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RESEARCH ARTICLE

Black Garlic (Allium Sativum L.) In Complementary Medicine: A Concise Phytochemical and Pharmacological Review

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ABSTRACT

Black garlic is modified raw white garlic (Allium sativum L.) obtained by treating it at a highly controlled temperature and humidity. They contain a high number of antioxidants versus white garlic, hence possesses higher antioxidative activity. Black and white garlic differ in physicochemical properties, phytochemical constituents, and pharmacological activities. This study reviews and summarizes the multi-activity properties of black garlic from the recent scientific findings. The study aims to provide a concise review related to all the information available on black garlic. The references in this review were gathered from several databases and resource providers like Pub Chem, Pub Med (National Center for Biotechnology Information, NCBI), Scopus (Elsevier), Web of Science, SpringerLink (Springer), and Google Scholar (Google). The current review shows that black garlic's phytochemical constituents and pharmacological activities make it a promising plant-derived remedy in complementary medicines.

KEYWORDS:
Allium sativum L.; black garlic; pharmacological activities; phytochemistry

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INTRODUCTION

Since ancient times, folks have utilized plants for dietary and therapeutic purposes. Thus, many researchers have developed techniques to find the therapeutical parts of plants which can be used as remedies. For ages, raw or white garlic (Allium sativum L.) is a widely used herbal plant for cooking and as a medicine. This herbaceous plant belongs to the family Liliaceae, which as also include Allium cepa L. (onion and shallot), Allium schoenoprasum L. (chives), Allium tuberosum L. (garlic chives), and Allium fistulosum L. (Japanese bunching onion). 1

The therapeutic and prophylactic effects of white garlic are well known. They are used as a phytomedicine to treat certain cardiovascular diseases such as high cholesterol levels, hypertension, and heart attack.1 They also possess anti-inflammatory, anticancer, and antimicrobial agents.1 All these effects are because of their phytochemical constituents. Phytochemicals are natural plant- derived compounds such as carbohydrates, lipids, phenolic, terpenoid, and alkaloid that exhibit therapeutic activities.2 Garlic contains high amounts of organosulfur bioactive compounds (alliin and gamma-L-glutamyl peptides), saponins, and antioxidants (flavonoids, polyphenols).1,3 The crushed garlic also contains thiosulfinate and active sulfur compounds (ajoene and allicin) degradation products derived from naturally occurring alliin in the presence of enzyme alliinase.1,3 The degradation of alliin to allicin produces sulfur-containing gases, allyl methyl sulfide (AMS), responsible for the pungent smell of garlic. An in vitro study by Toledano et al.4 has shown a high concentration of genotoxic activity in white garlic.

The unpleasant flavor of white garlic makes it intolerable for some people.5 Hence, garlic was modified in different forms like black garlic, garlic oil, smoke garlic, aged garlic, pills, supplements, etc. Black garlic (Figure 1) is one of the most famous processed white garlic, treated with thermal processing by fermenting the whole bulb or clove at controlled temperatures (60–90°C) and humidity (70–90%) for fixed periods that vary depending on cultures, manufacturers, and environments.6,7 Black garlic has originated from Asian regions and is used for dietary consumption for centuries in Thailand, South Korea, and Japan.6 But in the past few decades, black garlic is slowly gaining popularity in other parts of the globe.6,8

Black garlic has different organoleptic features like color, texture (tender and chewy), sweet flavor (sweet), and less odor versus raw fresh garlic.9 These features make people consume garlic without being distracted by its distinctive unpleasant taste. The color change of white garlic to black or dark brown is because of the Maillard reaction,5 that results in the browning process of the white garlic.10 Because of long periods of heat, black garlic contains less moisture compared with white garlic.9 Prolonged exposure to high temperature also seen to affects other physicochemical properties like the pH and browning intensity.8

According to Tran et al.,6 black garlic contains a higher amount of polyphenol (flavonoid) and sulfur-containing compounds versus white garlic, and all these compounds act synergistically as antioxidants. S-Allyl cysteine (SAC, sulfur-containing amino acid cysteine), a product of γ-glutamyl cysteine and S- allyl-mercapto cysteine (SAMC) are the antioxidants are produced during the thermal processing of white garlic. Other compounds such as fructose, xylose, glucose, pyruvate, and ash contents also increase significantly during the black garlic production.9,11

Phytochemistry of Black Garlic

Changes during thermal processing of black garlic

Black garlic is produced by treating white garlic at a highly controlled temperature and suitable humidity (70–90%) for a certain period. During this thermal processing, the Maillard reaction takes place. It is a nonenzymatic chemical reaction between reducing sugar and free amino acid-containing compounds, such as polypeptides (protein) and amino acid, which results in different physical properties such as color, taste, and aroma. This Maillard reaction also causes rearrangement or modification of the sugar rings and amino groups that give rise to the key intermediate products such as fructose-amino acids derivatives “Heyns” (N-substituted 2-amino-2-deoxyaldoses) and glucose-amino acids derivatives “Amadori” (N-substituted 1-amino-1-deoxyketoses) that contributes to the brown color of the black garlic.5

Raw white garlic contains fructan (polysaccharide form of the monomer fructose) that breaks down to glucose and fructose when reacts with the hydrolase enzyme. According to Yuan et al.’s study,5 fructan levels decreased, and fructose highly increased during the thermal processing of white garlic. The amount of Amadori is higher than Heyns compounds because of a faster reaction between glucose and amino acid than fructose and amino acid, which explains the lowered amount of glucose in black garlic that is approximately the same in white garlic when compared with fructose levels.5 This infers that a high fructose level contributes to the formation of intermediate Heyns compounds that enhance the sweet taste of the black garlic. During the late stages of the Maillard reaction, the Amadori and Heyns compounds eventually transform to form much smaller products and melanoidin.5,14

Figures 2 and 3 show the formation of Amadori and Heyns compounds from glucose and fructose. Several complex steps are involved in the Maillard reaction to form Amadori and Heyns compounds. Based on Hodge’s Diagram, during the initial stage, the aldehyde group in glucose react with free amino groups to form N-substituted glucosylamine which rearranges to form Amadori products.15 These Amadori products undergo oxidation degradation into carbonyl and dicarbonyl compounds (furfural hydroxymethylfurfural 2-furaldehyde and pyruvaldehyde), react with amino compounds to form melanoidin, the final product in the Maillard reaction. A few mixtures of different forms of Amadori compounds may exist because of the complexity of the Maillard reaction, which eventually causes the color changes of white garlic to black.15,16

Physicochemical changes in black garlic during browning process

The changes in organoleptic properties of the black garlic can be observed during the thermal process. These physical changes include color, taste, odor, and texture. Color plays a crucial part because it can affect the consumer’s appetite. The color of the white garlic turns gradually from white to yellow, caramel brown, dark brown, and will eventually turn to black depending on the aging period. The black color is because of the chemical melanoidin, the late-stage product of the Maillard reaction.17 Choi et al.13 showed that different stages in the Maillard reaction showed different colors based on their calculated absorbance. The optimum temperature to produce black color garlic is between 70 and 80 °C, although, at 90°C, large quantities with less quality can be produced.9

Black garlic possessed a sweet-sour taste at the final stage because of the abundant amount of sucrose and glucose. The sour taste is because of the reduction in pH value during the aging process. 3,5,13,18,19 The degree of the temperature also plays a pivotal role in the taste of the black garlic. For example, when heated at 80 or 90°C, it does not have definite sweet flavor because of the accelerating consumption of sugar content in the Maillard reaction.8 The melanoidin produced at the later stage contributes the bitter-sweet taste of black garlic.5,20 Black garlic has a softer and rubbery jelly-like texture. The high temperature will disrupt the the cell wall polysaccharides of black garlic that will further enhance tissue softening and, in turn contributes to the balminess texture of black garlic.19

Other physicochemical changes occurring during the browning process of black garlic include changes in pH, moisture content, and browning intensity. The pH of the black garlic significantly decreases during thermal processing that increases the acidity of the black garlic.4,5,13,19–21 The decline in pH is because of the formation of organic acid upon cell disruption during thermal processing. For example, acetic acid is the degradation product of hexose and pentose during the thermal process, and carboxylic acid is the oxidation product of aldohexose. Besides, there is a decrease in amino acid because of the reaction with sugar and other acidic compounds.5,21 Lu et al.22 stated that the black garlic contains high amounts of organic acids, like lactic acid contributes to the unique lactic sourness. However, the increased level of acidity gives an unpleasant acidic taste to the black garlic. Medina et al.3 (3) reported that the optimum acidity of the garlic needs to be approximately 2% to 2.5%, higher than 4% will generate an unpleasant acid taste. Temperature and thermal processing time affect the pH and acidity. Increased temperatures will decline the pH to rapidly, while longer manufacturing periods gradually reduce the pH.

The moisture content of the black garlic is reduced throughout the thermal processing. The study by Kang19 found that the moisture content of black garlic was significantly lower than its white counterpart, which may be because of the high temperature applied during the manufacturing process of black garlic that can alleviate the water content. The moisture content is related to the softness and elasticity of the black garlic. If the moisture content is low, the elasticity reduces and makes the black garlic too hard when eaten.8

The browning intensity of the black garlic is highly related to the Maillard reaction. It visually indicates the extent of the Maillard reaction which has occurred by the color of the black garlic.19 Yuan et al.5 showed the browning degree at 420 nm. Increased thermal processing period during the Maillard reaction increases the browning intensity rate.21 This occurs because of the black color of melanoidin produced during the late stages of thermal processing and also because of other Maillard reaction products.5

Phytochemical composition of black and white garlic

During the heat treatment of white garlic to produce black garlic, some compounds may be altered, increased, or reduced because of several processes like the Maillard reaction, caramelization, and oxidation of phenols.6,23 The period of the heating process may also affect the chemical composition of the black garlic. Thus, heating period needs to be optimized to get maximum bioactive compounds.

Black garlic also possesses an abundant amount of water-soluble SAC, the primary active ingredient that contributes to the high antioxidant capacity of the black garlic. This organosulfur compound is much more stable and odorless. The amount of SAC in black garlic is five to six times higher than in white garlic.24

SAC is produced by γ-glutamyl cysteine and is catalyzed γ-glutamyl by the enzyme γ-glutamyl transpeptidase. This enzyme is not actively productive in dried white garlic bulbs because it is present in the cell membrane of the garlic while its substrate, γ-glutamyl cysteine, is in the vacuole, leading to less SAC production.25

Non-treated white fresh garlic contains a high amount of γ-glutamyl cysteine. That will be naturally converted into alliin by the hydrolyzation and oxidization reactions. Alliin then will be further converted into allicin which exhibits unpleasant odor and cytotoxic effect. Meanwhile, in black garlic, SAC is produced instead of alliin from γ-glutamyl cysteine. The amount of allicin in black garlic is reduced because of the inactivation of enzyme alliinase during thermal processing of black garlic, thereby eliminating the distinct odor of black garlic.26 The temperature and the SAC content is inversely related as it decreases with an increase in temperature.18 The processing period also affects the content of SAC, which is directly related to the SAC content. Following an increase in the processing period, an increase in the SAC level is noticed.18

The most abundantly found nutrients in black garlic is carbohydrates and fructose.9 They also possess other reducing sugar like glucose, xylose, arabinose, and galactose. The amount of nonreducing sugar, sucrose, is lower when compared with the white garlic.3.9.19 This may be because of the hydrolysis of fructan into glucose and fructose during thermal processing.3 Moreover, the degradation of other polysaccharides may occur because of high temperature and acidic conditions. The increased acidity of black garlic may lead to the hydrolysis of sucrose into fructose and glucose, which reveals the abundance of fructose and glucose versus sucrose, and in turn, explains the sweet flavor of black garlic. The sugar content can decrease with a prolonged thermal processing period. 19

Due to the enzymatic hydrolysis of protein into amino acid at a high processing temperature and acidic condition, black garlic contains increased levels of leucine, isoleucine, tryptophan, phenylalanine, histidine, and aspartic acid.13,19 But the concentrations of other amino acids like cysteine(precursor of the sulfur-containing compound), tyrosine, threonine, glycine, and serine are reduced because of the Maillard reaction that occurs between amino acids and carbohydrates. Here the amino acids are used to produce an intermediate browning product, which is manifested by the complex formation of sugar-cysteine and sugar-tyrosine that exhibit higher antioxidant capacity in black garlic.13,19

Black garlic contains higher amounts of phenolic compounds like polyphenol and flavonoid, responsible for their high antioxidant activity versus white garlic.17,20 Two previous studies showed that the amount of phenolic content in black garlic significantly increased throughout the heating process until day 21 and didn't show much difference later.3,13 This outcome was also similar in another finding that reported a higher antioxidant content in 21 days versus 35 days of the manufacturing process.18 Total polyphenol and flavonoid compounds can be derived from 5-hydroxymethylfurfural (5-HMF), uridine, and adenosine during browning reaction, which have been observed in different fraction (chloroform: methanol) of ethyl acetate extracts of black garlic extraction.22 The flavonoids detected in black garlic include catechin, epicatechin, quercitrin, and myricetin, and phenols include gallic acid, p-coumaric acid, ferulic acid, and caffeic acid.27

Kang19 reported the declined concentration of thiosulfinate (responsible for the odoriferous smell of white garlic) in black garlic. This reduction was linked to its conversion into SAC, SAMC, arginine, or other unknown compounds during heat treatment, and degradation into allicin which is not significant in black garlic. Examples of thiosulfinate in the garlic are diallyl sulfide and diallyl disulfide.

Several alkaloids were also reported to present in black garlic, such as 2-acetyl- pyrrole responsible for the pleasant aroma of the black garlic.22,31,38 This is one of the products derived from the Maillard reaction. Another alkaloid found is tetrahydro-ß-carboline derivatives, which is the antioxidant component of black garlic.18,19 Tetrahydro-ß-carboline might be derived from the reaction between amino acid L-tryptophan and α-oxo acid, for instance, pyruvic acid, or aldehyde that were produced from Maillard reaction.19

The increased concentrations of pyruvate in black garlic improves its antioxidant and anti-inflammatory properties.18 The study by Jeong et al.28 showed that pyruvate significantly reduced the reactive oxygen species, which causes oxidative stress and cell death because of inflammatory effects. The amount of pyruvic acid in black garlic increases at the early processing stage but continuously decreases later.19 Pyruvic acid is responsible for the pungent smell in black garlic.19 The differences in the chemical compositions between black garlic and white garlic are presented in Table 1.

Pharmacological Activities of Black Garlic

Several studies have assessed the pharmacological activities of black garlic and proved that it has promising therapeutic potential. These include anticholesterol and antitriglycerides,14 anti-inflammatory,28 antimicrobial,24 anticancer,24 antioxidant,3,20,22,30 cardioprotective,31 and neuroprotective, activities.32,33 In addition, more studies on various pharmacological activities are continuously carried out in recent years. The pharmacological activities that have been assessed and scientifically proven are summarized and depicted in Table 2.

CONCLUSION

With the numerous plant bioactive constituents identified in black garlic and its therapeutic potential that has been proven to be pharmacologically active through various studies, the benefits of black garlic in complementary medicine are evidence based. Indeed, the fermented form of garlic should be sought after not only for its acceptable taste but also for its therapeutic and prophylactic properties.

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DISCLOSURE STATEMENT

The authors declare that there is no conflict of interest.

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Table 1: Differences in phytochemical composition between black and white garlic

Phytochemical composition	Black garlic	White garlic	Extract /form of garlic	Reference study
Carbohydrates	35 ± 3 g/100 g fw	28 ± 2 g/100 g fw	Methanol	Botas et al. [9]
	47.0 %	28.7 %	Water at 100°C	Sasaki et al. [12]
Total free sugars	33.6 ± 0.7 g/100 g fw	1.32 ± 0.05 g/100 g fw	Methanol	Botas et al. [9]
	4010.59 ± 18.72 mg/100 g,	292.54 ± 2.01 mg/100 g	Powder	Kang[19]
	16.07 ± 0.38 g/kg	1.52 ± 0.01 g/kg	Deionized water	Choi et al.[13]
Total amino acid	167.65 ± 1.08 mg/100 g	843.11 ± 3.75 mg/100 g	Powder	Kang[19]
	1486.65 ± 112.62 mg	1943.77 ± 161.22 mg	Sodium chloride and distilled water	Liu et al.[29]
Thiosulfinate	0.34 mmol/100 g	10.47 ± 0.35 mmol/100 g	Hexane	Kang[19]
SAC	2.12 ± 10.17 mg/g	1.24 ± 9.22 mg/g	Distilled water	Jeong et al.[28]
	194.3 µg/g	23.7 µg/g	Water at 100°C	Sasaki et al. [12]
Allicin	Not detected	Detected	Solid phase micro extraction	Czompa et al. [11]
	Not detected	3.62 ± 0.01 mg/g	Distilled water	Jeong et al.[28]
Total polyphenols	48.35 ± 1.14 mg GAE/g	13.91 ± 1.62 mg GAE/g	Deionized water	Choi et al.[13]
	2.68 ± 0.31 µg/mg	2.18 ± 0.24 µg/mg	Water at 80°C	Hee et al.[17]
	17.56 ± 0.31 g GAE/kg dw	3.20±0.07 g GAE/kg dw	50% v/v ethanol	Angeles et al.[20]
	16.17 ± 0.29 g GAE/kg	4.30 ± 0.04 g GAE/kg	50% v/v ethanol	Toledano Medina et al.[4]
Flavonoids	15.70 ± 2.11 mg RE/g	3.22 ± 0.07 mg RE/g	Deionized water	Choi et al.[13]
	1.92 ± 0.32 µg/mg	1.40 ± 0.26 µg/mg	Water at 80 °C	Hee et al.[17]
5-HMF	8.732 ± 0.17 mg	0 mg	Sodium chloride and distilled water	Liu et al.[29]
Pyruvate	2456.54 ± 23.93 µM/g	486.71 ± 12.08 µM/g	Distilled water	Jeong et al.[28]
2-acetyl-1- pyrroline	Detected	Not detected	Solid phase micro-extraction	Czompa et al.[11]

g/100g fw, grams per 100 g of fresh weight; GAE, gallic acid equivalents; g GAE/KG dw, grams of gallic acid equivalent per kg of dried weight; RE, rutin equivalents.

Table 2: Pharmacological activities of black garlic.

Pharmacological activity	Black garlic extract / form	Findings	Reference study
Anti-hepatotoxicity	Three fractions of solvent: water layer extract, n-butanol layer extract, and ethyl acetate layer extract.	n-butanol layer and water layer extract significantly reduced proinflammatory cytokines and other intermediators which improved the hepatic injury.	Tsai et al.[34]
	Deionized water at ratio 1:10 (solid: liquid).	Black garlic extracts significantly reduced cell death in rat clone-9 hepatocytes by inhibiting glutathione depletion, accumulation of melondialdehyde, and production of interleukin -6/ 8.	Lee et al.[35]
Antioxidant and antigenotoxicity	50% methanol	Black garlic can inhibit hydrogen peroxide (toxicant/potent genotoxic) action in dose dependent manner.	Toledano Medina et al.[4]
Anticholesterol and antitriglycerides (metabolic effect)	Powder	The level of triglycerides and low-density lipoprotein was significantly decreased and high-density lipoprotein levels increased.	Amor et al.[7]

Anti-inflammatory	80% methanol and ethyl acetate	ABG significantly suppress production of inflammation mediators (nitric oxide (NO), interleukin-6, PGE_2, and TNF-α) and inhibit enzyme (NO synthase and cyclooxygenase (COX-2) that catalyzed biosynthesis of prostaglandin.	You et al.[36]
Improve gastrointestinal performance	1:5 n-hexane. Further extract by five different polar solvents, n- hexane, dichloromethane, ethyl acetate, n-butanol, and water.	Black garlic extract in n-butanol and water extracts increased 5-HT_4 receptor, located in the gastrointestinal tract and have motility effect of GIT.	Chen et al.[37]
Cardioprotective effect	Black garlic cloves	There is significant increase in cardiac function with black garlic treated group by enhancing the aortic flow after 30 minutes of ischemia and 120 minutes of reperfusion.	Czompa et al.[11]
	50% ethanol	In combination with conventional treatment, it improved left ventricular ejection fraction and inhibited neuroendocrine activation of CHD patients, and decreased N-terminal pro-body BNP levels.	Liu et al.[29]

Fig.1: A whole bulb and cloves of black garlic.

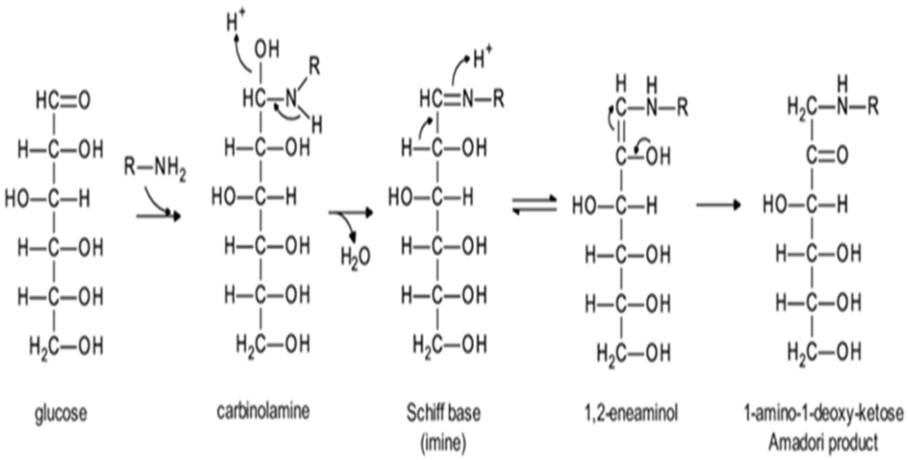

Fig.2: Amadori product formation.

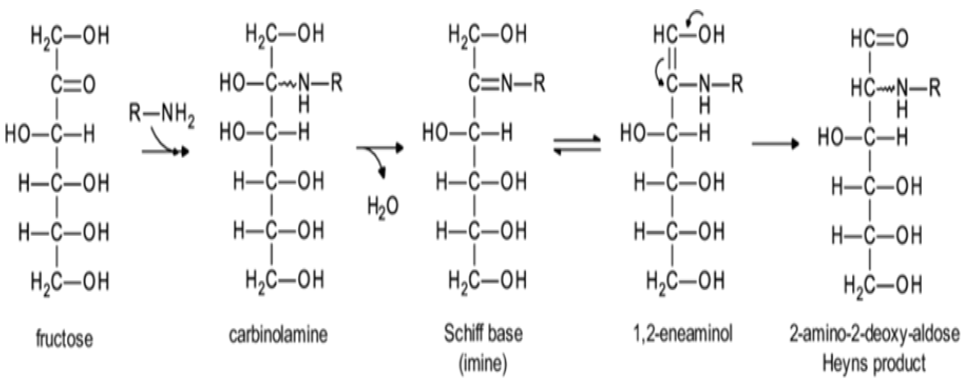

Fig.3: Formation of Heyns product.