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Prospect of The Black Pepper (*Piper nigrum* L.) as Natural Product Used to an Herbal Medicine

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Abstract

Black pepper (*Piper nigrum* L.) is a popular spice that is grown as tropical and subtropical plant throughout the world. The leaf, flower, fruit, and root are the most important elements of the plant. Asexual or vegetative propagation is becoming highly popular, although the sexual approach is still used for pepper vine cultivation. For mass production of the pepper plant, *in vitro* culture is also used. The bioactive components contained in them are extremely important because of their therapeutic potential against a number of diseases. They are usually classed as functional foods because, in addition to providing basic nutrition, provide physiological benefits and help to avoid chronic illness. The main component of black pepper is piperine. It has a complex phyto-chemistry includes: Volatile oil, alkaloids, and oleoresins. Because of its free-radical scavenging properties, black pepper and its active components can be prevention and control of tumor growth. Piperine, which can bind and inhibit the SARS-CoV-2 virus that causes the sickness, is present in black pepper and has antibacterial and antiviral effects. Piperine, a key alkaloid component of black pepper, it also helps to cognitive brain function, nutritional absorption, and gastrointestinal health. Black pepper is known as the "King of Spices" as well as the "King of Medicinal Agents," since it includes a wide variety of bioactive compounds with nutraceutical and pharmacological applications. An overview of the most common applications for black pepper, along with a strong evidence is present in this review.

Introduction

Black pepper is a popular spice crop all over the world. It's a basal angiosperm blooming vine that's generally dried and used as a spice fruit [1]. The spice belonging to the Piperaceae family. The climbing shoot, also known as the "main shoot," has internodes; the laterals, which develop off the main shoot, have shorter internodes and bear the spike. Spice is one of the most precious commodities, and it dominates the global trading market [2]. Black pepper has known as the "King of Spices" [3], [4] and it is called "Golmarich" in Bangladesh. Its grew in Kerela at Southwestern India, Malaysia, Indonesia, West Indies, and South America [5], [6]. The dried of black pepper has been used for flavor and old-fashioned medicine since antiquity. Black pepper is the most widely used spice in food preparation and distribution, as well as in perfumery [7], [8]. It is the most economically significant and widely used spice crop in the world, especially in Bangladesh [9]. The quality of a spice is determined by the odor, color, and pungency of the peppercorn [10], [11]. "*In vitro* cultivation of all parts of the plant on nutrient media develops under controlled conditions," according to Anandaraj [12]. At present, *in vitro* cultivation is a very common method for science breeders to propagate plants that are not easy to grow but have economic value in the world market.

Spicy fruits, resinous oils, and essential oils are used as flavoring ingredients in the food preservation, cosmetic, and perfume industries [13]. The spicy taste comes from Piperine essential oil, which is a pungent alkaloid. Piperine can increase the bioavailability of many drugs [14], [15]. In small amounts, safrole, sabinene, pinene, limonene, linaonol, and caryophyllene compounds are found. According to Santra *et al*. [16], black pepper has anesthetic properties, antimicrobial, antimutagenic, free-radical scavenger, immunomodulator, antitumor, antidepressant, antiapoptotic, antimetastatic, antithyroid, antitumor, antidepressant, antiapoptotic, antimetastatic, anti-thyroid, hepatoprotective, immune stimulator, and anti-spasmodic

[17], [18], [19], [20], [21], [22], [23], [24], [25], [26]. The black pepper fruit can use for pulmonary diseases, cold extremities, intermittent fever, gastric ailments, colic disorder, and diarrhea [27], [28], [29], [30]. It is suggested that phyto-compounds produced from black pepper may be very useful in combating the COVID-19 pandemic [31], [32], [33], [34], [35]. Insecticidal activity against pests has been found in black pepper [36], [37]. The secondary metabolite of nerolidol is used to control mites. Pipene, a well-known odor, is another component of essential oils [38], [39]. It has a bright future in the global market, but the factory has certain problems. Seeing the facts above, this review study was conducted to evaluate information about black pepper's growth, morphology, climate, and therapeutic efficacy.

Methodology

A study of the available journal literature, books, reports, blogs, and newspapers was conducted to assess the current level of research on the propagation, morphology, and therapeutic value of black pepper. Keyword searches in Google, Google scholar, web of science database, research gate, and a full-text search of the Science Direct database were conducted (Table 1). Personal communication was also used to get information from government agencies and non-governmental groups.

Morphology of Black Pepper Plant

The pepper plant is a perennial woody vine that grows to a height of 4 m (13 feet) on secondary trees, poles, or trellises [40]. The black pepper plant is a woody climber that reaches at least 10 m in height or length. The central stem develops many lateral branches to form a bushy column after it has established itself. The plants form adventitious roots, which are tiny roots that attach themselves to surrounding supports.

Leaf

The plant produces clusters, or spikes, of 50–150 blooms and has simple, alternate leaves that are varied in form (Figure 1). The leaves are dark green and lustrous on top and lighter green on the bottom, alternately arranged on the stalks above, dark green and sparkling, below, paler green. Dark green and shining above, lighter green below. Almond-shaped, tapering toward the tip, dark green and dazzling above, paler green below. The leaves are 5–20 cm long and 3–6 cm wide, with a length of 5–20 cm and a breadth of 3–6 cm. According to Shango *et al*. [41], the leaves blade (17.9 cm), leaf petiole (2.8 cm), and wider leaves (12.9 cm) are all from Tanzania. Leaf laminae can be cordate, oblong, ovate-lanceolate, or ovate-elliptic.

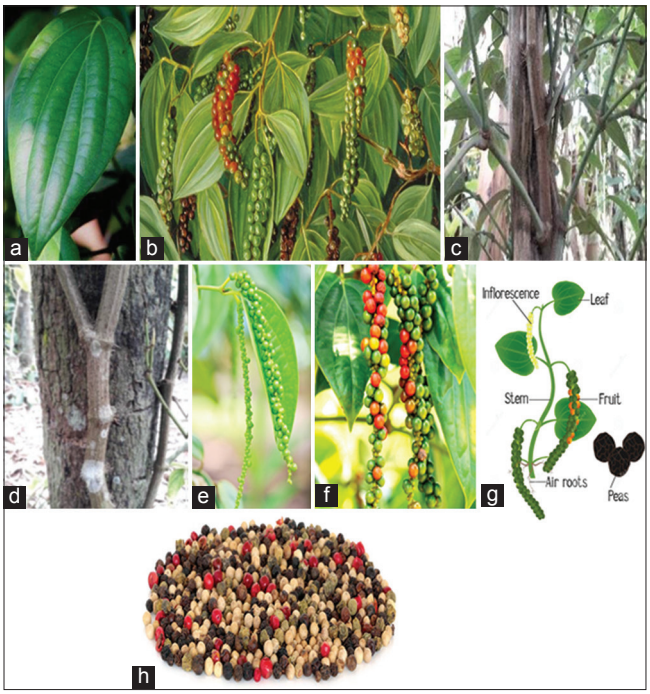

Figure 1: (a) Leaf; (b) stem of the black pepper plant with the fruits in different stages of fruiting; (c) erect shape of lateral branch habit; (d) round shape of stem; (e) inflorescence; (f) mature fruit; (g) parts of the black pepper plant (h) prepared fruit

Stem

Black pepper stems may grow up to 10 m long and 6 cm in diameter. The stem is herbaceous, delicate, and green (Figure 1). The leaf, blossom, and fruit are all found on the stem. Primary stems, runner shoots, and fruit producing stems are the three types of stems found on pepper plants. 20–30 fruiting spikes can be supported by a single stem [42].

Inflorescence

The flowers are tiny and are produced on pendulous spikes that are 4–8 cm long at the leaf nodes and can grow up to 7–15 cm in length (Figure 1). The bloom emerges from the opposing leaves' main stem node. It's a spike that grows from the nodes opposing the leaves. Sessile, bracteate, achlamydeous, and uni/bisexual, the flower is sessile, bracteate, achlamydeous, and uni/bisexual. Filiform, cylindrical, globular, and conical spike morphologies were identified. The spike is 3–15 inches long and has around 70 small blooms on it (up to 100 flowers). Greenish yellow blooms are placed in a spiral around the spine. Spikes are flower-bearing stalks that produce clusters of blooms. 50–150 white to yellow-green flowers are produced per spike [43].

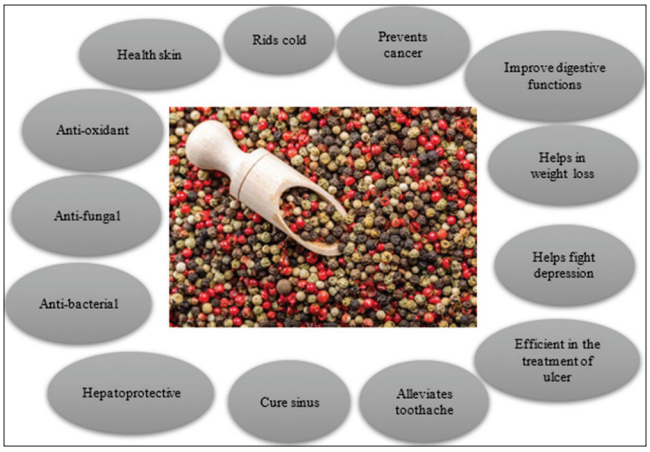

Figure 2: *Health benefits of black pepper*

Table 1: Keyword search

S. No.	Keyword search	Articles number
1.	Black pepper, *Piper nigrum* L.	278
2.	Medicinal importance	88
3.	Health benefits	117
4.	COVID-19	24
5.	Cancer	16
6.	Morphology	168
7.	Neuroprotective	32
8.	Propagation	68
9.	Limit of article	98
10.	Manually screened	97
11.	Articles included in the review	126

Fruit

Peppercorns, which are drupes with a diameter of 6 mm, are the most common fruit. At first, the fruits are green, but as they mature, they turn a reddish red colour (Figure 1). Each spike yields 50–60 fruits. The berries are divided into three categories: Large (5.8 mm), middle (>4.26 mm), and little (<4.26 mm) (4.8 mm). The quantity of berries per spike was classified as few (fewer than 25), medium (25–50), or many (more than 50) [41]. It's picked when the fruit is still green and immature; black pepper is picked when the fruit is fully matured but still green and shiny; and white pepper is picked when the fruit is somewhat riper [44]. The flavor is spicy, stinging, and highly strong, while the odor is intense and aromatic.

Table 2: Macronutrient composition of black pepper (100 g edible portion)

Name of the nutrition	Amount (Unit)
Water	12.5 g
Energy	251 kcal/1050 kJ
Protein	10.4 g
Total lipid	3.26 g
Carbohydrate	64 g
Fiber, total dietary	25.3 g
Galactose	0.15 g

Roots

There are two types of roots on pepper vine plants: Main and secondary roots. The adventitious roots adhere to the standards and strike at each node, forming roots (Figure 1). The ideal soil temperature for root development is (26–28°C). For black pepper, a well-distributed annual rainfall of 125–200 cm is ideal. The leaf area of cuts affects the roof of the black pepper root [45].

Propagation Practices in Black Pepper

Black pepper can be propagated by the asexual and sexual processes. The seeds are as sexual and cuttings, layering, and grafting as asexual propagation. Seed propagation is time consuming, slow process, and genetic variation occurred [11], [46]. In India, seeds are the main material to produce pepper but vegetative propagation is very much effective to cultivate black pepper [27]. Stem cutting and seed are the traditional propagated method [46], [47] and storage seed infested by pests in storage conditions [27], [48]. The cutting is commonly crawling by fungal, virus, bacterial, and mycoplasma pathogens in nursery and field conditions. The growing plant, quality, and quantity loss by the infestation of pathogens especially viruses [49], [50], [51], [52], [53], [54]. However, the vegetative propagation is cuttings, layering, grafting, budding, and rooted cuttings are favored for marketable cultivation [49], [50], [55], [56], [57], [58], [59].

Climatic Condition of Black Pepper

For its high demand in the global and it is referred as "Black gold" due to its higher prized trade. According to DEA [60], reported that Sri Lanka exported (7930–16,656) MT from 2014 to 2015, and export earnings have increased by 116% over previous years from (9029 to 19,543) Rs. Mn, in 2015. Sri Lanka mainly sells in India and procurements included 54% of pepper export in 2015. The pepper is mainly grown in low and mid wet and intermediate agroclimatic zones in the forest or any field. The pepper plant needs regular watering to improve growth and high-quality product in the nursery and main field. However, the unpredictable environmental condition is impacted by climate change and global warming. Decrease the rainfall but increase the temperature. For water stress, plant growth and development are hampered due to decrease rainfall in Sri Lanka [61], [62]. Increased temperature stress can alter crop physiological systems, resulting in reduced photosynthetic activity, reduced nitrogen absorption, and increased protein catabolism [62]. In reaction to heat stress, the plant displayed a variety of morphological signs [63]. The influence of crop physiology, water is the major issue [64] but temperature effect quality yield [65]. To overcome the water problem, the researcher develops the Super

Absorbent Polymers (SAPs) method where water is insufficient [66], [67]. Hutterman *et al.* [68] stated that the SAPs long water available for plant use when less water is found. SAPs also help to increase the moisture level but reduce the water stress of plants [69]. The method can absorb 1000 times more water than its original size and weight [70].

Nutraceutical and Functional Black Pepper

In traditional medicine, black pepper is used as a food additive to help the digestive system by improving appetite and absorption, as well as reducing dyspepsia and fleshiness. CVDs, diabetes mellitus, inflammatory illness, and cancer insurgence are among the current health issues that concern mankind [71]. Several animal studies have clarified the significance of black pepper can prevent of diseases [72], because of per 100 grams contain high energy, protein, carbohydrate, fibre, etc (as shown in Table 2). It is a good source of tryptophan (0.058 g), isoleucine (0.366 g), threonine (0.244 g), leucine (1.01 g), lysine (0.244 g), cystine (0.138 g), methionine (0.096 g), tyrosine (0.483 g), phenylalanine (0.446 g), valine (0.547 g), histidine (0.159 g), arginine (0.308 g), glycine (0.441 g), alanine (0.616 g), serine (0.409 g), and proline 1.41 g) (Table 3). The following are some highlights of the health-promoting potential of bioactive compounds found in black pepper.

Table 3: Micronutrient composition of black pepper (100 g edible portion)

Name of the nutrition	Amount (Unit)
Calcium, Ca	443 mg
Iron, Fe	9.71 mg
Magnesium, Mg	171 mg
Phosphorus, P	158 mg
Potassium, K	1330 mg
Sodium, Na	20 mg
Zinc, Zn	1.19 mg
Copper, Cu	1.33 mg
Manganese, Mn	12.8 mg
Selenium, Se	4.9 μg
Fluoride, F	34.2 μg
Thiamin	0.108 mg
Riboflavin	0.18 mg
Niacin	1.14 mg
Pantothenic acid	1.4 mg
Vitamin B-6	0.291 mg
Betaine	8.9 mg
Carotene beta	310 μg
Cryptoxanthin beta	25 μg
Vitamin A	547 IU
Lycopene	20 μg
Vitamin E	1.04 mg
Vitamin K (phylloquinone)	164 μg
Fatty acids, total saturated	1.39 g
Fatty acids, total monounsaturated	0.739 g
Fatty acids, total polyunsaturated	0.998 g
Histidine	0.159 g
Alanine	0.616 g
Aspartic acid	1.41 g
Glutamic acid	1.41 g
Glycine	0.441 g
Proline	1.41 g
Serine	0.409 g

Source: [76].

Ethnomedicine and Biological Activities

The black piper produced secondary metabolites that aid body metabolism and serve as a defensive mechanism [73], [74], [75], [76], [77]. Piper plants are being screened by scientists from many biological areas for a variety of secondary metabolites that might be utilized to make medications and biocontrol agents [78]. Anti-apoptotic [79], anti-bacterial [80], anti-Colon toxin [81], anti-depressant [82], anti-fungal [83], analgesic [84], anti-diarrhea and anti-inflammatory [85], anti-mutagenic [18], anti-metastatic activity [86], antioxidative [79], [87], antioxidative [79], [87], anti-pyretic [84], immuno-modulatory, anti-spermatogenic [88], anti-thyroid [23], anti-tumor [22], ciprofloxacin potentiator [89], [90], colic, cold extremities, gastric ailments [91], hepatoprotective [92], increase plasma [93], increase pancreatic enzymes [94], inhibit cytochrome [95], inhibit transcription [96], insecticidal activity [97], intermittent fever [91], and larvicidal activity [81] as mentioned in Figure 2.

Antioxidant Potential

Oxidation is an unavoidable process that occurs in body cells and is accompanied by certain unwanted reactions. Reactive oxygen species (ROS) is commonly regarded as the causal agent for a variety of diseases, including cancer, inflammation, atherosclerosis, and aging. Excessive ROS generation outperforms defensive capabilities as a result of oxidative anxiety in the body. A large variety of spices and fragrant plants have been identified. The bioactive compounds which are present, have antioxidant capacity molecules included in them [98].

With 0.43 mm of black pepper, 50% suppression of free radicals. In another research, Chavarria *et al*. [99], found that water and ethanol excerpts (75 g/ml) of black pepper prevent lipid peroxidation by 95.5% and 93.3%, respectively, in the previous experiments, and total phenolics content should be inhibited, which is 54.3 and 42.8 g/mg, respectively. Polyphenol concentrations were greater at 191 mg/100 g. Antioxidant activity was determined by various *in vitro* tests, which yielded some solid results. It was also suggested that black pepper might be a good source of normal antioxidants in the diet. As a result, black pepper's inclusion of these functional components makes it a great option for reducing oxidative stress [100]. Its strong hydrogen-donating capacity, metal chelating ability, and ability to scavenge free radicals all contribute to these effects. Furthermore, piperine's synergistic effects with other antioxidants like curcumin make black

pepper beneficial in disease preventive strategies that include ROS and related species [101]. Piperine at a dose of 10 mg/kg/day injected intraperitoneally repaired diabetes-induced abnormalities in Sprague–Dawley rats in another research, which employed diabetes mellitus development as a model of oxidative damage. The advantages come from antioxidants, which reduce LDL oxidation by regulating prostaglandin and leukotriene synthesis [102]. As a consequence, black pepper has antioxidant potential, but it has to be tested further in randomized controlled studies. The findings of such studies will ensure that black pepper and its bioactive components are used as a natural antioxidant.

Anti-inflammatory Potential

Inflammation can result in the growth of cancer cells. Insurgence is connected to a variety of illnesses such as arthritis, Alzheimer's, Parkinson's, and even cancer. Functional elements in diets may have anti-inflammatory properties. The inflammatory burst is a term used to describe a sudden increase in inflammation. Several methods, including inhibition of enzymes involved in the inflammatory cascade [103], are used to combat inflammation [104]. Recent animal and cell-level pharmacological research has revealed piperine, one of the active compounds in black pepper, might be effective in combating negative reactions. Black pepper's anti-inflammatory properties were originally documented about two decades ago. Piperine, according to Mujumdar *et al*. [105], works by activating the pituitary-adrenal axis, which helps to reduce acute inflammation. Bang *et al.* [106] used *in vitro* studies to further improve piperine's anti-inflammatory properties (20 and 100 mg/kg/day). Interleukin inhibition, matrix metalloproteinase inhibition, prostaglandin E2 inhibition, and activator protein 1 inhibition were proposed as potential pathways explaining their characteristics. Overall, the anti-inflammatory perspectives of black pepper and its active ingredients should be tested in disease prevention and management associated with inflammation.

Antimicrobial Potential

Plants have been used as antibacterial agents for a long time. The use of natural items, particularly spices, as antimicrobials has two benefits: prevention of infectious disease and improved health. The antibacterial activity of phytochemicals included in these items has been widely researched in recent years. Among these, phenolics have been shown to have antibacterial properties. Antimicrobial characteristics of black pepper and piperine can significantly reduce the development of *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Salmonella typhi*, Black pepper extracts inhibited the growth of bacteria such as *Staphylococcus*, *Bacillus*, and *Streptococcus*, according to Weerakkody *et al*. [107]. With minimum inhibitory concentrations (MIC) of 125, 250, and 500 ppm, black pepper extracts inhibited the growth of bacteria such as *Staphylococcus*, *Bacillus*, and *Streptococcus*. Brahma *et al*. [108] discovered that black pepper alkaloids had the potential to repel insects and rodents in this setting.

Many animals are repelled by black pepper and other freshly ground peppers. It is also said to be effective against houseflies, as well as having the capacity to prevent egg-laying antiparasitic properties against Giardia and Entamoeba species. Black pepper essential oil can also be used to protect cereals from insect damage and prevent worm infestations. Some of the black pepper's bioactive compounds have been discovered due to their use in the allelopathic management of insect infestations their effectiveness. Black pepper oil is also useful and has shown strong antibacterial efficacy against animal pathogens microbial pathogens [108], [109]. Overall, black pepper has significant antibacterial action against a wide range of pathogens that can be used for a variety of things, from preserving food to Infections that are avoided.

Gastrointestinal Activity

Black pepper and its active components have been used as traditional treatments for stomach problems. It is widely thought to help in the prevention and treatment of gastrointestinal problems. Black pepper stimulates the production of hydrochloric acid in the stomach by activating histamine (H2) receptors, which helps digestion. Diaphoretic (sweating-inducing) and diuretic (urination-inducing) properties are also present in black pepper [110]. Piperine is absorbed in the gut serosal fluids and tissue in a similar fashion to other amino acids absorbed from the mucosal side (44–63%). The gastrointestinal tract's functioning is improved by piperine. Improved nutrient absorption, improved enzyme synthesis, and improved defense capabilities are some of the mechanisms of action. Improved intestinal absorption of nutrients is one of the examples. Furthermore, due to its antioxidant capacity, it defends intestine from gastric secretions and ROS damage. In addition, "black pepper increased the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione reductase, and glutathione-S-transferase." These systems work together to offer gastro-protection by balancing mucosal health [111]. Piperine consumption may reduce body weight and visceral fat in mice by

increasing "thermogenic protein uncoupling protein-1." Black pepper has the ability to speed up the metabolic processes in the human body that produce energy. Although same process is involved in weight loss maintenance, it is also thought to have a function in nutrient absorption from the diet. When piperine is administered to perfuse hind limbs of experimental rats, it increases oxygen absorption [4]. Constipation and diarrhea can be treated with black pepper and its bioactive compounds [110].

Neuroprotective Property of Black Pepper

Globally, data collection on mental and brain disorders is frightening. More than 450 million individuals are thought to be affected by neurological disorders and depression [112]. The neuroprotective effects of functional meals have lately been highlighted as a possible therapy for a range of illnesses. In this sense, black pepper's antioxidant capacity and bioactive compounds are critical for improving brain function. In addition, piperine supplementation (5, 10, and 20 mg/kg body weight/day) promotes neuroprotection as well as enhanced cognitive performance. Piperine alleviated chronic moderate stress caused by variations in sucrose intake, according to their findings. "Piperine treatment enhanced the expression of brain-derived neurotrophic factor and mRNA. Piperine (10 and 20 mg/kg) relieved depression by decreasing adrenocorticotropic hormone and corticotropin-releasing hormone levels, thereby modulating the hypothalamic-pituitary-adrenal axis," according to Lindheimer *et al*. [113]. Piperine and curcumin have lately been recommended as a treatment for depressive disorders by Bhutani *et al*. [114]. According to behavioral testing using the forced swimming test, piperine is a strong antidepressant medication at 10 and 20 mg/kg, which is one of the most successful techniques for avoiding neurodegenerative illnesses such as Alzheimer's and Parkinson's. Piperine's effects on neurogenesis have not been fully investigated in humans, although mechanisms of action might include reduced lipid peroxidation and acetylcholinesterase enzyme activity. Black pepper and its active ingredients can assist with depression, Alzheimer's disease, and epilepsy, among other nervous system disorders.

Black Pepper Against Cancer

According to estimates, eating habits can lower cancer prevalence by 30–40%. Consumption of foods high in bioactive compounds has also been shown in population-based research to reduce the risk of many diseases, including cancer. In Asian and Mediterranean regions, spice intake is related to a decreased incidence of cancer. Reduced spice intake has also been related to a greater risk of cancer in poor nations [115]. Regulation of Phase I and Phase II detoxification processes, avoidance of lipid peroxidation, and an overall increase in antioxidant status are all anticancer characteristics of black pepper. Yang *et al*. [29] provided evidence that piperine's ability to interact with the cytochrome P450 enzyme system is responsible for piperine's anticancer effects in mice when exposed to benzo-pyrene. Piperine (50 mg/kg) was found to have chemopreventive effect against 7,12-dimethylbenz[a]anthracene (DMBA)-induced skin carcinogenesis by Vellaichamy *et al*. [116]. Piperine inhibited lipid peroxidation through regulating Phases I and II detoxification processes. The restoration of antioxidant status to normal is essential for health care, in addition to the aforementioned benefits. Khan *et al*. [30] observed similar results in oral cancer-bearing mice. Pellitorine (a terpine found in black pepper) has been demonstrated to be effective against the MCT-7 and HL60 cell lines [117]. Piperine's significant antioxidant effects have also been verified, suggesting that it may reduce protein expression, therefore controlling cell proliferation and transformation. Pepper has been revealed to have a free-radical scavenging effect that assists in the regulation of cancer development. In certain conditions, the same feature can be useful in delaying the growth of cancer cells. Almost all bioactive chemicals identified in black pepper, according to Liu *et al*. [118], can suppress TNF-induced NF-kappa B activation. Black pepper extracts and compounds decreased lipid peroxidation by 45–85% at 200 mg/mL, COX enzymes by 31–80%, and cancer cell proliferation by 3.5–86.8%. Some chemicals can be made less hazardous using black pepper and its components. Black pepper and piperine (60 M), according to numerous experts, mediate the adverse effects of DMBA, carbon tetrachloride, tertbutyl hydroperoxide, dioxin, and AFB1. Because these hazardous metabolites penetrate the food chain, they can induce reproductive toxicity, teratogenicity, immunological dysfunction, hepatotoxicity, and endocrine abnormalities in humans and animals [119]. Black pepper and its bioactive components are antigenotoxic, which means they can stop cancer from spreading.

Additional Health Benefits

The antioxidant and hypocholesterolemic properties of black pepper have a wide variety of nutraceutical uses. Triglycerides, total cholesterol, and LDL cholesterol levels are all important CVD risk factors. Some dietary recommendations can aid in the prevention and progression of CVDs. One way to enhance the lipid profile is to improve the peroxisome

proliferator-activated receptor. With EC (50) values of 84 M and 49 M, respectively, piperine had the greatest transactivational activity [103]. It looked into using black pepper extract to treat vitiligo, a skin condition marked by depigmentation lesions. The main alkaloid in black pepper encourages melanocyte proliferation. One of the most frequent oils discovered in individuals is black pepper oil. Inhalation is one of the most powerful appetizers since it encourages swallowing. Dysphagia is a condition that affects persons who have had a stroke. Another study is now underway. Information on the health benefits of black pepper tea is also available [120].

Time to Recover from COVID-19 Infection

COVID-19 is severely infected as a result of the development of a new COVID-19 stain in humans, and the infestation is spreading throughout the world [32], [121]. This viral illness has a significant influence on individuals all across the world, including Bangladesh [122], [123]. It also has an influence on the trade system's agriculture sectors [124]. Early statistics indicate that the median time from onset to clinical recovery for moderate cases is about 2–3 weeks. COVID-19 infection was severe in human lungs. Pneumonia was revealed to be caused by a new virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus's name is COVID-19, and the disease it causes is COVID-19. Wilson argues that when COVID-19 patients develop a cough and fever, it's because the infection has spread to the respiratory tree, or the air tubes that connect the lungs to the rest of the body. When the lining of the respiratory tree is injured, it irritates the nerves in the airway lining, causing inflammation. A cough can be triggered by a dust particle, but if it persists, it can extend beyond the airway lining to the gas exchange units at the end of the air passages. They discharge inflammatory material into the air sacs towards the bottom of our lungs when they get infected. The most prevalent cause of death is severe pneumonia. An emphasis on nutrition Immunotherapy is a coronavirus treatment that includes boosting or inhibiting the immune system's capacity to fight the virus. Immunotherapy may take many different forms, including cytokines, vaccines, viruses, adoptive cell transfer, and monoclonal antibodies, as we all know. Nutrition-based immunotherapy has demonstrated to be effective and efficient in individuals who have been infected with COVID-19. Piperine is a bioactive phytochemical discovered in *Piper nigrum* with a wide range of physiological and pharmacological effects. Molecular docking was used to test twenty-six bioactive compounds found in various species for activity against SARS-CoV-2, and the results revealed that piperine, "found in black pepper, had a higher binding affinity (−7.0 kCal/mol) than adenosine monophosphate (−6.4 kCal/mol) towards the nucleocapsid's RNA-binding pocket. The stability of piperine attached to nucleocapsid protein as a possible RNA-binding site inhibitor was validated by molecular dynamics simulations of the docked complexes." As a result, piperine appears to be a promising option for suppressing RNA packing in the nucleocapsid, and therefore viral multiplication. In addition to its immunomodulatory properties, black pepper intake may aid in the direct battle of SARS-CoV-2 through potential antiviral actions, according to this study [125]. Free radicals, ROS, and lipid peroxidation are all inhibited by piperine's flavonoids and phenolic content. Black pepper's antioxidant activity was measured using SOD, CAT, glutathione peroxidase, including reduced the amount of malondialdehyde, and protein carbonyl levels in the hippocampus [124], [125], [126]. Black pepper phyto-compounds could be very useful in combating the COVID-19 pandemic era [36]. For the treatment of COVID-19 from *P. nigrum*, this study employed 26 drugs. Using the molecular docking approach, structure of black pepper, clove, and ginger, it is possible to improve inhibitory viability against COVID-19.

Conclusion

The fruit of black pepper is a very important spice in the world market. This spice is very sensitive to the climate. The fruit is not only used in cooking material but also used as a medicinal or biological agent in the world as it contains bioactive compounds. Piperine, oleoresins, and essential oil are all useful components in black pepper, and it regulates gastrointestinal function. It also has anti-inflammatory properties. Black pepper can protect the body against depression and Alzheimer's disease by providing neuroprotection. Black pepper possesses antibacterial and antiviral properties, which may aid in the treatment of COVID-19 patients. The relevance of black pepper's synergistic impact in increasing the bioavailability of minerals and medicines cannot be overstated. Overall, health-care consultants should consider black pepper from a nutraceutical standpoint. Additional efforts will be necessary to assess its correct application in various goods, and the findings of such research will add meticulousness to the worries.

Authors Contributions

This work was conducted in collaboration with all authors. Author AUK planned, structured, wrote,

revised, and rechecked the manuscript thoroughly. SN and YSP rearranged and improved the draft copy. MSAT and MD were contributed to revising and improving the manuscript thoroughly. All authors reviewed carefully and approved the final version of the manuscript.

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