

# Fermented Black Garlic

## INGREDIENTS



Garlic (*Allium Sativum L.*) has been used as a culinary seasoning and medical herb since ancient times.<sup>1</sup> However, the consumption and use of fresh garlic in foods and medicine has been limited due to its pungent odor and flavor. The organosulfur compounds like allicin and diallyl disulfide (DADS) are the main compounds responsible for its pungency effects and spicy aroma.<sup>2</sup> Fresh garlic has also a tendency to cause an upset stomach and bad breath.

Consequently, various garlic preparations such as black garlic (also known as Aged Black Garlic (ABG)), have been developed to aim to reduce these characteristics without losing biological functions. A wide array of therapeutic effects of fresh garlic and aged black garlic has also been observed including cardioprotective, hepatoprotective, and antioxidant effects, as well as immune enhancement.\*<sup>3,4</sup> These effects are attributed to a high concentration of organosulfur compounds (OSCs).

ABG is traditionally produced by aging whole bulbs of fresh garlic at high humidity and temperatures. During this fermenting aging process, odorous, harsh and irritating compounds in fresh garlic are converted naturally into stable and safe sulfur compounds and a deep black hue as well as a soft, jelly-like texture and sweet syrupy flavor are created. At the same time, the amount of allicin, the main component of fresh garlic known to have potent antioxidant activity, is reduced, removing the pungent flavor and odor. Allicin is also converted into a stable and more potent antioxidant known as S-Allyl-Cysteine (SAC). In fact, based on a body of literature, SAC is proven to have twice the antioxidant capacity and to be absorbed better than allicin. Moreover, SAC was found to exhibit beneficial effects on the immune system, cognitive and cardiovascular functions, making ABG extracts an ideal natural functional food to support overall human health.\*<sup>1,5-6</sup>

Doctor's Best uses a new generation of aged black garlic extract named ABG10+. It is derived from fresh garlic and is the first extract standardized to a higher concentration of the bioactive compound S-allyl cysteine (SAC) than in standard black garlic. ABG10+ is produced via a proprietary optimized aging process through a naturally occurring chemical reaction called "autocatalysis" under rigorous temperature and humidity controls.\*<sup>7</sup> This technique naturally enriches the garlic with its unique composition of SAC, polyphenols, and melanoidins, all known to exert potent antioxidant effects.

## BENEFITS

- Helps provide potent antioxidant activity to fight oxidative stress\*
- Helps support cardiovascular health\*
- Helps maintain healthy cholesterol levels and blood

- pressure already within the normal range.\*
- Helps support healthy immune response\*
- Helps support healthy cognitive functions\*

## EXTENDED BENEFITS

Helps provide potent antioxidant activity to fight oxidative stress\*

Oxidative stress is a phenomenon caused by an imbalance between production and accumulation of oxygen reactive species (ROS) in cells and tissues and the ability of a biological system to detoxify these reactive products.<sup>8</sup> This is a harmful process that can negatively affect several cellular structures, such as membranes, lipids, proteins, lipoproteins, and deoxyribonucleic acid (DNA).

Garlic has been known not only as a flavor enhancer, but also as a food that has high potential antioxidant activity. However, some people are reluctant to ingest raw garlic due to its unpleasant odor and taste. Therefore, many types of garlic preparations have been developed to reduce these attributes without losing biological functions.

Aged Black Garlic (ABG) is a garlic preparation with a sweet and sour taste and no strong odor. Extensive in vitro and in vivo studies

## Fermented Black Garlic 60 Veggie Caps Supplemental Facts

### Supplement Facts

Serving Size 2 Veggie Capsules  
Servings Per Container 30

Amount Per Serving		% Daily Value
Black Garlic Ext.	500 mg	†
<i>(Allium sativum L.)</i> (bulb)(ABG10+®) Standardized to contain 0.1% S-Allyl Cysteine (500 mcg)		

† Daily Value not established.

**Other Ingredients:** Hypromellose (vegetarian capsule), maltodextrin, microcrystalline cellulose, silicon dioxide, magnesium stearate (vegetable source).

**Suggested Adult Use:** Take 2 capsules daily, or as recommended by a nutritionally informed physician.

**WARNING:** Consult a physician before use if you are pregnant, nursing, or taking medications for diabetes or blood thinners.

**Non-GMO / Gluten Free / Soy Free / Vegan**

This product contains natural ingredients that may vary in color. Store in a cool dry place.

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have demonstrated that ABG shows higher antioxidant activity than fresh garlic.<sup>9-10</sup> ABG contains antioxidant bioactive compounds, such as phenols, flavonoids, pyruvate, thiosulfate, S-allylcysteine (SAC), S-1-Propenyl-L-Cysteine (S1PC), and S-allylmercaptocysteine (SAMC).<sup>11-12</sup> In ABG extracts, SAC and SAMC are the major water soluble organosulfur compounds (OSCs). Others, such as Diallyl sulfide (DAS), diallyl disulfide (DADS), and diallyl tetrasulfide are oil soluble organosulfur compounds. All these OSCs, derived from allicin, are responsible for the potent antioxidant activity of ABG extracts.<sup>13-16</sup>

In recent years, many studies have been conducted to investigate the bioactive compounds in ABG and their antioxidant activities.<sup>17</sup> In particular, it was found that tetrahydro-b-carboline, SAMC, and SAC are compounds that were shown to have the most antioxidant and protective effects against oxidative stress by inhibiting the production of ROS and/or scavenging them.<sup>18-19</sup> More, the content of SAC and SAMC in ABG extracts is very high because they are produced during the process of aging, thus providing AGE with higher antioxidant activity than fresh garlic and other commercial garlic supplements.<sup>\*20-24</sup>

### Helps supports cardiovascular health\* Helps maintain healthy cholesterol levels and blood pressure already within the normal range.\*

Garlic has been used for centuries in folk medicine but also in modern medicine for its beneficial cardiovascular health effect.<sup>\*25</sup> Although its positive impact on cardiovascular health has been clinically recognized by the scientific community worldwide, consumers have been reluctant to make good use of its medicinal properties due mainly to its pungent taste and odor.<sup>\*5,26</sup>

With a growing awareness of the health benefits of garlic, black garlic or aged black garlic extracts have emerged as one of the fastest-growing health-oriented food products in the world.<sup>16</sup> In recent years, many studies (in vitro, in vivo, and animal studies) have been conducted to investigate the possible mechanisms involved in the beneficial effects of black garlic extracts on cardiovascular system.\* Thus, García-Villalón et al. analyzed the in vitro cardiovascular effects of an ABG extract enriched in S-allylcysteine and polyphenols (ABG10+) in Sprague-Dawley rats. Their study demonstrated that ABG10+ induced a relaxing effect on coronary arteries. Therefore, ABG10+ exerted a protective effect on the heart during ischaemia-reperfusion, which could be due to the induction of adaptive antioxidant mechanisms in the tissue.<sup>\*27</sup> Ha et al. conducted an experiment in rats and showed that consumption of black garlic extract lowers SREBP-1C mRNA expression, which caused downregulation of lipid and cholesterol metabolism. As a result, ABG was found to decrease the blood levels of total lipids, triacylglycerides, and cholesterol.<sup>28</sup>

Another research team also highlighted the beneficial effect of ABG on blood pressure. They demonstrated that AGE safely improved several factors related to blood vessel physiology in rats compared to raw garlic.<sup>29</sup> Moreover, based on many clinical studies, ABG extracts were found to be a potent natural supplement that can protect and support a healthy cardiovascular system by maintaining healthy cholesterol levels and blood pressure, improving endothelial function, vascular function, and reducing platelet aggregation and artery calcification.<sup>\*30-43</sup>

### Helps support healthy immune response\*

While ABG has been well known for years for its beneficial impact on cardiovascular health, its proven therapeutic qualities also include its positive effects on the immune system.<sup>\*44-45</sup> Studies in animals and humans showed that ABG extracts supplementation

may enhance the immune function by increasing the proliferation rate of some key components of the immune system such as the  $\gamma$ T cells, T lymphocytes helper 1, cytokine IFN- $\gamma$ , TNF- $\alpha$ , and natural killer (NK) cells.<sup>\*46-47</sup>



### Helps support healthy cognitive functions\*

Because the burden of disease in individuals increases with age, many studies have found that oxidative stress may be involved in the process of aging that could also affect cognitive functions in the ageing population.\* Several findings suggest oxidative stress plays an important role in neurodegenerative processes accompanying cognitive impairment due the fact that the brain is particularly vulnerable to reactive oxygen species (ROS) as its metabolism accounts for approximately 20% of all oxygen consumption within the body.<sup>48</sup>

Many studies suggest that dietary antioxidants may affect cognition directly through reducing oxidative stress at the neuronal cell level in areas of the brain that relate to memory and other cognitive domains or indirectly by affecting oxidative stress in areas that were linked to mood health which in turn can affect cognitive performance.\* Therefore, since ABG is known to have potent antioxidant activity, investigators have conducted various studies to show the positive effect of aged black garlic extracts on brain health and cognitive functions.<sup>42,49-52</sup> Thus, Numagami et al. was able to characterize the pharmacologic features of S-allylcysteine (main active compound of ABG) as a free radical scavenger in rat brain ischemia models. Their results support the idea that SBG has neuroprotective effects and may support healthy brain functions in humans.<sup>\*53</sup> Similar results were found when Ray et al. showed that aged garlic extract (AGE) and S-allyl-L-Cysteine (SAC) treatment prevented the oxidative insults to neuronal cells in a mouse model experiment.<sup>\*54</sup>

## CLINICAL STUDIES

A double-blind parallel randomized placebo-controlled trial was conducted to assess the effect and tolerability of aged garlic extract as a supplement therapy to existing antihypertensive medications taken by 50 participants known to have uncontrolled blood pressure levels. The active group received four capsules of aged garlic extract (960mg containing 2.4mg S-allylcysteine) daily for 12 weeks, and the control group received matching placebos. Results showed that systolic blood pressure was on average  $10.2 \pm 4.3$ mmHg ( $p = 0.03$ ) lower in the garlic group compared with the control group and aged garlic extract was generally well tolerated. The authors concluded that aged garlic extract is superior to placebo in maintaining healthy systolic blood pressure and that aged black garlic extract may be a useful natural supplement to conventional medications in helping with maintaining blood pressure within normal range.<sup>\*34</sup> Similar results and conclusions were found in another 12-week, double-blind, randomized placebo-controlled dose-response trial which reported a reduction of mean systolic blood pressure in subjects supplemented with 480 or 960 mg black garlic (containing 1.2/2.4mg of SAC) compared to placebo.<sup>\*35</sup>

A placebo-controlled, double-blind, randomized trial was designed to assess whether aged garlic extract therapy with supplements (AGE+ S: capsule containing aged garlic extract (250 mg) plus Vitamin B12 (100  $\mu$ g), folic acid (300  $\mu$ g), Vitamin B6 (12.5 mg) and

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L-arginine (100 mg) favorably affects inflammatory and oxidation biomarkers, vascular function and adipose tissue progression as compared to placebo. Sixty-five participants (age 60± 9 years, 79% male) were treated with a placebo capsule or a capsule containing AGE + S given daily for a 1 year. All patients underwent coronary artery calcium scanning (CAC), temperature rebound (TR) as an index of vascular reactivity, and measurement of lipid profile, and other biological parameters were measured at baseline and 12 months. CAC progression was defined as an increase in CACN15% per year and an increase in TR above baseline was considered a favorable response. Results showed that at 1 year, CAC progression was significantly lower and TR significantly higher in the AGE+ S compared to the placebo group after adjustment of cardiovascular risk factors. Total cholesterol and LDL-C were decreased, whereas HDL and other biomarkers for lipid profile significantly increased in AGE + S compared to placebo. The authors concluded that AGE+ S is associated with a favorable improvement in oxidative biomarkers, vascular function, and reduced progression of fat tissue in the body. They also suggested that aged garlic extract and the other dietary supplements may help decrease long term adverse cardiovascular events.\*<sup>30</sup>

Similar results were found in another randomized controlled trial that evaluated the effect of aged garlic extract with supplements (AGE + S) versus placebo on adipose tissue progression. Sixty asymptomatic participants were randomized to receive either AGE + S or placebo. Adipose tissue measurements were performed at baseline and 1-year follow-up CAC scanning. All participants were educated regarding a low-cholesterol diet and instructed to avoid any direct form of garlic and antioxidant supplementation. Participants with established cardiovascular disease were excluded. After 12 months of treatment, overall results showed that adipose tissue progression was significantly lower in the AGE + S as compared with the placebo group (P < 0.05). The authors concluded that AGE + S is associated with favorable effects on reducing the progression rate of adipose tissue volumes hence AGE + S could have a beneficial effect on cardiovascular health.\*<sup>55</sup>

The Faith randomized clinical trial investigated the effects of aged garlic extract + coenzyme Q10 (AGE + CoQ10) on vascular elasticity and endothelial function, both considered as parameters linked to cardiovascular health. Sixty-five Los-Angeles County firefighters who met the eligibility criteria were enrolled in this placebo-controlled, double-blinded randomized trial. The firefighters were randomized to four tablets of AGE (300 mg/tablet) plus CoQ10 (30 mg/tablet) or placebo. The participants underwent quarterly visits and 1-year follow-up. The vascular elasticity was measured by pulse-wave velocity (PWV) and the endothelial function was measured by digital thermal monitoring (DTM). After one year of treatment, data obtained from this study showed that PWV and DTM significantly improved in the AGE+CoQ10 compared with the placebo group (P < 0.05). The authors concluded that AGE plus CoQ10 was effective in improving the vascular elasticity and endothelial function in firefighters with high occupational stress, independent of baseline blood pressure, statins use (statins belong to the class of lipid-lowering medications), or other cardiovascular risk factors. They also suggested that their study further highlighted the beneficial effects of AGE plus CoQ10 on improving cardiovascular and psychological health of individuals exposed to highly stressful environments.\*<sup>32</sup>

A double-blind, randomized placebo-controlled trial was conducted to study the effect of aged black garlic (ABG) on blood pressure. Fifty-five participants were randomly assigned to receive either ABG or placebo twice daily (total 6 g/day) before consumption of a meal every morning and evening for 12 weeks. Results showed that among lipid components, no significant differences

in triglycerides, low-density lipoprotein cholesterol, total cholesterol, or free fatty acid levels were observed between the two groups. However, ABG increased high-density lipoprotein cholesterol (known as "Good cholesterol") levels compared with the placebo group at the end of the study. Moreover, a significant decrease in the levels of apolipoprotein B (better measure of circulating LDL particle, known as "Bad cholesterol") and a significant increase in the ratio of low-density lipoprotein cholesterol/apolipoprotein B were observed in the ABG group. No significant adverse effects were reported by any of the participants. The authors concluded that aged black garlic supplementation may have a cardioprotective effect.\*<sup>56</sup>

A prospective randomized double-blind study investigated the effect of aged garlic extract (AGE) on the build-up of fat deposits (plaques) in the walls of arteries that supply blood to the heart. Fifty-five participants with known cardiovascular issues were prospectively assigned to consume 2400 mg AGE daily or placebo orally. Both groups underwent CCTA (Cardiac computed tomography angiography (CCTA), a non-invasive tool that evaluates the heart and coronary arteries) at baseline and follow-up 354 ± 41 days apart. Coronary plaque volume, including total plaque volume (TPV), dense calcium (DC), and low-attenuation plaque (LAP) were measured. based upon predefined intensity cutoff values. The use of multivariable linear regression analysis was performed to examine whether AGE affected each plaque change. Results showed that the %LAP change was significantly reduced in the AGE group compared with the placebo group. The authors concluded that AGE has the ability to stabilize vulnerable plaque and decrease adverse cardiovascular events.\*<sup>41</sup>

A 6-month long clinical trial explored the clinical effects of ABG on the cardiovascular system and quality of life (QOL) of 120 participants with heart conditions. Participants were randomly assigned into the ABG group and placebo group. Various cardiac functions were measured as well as quality of life. Results showed that ABG treatment improved cardiac function when compared with controls (P < 0.05). The QOL scores and LVEF (left ventricular ejection fraction) values were higher in the BG group than in the CG group. It was also found that the circulating antioxidant levels were higher in the BG group than in the CG group. Since antioxidant levels had a positive link with QOL and LVEF values, the authors concluded that BG improves the QOL and cardiac functions by increasing antioxidant levels. They also concluded that ABG, combined with traditional medicine treatment of heart diseases, can improve cardiovascular health.\*<sup>57</sup>

In the study by Amor et al., one month of treatment with aged black garlic extract (ABG10+ from Pharmactive Biotech Products) resulted in a 22% decrease in circulating levels of low-density lipoprotein cholesterol (LDL), improving cardiovascular health.\* The supplement also increased beneficial high-density lipoprotein cholesterol (HDL) by 46%, while improving the overall HDL/LDL ratio by 70%. In addition, the animal subjects treated with ABG10+ showed lower body weight, lower triglyceride levels, and lower insulin and leptin serum concentrations in comparison to non-treated controls. ABG10+ also attenuated vasoconstriction via its ability to reduce oxidative stress.\*<sup>31</sup>

A randomized double-blind, placebo-controlled clinical trial

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examined the effect of aged garlic extract (AGE) on arterial elasticity in 57 subjects over a period of 12 weeks, using the EndoPAT™ technology. In addition, changes in blood pressure were also analyzed. The daily uptake amount of AGE was 2 ml (with 1 ml taken twice per day at mealtimes) for a duration of 84±3 days. In order to maintain the 'blind' factor with respect to the odor, the placebo contained 3% concentrated AGE, which is considered as inactive with respect to any potential beneficial effect. The results revealed a significant decrease in blood pressure in the AGE group, and in particular diastolic blood pressure. Using the EndoPAT™ technology, the augmentation index (AI) was analyzed, which measures arterial stiffness calculated via pulse waveform analysis of the PAT signal; lower AI values reflect better arterial elasticity. The AGE group exhibited a significant improvement in arterial elasticity, measured as AI75, by 21.6%. The result of this well-controlled clinical trial confirmed the positive effect of AGE on blood pressure. The authors concluded that these results not only demonstrate the positive effects of AGE on the relevant risk factors of cardiovascular diseases, but also the direct effect on arterial elasticity. These data clearly indicate that AGE may exert several positive direct effects on cardiovascular health.\*<sup>36</sup>

A double-blinded placebo controlled, randomized clinical trial investigated the effects of AGE on vascular endothelial function of participants known to have some cardiovascular issues. A total of 65 individuals were randomized to ingest either AGE (2 capsules twice daily -- each capsule containing 2,400 mg of AGE) or placebo for three months. After three months, results showed that AGE had a favorable effect on arterial stiffness by improving endothelial function compared to placebo. The authors concluded that AGE has a positive impact on cardiovascular health.\*<sup>38</sup>

A randomized, double-blind, placebo-controlled parallel-intervention study was conducted to evaluate the effect of AGE on the immune system. Healthy human participants (n = 120), (21-50 years of age), were recruited to consume 2.56 g of AGE daily or placebo supplements for 90 days during the cold and flu season. Peripheral blood mononuclear cells were isolated before and after consumption and NK cell function was assessed by flow cytometry. The effect on cold and flu symptoms was determined by using daily diary records of self-reported illnesses. After 45 days of AGE consumption, natural killer (NK) cells proliferated better and were more activated than cells from the placebo group. After 90 days, although the number of illnesses was not significantly different, the AGE group showed reduced cold and flu severity, with a reduction in the number of symptoms, the number of days participants functioned suboptimally, and the number of work/school days missed. Based on these results, the authors suggested that AGE supplementation may enhance immune cell function and may be partly responsible for the reduced severity of colds and flu reported\*. They also suggested that the immune system functions well with AGE supplementation.\*<sup>47</sup>

A parallel, double-blind, placebo-controlled, randomized study investigated whether daily supplementation with aged garlic extract (AGE) could improve immune function in overweight adults. Fifty-one healthy adults (mean age 45.6 ± 1.6 years, mean BMI 36.1 ± 0.9 kg/m<sup>2</sup>) were randomized into the AGE supplementation or placebo group. Participants took a divided daily dose of 3.6 g AGE or placebo, with food for 6 weeks. Blood lipid panel was assessed at baseline and after 6 weeks of supplementation. Results obtained showed a positive impact on the immune system (increase in γδ-T cells and decrease of L-6 and TNF-α) and a reduction in LDL (known as "bad cholesterol") in the AGE group compared to the placebo group. In conclusion, the authors suggested that AGE, taken consistently, may be beneficial in supporting healthy immune function and cardiovascular health in overweight individuals.\*<sup>58</sup>

Jeong et al. investigated the antioxidant activities of ABG on Aβ-induced (Amyloid-(Aβ) is known as a major cause of cognitive impairment) cognitive dysfunction in neurons like PC 12 cells and mice. Their findings suggest that aged garlic extracts with antioxidant activities may improve cognitive impairment against Aβ-induced neuronal deficit and may possess a wide range of beneficial activities for neurodegenerative disorders in humans.\*<sup>49</sup>

Thorajak et al. investigated the effects of AGE on Aβ-induced cognitive dysfunction with a biochemical basis in the cholinergic, glutamatergic, and GABAergic systems in rats. Adult male Wistar rats were orally administered three doses of AGE (125, 250, and 500 mg/kg) daily for 65 days. At day 56, they were injected with aggregated Aβ into each lateral ventricle, bilaterally. After six days of Aβ injection, the rats' working and reference memory was tested. The results showed that AGE significantly improved the working memory and tended to improve the reference memory in cognitively impaired rats. In addition, AGE significantly ameliorated the loss of cholinergic neurons in the hippocampus of rat brains with Aβ-induced toxicity. The authors concluded that AGE was able to attenuate the impairment of working memory via the modification of cholinergic neurons in the hippocampus of Aβ-induced rats. They also concluded that the consumption of aged garlic may have beneficial brain health benefits in humans.\*<sup>51</sup>

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\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.