadine Juice and Elderberry Preparations on Wild-Type H1N1 Influenza Virus-Induced Cytotoxicity. Susan Elrod and Phillip Greenspan. The FASEB Journal 2015 29:1 supplement


