

NANOFORMULATED



# AMPK CHARGE+™

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**AMPK Charge+** is an innovative phytonutrient blend designed to support the AMPK pathway, a critical metabolic pathway that is responsible for regulating glucose and lipid metabolism, cellular clarity, mitochondrial biogenesis, and body weight.\* The blend of botanicals and nutraceuticals in AMPK Charge+™ includes diindolylmethane (DIM), quercetin dihydrate, milk thistle seed extract, resveratrol, berberine HCL, and cinnamon bark oil for potent AMPK support.\*

## EDUCATION

### THE SIGNIFICANCE OF THE AMPK PATHWAY IN OUR MODERN-DAY WORLD

The AMP-activated protein kinase pathway, AMPK for short, is an evolutionarily-conserved pathway present in all complex life forms, from mice to humans. AMPK is a central regulator of metabolism, growth, and energy, and helps coordinate metabolism in the liver, muscles and fat.<sup>1</sup> AMPK is an exquisite nutrient sensor and is activated whenever intracellular energy (in the form of ATP) is low.<sup>2</sup> AMPK activation restores cellular energy levels by stimulating pathways and processes that generate ATP.<sup>3</sup>

AMPK also has anti-inflammatory effects, regulates insulin sensitivity, upregulates pathways involved in longevity, and enhances muscle performance and contraction.<sup>4,5,6,7</sup> It also governs autophagy, a process whereby cells engulf and clear out debris, damaged proteins, and dysfunctional organelles, and then recycle or dispose of them.<sup>8,9</sup> AMPK is a truly pluripotent pathway essential for whole-body health.

AMPK is activated by a variety of inputs, including fasting, low blood insulin levels, and exercise.<sup>10</sup> Unfortunately, very few people routinely engage in AMPK-activating lifestyle practices. A confluence of factors central to modern-day life inhibit AMPK, including chronic overnutrition (i.e., overeating), a sedentary lifestyle, hyperinsulinemia, and overweight and obesity.<sup>11,12</sup> In particular, AMPK is suppressed by excess glucose, fatty acids, and amino acids present in the blood after eating, when the body is in the "fed" state.<sup>13</sup> Most people in the modern Western world live in a chronic fed state, rarely entering the fasted state necessary for AMPK activation. AMPK



## Supplement Facts

Serving Size: 5 mL (1 tsp.)  
Servings Per Container: 20

	Amount Per Serving	% Daily Value
<b>Proprietary Blend:</b>	415mg	**
Phospholipids (from purified sunflower seed lecithin), Diindolylmethane, Quercetin Dihydrate (from Sophora japonica flower), Milk Thistle Seed Extract (80% Silymarin), Resveratrol (from Polygonum cuspidatum root), Berberine HCL (from Phellodendron amurense bark), Cinnamon bark oil		

\*\*Daily Value not established

**Other Ingredients:** Glycerin, water, ethanol, medium chain triglycerides, tocopherols, natural citrus oils, natural flavoring, natural mixed tocopherols, propolis extract

activity also decreases during the aging process.<sup>14,15</sup> As a result, most people today rarely realize the spectrum of health benefits offered by AMPK activation.

When AMPK is inhibited, its opposing pathway, mTOR is activated.<sup>16,17</sup> The mammalian target of rapamycin pathway, or mTOR, is a central regulatory pathway that orchestrates cellular growth and homeostasis. AMPK controls mTOR signaling.<sup>18</sup> While mTOR has beneficial roles in the body, supporting muscle growth and development, chronic mTOR activation compromises metabolic health and promotes body fat storage and cellular proliferation.<sup>19</sup> For optimal metabolic health, our bodies must alternate between AMPK (fasted state) and mTOR (fed state) activity.<sup>20</sup> In our mTOR-dominant world, targeted activation of the ancient, powerful AMPK pathway is essential for overcoming the harmful effects of the modern diet and lifestyle and promoting metabolic clarity and longevity.

## **HOW DOES AMPK BENEFIT OUR HEALTH?**

AMPK benefits whole-body health across the lifespan by improving metabolic function, attenuating inflammation, enhancing mitochondrial function, and supporting a healthy aging process.

### **Metabolic Clarity**

AMPK flips the body's "metabolic switch" from burning primarily glucose for fuel to burning fat (as ketones) for fuel.<sup>21</sup> AMPK activation stimulates lipolysis, which allows the body to tap into its fat stores to create cellular energy. Utilizing ketones for fuel is a cleaner form of cellular energy production that minimizes oxidative stress and inflammation while maximizing the amount of energy, in the form of ATP, your cells can make.

Amplification of AMPK signaling also improves other aspects of metabolic health. It improves blood sugar control by enhancing insulin sensitivity and promoting efficient glucose uptake from the blood into cells.<sup>22</sup> This prevents glucose from lingering in the blood for too long, where it can wreak havoc on blood vessel integrity.

AMPK activation also supports healthy blood lipid levels. It prevents fat from accumulating in the liver, a phenomenon closely tied to blood sugar control and, if allowed to continue unabated, significantly compromises liver function.<sup>23</sup>

AMPK is essential for the activation of autophagy, the body's cellular "housekeeping" system that clears out damaged and dysfunctional cell components so that the body can recycle or dispose of them.<sup>24</sup> By elegantly maintaining cellular homeostasis, a proper level of autophagy ensures that we stay healthy, fit, and age with grace. Autophagy is inhibited by the postprandial surge in insulin and is stimulated during periods of fasting or when nutrients are in short supply. Without optimal AMPK activation, autophagic activity may be insufficient to support whole-body health.

Together, the beneficial effects of AMPK on fuel utilization, blood sugar, blood lipids, and autophagy help to clean up the body's metabolic machinery, supporting metabolic clarity.

### **AMPK Supports a Healthy Inflammatory Balance**

Inflammation is a central component of many of the chronic diseases we face in Westernized society today, including cardiovascular disease, type II diabetes, neurodegenerative diseases, and uncontrolled cellular proliferation.<sup>25</sup> Chronic activation of mTOR and insufficient AMPK activity exacerbates inflammation; this imbalance in cellular signaling pathways is increasingly implicated in chronic disease development.<sup>26</sup>

Conversely, AMPK activation has been found to reduce inflammation, stemming the tide of unproductive inflammatory processes that contribute to chronic diseases such as cardiovascular disease and type 2 diabetes.<sup>27,28</sup>

### Supports Healthy Mitochondrial Function

Mitochondria are the energy powerhouses of cells, responsible for generating a constant supply of cellular energy in the form of ATP. AMPK activation increases mitochondrial efficiency, supporting ATP production while minimizing harmful free radical byproducts. It also activates mitophagy, the selective degradation of defective mitochondria, and promotes the creation of new, healthy mitochondria.<sup>29</sup>

### Supports Healthy Cellular Senescence

Cellular senescence is the process by which cells cease to be functional, instead transitioning into a state of cell cycle arrest and secreting a variety of pro-inflammatory mediators that harm surrounding healthy cells. Cellular senescence is triggered by oxidative stress, DNA damage, and is a part of the aging process. Senolytics, or compounds that selectively kill senescent cells, reduce the body's senescent cell burden and may promote metabolic health and longevity. A variety of natural compounds exert senolytic effects, rejuvenating the body at the cellular level.

### AMPK Activation Promotes Longevity

AMPK activates an ancient network of genes and proteins that regulate longevity, including the sirtuins. Sirtuins are proteins that play a vital role in regulating cellular health and homeostasis. Therapeutic sirtuin activation has been shown to support healthy aging and metabolism.<sup>30</sup> Interestingly, AMPK and sirtuins appear to engage in crosstalk to ultimately impact cellular health and lifespan.<sup>31</sup>

Sirtuins require NAD<sup>+</sup> to function properly; a lack of NAD<sup>+</sup> thus inhibits AMPK activation. Fortunately, some of the lifestyle practices that activate AMPK, such as fasting, also support NAD<sup>+</sup> generation, providing powerful synergistic support for longevity.<sup>32,33</sup>

### AMPK Activation Acts As An Exercise Mimetic

In an ideal world, we would all engage in daily physical activity to support optimal health. However, the reality is that this is not feasible for many people. This realization has led to increased scientific interest in compounds that induce physiological benefits similar to those seen with exercise;<sup>34,35</sup> such compounds are referred to as "exercise mimetics."

AMPK activation drives energy metabolism in skeletal muscle, the cardiovascular system, and mitochondria and plays an essential role in mediating the beneficial effects of physical activity. Several AMPK activators thus act as exercise mimetics, with resveratrol one of the most-studied compounds thus far. In animal studies, resveratrol has been found to increase running endurance and improves cardiac and mitochondrial function via mechanisms that parallel those seen with exercise.<sup>14,15</sup> Quercetin may offer similar, albeit milder effects; its benefits for exercise may come, in large part, from its ability to attenuate exercise-induced oxidative stress.<sup>36</sup>

## PHYTOCOMPOUNDS THAT SUPPORT AMPK

**Resveratrol** stimulates AMPK, inhibits the mTOR pathway, activates sirtuins, and induces autophagy by targeting a complex array of autophagy-associated proteins.<sup>37,38</sup> Resveratrol is widely known for its ability to increase NAD<sup>+</sup>, which is needed for sirtuin activation and AMPK/sirtuin crosstalk involved in longevity.<sup>39</sup> Resveratrol also increases mitochondrial biogenesis, supporting robust cellular energy production.<sup>40</sup>

**Berberine** modulates autophagy in the liver, protecting against excessive hepatic fat accumulation that can contribute to non-alcoholic fatty liver disease.<sup>41</sup> Berberine also activates AMPK and inhibits mTOR, improves glucose metabolism and insulin sensitivity, and promotes mitochondrial biogenesis.<sup>42,43</sup>

**Quercetin's** powerful antioxidant properties are due in part to its AMPK-activating effects. Multiple studies indicate that quercetin blocks mTOR, activates autophagy, increases mitochondrial biogenesis and reduces inflammation.<sup>44,45,46</sup> Exciting research has shown that quercetin may also act as a senolytic, a compound that

selectively induces the death of senescent cells, or cells that have ceased to be functional and instead secrete pro-inflammatory molecules that harm healthy cells around them.<sup>47</sup> Research indicates that targeting senescent cells may stem the tide of aging and promote a youthful physiology.<sup>48</sup> Finally, quercetin's ability to stabilize mast cell degranulation offers additional anti-inflammatory, antihistamine and immune support.<sup>49</sup>

**Milk thistle** is well-known for its liver-protective properties and ability to induce autophagy in cultured cell lines.<sup>50</sup> Silymarin, a group of phytochemicals found in milk thistle, has been found to inhibit mTOR, allowing AMPK to perform its vital roles in the body.<sup>51</sup> Silybin also increases mitochondrial biogenesis and can restore healthy NAD+ levels in liver tissue impacted by non-alcoholic fatty liver disease.

**Diindolylmethane (DIM)** induces protective autophagy and increases the transcription of autophagy-associated genes in cell lines in part by activating AMPK.<sup>52</sup> DIM is also immune-balancing, shifting the balance towards calming T-regulatory cells.<sup>53</sup>

**Cinnamon** directly activates AMPK and inhibits mTOR.<sup>54,55</sup> Cinnamon also supports metabolism by lowering fasting glucose levels and hemoglobin A1c, a measure of average blood glucose levels over time.<sup>56</sup>

**Quicksilver Delivery Systems®** improve upon liposomal and emulsification technology with smaller, more stable particles made from the highest-grade ingredients available. In addition to exceptional absorption rates, these tiny liposomal and nanoemulsified particles increase diffusion across mucous membranes, enhance lymphatic circulation of nutrients and support cellular delivery.\*

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References available at [quicksilverscientific.com/ampkchargereferences](http://quicksilverscientific.com/ampkchargereferences)

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WARNING: NOT FOR USE BY INDIVIDUALS UNDER THE AGE OF 18 YEARS. DO NOT USE IF PREGNANT, BREAST-FEEDING, OR PLANNING TO BECOME PREGNANT. KEEP OUT OF REACH OF CHILDREN. Consult a healthcare professional before use if you have any medical condition or are taking any other supplements or medications. Do not exceed recommended dosage. See [www.quicksilverscientific.com](http://www.quicksilverscientific.com) for additional safety information.

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