Multifarious Benefits of Black Garlic in Health and Nutrition

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Abstract

Garlic is one of the most important foods and spices for centuries. Garlic is used as a basic resource material for modern pharmaceuticals which are thought to be powerful instrument in maintaining public health and act against nutritionally induced acute and chronic diseases, Black garlic, endowed with nutritional and therapeutic potential, is produced by fermentation from fresh garlic under controlled conditions of high temperature and humidity by eliminating its unpleasant odor. After processing, the black garlic products have a high content of polysaccharides, reducing sugar, protein, phenolic compounds, organic sulfur compounds, and melanoidins. Compared to fresh garlic, BG does not release a strong off-flavor due to the reduced content of allicin, which was converted into antioxidants bioactive alkaloids and flavonoid compounds during the aging process. Apparently, BG exhibits several advantages when compared with fresh garlic. Since garlic has long been consumed in the human society and has been recognized as one of the safe food substances, there will be no constraints for further invention of BG products for such functional food, food supplements, as well as medical purposes. Today as herbal medicine garlic is attracting public health authorities, pharmaceutical industries because of its larger use in prevention and treatment of so many diseases and disorders. Garlic is used as a basic resource material for modern pharmaceuticals which could be a powerful instrument in maintaining public health and act against nutritionally induced acute and chronic diseases. This review insights on the multifunctional pharmaceutical applications of this natural herb with a wider scope for commercialization.

Keywords: Black Garlic, Allicin, S-allyl cysteine (SAC), Diallyl trisulfide (DATS), diallyl disulfide (DADS), colorectal cancer, hepatocarcinogenesis

Introduction

An excipient (derived from words excipere to take out, receive) may be defined as any substances mixed with the active pharmaceutical ingredient to give it consistency or used as a vehicle for its administration. Natural excipients and derivatives occur ubiquitously throughout the plant and animal kingdoms[1].In recent years, plant derived polymers have evoked tremendous interest due to their diverse pharmaceutical applications such as diluent, binder, disintegrants in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppository, they are also used in cosmetics, textiles, paints and papermaking[2]. Classification of excipients is based on their role in the pharmaceutical formulation, their interactions influencing drug delivery, or their chemical and physico-chemical properties[3].Natural gums and mucilages are preferred over the synthetic ones because they are biocompatible, cheap, and easily available than the synthetic ones. Also, the natural excipients are preferred on the synthetic and semisynthetic ones because of their lack of toxicity, low cost, soothing action, availability, and non-irritant nature of the excipients. India, because of its geographical and environmental position, has traditionally been a reliable source for such products among the Asian countries[4]. For thousands of years, man has relied on nature as a source of medicines to treat and cure illnesses. Only in the twentieth century has the pharmaceutical industry turned to modern methods of combinatorial chemistry and rational drug design as a means of obtaining new chemical structures with potential drug uses[5].

Allium sativum, commonly known as lahsun in Hindi (Garlic in English) belongs to the family Alliaceae and plant order liliales[6]. Garlic is a perineal, erect, bulbous herb indigenous to Asia, but it is commonly grown in many parts of the world. Plant prefers sunny dry places in relatively arid climate. Garlic is one of the important *Alliums* which are used for both culinary and medicinal purpose by many cultures for centuries[7]. Both cultivated and wild species of garlic are available in different climatic regions. Members of the Garlic family include *Allium cepa* (Onion), *Allium ascalanicum* (shallot), and *Allium porrum* (Leek)[8].Garlic is the most important of all the species because of the presence of sulfur compounds allicin, helps to decrease serum levels of glucose, insulin, triglycerides, and uric acid, as well as insulin resistance, and reduces cytokine levels. S-allyl cysteine (SAC), a superstar antioxidant found abundantly only in black garlic (compared to other garlics)[9]. S-allyl cysteine (SAC) is a water-soluble garlic derivative which acts on human ovarian cancer cells *in vitro*[10]. Diallyl trisulfide

(DATS), diallyl disulfide (DADS), a major organosulfur component of garlic that inhibits cell proliferation by triggering either cell cycle arrest or apoptosis, but the exact mechanisms of its action in human bladder cancer cells is remain unknown[11].Garlic products act on several signalling pathways, including the inflammatory and apoptotic ones, and strongly target cancer. Its components/formulations can scavenge free radicals and protect membranes from damage and maintains cell integrity.

It also provides cardiovascular protection mediated by lowering of cholesterol, blood pressure, antiplatelet activities, and thromboxane formation thus providing protection against atherosclerosis and associated disorders. Besides this, it possesses antimutagenic and antiproliferative properties that are interesting in chemo preventive interventions[12].Organosulfur compounds from garlic effectively inhibit the growth of transplanted as well as spontaneous cancers in preclinical animal models without any adverse side effects[13]. Garlic supplementation inhibits platelet aggregation and high intakes of garlic and other Allium vegetables (e.g., onions and leeks) may help protect against gastric, colorectal cancer (CRC) and relieve from hepatocarcinogenesis[14].

Garlic products that contain the most safe, effective, stable, and odourless components are the most valuable as dietary supplements. Garlic also contains non sulfur compounds such as steroid saponins. These have characteristic properties, including the production of stable foam when shaken with water, haemolytic activity, and a bitter taste.Garlic natural products of therapeutic and dietary use are most preferred items used by nutritionists, physicians, food technologists, food chemists. Raw garlic or half processed garlic pastes are used as pharmaceuticals for maintaining health and act against nutritionally induced acute and chronic diseases. Its therapeutical potential has been known for many ages[15].

Today as herbal medicine garlic is attracting public health authorities, pharmaceutical industries because of its larger use in prevention and treatment of so many diseases and disorders. Garlic is used as a basic resource material for modern pharmaceuticals which are thought to be powerful instrument in maintaining public health and act against nutritionally induced acute and chronic diseases[16]. However, garlic consumption is still limited because of its strong flavour and odour. Moreover, fresh garlic causes some adverse effects including gastrointestinal disorder, haemolytic anaemia and allergic reactions. Recently, a preparation of garlic called black garlic was marketed widely. It is produced by heating whole garlic bulbs at high temperature (70˚C) and high humidity (90%). Unlike fresh garlic, black garlic has a

sweeter taste as a fruit so that it can be used easily. Particularly, there is a significant increase in the amounts of S-allyl cysteine (SAC), amino acids, flavonoids, and polyphenols, etc., [17]. Black garlic gets its name from the black hue of the cloves, but retains the same shape as raw garlic.

Black Garlic contains approximately 850mg S-allyl-cysteine (SAC) per bulb, which is 30 times less toxic than allicin in garlic. (Allicin is regular garlic is the compound that is responsible for garlic's health benefits, however it can also be toxic, when consumed in large quantities). A person can consume significantly more black garlic with no side effects. Black garlic also contains the following crucial nutrients: Magnesium, Calcium, Phosphorous, Selenium, Vitamin B6, Vitamin C[36].Exact origin of BG is unknown and controversial. However, BG has long been consumed in Thailand, South Korea and Japan for centuries and was introduced into Taiwan and other countries around 10 years ago[18]. Compared to fresh garlic, black garlic showed stronger antioxidant and free radical scavenging ability. Furthermore, black garlic has been reported to have a better immunomodulatory effect than raw garlic[17].In 1990, Designers Food Programme listed Garlic at the top of cancer-fighting candidates[20]. When compared with fresh garlic, BG does not release a strong off-flavor due to the reduced content of allicin, which was converted into antioxidant compounds such as bioactive alkaloids and flavonoid compounds during the aging process. The changes of physicochemical properties are the main reasons for enhanced bioactivity of BG compared with fresh garlic. Besides daily consumption, several studies have reported that BG extract demonstrates several nutritive and therapeutic functions. Black garlic is already enjoyed in Asian countries where preparing food by fermentation is part of the culture. Pre-packed black garlic cloves and black garlic dietary supplements are alsowidely available.

The present review attempts to emphasize the technical aspects of the compositional change, production, and pharmaceutical applications of BG with their future prospects on their possible applications as a functional food product.

PRODUCTION OF BG

- The aging period of BG is shorter at a high temperature; however, controlling the amount of some components might be difficult at a high temperature because their contents change rapidly during the aging process.

- In the case of aging process at 70˚C, the speed of aging is two-fold faster than that at 60˚C. However, the quality of BG is affected by not only temperature, but also other factors such as humidity and fermentation.

Therefore, further investigations are also required to ascertain the influence of such factors on the extent of change in the composition[18]. During fermentation, the pearly white cloves of fresh garlic *(Allium sativum)* gradually darken to their final black appearance, and the process converts the compounds found in fresh garlic into a whole new range of compounds.

Procedure

Primarily, as a pre-treating procedure, the raw garlic must be prepared by distinguishing garlic with the same condition.After the preparation for aging as above is completed, the inner temperature and humidity of the aging chamber and the weight of the stored garlic are checked, furthermore, the information must be confirmed. After the above-mentioned preparations, The whole manufacturing procedure of the black garlic according to its method of preparation, can be divided into five steps: preparatory stage, main aging step, after aging step, and low temperature after aging step (Figure 1).

1. Initially, preparatory steps are performed: the peeled garlic is stored by 10 kg, sealed, and stored at each tray.
2. Step 1: the prepared garlic is steam-treated at a high temperature and high humidity condition.
3. In this procedure, steam and heat are applied for 1-3 hrs while maintaining the temperature of 80-100° C. At this time, the humidity condition must be maintained at 100% RH. By this procedure, heat and water produced from the steam are applied to the garlic, making the tissue of the garlic smooth and soft.
4. The water in these garlic is later changed in phase to steam and discharged into outer air. Thus, the weight of the garlic is decreased. If the weight change of the garlic is about 0-29%, the steam processing is finished, and the next step is carried out. Once this step is finished, the hot taste of the garlic is broken down; the hard tissue of the garlic becomes smooth and soft because of the heat-treating action of the enzyme inside of the garlic.

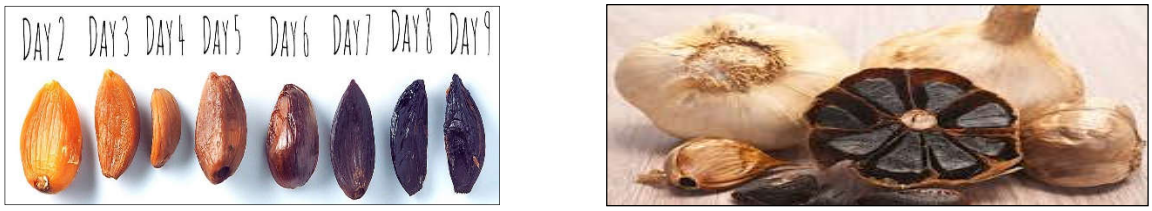
5. In the next main aging step, heat is applied by the temperature of 72-77° C.; the inner humidity is maintained at 60-70% RH for about 198 hrs. After this main aging procedure is finished, the weight change of the garlic becomes about 30-49%.
6. Through this procedure, the garlic preserves a constant amount of water in its tissue. At this stage, the browning reaction is promoted.
7. After the main aging procedure is finished, the after-aging procedure is begun.
8. In the after-aging procedure, the temperature of 60-69° C. is maintained; the humidity condition is maintained at 50-60% RH for 35 hrs. By maintaining these conditions, the hot taste of the garlic disappears, and good sugar content with the sweet and sour taste good for eating develops.
9. The next step is the drying. This step is done by maintaining a temperature of 50-58° C., and humidity condition of 40-50% RH for 51 hrs. After this step, the surface of the black garlic becomes dry. Thus, each particle of the black garlic is not sticky as it was, as caused by the water and resin in the surface. The garlic becomes gentler to consumer's hands, and Handling it is now easy owing to its non-sticky quality. Storability is also improved.
10. Next, the low temperature after-aging follows. At this stage, the temperature is maintained at 0-5° C., and the humidity condition at 20-30% RH for 168 hrs. By keeping these required conditions, the chilly air is supplied into the inner of the aging chamber using the chilly air compressor that is installed in the aging device.
11. With the supplied chilly air, garlic is kept at a low-temperature. Once the after-aging step is finished, the best black garlic is produced. Its surface is dry; its inner part is chewy due to proper water content; its taste, sweet and sour; and its handling and storability, easier (KO *et al.,* 2011).

The possible differences between fresh garlic and fermented black garlic in terms of physicochemical and biochemical attributes are clearly present in the table 1. Several studies have reported that water-soluble sugars, amino acids, total polyphenols, and flavonoids increased or decreased during thermal processing (table 2).

Table 1: Comparison between Black Garlic and Raw Garlic[21]

Parameters	Raw garlic	Black garlic

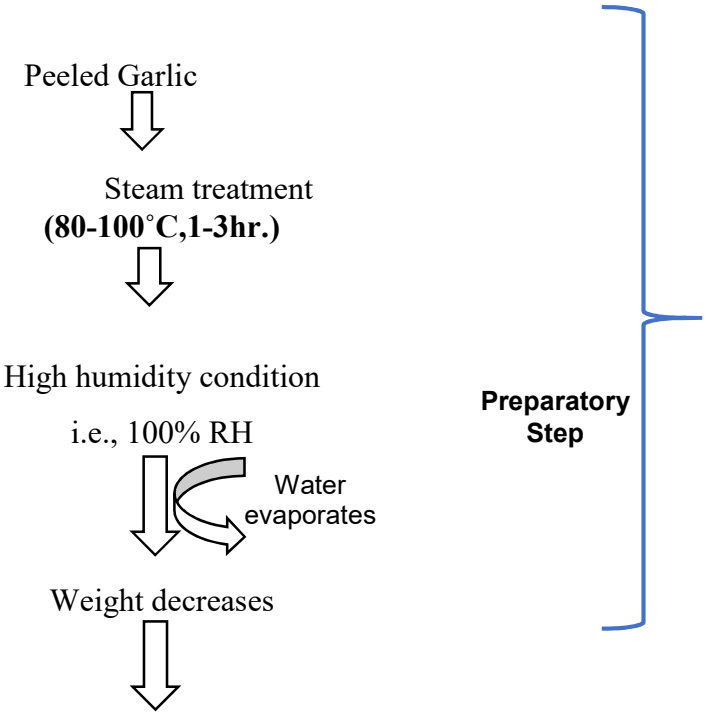
Order & taste	Spicy, garlic odour	Sweet, No smell & odour
Moisture/ % w. B	65.4	34.0
Sugar/bx	9.1	14.6
Total acid contents	18.2	46.5
Volatile organic sulfur compounds % d. B	0.65	0.06
Polyphenols %	0.22	3.1
Free radical scavenging capacity g/kg	6.8	57.7



A **B**

Figure 1. Black garlic. (A) Sequential changes in garlic during fermentation process (left to right): (B) Black garlic cloves.

Production of Black garlic



(If Weight change of the garlic is about 0-29%, the steam processing is finished)

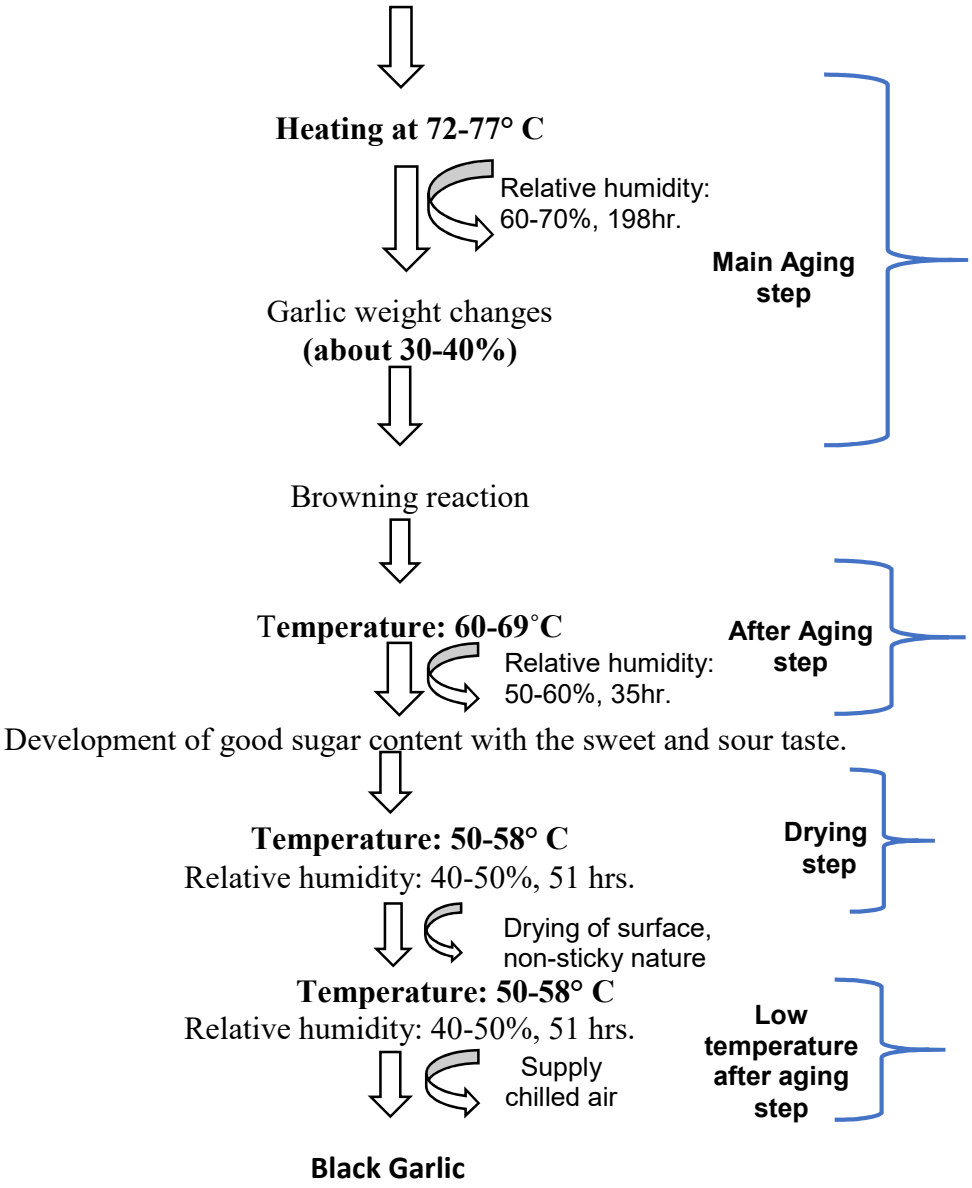


Fig 1: flow chart indicating the stages of black garlic production at various conditions

Table 2: Comparison of the biochemical components of BG and fresh garlic

components	Components of black garlic compared with fresh garlic	Original concentration
Water-soluble sugar	Increased 1.88e7.91-fold	450 mg/g
Polyphenol	Increased 4.19-fold	13.91 mg GAE/g
Flavonoid	Increased 4.77-fold	3.22 mg RE/g
Amadori & Heyns	Increased 40e100-fold	10 mg/g
Fructan	Decreased 0.15e0.01-fold	580 mg/g

Leucine	Increased 1.06-fold	58.62 mg/100 g
Isoleucine	Increased 1.67-fold	50.04 mg/100 g
Cysteine	Decreased 0.58-fold	81.06 mg/100 g
Phenylalanine	Increased 2.43-fold	] 55.64 mg/100 g
Tyrosine	Decreased 0.18-fold	449.95 mg/100 g
GAE ¼ gallic acid equivalents; RE ¼ rutin equivalents		

Bioactivities of Black Garlic:

1. Garlic has been used as a medicine since ancient times and has long been known to have antibacterial, antifungal, and antiviral properties. Garlic extracts has preliminary evidence for the antimicrobial activity against periodontal pathogens, *P. gingivalis*, *A. actinomycetemcomitans*. Its action against *P. gingivalis* includes inhibition of total protease activity, and this raises the possibility that garlic may have therapeutic use for **periodontitis** and possibly other oral infections[22].
2. Black garlic has high content of polyphenol. BGP (Black Garlic Polyphenol) has obvious DPPH· radical and ·DH radical scavenging activities and can significantly decrease the serum MDA(Malondialdehyde) content in mice and increase the serum SOD (Superoxide Dismutase) and GSH-Px (Glutathione peroxidase) activities. This indicates that, the BGP has **good *in vivo* antioxidant activities**, which are basically in accordance with the *in vitro* antioxidant activities[23].
3. Administration of 0.5% or 1.5% black garlic extract was effective, dose-dependently, in improving blood lipid profiles, especially TG, and blood glucose levels in rats fed a high fat diet, as evidenced by decreased expressions of SREBP-1c and its related enzymes, along with increased expression of CPT-1. Thus, appropriate intake of black garlic will be beneficial in the **prevention of hyperlipidaemia and hyperglycaemia** caused by a high fat diet[24].
4. Several studies *in vitro*, have **confirmed the cardioprotective effects** of garlic on primary cultured cardiac myocytes, fibroblasts, and endothelial cells, by reducing the production of ROS and blocking ROS-dependent extracellular signal-regulated kinase (ERK)1/2, JNK1/2, AKT, NF-*κ*B, and SMADS signalling[25].
5. **Anti-bacterial potency** was admitted in the extracts of the black garlic against MRSA (Methicillin-Resistant Staphylococcus aureus), enterohemorrhagic E. coli O157, Pseudomonas spp. (a causative agent of opportunistic infection), Candia albicans. However, bacteria killing potency was less than that of general fresh garlic. Difference

in its activity between them might be caused by different amount of volatile allicin contained, which was powerful bacteria killing agent. Great benefit of the black garlic is to have worked to the drug resistant MRSA [26].

6. Aged Black Garlic extract modulated the PI3K/Akt signalling pathway in HT29 cells through the upregulation of PTEN, downregulation of Akt expression, reduction of p-Akt and p70S6K1 expression at the mRNA level which may be effective in the prevention and treatment of **colon cancer** in humans[27].
7. Aged Black garlic, which was known to have strong antioxidant effects, protected rats from CCl_4 and D-galactosamine-induced hepatic injury also suggests that the treatment with anti-oxidants might be beneficial for **protection from liver injuries** induced by CCl_4 and D-galactosamine and also HFD (High fat diet)-induced increase in liver weight was significantly inhibited by treatment with aged black garlic[28].
8. HEABG (Hexane extract of aged black garlic extract) reduces leukemic cell growth by inducing caspase-dependent apoptosis through both intrinsic and extrinsic pathways, implying its potential therapeutic value in the **treatment of leukaemia[29].**
9. Garlic and aged black garlic, to a greater extent, could decrease hydrogen peroxides and contribute to protection against **diabetic complications** by exerting strong anti-oxidant activities[30].

THERAPEUTIC USES OF BLACK GARLIC:

1. Garlic and its derivatives can reduce the risk of several types of **human cancer**. Locals use garlic products to prevent **colon cancer, rectal cancer, breast cancer, prostate cancer, and lung cancer. It is also used to treat prostate cancer**. The overall activity of garlic is mainly due to the presence of sulfur compounds such as alliin, allicin, ajeone and others[31].
2. Black garlic could restrain the development of **atherosclerosis** by cleaning cholesterol to **improve hyperlipidaemia** and reduce weight and blood lipids. Furthermore, researchers found that black garlic had a strong antioxidant activity both *in-vivo* and *in-vitro*[19].
3. While “good” cholesterol, or HDL, is essential for survival, keeping LDL, or “bad” cholesterol in check is important for reducing the risk of heart disease, stroke and premature death. Although raw garlic has gotten most of the praise when it comes to heart healthy benefits, black garlic has recently been the subject of multiple studies, and

as it has a slightly different phytochemical makeup compared to raw garlic, it offers even greater benefits for supporting the heart. A 2014 study conducted at Chonbuk National University Hospital in South Korea found that participants who took black garlic extract daily for 12 weeks say an average increase in HDL ("good" cholesterol), as well as a decrease in allpoprotein B in blood lipids – something that's considered to be a strong indicator of heart disease risk[35].

4. Garlic is also high in antioxidants. The total phenolic content in black garlic is 5-8 times higher than that of fresh garlic, so the black garlic has higher **antioxidant activity** than fresh garlic [23,34]. Black garlic has been found to have twice the antioxidant properties of conventional garlic. Antioxidants protect the cells from disease and are thought to slow down the aging process, according to OrganicAuthority.com. Because black garlic is so potent, the heightened levels of antioxidants offering protection from free radical damage make it an ideal food for thwarting chronic disease. Free radicals damage cells leading to heart disease, Alzheimer's, circulatory problems, rheumatoid arthritis and other chronic diseases[34].
5. Aged Black Garlic Extract(ABGE) can inhibit the growth and **induce apoptosis in HT29 cells** through the inhibition of the PI3K/Akt pathway, suggesting that ABGE may be effective in the prevention and treatment of **colon cancer** in humans[27].
6. Aged Black Garlic has **hepatoprotective effects** and suggest that ABG supplementation might be a good adjuvant therapy for the management of liver injury[28].
7. Aged Black Garlic showed an increased **anti-tumor** action with a high curative rate against Meth A fibrosarcoma, which fresh garlic extracts failed to cure[32].
8. Hexane Extract of Aged Black Garlic reduces leukemic cell growth by inducing caspase-dependent apoptosis through both intrinsic and extrinsic pathways, implying its potential therapeutic value in the treatment of **leukaemia**[29].
9. Intake of black garlic will be beneficial in the prevention of hyperlipidaemia and hyperglycaemia caused by a high fat diet[24].
10. The black garlic extract was more effective than the raw garlic extract regarding **immunostimulatory activities**[33].
11. White garlic contains antimicrobial, antibiotic and antifungal agents in its active ingredient, allicin. In black garlic, S-allyl cysteine assists with the absorption of allicin, helping it metabolize more easily, which could offer boosted protection **against infections**[34].

Conclusion

BG, a potential natural supplement, exhibits multifarious benefits when compared with fresh garlic slices. Whereas fresh garlic is pungent, black garlic has a mild, sweetish taste and smell which is similar to that of oven-roasted garlic. Since garlic has long been consumed in the human society and has been recognized as one of the safe food substances with inherent medicinal properties, demanding deeper scientific investigation and validation of its multiple benefits. However, it is commonly known that excessive consumption of garlic can cause problems such as odor of the breath and skin, occasional allergic reactions, and toxicity. The main constituents of black garlic extract are water soluble compounds, thus it lacks the toxicity and has no peculiar garlic smell. Therefore, it can be taken by humans for a long time without presenting toxic side effects or contraindications with medications to prevent or reduce specific clinical problems. Scientific investigations in the field of nutrition led to the discovery of phenomena credited for prevalence and pathogenesis of various health discrepancies. Significance of natural products revitalized nowadays to alleviate such maladies. There exists an immediate need to optimize the BG manufacturing process at an industrial scale by exercising a proper control over the intermediate products as it has been scientifically proven to provide multifunctional health and nutritional benefits to the suffering mankind. Functional food and related therapies are often patterned with phytochemicals; studying the influence of each compound on human health can provide better insight regarding these nutraceutical agents Undoubtedly, BG has considerably enhanced the overall health and quality of life by its versatile nature. Apparently, a range of evidence has been documented in its favor but still necessitates the demand for further research before claiming its vitality.

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