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Allium sativum, a potential phytopharmacological source of natural medicine for better health

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Abstract

Allium sativum, is a perennial flowering bulb which has been consumed worldwide as a functional food and known from thousands of years for its medicinal and culinary properties. Therapeutic potential of garlic is attributed to presence of its vital phytoconstituents. In present review, a complete therapeutic profile of drug is summarized by discussing its potential benefits highlighting the bioactive constituents. Phytoconstituents of crude drugs are used as antiviral, antioxidant, anti-inflammatory, antibacterial, antifungal, immunomodulatory, cardioprotective, anticancer, hepatoprotective, anti-diabetic, anti-obesity, neuroprotective, etc. Thus, it could conclude that garlic is one of the superior natural sources of bioactive compounds and has promising applications in the development of functional foods and nutraceuticals to improve health, and to prevent chronic diseases in the human.

Keywords: *Allium sativum;* Phytochemistry; Phytoconstituents; Pharmacological Activities

1. Introduction

Since more than five thousand years, medicinal plants have been widely used as food supplements, condiments, prophylactic agents and as therapeutic agents in the treatment various diseases and disorders of human beings and animals. Without medicinal plants, we cannot imagine the existence of human life [1]. Even today in 21st century, the livelihood of tribal people are depend on daily use of plants as food or as medicine. Herbal plants wholly or parts thereof are commonly used in cooking. Along with vegetables, medicinal plants such as *Allium sativum* (garlic), *Allium cepa* (onion), *Elettaria cardamomum* (cardamonm), *Cuminum cyminum* (cumin), *Myristica fragrans* (nutmeg], *Pipper nigrum*(black pepper), *Madhuca indica* etc are also being used in the kitchen [2-7].

Almost 25 centuries ago, Hippocrates, father of medicine, said that let food be thy medicine and let medicine be thy food. Supporting this statement, Hippocrates prescribed garlic for a variety of conditions. In the light of COVID-19 situation, WHO encouraging the people across the world to use medicinal plants. Some of the medicinal plants that are commonly used are *Withania somnifera* (ashwagandha), *Capsicum annuum* (capsicum), *Hypericum perforatum* (St. John's wort), *Aloe barbadensis* (Aloe vera), *Oroxylum indicum,* etc [8-16].

Allium sativum (Fig. 1) known by its common name Garlic has been used as condiment during cooking of foods. Garlic has become common ingredient of kitchen in India and Indian subcontinental countries. cousins'. as potential health benefits and food properties of Garlic [17,18]. It is one of the earliest examples of herb effective for the treatment of various diseases and maintenance of general health. It was found in Egyptian and ancient Greek temples. Therapeutic

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applications of garlic have been recorded in ancient medical texts from Egypt, Greece, Rome, China and India. Garlic was administered to provide strength and increase work capacity for labourers in many cultures [19]. Garlic was consumed to provide strength and increase work capacity for labourers in many cultures. Perhaps, It was given as one of the earliest "performance enhancing" agents to the original Olympic athletes in Greece [20]. Avicenna, a Persian physician-philosopher wrote in his book *Canon of Medicine* that the garlic for the treatment of a wide variety of ailments including arthritis, snake and insect bites, parasites, chronic cough, and as antibiotic for infectious diseases [21].

Figure 1 *Allium sativum* (garlic)bulb with petals

Clinically, garlic has been investigated for a variety of indications, namely, hypertension, hypercholesterolemia, diabetes and for the prevention of arteriosclerosis and cancer. Researchers have increasingly focused on black garlic, a processed garlic product with increased polyphenol and flavonoid contents, as well as better antioxidant properties, compared to the fresh garlic [22].

2. Potential bioactive compounds

Medicinal properties of the herb are attributed to their active chemical compounds (ACC). These compounds may be volatile or non-volatile. There are various analytical techniques by which active chemical compounds are determined. These methods can also be used for analysis of ACC in pharmaceutical formulations including ayurvedic products [23-42]. In order to justify the writing of Galen from second century "*Garlic as the rustic's theriac"* means garlic possesses potential to cure all ailments, we searched high quality studies published in renowned journals, reviewed the therapeutic functions of garlic and the bioactive components responsible for it.

Bioactive compounds of garlic include organosulfur compounds, saponins, phenolic acids, flavonoids and polysaccharides [43-46]. It contains at least thirty three sulfur compounds, several enzymes and the minerals germanium, calcium, copper, iron, potassium, magnesium, selenium and zinc; vitamins A, B1 and C, fiber and water. Seventeen amino acids are found in garlic, lysine, histidine, arginine, aspartic acid threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan and phenylalanine [47]. The major active components of garlic are organosulfur compounds which includes diallyl thiosulfate [allicin], diallyl sulfide [DAS], diallyl disulfide [DADS], diallyl trisulfide [DATS], E/Z-ajoene, S-allyl-cysteine [SAC] and S-allyl-cysteine sulfoxide [alliin] [48-52].

3. Pharmacological activities

Hundreds of successful clinical investigations have been carried out for estimation of broad-spectrum therapeutic benefits of garlic. Contemporary investigations are going on to confirm many of the beliefs of ancient cultures regarding garlic, defining mechanisms of action and exploring potential of garlic for disease prevention and treatment.

3.1. Effects on cardiovascular diseases

Garlic has history of being used for treatment of cardiovascular diseases. A scientific literature review shows garlic consumption has significant effect on lowering blood pressure, prevention of atherosclerosis, reduction of serum cholesterol and triglyceride, inhibition of platelet aggregation and increasing fibrinolytic activity [55]. Garlic lower hypertension by reducing oxidative stress, increasing the production of nitric oxide and hydrogen sulphide and inhibiting the angiotensin converting enzyme [56-61]. *In-vivo* animal experiments on wistar rats demonstrated that garlic significantly alleviated isoproterenol induced myocardial necrosis [62]. In another study, when garlic powder was

given in addition to hydrochlorothiazide plus triampterene baseline therapy showed a mean reduction of systolic blood pressure by 10-11 mmHg and diastolic blood pressure by 6-8 mmHg versus placebo [63,64].

It has been demonstrated that the intake of garlic powder can effectively reduce blood pressure, total cholesterol, low-density lipoprotein cholesterol and other risk factors related to cardiovascular diseases [65]. Preparations of garlic including garlic paste, garlic oil, allicin, and ajoene have been found to significantly reduce cholesterol biosynthesis in rat hepatocytes via inhibiting 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase and 14-a-demethylase [66,67]. In rabbits that were fed with a high-cholesterol diet and supplemented with garlic or allicin, it was found that hypercholesterolemia was significantly inhibited by 50% and showed a decrease in tissue cholesterol and low-density lipid [LDL] concentrations and raised high density lipid [HDL] concentrations along with reduced atheromatous changes [68]. It was reported that raw garlic possibly works via its active metabolite allicin action on coronary endothelial function and vaso reactivity [69].

The electrophysiological correlation to vasodilatation in human coronary arteries under the influence of garlic extract showed decrease in the isometric wall tension. Allicin and ajoene hyperpolarized the cell membrane and relaxed the vascular strips in a concentration dependent manner and suggested that garlic extract and its compounds can be classified as phytopharmacological K+ channel openers [70]. The studies have revealed that garlic might reduce platelet aggregation so that the patients who are on treatment of anticoagulant medication need to be warned about consuming garlic [71,72].

3.2. Antioxidant activity

Garlic and its active ingredients such as phenols and saponins have certain antioxidant effects. Whole garlic and aged garlic extract [AGE] exhibit direct antioxidant effects and enhance the serum levels of two antioxidant enzymes, catalase and glutathione peroxidase [73]. Garlic extract has shown efficiency in removal of hydroxyl radicals in a dose dependent fashion, but their effectiveness was reduced about 10% by heating to 100°C for 20 min. Other garlic constituents, such as S-allyl cysteine, also confirmed significant antioxidant effects. The sulfur compounds found in fresh garlic appear to be nearly 1000 times more potent as antioxidants than crude and aged garlic extract. Garlic was able to reduce the radicals present in cigarette smoke [74]. A study evaluated the antioxidant capacities of both raw and cooked garlic, and found that the raw garlic exhibited stronger antioxidant activity. Stir-fried garlic was also shown to have stronger antioxidant capacities indicating that the processing could affect the antioxidant property of garlic [75]. Different processing methods also affected the antioxidant activity of garlic. Usually, raw garlic had a stronger antioxidant activity than cooked garlic and the antioxidant activity of fermented garlic, such as black garlic, was stronger than that of crude garlic.

3.3. Antimicrobial activity

Garlic shows broad spectrum antimicrobial activities against many species of bacteria, viruses, parasites, protozoan and fungi [76]. Antimicrobial studies of essential oil obtained by steam distillation of garlic bulbs were found rich in diallyl disulphide, diallyl trisulphide and diallyl tetrasulphide and possesses potent antimicrobial activities, it inhibits the growth of Gram positive and Gram negative bacteria, such as *Staphylococcus, Streptococcus, Micrococcus, Enterobacter, Escherichia, Klebsiella, Lactobacillus, Pseudomonas, Shigella, Salmonella, Proteus,* and *Helicobacter pylori* [77]. Garlic oil also showed antibacterial activities against *Staphylococcus aureus, Staphylococcus albus, Staphylococcus saprophyticus, Shigella flexneri, Shigella sonnei, Salmonella typhi* and *Escherichia coli* [78].

In a study of garlic oil with *Penicillium funiculosum* as a model strain inhibited the fungus probably by penetrating into hyphae cells and even their organelles, destroying the cell structure and inducing the leakage of cytoplasm and macromolecules [79]. Another study of garlic oil for its antifungal activity revealed that it could penetrate the cellular membrane of *C. albicans* as well as the membranes of organelles such as the mitochondria, resulting in organelle destruction and ultimately cell death [80]. Garlic might be promising in treatment of fungal diseases from important pathogenic genera *Candida, Malassezia* and the *Dermatophytes* and have shown to inhibit growth of fungal diseases as equally as the drug ketoconazole [81]. Allitridin possesses anti-human cytomegalovirus activity [HCMV] activity and the mechanism is associated with suppression of i.e. gene transcription [82]. The above studies summarized that bioactive components present in garlic destroy the cell structure and the metabolic process of bacterial and fungal cells.

3.4. Anti-inflammatory activity

Garlic has been described as an anti-inflammatory agent of plant origin. Investigation revealed anti-inflammatory activity of garlic is equivalent to indomethacin [83]. Garlic was also recommended to be used as an adjuvant in various inflammatory disorders. A study with carrageenin induced paw-edema animal model has shown anti-inflammatory

activity of garlic is as effective as piroxicam [84]. In another study, the ethyl linoleate in garlic reduced the production of nitric oxide [NO] and prostaglandin E-2 by down regulating the expression of inducible NO synthase [iNOS] and cyclooxygenase-2 [COX2] in lipopolysaccharide stimulated RAW 264.7 macrophages [85]. Garlic supplements are effective in osteoarthritis in obese or overweight patients as it reduces the pro-inflammatory adipocytokine and resistin [86]. Many studies have shown that anti-inflammatory effects of garlic are associated with inhibition of inflammatory mediators.

3.5. Immunomodulatory effects

In wake of novel viruses like Covid-19 and Ebola, boosting immunity is receiving new attention. Garlic has been suggested as a promising candidate for maintaining the homeostasis of the immune system. Sulfur containing amino acids and polysaccharides present in garlic are the main immune-modulating components [87]. A randomized, double-blind, placebo-controlled parallel intervention revealed that aged garlic extract has potential to improve both natural killer [NK] and γδ-T cell function and can reduce the severity of cold and flu symptoms [88]. In a study, the combination of garlic oil and levamisole have shown additive up regulatory effect on immunity by stimulating T-helper 1 and T-helper 2 [89]. AGE consumption was found to reduce the occurrence and severity of the cold and flu and improve the immune system functions in humans [90].

3.6. Antineoplastic activity

Cancer or malignant neoplasm is a broad group of diseases involving unregulated cell growth. Cancer is a primary cause of death in the world and accounts for approximately 8.8 million deaths per year [91]. Many herbs, fruits and rhizomes like berries, cruciferous vegetables, tomatoes, garlic and ginger are reported to have anticancer properties [92,93,94]. Some photochemical present in garlic are capable of selective killing of cancer cells[95]. A study revealed that garlic and its sulfur compounds have potential to decrease or abolish the activation of carcinogens, thus reducing the risk of cancer [96]. Carcinogenic nitrosamines produced during cooking are reported to be inhibited by organic allyl sulfides present in garlic [97,98]. Moreover, garlic allyl sulfides have shown activity to block DNA alkylation, which is a preliminary step of nitrosamine carcinogenesis. Biactive compounds present in garlic are capable to arrest call cycle at the G0/G1 phase and G2/M phases in cancer cells, increase the expression of tumor suppressor genes, inhibit the angiogenesis process, induction of apoptosis and modulation of various other genetic pathways [99]. A case-control study on Chinese population in Taiyuan revealed raw garlic consumption is associated with reduced risk of lung cancer [100].

A study found that ethanol-based garlic extract [GE] suppressed the growth of multiple myeloma and prostate cancer cells in vitro. GE influenced hundreds of proteins involved in cellular signaling, including changes in vital cell signaling cascades regulating proliferation, apoptosis, and the cellular redox balance. The growth of mammary tumor cells was also suppressed in vivo by GE by increasing stress on the endoplasmic reticulum [101]. The intake of raw and crushed garlic upregulates apoptotic related genes and proto-oncogene which stimulates expression of genes related to immunity and cancer in the blood of human beings [102]. A study revealed that cisplatin induced renal, ultrastructural and biochemical changes such as hemorrhaging, glomerular atrophy, tubular necrosis and degeneration in adult male rats were improved by AGE therapy [103].

Thus, bioactive active components of garlic act as prophylactic to prevent and manage different malignancies. Antineoplastic mechanism of garlic includes regulation of carcinogen metabolism, inhibition of cell growth and proliferation, induction of apoptosis, suppression of angiogenesis and inhibition of invasion and migration. Garlic has shown potential to prevent or cure negative effects of antineoplastic therapies.

3.7. Hepatoprotective activity

Multiple studies have revealed that garlic has hepatoprotective effects [104,105,106]. In a study revealed reduction in lipid level by garlic oil [150 mg/kg bw/d] in ethanol and high lipid diet feeding induced significant fat accumulation in rat liver [107]. Another study have evaluated the therapeutic effects of raw garlic on alcoholic liver disease patients. In that study, 20 alcoholic patients were enrolled and received about 2.4 g raw garlic bulbs daily in the morning for 45 days. Results showed that raw garlic alleviated liver damage indicated by the decline of serum ALT, AST, ALP, gamma glutamyl transferase [GGT] and LDH activities [108]. In an in vitro study, the black garlic extract reduced the damage of tert-butyl hydroperoxide in rat clone-9 hepatocytes by inhibiting apoptosis, lipid peroxidation, oxidative stress, and inflammation [109].

In another study, garlic attenuated liver damage induced by alloxan in rats and improved the biochemical plasma factors of hepatic functions, such as urea, creatinine, aspartate transaminase, and alanine transaminase [110]. Also, it was reported that the active compounds such as DAS, DADS, and S-methyl-l-cysteine present in garlic, could prevent and

treat liver damage, such as acute and chronic ethanol-induced liver damage [111]. Compared with unfermented garlic extract, the fermented garlic extract by Lactobacillus plantarum was able to more effectively reduce liver lipid levels and improve hepatic steatosis in mice [112]. A study revealed that garlic with high dose has the potential ability to induce liver damage and low doses are safe doses of garlic [113]. The above studies revealed that garlic can effectively alleviate acute or chronic liver injury, but the side effects of excessive consumption of garlic also need to be considered. It is necessary to evaluate the safe dose and duration of garlic usage in humans.

3.8. Gastro intestinal tract effects

Garlic has been reported to have protective effects on digestive disorders. Raw garlic has reported to have anti-bacterial effects against *H. pylori* residing in the stomach and may be prescribed along with routine drugs for the treatment of gastric *H. pylori* infection [114]. Extract of black garlic effectively promoted gastrointestinal motility by increasing 5-HT_4 content effectively which stimulated the gastrointestinal peristalsis and enhanced its gastrointestinal tract emptying and promoted defecation [115]. Both the garlic and silymarin have shown the hepatoprotective effect against the isoniazid induced hepatotoxicity in rats [116].

AGE supplementation reversed the hepatic injury through its antioxidant activity in hepatotoxicity induced by ethephon in Wistar albino rat [117]. AGE was effective in preventing indomethacin-induced ulcers in rats by reducing oxidative stress and elevating prostaglandin E-2, glutathione, and NO in gastric tissue [118]. Overall, bioactive compounds present in garlic shows antibacterial effect against *H. pylori*, improve gastrointestinal functions and alleviate colitis and gastric ulcers by reducing oxidative stress and inhibiting inflammation.

3.9. Anti-diabetic activity

Garlic is called as insulin secretagogue and insulin sensitizer based on its antioxidative, anti-inflammatory and antiglycative properties which are responsible for its role in preventing diabetes progression and the development of diabetes related complications [119]. Aqueous extract of garlic exhibited promising hypoglycemic and hypolipidemic activity in alloxan-induced diabetic rats [120]. A study revealed that oral administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels, while increased serum insulin in diabetic rats but not in normal rats [121]. AGE exhibits a dose-dependent ameliorative action on indicators of diabetes in streptozotocin-induced diabetic rats [122].

Garlic decreased pancreatic β-cell damage, hepatic injury and showed more promising effect in terms of reducing oxidative stress and pathological changes when compared to resveratrol and metformin groups [123]. In a study of streptozotocin induced diabetic retinopathy in rats, administration of an extract of raw garlic by gastric gavage for seven weeks showed marked decrease in body weight, significant increase in blood glucose and glycated hemoglobin levels and improved effects on the retina [124]. A lack of scientific evidence from human studies and inconsistent data from animal studies warrant large scale clinical studies with diabetic patients to confirm the usefulness of garlic in the treatment and prevention of diabetes.

3.10. Anti-obesity activity

Garlic and its constituents have been shown to possess potent regulatory activities on lipid metabolism. Garlic oil suppressed body weight gain and white adipose tissue mass in the rat model of high-fat diet-induced obesity by increasing UCP1 expression and by enhancing fat oxidation and energy expenditure [125]. Garlic oil has shown to counteract the influence of a high-fat diet on the weight of body and adipose tissue in hyperlipidemia rats [126]. Methanolic extract of black garlic was found to reduce the weight of rats fed with a high-fat diet. This treatment regulated lipid metabolism by up-regulating the expression of AMPK, fork head box protein O1, perilipin, and adiponectin in the adipose tissue of the rats and down-regulating the cluster of differentiation 36 [CD36], plasminogen activator inhibitor 1, resistin, and TNF-α [127]. From studies it was seen that fermented garlic products have certain positive effects on obesity by inhibiting lipogenesis and regulating lipid metabolism.

3.11. Wound healing activity

Several animal studies have shown that garlic extracts increase the rate of wound healing and decrease the rate of infection. A study on rats showed that allicin acted on fibroblasts and treated the wounded site faster compared to Vaseline treated site. [128]. Another study on the chicken dorsum skin excision wound assay to investigate the influence of different concentrations of aged garlic solution [AGS] on wound healing revealed that a very highly significant increase in angiogenesis was observed among all groups treated with aged garlic solution and no significant change was observed among control and skin lotion-treated groups [129]. Overall, allicin appear to be the main wound healing components in garlic.

3.12. Neuroprotection

Investigations have revealed that garlic contains organic sulfur compounds which are effective in treatment of neurological diseases. Active component N-α-[1-deoxy-D-fructos-1-yl]-L-arginine [FruArg] from AGE alleviated neuroinflammation by inhibiting the production of NO and regulating the expression of multiple protein targets related to oxidative stress in lipopolysaccharide activated murine BV-2 microglial cells [130]. S-allyl-L-cysteine [SAC] exerts significant protective effects against endoplasmic reticulum stress-induced neurotoxicity in cultured rat hippocampal neurons and organotypic hippocampal slice cultures [131]. SAC and FruArg are prototype for developing novel therapeutic drugs for neurological diseases.

3.13. Renal Protection

Garlic was reported to possess renal protective effect [132]. A study revealed that garlic has regenerative potential after tubular injury induced by gentamicin in animal models [133]. In another gentamicin induced nephrotoxicity study in rats, administration of pulverized garlic supplemented diet showed nephron protective effect [134]. The aqueous extract of garlic was shown to reduce the oxidative stress in the kidneys of diabetic rats [135]. Another study revealed that allicin may play a role in chronic kidney disease, reducing hypertension, oxidative stress and improving renal dysfunction. Silico analysis suggested that allicin could have acted on angiotensin II receptor type 1. Allicin showed antihypertensive, antioxidant, and nephroprotective effects. The beneficial effects showed by allicin are similar, or even better, than those of losartan [136].

4. Conclusion

Therapeutic potential of garlic in treatment of diseases and preventing or reducing associated symptoms have been recognized worldwide. Microorganisms are getting resistant to allopathic antimicrobial medicines because of their vast use in treatment; however, intake of garlic is able to provide some level of anti-microbial activities and can boost the immune system. More clinical studies should be conducted to illustrate mechanisms of actions of the bioactive compounds present in garlic. In addition, the effects of the processing, such as fermentation and heat, on garlic should be further studied because they could impact the biological functions and safety of garlic. Furthermore, more clinic trials should be carried out to confirm the health benefits of garlic on humans, and special attention should be paid to the side effects and safety of garlic.

Compliance with ethical standards

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Disclosure of conflict of interest

The author declares no conflict of interest.

References

[1] Ayurvedic Formulary of India, Ministry of Health and Family Planning, Government of India. The Controller of Publications: New Delhi;2001.

[2] Badukale NA, et al. Phytochemistry, pharmacology and botanical aspects of *Madhuca indica*: A review. Journal of Pharmacognosy and Phytochemistry. 2021; 10(2): 1280-1286.

[3] Qiblawi S, Dhanarasu S, Faris MA. Chemopreventive Effect of Cardamom (Elettaria cardamomum L.) Against Benzo(α)Pyrene-Induced Forestomach Papillomagenesis in Swiss Albino Mice. J Environ PatholToxicol Oncol. 2015;34(2):95-104. doi: 10.1615/jenvironpatholtoxicoloncol.2015010838.

[4] Johri RK. *Cuminum cyminum* and Carum carvi: An update. Pharmacogn Rev. 2011;5(9):63-72. doi:10.4103/0973-7847.79101.

[5] Tajuddin, Ahmad S, Latif A, Qasmi IA. Aphrodisiac activity of 50% ethanolic extracts of Myristica fragrans Houtt. (nutmeg) and Syzygiumaromaticum (L) Merr. & Perry. (clove) in male mice: a comparative study. BMC Complement Altern Med. 2003;3:6. Published 2003 Oct 20. doi:10.1186/1472-6882-3-6.

[6] Takooree H, Aumeeruddy MZ, Rengasamy KRR, Venugopala KN, Jeewon R, Zengin G, Mahomoodally MF. A systematic review on black pepper *(Piper nigrum* L.): from folk uses to pharmacological applications. Crit Rev Food Sci Nutr. 2019;59(sup1):S210-S243. doi: 10.1080/10408398.2019.1565489. PMID: 30740986.

[7] Prasan R. Bhandari. Garlic (*Allium sativum* L.): A review of potential therapeutic applications. International Journal of Green Pharmacy.2012;118-129.

[8] Manwar JV, Mahadik KR, Sathiyanarayanan L, Paradkar AR, Patil SV. Comparative antioxidant potential of *Withania somnifera* based herbal formulation prepared by traditional and non-traditional fermentation processes. Integr Med Res. 2013; 2:56-61. http://dx.doi.org/10.1016/j.imr.2013.04.002

[9] Khadatkar SN, Manwar JV, Sahare AY. Preparations and evaluation of Microcapsules of Capsaicin. International Journal of Chemical Sciences. 2007; 5(5):2333-2341.

[10] Sahare AY, Padgilwar SS, Chaudhari Y, Manwar JV. *Hypericum perforatum:* A Medicinal plant. Plant Archives. 2007; 7(2):463-468.

[11] Manmode R, Manwar J, Vohra M, Padgilwar S, Bhajipale N. Effect of preparation method on antioxidant activity of ayurvedic formulation kumaryasava. J HomeopAyurv Med. 2012; 1:114. doi:10.4172/2167-1206.1000114.

[12] Padgilwar S, Manwar J, Vohra M, Banginwar Y. Traditional Uses, Phytochemistry and Pharmacology of *Oroxylum Indicum*: A Review. International Journal of Pharmaceutical and Phytopharmacological Research. 2014; 3 (6):483-486.

[13] Manwar J, Mahadik K, Paradkar A, Sathiyanarayanan L, Vohra M, Patil S. Isolation, biochemical and genetic characterizations of alcohol-producing yeasts from the flowers of *Woodfordia fruticosa*. J Young Pharm. 2013;5(4):191-194.

[14] Khadatkar SN, Manwar JV, Bhajipale NS. In-vitro anthelmintic activity of root of *Clitoria ternatea*linn. 2008; 4(13):148-150.

[15] Sahare AY, et al. Antimicrobial activity of *Pseudarthria viscida* roots. Asian Journal of Microbiology Biotechnology & Environmental Sciences. 2008; 10(1):135-136.

[16] Wadekar AB, et al. Morphology, phytochemistry and pharmacological aspects of *Carica papaya*, an review. GSC Biological and Pharmaceutical Sciences. 2020; 14(03).

[17] Prasan R. Bhandari. Garlic (*Allium sativum* L.): A review of potential therapeutic applications. International Journal of Green Pharmacy.2012;118-129.

[18] Adaki S, Adaki R, Shah K, Karagir A. Garlic: Review of literature. Indian J Cancer. 2014; 51:577-81.

[19] Rivlin RS. Historical perspective on the use of garlic. J Nutr. 2001; 131:951S-954S.

[20] Onuora C, et al. Therapeutic Effects of Garlic: A Review. Scientific Journal of Biology & Life Sciences. 2019;1(1):SJBLS.MS.ID.000502.

[21] Bayan, L, Koulivand PH, Gorji A. Garlic: A Review of Potential Therapeutic Effects. Avicenna Journal of Phytomedicine. 2014; 4(1):1-14.

[22] Kimura S, Tung YC, Pan MH, Su NW, Lai YJ, Cheng KC. Black garlic: A critical review of its production, bioactivity, and application. J Food Drug Anal. 2017; 25:62-70.

[23] Panchale WA, et al. Chromatographic analysis of famotidine, paracetamol and ibuprofen from tablet formulation. Research Journal of Pharmacy and Technology, 2019; 12:231-263.

[24] Panchale WA, et al. Concurrent analysis of ambroxol HCl and salbutamol sulphate from tablet formulation by RP-HPLC. GSC Biological and Pharmaceutical Sciences. 2020; 13(03):197-202.

[25] Sabhadinde AF, et al. Novel RP-HPLC method for simultaneous analysis of chlorthalidone and telmisartan from combined dosage form. International Journal of Pharmacy and Pharmaceutical Research. 2020; 20(1):491-502.

[26] Panchale WA, et al. RP-HPLC method for simultaneous determination of escitalopram oxalate and flupentixol HCl in tablet dosage form. GSC Biological and Pharmaceutical Sciences. 2021; 14(01):169-174. https://doi.org/10.30574/gscbps.2021.14.1.0004.

[27] Nimbokar SW, et al. Development and validation of RP-HPLC method for determination of zonisamide from tablet formulation. World Journal of Pharmaceutical and Medical Research. 2021;7(2):196-200

[28] Manwar JV, et al. Development of newer RP-HPLC method for simultaneous estimation of cefixime and linezolide in bulk drugs and combined dosage form. International Journal of Pharmacy and Life Sciences. 2021;12(1):26-31.

[29] Panchale WA, Gulhane CA, Manwar JV, Bakal RL. Simultaneous estimation of salbutamol sulphate and ambroxol HCl from their combined dosage form by UV-Vis spectroscopy using simultaneous equation method. GSC Biological and Pharmaceutical Sciences. 2020;13(03):127-134.

[30] Pophalkar PB, et al. Development and evaluation of ondansetron medicated jelly. World Journal of Pharmaceutical Research. 2018; 7(19):1252-1263.

[31] Panchale WA, Bakal RL. First-order derivative spectrophotometric estimation of gemifloxacin mesylate and ambroxol HCl in tablet dosage form. GSC Biological and Pharmaceutical Sciences.2021; 14 (2):029-036.

[32] Bakal RL, et al. Spectrophotometric estimation of amitriptyline HCL and chlordiazepoxide in tablet dosage form. International Journal of Chemical Sciences. 2007; 5(1):360–364.

[33] Manwar JV, et al. Application of simultaneous equation method for the determination of azithromycin and cefixime trihydrate in tablet formulation, Research Journal of Pharmacy and Technology. 2017;10(1):108-112.

[34] Manwar JV, et al. Response surface based optimization of system variables for liquid chromatographic analysis of candesartan cilexetil. Journal of Taibah University for Science. 2017; 11:159–172.

[35] Gulhane CA, et al. Liquid chromatographic method for simultaneous estimation of thiocolchicoside and etoricoxib from tablet formulation. Asian Journal of Pharmaceutical Analysis. 2021;11(3).

[36] Manwar J, Mahadik K, Paradkar A, Patil S, Sathiyanarayanan L, Manmode R. Gas chromatography method for the determination of non-ethanol volatile compounds in herbal formulation. International Journal of Analytical and Bioanalytical Chemistry. 2013; 3(1):12-17.

[37] Wadekar AB, et al. Formulation and evaluation of extended release tablet of metoprolol succinate. World Journal of Pharmacy and Pharmaceutical Sciences.2016; 5(6):1302-1316.

[38] Wadekar AB, et al. An overeview on exosome: Natural drug delivery vehicle. World Journal Of Pharmacy and Pharmaceutical Sciences. 2013; 2(1):75-88.

[39] Kadam CY, et al. Design and in vitro characterization of phase transition system using rivastigmine tartrate for nasal drug delivery system. World Journal of Pharmaceutical Research. 2018; 8(1):815-829.

[40] Suroshe RS, et al. Development and Characterization of Osmotic Drug Delivery System of Model Drug. World Journal of Pharmaceutical Research. 2018; 7(18):1158-1171.

[41] Patil SS, Kumbhar DD, Manwar JV, Jadhao RG, Bakal RL, Wakode S. Ultrasound-Assisted Facile Synthesis of Nanostructured Hybrid Vesicle for the Nasal Delivery of Indomethacin: Response Surface Optimization, Microstructure, and Stability. AAPS PharmSciTech. 2019 Jan 29;20(3):97. doi: 10.1208/s12249-018-1247-1.

[42] Nimbalwar MG, Upadhye K, Dixit G. Fabrication and evaluation of ritonavir proniosomal transdermal gel as a vesicular drug delivery system. Pharmacophore. 2016; 7(2):82-95.

[43] Diretto G, Rubio-Moraga A, Argandona J, Castillo P, Gomez-Gomez L, Ahrazem O. Tissue-specific accumulation of sulfur compounds and saponins in different parts of garlic cloves from purple and white ecotypes. Molecules 2017; 22:1359.

[44] Szychowski KA, Rybczynska-TkaczykK, Gawel-Beben K, Swieca M, Karas M, Jakubczyk A, Matysiak M, Binduga, UE, Gminski J. Characterization of active compounds of different garlic (*Allium sativum* L.) cultivars. Pol. J. Food Nutr. Sci. 2018; 68:73-81.

[45] Bradley JM, Organ CL, Lefer DJ. Garlic-derived organic polysulfides and myocardial protection. J. Nutr. 2016; 146:403S-409S.

[46] Wang YC, Guan M, Zhao X, Li XL. Effects of garlic polysaccharide on alcoholic liver fibrosis and intestinal microflora in mice. Pharm. Biol. 2018; 56: 325-332.

[47] Hahn G, Koch HP, Lawson LD. Garlic: the science and therapeutic application of *Allium sativum* L and related species 1996. 2nd ed. Lippincott Williams and Wilkins.

[48] Josling PA. The heart of garlic Nature's aid to healing the human by chronic inhibition of nitric oxide synthesis. Life Sci. 2005; 62:71-77.

[49] Yoo DY, Kim W, Nam SM, Yoo M, Lee S, Yoon YS, Won MH, Hwang IK, Choi JH. Neuroprotective effects of Z-ajoene, an organosulfur compound derived from oil-macerated garlic, in the gerbil hippocampal CA1 region after transient forebrain ischemia. Food Chem Toxicol. 2014; 72:1-7.

[50] Kodera Y, Ushijima M, Amano H, Suzuki J, Matsutomo T. Chemical and biological properties of S-1-propenyl-l-cysteine in aged garlic extract. Molecules. 2017; 22:570.

[51] Yoo M, Lee S, Kim S, Hwang JB, Choe J, Shin D. Composition of organosulfur compounds from cool and warm-type garlic (*Allium sativum* L.) in Korea. Food Sci Biotechnol. 2014; 23:337-344.

[52] Mansingh DP, Dalpati N, Sali VK, Rachel Vasanthi A H. Alliin the precursor of allicin in garlic extract mitigates proliferation of gastric adenocarcinoma cells by modulating apoptosis. Phcog Mag. 2018;14, Suppl S1:84-91

[53] Lanzotti V. The analysis of onion and garlic. J Chromatogr A. 2006; 1112(1-2):3-22. https://doi.org/10.1016/j.chroma.2005.12.016.

[54] Finley JW. Reduction of cancer risk by consumption of selenium-enriched plants: enrichment of broccoli with selenium increases the anticarcinogenic properties of broccoli. J Med Food. 2003; 6:19-26.

[55] Chan JY, Yuen AC, Chan RY, Chan SW. A review of the cardiovascular benefits and antioxidant properties of allicin. Phytother Res. 2013; 27:637-646.

[56] Cruz C, et al. Renoprotective and antihypertensive effects of S-allylcysteine in 5/6 nephrectomized rats. Am. J. Physiol. Renal Physiol. 2007; 293:F1691-F1698.

[57] Fasolino I, et al. Orally administered allyl sulfides from garlic ameliorate murine colitis. Mol. Nutr. Food Res. 2015; 59:434-442.

[58] Takashima M, Kanamori Y, Kodera Y, Morihara N, Tamura K. Aged garlic extract exerts endothelium-dependent vasorelaxant effect on rat aorta by increasing nitric oxide production. Phytomedicine. 2017; 24:56-61.

[59] Asdaq SM, Inamdar MN. Potential of garlic and its active constituent, S-allyl cysteine, as antihypertensive and cardioprotective in presence of captopril. Phytomedicine. 2010; 17:1016-1026.

[60] Sausbier M, Schubert R, Voigt V, Hirneiss C, Pfeifer A, Korth M, Kleppisch T, Ruth P, Hofmann F. Mechanisms of NO/cGMP-dependent vasorelaxation. Circ Res. 2000 Oct 27;87(9):825-30. doi: 10.1161/01.res.87.9.825.

[61] Li X, Kim HY, Cui HZ, Cho KW, Kang DG, Lee HS. Water extract of *Zanthoxylum piperitum* induces vascular relaxation via endothelium-dependent NO-cGMP signaling. J Ethnopharmacol. 2010 May 27;129(2):197-202. doi: 10.1016/j.jep.2010.03.003.

[62] Mukthamba P, Srinivasan K. Dietary fenugreek (*Trigonella foenum-graecum*) seeds and garlic (*Alliumsativum*) alleviates oxidative stress in experimental myocardial infarction. Food Science and Human Wellness. 2017; 6:77-87.

[63] Kandaziora J. Blood pressure and lipid lowering effect of garlic preparations in combination with a diuretic.ArtzlicheForschung. 1988;35:1-8.

[64] Stabler SN, Tejani AM, Huynh F, Fowkes C. Garlic for the prevention of cardiovascular morbidity and mortality in hypertensive patients. Cochrane Database Syst Rev. 2012 Aug 15;(8):CD007653. doi: 10.1002/14651858.CD007653.pub2.

[65] Kwak JS, Kim JY, Paek JE, Lee YJ, Kim HR, Park DS, Kwon O. Garlic powder intake and cardiovascular risk factors: a meta-analysis of randomized controlled clinical trials. Nutr Res Pract. 2014;8(6):644-54. doi: 10.4162/nrp.2014.8.6.644.

[66] Gebhardt R, Beck H. Differential inhibitory effects of garlic-derived organosulfur compounds on cholesterol biosynthesis in primary rat hepatocyte cultures. Lipids. 1996; 31(12):1269-1276.

[67] Yeh YY, Yeh SM. Garlic reduces plasma lipids by inhibiting hepatic cholesterol and triacylglycerol synthesis. Lipids. 1994; 29(3):189-193.

[68] Kwon MJ, Song YS, Choi MS, Park SJ, Jeong KS, Song YO. Cholesteryl ester transfer protein activity and atherogenic parameters in rabbits supplemented with cholesterol and garlic powder. Life Sci. 2003; 72(26):2953-2964.

[69] Sun X, Ku DD. Allicin in garlic protects against coronary endothelial dysfunction and right heart hypertrophy in pulmonary hypertensive rats. Am J Physiol Heart Circ Physiol. 2006; 291(5):H2431-H2438.

[70] Siegel G, Nuck R, Schnalke F, Michel F. Molecular evidence for phytopharmacological K+ channel opening by garlic in human vascular smooth muscle cell membranes. Phytother Res. 1998; 12(l1):S149-S151.

[71] Rahman K. Effects of garlic on platelet biochemistry and physiology. Mol Nutr Food Res. 2007; 51(11):1335-1344.

[72] Borrelli F Capasso, A Raffaele, Angelo A. Antioxidant action and therapeutic efficacy of *Allium sativum* L. Molecules. 2013; 18(1):690-700.

[73] Prasad G, Sharma VD, Kumar A. Efficacy of garlic (*Allium sativum* L.) therapy against experimental dermatophytosis in rabbits. Indian J Med Res. 1995; 75:465-467.

[74] Torok B, Belagyi J, Rietz B, Jacob R. Effectiveness of garlic on the radical activity in radical generating systems. Arzneimittelforschung. 1994; 44:608-611.

[75] Locatelli DA, Nazareno MA, Fusari CM, Camargo AB. Cooked garlic and antioxidant activity: Correlation with organosulfur compound composition. Food Chem. 2017; 220:219-224.

[76] Jaber MA, Al Mossawi A. Susceptibility of some multiple resistant bacteria to garlic extracts. African Journal of Biotechnology. 2007; 6(6):771- 776.

[77] Tsao SM, Yin MC. In vitro antimicrobial activity of four diallyl sulphides occurring naturally in garlic and Chinese leek oil. J Med Microbiol. 2001; 50(7):646-649.

[78] Guo YJ. Experimental study on the optimization of extraction process of garlic oil and its antibacterial effects. Afr. J. Tradit. Complement. Altern Med. 2014; 11:411-414.

[79] Li WR, Shi QS, Liang Q, Huang XM, Chen YB. Antifungal effect and mechanism of garlic oil on penicillium funiculosum. Appl Microbiol Biot. 2014; 98:8337-8346.

[80] Li WR, Shi QS, Dai HQ, Liang Q, Xie XB, Huang XM, Zhao GZ, Zhang LX. Antifungal activity, kinetics and molecular mechanism of action of garlic oil against Candida albicans. Sci Rep. 2016; 6:22805.

[81] Shams Ghahfarokhi M, Shokoohamiri MR, Amirrajab N, Moghadasi B, Ghajari A. In vitro antifungal activities of Allium cepa *Allium sativum* and ketoconazole against some pathogenic yeasts and dermatophyte. Fitoterapia. 2006; 77(4):321-323.

[82] Zhen H, Fang F, Ye DY, Shu SN, Zhou YF, Dong YS, Nie XC, Li G. Experimental study on the action of allitridin against human cytomegalovirus in vitro: inhibitory effects on immediate early genes. Antiviral Res. 2006; 72:68-74.

[83] OlimovNemat, AbrorMuhitdinov, Sobir Aminov, Xabibullo Aliyev, Anti-Inflammatory Activity of Garlic Oil Extract, Medical and Health Science Journal. 2013; 14(2):84-86.

[84] Jayanthi MK, Murali Dhar, Anti-inflammatory effects of *Allium sativum* (Garlic) in experimental rats. Biomedicine. 2011; 31(1):84-89.

[85] Park SY, Seetharaman R, Ko MJ, Kim DY, Kim TH, Yoon MK, Kwak JH, Lee SJ, Bae YS, Choi YW. Ethyl linoleate from garlic attenuates lipopolysaccharide-induced pro-inflammatory cytokine production by inducing heme oxygenase-1 in RAW 264.7 cells. Int Immunopharmacol. 2014; 19:253-261.

[86] Dehghani S, Alipoor E, Salimzadeh A, Yaseri M, Hosseini M, Feinle-Bisset C, Hosseinzadeh-Attar MJ. The effect of a garlic supplement on the pro-inflammatory adipocytokines, resistin and tumor necrosis factor and on pain severity, in overweight or obese women with knee osteoarthritis. Phytomedicine. 2018; 48:70-75.

[87] Li M, Yan YX, Yu QT, Deng Y, Wu DT, Wang Y, Ge YZ, Li SP, Zhao J. Comparison of immunomodulatory effects of fresh garlic and black garlic polysaccharides on RAW 264.7 macrophages. J Food Sci. 2017; 82:765–771.

[88] Nantz MP, Rowe CA, Muller CE, Creasy RA, Stanilka JM. Supplementation with aged garlic extract improves both NK and γδ-T cell function and reduces the severity of cold and flu symptoms: a randomized double-blind placebo-controlled nutrition intervention. Clin Nutr. 2012; 31(3):337-344.

[89] Mohamed EH, Baiomy AAA, Ibrahim ZS, Soliman MM. Modulatory effects of levamisole and garlic oil on the immune response of wistar rats: Biochemical, immunohistochemical, molecular and immunological study. Mol Med Rep. 2016; 14:2755-2763.

[90] Percival SS. Aged garlic extract modifies human immunity. J Nutr. 2016; 146:433S-436S.

[91] GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388(10053):1459-1544.

[92] Bom J, Gunutzmann P, Hurtado ECP, MaragnoCorrea, JMR, Kleeb SR, Lallo MA. Long-term treatment with aqueous garlic and/or tomato suspensions decreases Ehrlich ascites tumors. Evid. Based Complement. Altern. Med. 2014;381649.

[93] Smith MT, Guyton KZ, Gibbons CF, Fritz JM, Portier CJ, Rusyn I, DeMarini DM, Caldwell JC, Kavlock RJ, Lambert PF. Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. Environ. Health Perspect. 2016; 124:713-721.

[94] Nicastro HL, Ross SA, Milner JA. Garlic and onions: Their cancer prevention properties. Cancer Prev. Res. 2015; 8:181-189.

[95] Zhang Y, Liu X, Ruan J, Zhuang X, Zhang X,Li Z. Phytochemicals of garlic: Promising candidates for cancer therapy. Biomed Pharmacother. 2020; 123:109730.

[96] Nicastro HL, Ross SA, Milner JA. Garlic and onions: Their cancer prevention properties. Cancer Prev. Res. 2015; 8:181-189.

[97] Jakszyn P, Agudo A, Ibanez R, Garcia-Closas R, Pera G, Amiano P, Gonzalez CA. Development of a food database of nitrosamines, heterocyclic amines, and polycyclic aromatic hydrocarbons. J. Nutr. 2004; 134:2011-2014.

[98] Milner JA. Mechanisms by which garlic and allyl sulfur compounds suppress carcinogen bioactivation- Garlic and carcinogenesis. Adv. Exp. Med. Biol. 2001; 492:69-81.

[99] Almatroodi SA, Alsahli MA, Almatroudi A, Rahmani AH. Garlic and its Active Compounds: A Potential Candidate in The Prevention of Cancer by Modulating Various Cell Signalling Pathways. Anticancer Agents Med Chem. 2019; 19(11):1314-1324.

[100] Myneni AA, Chang SC, Niu R, Liu L, Swanson MK, Li J, Su J, Giovino GA, Yu S, Zhang ZF, Mu L. Raw Garlic Consumption and Lung Cancer in a Chinese Population. Cancer Epidemiol Biomarkers Prev. 2016;25(4):624-633.

[101] Petrovic V, Nepal A, Olaisen C, Bachke S, Hira J, Sogaard CK, Rost LM, Misund K, Andreassen T, Melo TM. Anti-cancer potential of homemade fresh garlic extract is related to increased endoplasmic reticulum stress. Nutrients. 2018; 10:450.

[102] Charron CS, Dawson HD, Albaugh GP, Solverson PM, Vinyard BT, Solano Aguilar GI, Molokin A, Novotny JA. A single meal containing raw, crushed garlic influences expression of immunity and cancer related genes in whole blood of humans. J. Nutr. 2015; 145:2448-2455.

[103] Nasr AY, Saleh HAM. Aged garlic extract protects against oxidative stress and renal changes in cisplatin treated adult male rats. Cancer Cell Int. 2014; 14:92.

[104] Qamar A, Siddiqui A, Kumar H. Fresh garlic amelioration of high fat diet induced fatty liver in albino rats. J. Pak. Med. Assoc. 2015; 65:1102-1107.

[105] Meng X, Li Y, Li S, Gan RY, Li HB. Natural products for prevention and treatment of chemicalinduced liver injuries. Compr. Rev. Food Sci. Food Saf. 2018: 17:472-495.

[106] Meng X, Li S, Li Y, Gan RY, Li HB. Gut microbiota's relationship with liver disease and role in hepatoprotection by dietary natural products and probiotics. Nutrients. 2018; 10:1457.

[107] Shoetan A, Augusti KT, Joseph PK. Hypolipidemic effects of garlic oil in rats fed ethanol and a high lipid diet. Experientia. 1984; 40:261-263.

[108] Mirunalini S, Arulmozhi V, Arulmozhi T. Curative effect of garlic on alcoholic liver diseased patients. Jordan Journal of Biological Sciences. 2010; 3:147-152.

[109] Lee KC, Teng CC, Shen CH, Huang WS, Lu CC, Kuo HC, Tung SY. Protective effect of black garlic extracts on tert-Butyl hydroperoxide-induced injury in hepatocytes via a c-Jun N-terminal kinase dependent mechanism. Exp Ther Med. 2018; 15:2468-2474.

[110] ApriokuJS, Amah Tariah FS. Garlic (*Allium sativum* L.) protects hepatic and renal toxicity of alloxan in rats. Br. J. Pharm. Res. 2017; 17:34909.

[111] Guan MJ, Zhao N, Xie KQ, Zeng T. Hepatoprotective effects of garlic against ethanol induced liver injury: A mini review. Food Chem. Toxicol. 2018; 111:467-473.

[112] Lee HS, Lee SJ, Yu HJ, Lee JH, Cho HY. Fermentation with Lactobacillus enhances the preventive effect of garlic extract on high fat diet-induced hepatic steatosis in mice. J Funct Foods. 2017; 30:125-133.

[113] Rana SV, Pal R, Vaiphei K, Singh K. Garlic hepatotoxicity: safe dose of garlic. Trop Gastroenterol. 2006; 27(1):26-30.

[114] Hoshino T, Kashimoto N, Kasuga S. Effects of Garlic Preparations on the Gastrointestinal Mucosa. The Journal of Nutrition. 2001; 131(3):1109S-1113S.

[115] Chen YA, Tsai JC, Cheng KC, Liu KF, Chang CK, Hsieh CW. Extracts of black garlic exhibits gastrointestinal motility effect. Food Res. Int. 2018; 107:102-109.

[116] Nasim I, Sadiq M, Jehangir A. Hepatoprotective effect of garlic (*Allium sativum*) and milk thistle (silymarin) in isoniazid induced hepatotoxicity in rats, Biomedica. 2011; 27:166-170

[117] Al Brakati A. Protective effect of aged garlic extracts against hepatotoxicity induced by ethephon in Wistar albino rat. Environ Sci Pollut Res Int. 2020; 27(6):6139-6147.

[118] El Ashmawy NE, Khedr EG, El Bahrawy HA, Selim HM. Gastroprotective effect of garlic in indomethacin induced gastric ulcer in rats. Nutrition. 2016; 32:849-854.

[119] Liu CT, Sheen LY, Lii CK. Does garlic have a role as an antidiabetic agent? Mol Nutr Food Res. 2007; 51(11):1353-64.

[120] Ozougwu JC, Eyo JE, Studies on the anti diabetic activity of *Allium sativum* (garlic) aqueous extracts on alloxan-induced diabetic albino rat. Pharmacologyonline. 2010; 2:1079-1088.

[121] Thomson M, Al Qattan KK, JS D. Anti-diabetic and antioxidant potential of aged garlic extract (AGE) in streptozotocin induced diabetic rats. BMC Complement Altern Med. 2015; 16:17.

[122] Eidia A, Eidib M, Esmaeilia E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin induced diabetic rats. Phytomedicine. 2006; 13:624-629.

[123] Kaur G, Padiya R, Adela R, Putcha UK, Reddy GS, Reddy BR, Kumar KP, Chakravarty S, Banerjee, SK. Garlic and resveratrol attenuate diabetic complications, loss of beta-cells, pancreatic and hepatic oxidative stress in streptozotocin-induced diabetic rats. Front Pharmacol. 2016; 7:360.

[124] Al brakati AY. Protective effect of garlic against diabetic retinopathy in adult albino rats. Res J Pharm Biol Chem Sci. 2016; 7:2748-2759.

[125] Kagawa Y, Ozaki Masuzawa Y, Hosono T, Seki T. Garlic oil suppresses high-fat diet induced obesity in rats through the upregulation of UCP-1 and the enhancement of energy expenditure. Exp Ther Med. 2020; 19(2):1536-1540.

[126] Yang C, Li L, Yang L, Lu H, Wang S, Sun G. Anti-obesity and Hypolipidemic effects of garlic oil and onion oil in rats fed a high-fat diet. NutrMetab (Lond). 2018; 15:43.

[127] Chen YC, Kao TH, Tseng CY, Chang WT, Hsu CL. Methanolic extract of black garlic ameliorates diet induced obesity via regulating adipogenesis, adipokine biosynthesis, and lipolysis. J Funct Foods. 2014; 9:98-108.

[128] Alhashim, Minhal, Lombardo, Jamie MD. Mechanism of Action of Topical Garlic on Wound Healing, Dermatologic Surgery. 2018; 44(5):630-634.

[129] Sohail Ejaz, Irina Chekarova, Jae Woo Cho, Seung Yeon Lee, Shoaib Ashraf, Chae Woong Lim. Effect of aged garlic extract on wound healing: A new frontier in wound management. Drug and Chemical Toxicology. 2009; 32(3):191-203.

[130] Zhou H, Qu Z, Mossine VV, Nknolise DL, Li J, Chen Z, Cheng J, Greenlief CM, Mawhinney TP, Brown PN, Fritsche KL, Hannink M, Lubahn DB, Sun GY, Gu Z. Proteomic analysis of the effects of aged garlic extract and its FruArg component on lipopolysaccharide induced neuroinflammatory response in microglial cells. PLoS One. 2014; 9(11):e113531.

[131] Kosuge Y. Neuroprotective mechanisms of S-allyl-L-cysteine in neurological disease. Exp Ther Med. 2020; 19(2):1565-1569.

[132] Seckiner I, Bayrak O, Can M, Mungan AG, Mungan NA. Garlic supplemented diet attenuates gentamicin nephrotoxicity in rats. Int. Braz. J. Urol. 2014; 40:562-567.

[133] Nasri H, Nematbakhsh M, Rafieian-Kopaei M. Ethanolic extract of garlic for attenuation of gentamicin-induced nephrotoxicity in Wistar rats. Iran J Kidney Dis. 2013; 7(5):376-82.

[134] Seckiner I, Bayrak O, Can M, Mungan AG, Mungan NA. Garlic supplemented diet attenuates gentamicin nephrotoxicity ın rats. Int Braz J Urol. 2014; 40(4):562-7.

[135] Nasiri A, Ziamajidi N, Abbasalipourkabir R, Goodarzi MT, Saidijam M, Behrouj H, Asl SS. Beneficial effect of aqueous garlic extract on inflammation and oxidative stress status in the kidneys of type 1 diabetic rats. Indian J. Clin. Biochem. 2017; 32:329-336.

[136] Garcia Trejo EMA, Arellano Buendia AS, Sanchez Reyes O, Garcia Arroyo FE, Arguello Garcia R, Loredo Mendoza ML, Tapia E, Sanchez Lozada LG, Osorio Alonso H. The Beneficial Effects of Allicin in Chronic Kidney Disease Are Comparable to Losartan. Int J Mol Sci. 2017; 18(9):1980.