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REVIEW ON USES OF GARLIC EXTRACT

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ABSTRACT

Garlic belongs to family Liliacae. The main objective of the review is to introduce some pharmaceutical uses of garlic. Garlic (Allium sativum) is used through-out the world It used as flavouring agent and medicinal agent. The extract of garlic used to treat many diseases which include Alzhiemer disease, Cardiovascular diseases, Cancer. It also used in treatment of diabetes mellitus. The extract of garlic have beneficial role in Hypertension, Thrombosis. The review includes the detail information about garlic and its use in different diseases.

KEYWORDS: Garlic, Cardiovascular diseases, Cancer, Hypertension, Thrombosis, Alzhiemer disease.

INTRODUCTION

Garlic has a long tradition as a food and as a medicinal plant. Therapeutic effects, routes of application and modes of preparation of garlic are very varied. In order to be able to assess which mode of preparation is suitable for which application, it is necessary to explain certain substance characteristics of garlic. The garlic bulb contains cysteine sulphoxides belonging to the secondary plant components. During the processing these compounds undergo a rapid enzymatic respectively non-enzymatic conversion. Depending on the mode of preparation, different substances with different effects can be found in the resulting products. Most of the data available on the chemopreventive and curative effects of garlic is based on the use of the freshly prepared garlic. Epidemiological studies prove that the risk for different malignant diseases, especially of the gastro-intestinal tract is significantly reduced by regular consumption of large amount of garlic. In numerous investigations it was possible to

demonstrate different pharmacological properties, for some cysteine sulphoxides, like antimicrobial, anticancer, and antioxidant activity. The antioxidant potential of garlic is of great interest in connection with the antiatherosclerotic and cardioprotective effects observed epidemiologically and clinically.

BOTANY

Garlic belongs to the Allium, which comprises of approximately 600 known species distributed over the whole northern hemisphere. Characteristic for Allium species are herbaceous, perennial bulbous plants having typical leek odour. The bulb of garlic, Allium sativum L., is of a compound nature, consisting of numerous bulbets, so-called cloves, of different size, the whole surrounded by layers of white scale leaves. The ovoid cloves are 3-4 sided with an acute summit, narrowed into a thread like portion of fibre, and the base truncate. Each clove is separately enclosed in a white scale and covered with pinkish-white skin. From the central clove, the plant shoots a quill-like, round, hollow, and unbranched stall, which is encased at the bottom by long, narrow and flat, grass-like leaves. The whitish flowers are placed at the end of a stalk rising direct from the bulb, and grouped together in a globular head. The flowers develop numerous egg-shaped bulbills, which have an important function in the propagation of the plant.[1, 2]

PHARMACEUTICAL USES OF GARLIC

TREAT CARDIOVASCULAR DISEASE

Disorders of the heart and the circulatory system claim more lives than any other diseases. It is the obstruction or clogging of the coronary arteries which causes more deaths than any other factors. The arteries, which supply the heart with blood and oxygen, become increasingly narrower as plaque builds up over time. When blood supply becomes restricted, a certain portion of the heart is deprived of oxygen and leads to heart attack. The two greatest means of heart disease are high blood pressure and high blood serum cholesterol levels; which are directly impacted by the therapeutic action of garlic. The relevant role of garlic in coronary heart disease was done on rabbits and found that even pre-existing athero-sclerotic deposits and lesions could actually be reversed if garlic was consistently consumed.[3] From a study conducted in India, 432 coronary artery patients were randomly grouped into two groups and half of them were supplied with garlic juice in milk, whereas the other group patients were not supplied with garlic juice. The result showed that within the three years of the study time, nearly twice as many patients had died in the group not supplied with garlic

juice.[4] It is well reported to scavenge oxidants, increase superoxide dismutase, catalase, glutathione peroxidase, glutathione levels, inhibit lipid peroxidation as well as it reduces cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl-CoA. It has been shown to reduce platelet aggregation, arterial plaque formation, decrease homocysteine, lower blood pressure, and increase microcirculation. It may also help prevent cognitive decline by protecting neurons from neurotoxicity and apoptosis, thereby preventing ischaemia or reperfusion-related neuronal death and by improving learning and memory retention.[5]

ALZHEIMER'S DISEASE

Known for its neuroprotective abilities in vitro[6], aged garlic has been looked to for multiple benefits that some researchers believe may address a number of underlying mechanisms which contribute to the classic Alzheimer beta-amyloid plaque. According to one author, garlic: "is expected to produce cumulative benefits and exhibit enhanced neuroprotection by virtue of being "natural statin", "natural NSAID", "natural anti-oxidant", "natural anti-apoptotic agent" and "memory enhancer", a combination of many single-ingredient synthetic pharmaceutical drugs currently used for Alzheimer's therapy, only with least adverse effects.[7]" Unfortunately, there is a dearth of clinical studies showing of aged garlic extract in relation to Alzheimer's pathology, except for reports showing improved behavior in senescence accelerated mice after garlic treatment.[8] Given the multiple-mechanistic possibilities and minimal risk associated with its use, garlic seems a prudent recommendation for prevention and treatment. Since aged garlic is best studied in relation to Alzheimer's it may be the best form to employ.

ANTIATHEROSCLEROTIC

One study by Wang and Ng (1999) showed that garlic compounds possess anti-atherosclerotic activity.[9] Also numerous animal studies have reported that garlic can have protective effect against atherosclerosis.[10] Sulfur-containing volatiles from garlic are the principal compounds responsible for such property and the most abundant volatile compound is diallyl disulfide followed by diallyl trisulfide.[11] These active constituent(s) of garlic responsible for its anti atherogenic action are shown to be mostly present in the oily fraction of the plant.[12] Among these constituents, allicin is another compound that plays an important role in anti-atherosclerotic activity of garlic. It is produced upon crushing of the garlic clove. A pure allicin preparation may affect atherosclerosis not only by acting as an antioxidant, but also by other mechanisms, such as lipoprotein modification and inhibition of LDL uptake and

degradation by macrophages.[13] In a study, 112 patients (47 men and 65 women) 40 to 60 years of age were examined. 56 patients had ischemic heart disease and/or equal disorders. Another 56 patients were free of any signs of atherosclerosis, but had one or more cardiovascular pathology risk factor. Six month therapy using allicor results in moderate hypolipidemic and antioxidative effect. A dosage of 600 mg per day decreases ten-year chance of fatal cardiovascular complications in patients with clinical signs of atherosclerosis, whereas in patients who have no signs of atherosclerosis the complications are decreased with dosage of 300 mg per day.[14] Another survey indicated that garlic indirectly affects atherosclerosis by reduction of hyperlipidemia. Garlic's direct effect on atherosclerosis may be explained by its capacity to reduce lipid content in arterial cells and to prevent intracellular lipid accumulation. This effect, in turn, is accompanied by other atherosclerotic manifestations, i.e., stimulation of cell proliferation and extracellular matrix synthesis. A study demonstrated that garlic reduces the atherogenic properties of cholesterol. As sited above, suppressed LDL oxidation may be one of the powerful mechanisms accounting for the anti-atherosclerotic properties of garlic.[15]

DIABETES MELLITUS

Although experimental studies demonstrated a clear hypoglycemic effect of garlic, the effect of garlic on human blood glucose is still controversial. Many studies showed that garlic can reduce blood glucose level in diabetic animals. Garlic was effective in reduction of blood glucose in streptozotocin- as well as alloxan-induced diabetes mellitus in rats and mice.[16] Short term benefits of garlic on dyslipidemia in diabetic patients were shown.[18] Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol as compared with placebo in diabetic patients.[18] *S*-allyl cysteine, a bioactive component derived from garlic, restored erectile function in diabetic rats by preventing reactive oxygen species formation through modulation of NADPH oxidase subunit expression. Metformin and Garlic treatment in diabetic patients for 12 weeks reduced fasting blood glucose (FBG), but the percentage of change in FBG was more substantial with metformin supplemented with garlic than with metformin alone. Chronic feeding of garlic extracts showed significant decrease in blood glucose level. However, some other studies showed no change of blood glucose level after that in human. Therefore, the role of garlic in diabetic patients needs to be further investigated.[19] The beneficial effect of garlic on diabetes mellitus is mainly attributed to the presence of volatile sulfur compounds, such as alliin, allicin, diallyl disulfide, diallyl trisulfide, diallyl sulfide, S-allyl cysteine,

ajoene, and allyl mercaptan. Garlic extracts have been reported to be effective in reducing insulin resistance.[20]

HOMOCYSTEINE

Elevated plasma homocysteine concentrations have been associated with an increased risk of vascular disease as high homocysteine is known to inhibit endothelial cell proliferation[21] and contribute to atherothrombotic events. In one animal study by Yeh et al., the addition of aged garlic extract decreased plasma total homocysteine concentration by 30% (2006). However, marked lowering of homocysteine concentrations by folic acid and Bvitamin supplementation seems to play no bearing on inflammatory and immune cytokine responses and may not reduce risk of cardiovascular events.[22] Accordingly, it is premature to state that garlic's hypohomocysteinemic effect would solely help protect cardiovascular function. Possibly, the effect of B vitamins, garlic and other healthful interventions would collectively create a more Protective response.

ANTIHYPERTENSIVE

Garlic has probably been most popularized as a complementary therapy for blood pressure control.[23] Hypertension (systolic blood pressure ≥ 140 mm Hg; diastolic pressure ≥ 90 mm Hg) the most important risk factor for chronic circulatory disease and is one of the major risk factors of atherosclerosis11, affecting an estimated 1 billion individuals worldwide.[24] The mechanism of antihypertensive activity of garlic is due to its prostaglandin-like effects, which decrease peripheral vascular resistance. The gamma-glutamylcysteines are the compounds in garlic that may lower blood pressure, as indicated by their ability to inhibit angiotensin-converting enzyme in *in vitro.* Garlic modulates the production and function of both endothelium derived relaxing and constricting factors and this may contribute to its protective effect against hypoxic pulmonary vasoconstriction. Garlic elicits nitricoxide- dependent relaxation in pulmonary arteries. Garlic pearls at a dose of 250mg/d for 2 months of supplementation; there was also a significant decline in both systolic and diastolic blood pressures. It could be suggested that dietary supplementation of garlic may be beneficial in reducing blood pressure and oxidative stress in hypertensive individuals.[25] Garlic also activated the synthesis of nitric oxide, which is a potent endogenous vasodilator.

ANTITHROMBOTIC

Garlic extracts and several garlic constituents demonstrated significant antithrombotic actions both in vitro and in vivo. Allicin and adenosine are the most potent antiplatelet constituents of

garlic.[26] A study suggested that odorless garlic not only activates fibrinolytic action by accelerating (tissue-type plasminogen activator) t-PA-mediated plasminogen activation, but also suppresses the coagulation system by down regulating thrombin formation, suggesting a beneficial role in preventing pathological thrombus formation in such cardiovascular disorders.[27] A study mentioned that aqueous extract of garlic inhibits platelet aggregation induced by several aggregation agents, including arachidonate in a dose-dependent manner.

Another survey indicated that garlic extracts act through inhibition of the ADP (adenosine diphosphate) pathway. Their mechanisms of action are comparable to that of the clinically used drug clopidogrel. The pharmacologically active component of the extracts appears to be lipophilic rather than hydrophilic.[28] One study mentioned that the aromatic thiosulfonate derived from garlic is a very effective inhibitor of platelet aggregation. Diallyl trisulfide (DATS) is one of the major constituents in garlic oil and has demonstrated various pharmacological activities, such as antithrombotic.[29] DAT-rich garlic oil showed anticoagulant action due to inhibition and/or inactivation of thrombin, in an animal study. The antiplatelet activity of methyl allyltrisulfide (MATS), a component commonly present in steam-distilled garlic oil, has also been demonstrated. MATS inhibits arachidonic acid cascade at the reaction site with PGH synthase. In a study allicin and thiosulfinates were considered as responsible compounds for the (in-vitro antiaggregatory activity) IVAA response. It was also shown that the loss of activity, and the partial loss of antithrombotic effect in crushed-cooked garlic may be compensated by increasing the amount consumed.[30]

ANTICANCER EFFECT

According to Hikino H *et al* in 1986, animal studies have reported protective effects of garlic against hepatotoxins, cyclophosphamide, Adriamycin, methylcholanthrene, gentamicin, 4-nitroquinoline 1-oxide, and bromobenzene.[31] Garlic has demonstrated strong inhibition of cancer development in the presence of known tumor promoters including 12-O. More recent studies seem to relate the consumption of garlic with cancer. Sulphurous components are believed to be responsible to avoid the developing of cancerous cells in stomach, liver. The exact mode of action was not fully understood, but several modes of action have been proposed. These include its effect on drug metabolizing enzymes, antioxidant properties and tumor growth inhibition. Recently, it has been observed that aged garlic extract, but not the fresh garlic extract, exhibited radical scavenging activity. The two major compounds in aged garlic, S-allylcysteine and S-allylmercapto-L-cysteine, had the highest radical scavenging

activity. In addition, some organosulfur compounds derived from garlic, including S-allylcysteine, have been found to retard the growth of chemically induced and transplantable tumors in several animal models. Therefore, the consumption of garlic may provide some kind of protection from cancer development.[32, 33] Garlic can alter the carcinogen metabolism either increasing the detoxifying enzymatic systems activity that increases the carcinogen polarity facilitating its excretion from the body 40 or inhibiting the procarcinogen activation by cytochrome P450. Glutathione-Stransferase is a well known detoxifying enzyme in phase II metabolism. This remarkable little bulb now tops the list of potential cancer-preventative foods. It contains multiple anticancer compounds and antioxidants, more than 30 at the last count, which such powerful compounds as quercetin, diallyl sulphide, allin and ajoene. These have the ability to block cancer causing agents such as nitrosamine and Aflatoxins which have been specifically linked to stomach, lung and liver cancer. Garlic's ajoene and allicin have also been shown to retard cancer cells as a type of natural chemotherapy. Garlic reduces risk of patients with prostate cancer, especially those with localized disease. Men in the highest of three intake categories of total allium vegetables (>10.0 g/day) had a statistically significantly lower risk (odds ratio = 0.51,P<.001) of prostate cancer than those in the lowest category (<2.2 g/day).[34] Additionally, garlic also contains a high concentration of selenium, which is responsible, in part, for garlic's antioxidant and cancerpreventive effects. Hence, some growers add selenium to the soil to increase garlic's selenium content. Treatment of human melanoma cells with S-allylcysteine reduces expression of cellsurface ganglisides, the tumor associated markers of differentiation and transformation. S180 tumor cells when exposed to a garlic extract displayed delayed progression to S phase.

DERMATOLOGIC APPLICATIONS

A study examined 43 persons for their topical use of two different garlic extracts for wart and corn treatment. Of these persons, 15 volunteers utilized a water extract of garlic, while 23 volunteers applied lipid extract to appropriate areas twice a day. Five controls applied only a neutral solvent. All lipid extract volunteers experienced complete resolution of wart and 80% of corn within one to two weeks. The water extract seemed to be less potent, with complete dissolution of smaller warts and corns, and only partial dissolution of larger ones. Controls showed no improvement from baseline. The lipid extract did cause some burning, redness, blistering and skin darken-ing, which was resolved after conclusion of use.[35]

ANTI MICROBIAL EFFECTS

ANTIVIRAL

Garlic and its sulfur constituents verified antiviral activity against coxsackievirus species, herpes simplex virus types 1 and 2, influenza B, para-influenza virus type 3, vaccinia virus, vesicular stomatitis virus, human immunodeficiency virus type 1 and human rhinovirus type 2. The order of compounds found in garlic for virucidal activity was, ajoene > allicin > allyl methyl thiosulfanate > methyl allyl thiosulfanate; no activity was found for the polar fractions, alliin, deoxyalliin, diallyl disulfide, or diallyl trisulfide. Several laboratory tests have shown that garlic is an effectual treatment for both the influenza B virus and herpes simplex virus. Two independent researchers in Japan and Romania have found that garlic is able to protect living organisms from the influenza virus.[36] Most recently, a double blind placebo con-trolled study has shown significant protection from the common cold virus. As conducted by The Garlic Centre, published in Advances in Therapy, this is the first serious work to show prevention, treatment and reduction of re-infection benefits from taking Allimax Powder capsules once daily.[37]

ANTIBACTERIAL

Garlic extract 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.[38] Its antibacterial activity is mainly due to the presence of allicin produced by the enzymatic activity of allinase on alliin. Allicin is considered to be the most potent antibacterial agent in crushed garlic extracts, but it can be unstable, breaking down within 16 h at 23°C. However, the use of a water-based extract of allicin stabilizes the allicin molecule due to the hydrogen bonding of water to the reactive oxygen atom in allicin or there may be water soluble components in crushed garlic that destabilize the molecule.[39] The disadvantage of this approach is that allicin can react with water to form diallyl disulphide, which does not exhibit the same level of antibacterial activity of allicin.[39]

ANTIFUNGAL

Antifingal activity was first established in 1936 by Schmidt and Marquardt whilst working with epidermophyte cultures.Many fungi are sensitive to garlic including Candida, Torulopsis, Trichophyton, Cryptococcus, Aspergillus, Trichosporon, and Rhodotorula.[40] Garlic extracts have been shown to decrease the oxygen uptake, reduce the growth of the

organism, inhibit the synthesis of lipids, proteins, and nucleic acids, and damage membranes.[41] A sample of pure allicin was shown to be antifungal. Removal of the allicin from the reaction by solvent extraction decreased the antifungal activity. Activity has also been observed with the garlic constituents, diallyl trisulfide, against cryptococcal meningitis, ajoene, and against Aspergillus.[42] Thiol reduced the activity, suggesting the blocking of thiol oxidation by allicin. Inhibition of respiratory activity is thought to be due to inhibition of succinate dehydrogenase. . The adhesion of Candida is also greatly reduced in the presence of garlic extract.[41] Again, this effect is diminished by the addition of thiol compounds. The addition of ajoene to some fungal growth mixtures, including Aspergillus Niger, C. albicans, and Paracoccidiodes, has resulted in inhibition at concentrations lower than that experienced with allicin.

OSTEOPOROSIS

Garlic may also confer phytoestrogenic effects to counter boneloss. One fascinating animal study examined the effects of garlic extracts on the intestinal movement calcium in rats as well as to study garlic's possible role in maintaining the bone mineral content and bone tensile strength in an ovariectomized rat model of osteoporosis. The results suggest that, in this experimental model, oil extract of garlic promotes intestinal transference of calcium by modulating the activities of both intestinal alkaline phosphatase and Ca (2+) activated ATPase. Also, the observed low bone mineral content and low bone tensile strength in these rats were significantly restored by garlic oil supplementation. Furthermore, garlic oil supplementation was able to revive partially the bilateral ovariectomy-induced decrease in the serum estrogen titer. Interestingly, the serum parathyroid hormone level was found unaltered in these rats. The garlic oil supplemented partial recovery in serum estrogen titer in bilaterally ovariectomized rat was found to be persistently associated with enhanced calcium transference and better preservation of bone mineral content.[43] It may then be useful to use garlic as a treatment strategy in post-menopausal women with osteoporotic 11tendency or for pre-mature menopausal women who have sustained low estrogen levels.

ROLE OF GARLIC AGAINST MULTI-DRUG RESISTANT TUBERCULOSIS (MDR-TB)

Scientific evidence from randomized clinical trials supports the use of garlic and enhances access for MDR-TB infected people, through the public health system. Its use can allow an effective MDR-TB management, due to its affordability and the absence of toxic effects.[44]

In view of the increased incidence of MDR-TB, the research of new anti-tubercular drugs based on affordable and more effective treatments has already begun. Studies on innovative alternative plant extracts of medicinal values need to be emphasized, as plants are an important source of new antimicrobial agents, with little toxicity, able to replace drugs to which Myco-bacterium resistance has occurred.[45]

As garlic is concerned, the in vitro tests undertaken about the inhibitory effect on MDR-TB are at an advanced stage whereas few researches in vivo have been conducted. The concentration of garlic extract re-quired was in the range of 1.34 to 3.35 mg/ml suggesting that there is only a slight variation in the susceptibility of the strains to allicin. The anti-tuberculosis activity in vivo of garlic oil preparation was demonstrated in a study of guinea pigs which were given an intra-peritoneal dose of 0.5 mg/kg. However, when garlic oil was used, a reduced causative process was noted in the organs involved, indicating that garlic oil administration causes less marked lesions in the viscera of the animals inoculated with tubercle bacilli. The high potential of garlic extract was revealed to inhibit the growth of Mycobacterium tuberculosis H37Rv and M. tuberculosis TRC-C1193, susceptible and resis-tant to isoniazid (first-line anti-tuberculosis medication), respectively. The minimum inhibitory concentration (MIC) of garlic was between 80 and 160 µg/ml for the susceptible strain and 100 and 200 µg/ml for the resistant strain.

STRESS

Among its many uses, garlic appears to have the fortunate capacity for protecting against the ravages of stress that affects the autonomic nervous and neuroendocrine sytem. Rats that were trained with endurance exercises to physical fatigue enjoyed improved parameters of aerobic glucose metabolism, attenuated oxidative stress, and vasodilation, when given garlic at a dosage of 2.86 g/kg 30 minutes before exercise.[46] In rats exposed to psychologically stressful situations, aged garlic extracts significantly prevented the decreases in spleen weight seen in control animals. Additionally, the garlic significantly prevented the reduction of hemolytic plaque-forming-cells in spleen cells and anti-SRBC antibody titer in serum caused by this psychological stress. Moreover, a reduction in NK activities was observed in the psychological stressexposed mice as compared with normal mice (non-stress), whereas NK activities in the garlic administered mice were almost equivalent to the mice not exposed to stressors. Garlic was able to block the lipopolysaccaride induced immune cytokine and plasma corticosterone and catecholamine changes following cold water immersion stress.[47]

Aged garlic extract is also effective to prevent adrenal hypertrophy, hyperglycemia and elevation of corticosterone in hyperglycemic mice induced by immobilization stress. Given the extreme chronic stress many people now face during daily life, garlic may prove useful to counter the negative impact this stress has on human physiology.

ADVERSE EFFECTS OF GARLIC

The main adverse effect commonly associated with garlic intake is breath odor, especially when raw forms of the herb are used. Nausea and vomiting are other major adverse effects and care should be taken in consuming high quantities. Although an entire bulb produces little juice, it is potent and can act as a strong emetic, even in small quantities. Although garlic generally poses little in terms of safety issues, there are isolated cases of topical garlic burns. Rare garlic allergy has been attributed to the protein allinase, which has induced immunoglobulin E (IgE) mediated hypersensitivity responses from skin prick testing. As a result, the literature has generally cautioned against using garlic while using anticoagulant therapy. There is a reported case of spontaneous spinal or epidural hematoma in an 87 years old man, with associated platelet dysfunction related to excessive garlic ingestion.[48]

CONCLUSION

Garlic is consumed through-out the world. Garlic used as flavoring agent but it have medicinal uses. The review includes some pharmaceutical uses of garlic. Garlic used to treat cardiovascular disease, used as antiatherosclerotic, antimicrobial and many more. Garlic used as antidiabetic and antihypertensive. The garlic has beneficial role in cancer, it also used as anticancer agent. Today, with the ever-growing resistant organisms, taking of garlic extract remains a powerful antimicrobial agent. Clearly more studies are needed to refine the use and improvement of the efficacy of this important medicinal plant.

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