Journal of Medicinal Plants Studies
www.PlantsJournal.com

ISSN (E): 2320-3862
ISSN (P): 2394-0530
NAAS Rating: 3.53
JMPS 2018; 6(2): 44-48

Received: 13-01-2018
Accepted: 16-02-2018

Md. Khairul Alam
Department of Unani Medicine, Hamdard University Bangladesh, Hamdard City of Science, Education & Culture, Gazaria, Munshiganj, Bangladesh

Mohammad Abu Bin Nyeem
Department of Unani Medicine, Hamdard University Bangladesh, Hamdard City of Science, Education & Culture, Gazaria, Munshiganj, Bangladesh

Md. Abdus Samad
Department of Applied Nutrition and Food Technology, Islamic University, Kustia, Bangladesh

Correspondence
Md. Khairul Alam
Department of Unani Medicine, Hamdard University Bangladesh, Hamdard City of Science, Education & Culture, Gazaria, Munshiganj, Bangladesh

Effects of garlic on hyperlipidemia: A review

Md. Khairul Alam, Mohammad Abu Bin Nyeem and Md. Abdus Samad

Abstract
Garlic is an important universal dietary and medicinal plant which is being used as food and herbal medicine since ancient times. Hyperlipidemia is considered one of the major risk factors causing cardiovascular diseases (CVDs). CVDs accounts for one third of total deaths around the world, it is believed that CVDs will turn out to be the main cause of death and disability worldwide by the year 2020. The aim of the present literature review was to evaluate the effect of garlic on hyperlipidemia. The medicinal importance of garlic is attributed to its lipids lowering and antiatherogenic effects. Being important spice in human food, garlic can contribute its lipids lowering and anti-atherogenic effects. So it has been evaluated so far by several clinical trials in hyperlipidemia. Most of the studies on the effect of oral garlic on serum lipids have shown positive results within the low range of hyperlipidemia. The lipids lowering effect of garlic remains for a few months only. The conclusion of the literature review is need of further planned clinical trials to evaluate its qualitative and quantitative aspect of hypolipidemic effect in clinical practice.

Keywords: Garlic, hyperlipidemia, lipids, lipids lowering, cardiovascular diseases (CVDs)

Introduction
Hyperlipidemia refers to disorder of lipid metabolism manifested by increase of plasma concentrations of the various lipid and lipoprotein such as increase of serum total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG) concentrations, and a decrease in the high-density lipoprotein (HDL) concentration [1-2]. Hyperlipidemia is the risk factor for cardiovascular disorders and has been reported as the most common cause of death in developing nations. Hyperlipidemia may be caused by specific genetic abnormalities called primary as the most common cause of death in developed as well as developing nations [3-5]. Hyperlipidemia may be caused by specific genetic abnormalities caused by lifestyle habits or medical diseases such as diabetes, kidney disease, hypothyroidism and heart disease. One has a greater chance of developing hyperlipidemia is a man (>45 years) or a woman (>55) or having familial history of hyperlipidemia [6].
Garlic (*Allium sativum* L. fam. Alliaceae) is used as one of common components of foods and condiments [7]. Many reports in the literature have shown that *A. sativum* has variety of pharmacological activities such as antihypertensive, antihypercholesterolaemic, cardioprotective, antiplatelet, hypoglycaemic, antimicrobial, antineoplastic etc. though all the data in the different researches are not concordant with each other. Garlic contains alliin, allicin, diallyl disulphide, S-allylcysteine and diallyl trisulfi de organosulfur compounds and allicin is responsible for characteristic garlic odour [8-11]. Out of these compounds, allicin is the most studied compound responsible for the different types of pharmacological effects [8]. Alliin is the precursor of allicin which is produced by the action of alliinase enzyme. This enzyme may be deactivated by gastric juice. So, enteric coated tablets of garlic are recommended for the therapeutic uses to inhibit the gastric inactivation of enzyme so that generation of allicin from alliin is not affected [12]. Allicin is hydrophobic and crosses the biological barrier easily and undergoes metabolic pathway instantly to produce different pharmacological effects [13].

Chemical composition of garlic
The flavor and functions promoted the health are usually attributed to sulfur compounds of garlic, namely alliin, γ-glutamyl and their derivatives [14]. It has been estimated that the cysteine sulfoxides and γ-glutamylcysteine peptides are non-volatile over 82% of the total sulfur content of garlic [15]. Allicin is the most predominant thiosulphate in garlic that is responsible for the characteristic odor and has an antibacterial effect and toxic to insects [16]. One milligram of alliin is considered equivalent to 0.45 mg of allicin [15].

The organosulfur compounds from *A. sativum* such as alliin, allicin and diallyl sulfide, provide the most powerful of its biological activity in protection against oxidative damage [17]. Organic-soluble allyl sulfur compounds are formed from the parent compound to give the alliin, ajoene, diallyl sulfide (DAS), diallyl disulfide (DADS) and diallyl trisulfide (DATS), while the water-soluble sulfur compounds of garlic may occur especially after alcoholic fermentation and the parent compound was alliin and gamma-glutamyl S-allylcysteine which is converted to S-allylcysteine (SAC), S-allylmercaptocysteine (SAMC) and others. Mei-chin Yin and al. conducted a study on antioxidant and antimicrobial protection of diallyl sulfide (DAS), diallyl disulfide (DADS), S-ethyl cysteine (SEC), and n-acetyl cysteine (NAC) for five inoculated pathogenic bacteria, *Salmonella typhimurium*, *Escherichia coli*, *Listeria monocytogenes*, *Staphyllococcus aureus* and *Campylobacter jejuni*. They showed that DAS and DADS exhibited both antioxidant and antimicrobial protection contrarily to both SEC and NAC that might directly stabilize the redox status or protein structure [18].

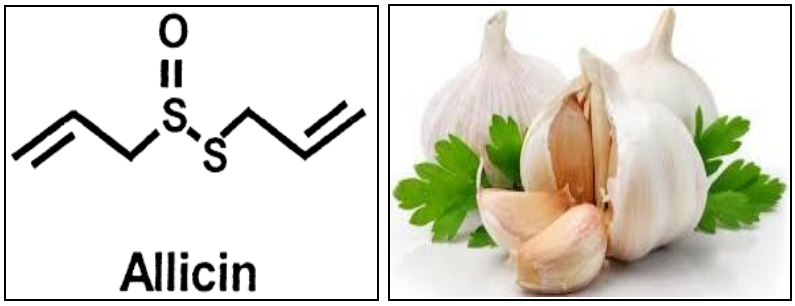

Fig: Allicin

Review of garlic on hyperlipidemia

The study evaluates the effects of garlic on one of the major cardiovascular risk factors like dyslipidemia in patients with type 2 diabetes mellitus. The result shows that garlic had a significant reduction in total cholesterol (-28 mg/dl, -12.03% *P*=<0.001), LDL-C (-30 mg/dl,-17.99% *P*=<0.001) while the placebo treated group (n=32) had a non significant decrease in total cholesterol (-2 mg/dl, -0.9% p= ns) and LDL-C (-3 mg/dl, -1.6% p=ns). HDL cholesterol was significantly increased in patients treated with garlic (3.35 mg/dl, 8.81% *P*=<0.05) compared with placebo group (0.62, 1.6% P= n.s) but there was no significant difference in triglyceride was observed between two groups. The findings indicate that Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol as compared to placebo [19].

The study investigated the effect of garlic powder at 5% and 10% level on plasma lipid profile in hypercholesterolemic rats. Male albino rats were fed a diet containing 20% fat and 1% cholesterol for two weeks to provoke hypercholesterolemia. The hypercholesterolemic rats were divided into three groups B, C and D. Group A rats were fed with normal diet, Group B were maintained on the hyper diet, Group C were fed hyper diet +5% garlic powder, Group D were fed hyper diet with +10% garlic powder. They were maintained on this diet for four weeks. Results showed that the plasma total cholesterol and LDL-C was significantly reduced in the treated groups (C and D) compared to the hypercholesterolemic control (Group B), while the HDL-C was significantly increased (*P*<0.05). Also plasma enzyme activities of Aspartate and Alanine Aminotransferases (AST. ALT) and Alkaline Phosphatase (ALP) showed a slight decrease in the treated rats. It is concluded that consumption of dry garlic powder at the level used in this study could be beneficial on the plasma lipid profile in hypercholesterolemia [20].

To evaluate the hypocholesterolemic effect of an enteric-coated garlic supplement standardized for allicin-releasing potential in mild to moderate hypercholesterolemic patients, this double-blind randomized, placebo-controlled intervention study was conducted in 46 hypercholesterolemic subjects who had failed or were not compliant with drug therapy. Each subject was given dietary counseling to lower fat intake and enteric-coated Australian garlic powder tablets with 9.6 mg allicin-releasing potential or matching placebo tablets. After 12 weeks it is found that the garlic supplement group had a significant reduction in total cholesterol and LDL-cholesterol while the placebo group had a non-significant increase in TC and LDL-C. HDL cholesterol was significantly increased in the placebo group, compared to the garlic group, and no significant difference in triglycerides or in LDL/HDL ratio was observed between groups.

The study demonstrates that enteric-coated garlic powder supplements with 9.6 mg allicin releasing potential may have value in mild to moderate hypercholesterolemic patients when combined with a low fat diet. Taken with other evidence, the efficacy of garlic for lipoprotein metabolism might require allicin bioavailability to be enhanced through the use of, for example, an enteric-coated dose form. If this is the case, the possibility remains that greater hypocholesterolemic efficacy may be evident at a higher allicin dose. Also noteworthy in this study was a small reduction in energy intake with garlic compared with placebo, attributable to reduction in fat, carbohydrate and alcohol intakes. This may also have contributed to the effects on blood lipids. This study suggests that garlic supplementation has a cholesterol-lowering effect, which may be mediated by direct action of a biologically active compound or compounds and in part through the effect on food and nutrient intake [21].

The study was evaluated to the effects of purified allicin on the cardiovascular system. For this twenty spontaneously hypertensive rats were treated for 6 weeks with a daily dose of 80 mg/kg/day of purified allicin added to their chow were compared to control rats that were fed regular chow. Weight, systolic blood pressure (SBP), triglycerides, cholesterol, insulin and adiponectin were measured at baseline and at the end of the study. The Results showed that allicin had no effect on body weight whereas it reduced SBP significantly from 190±7.5 mmHg to 168±5.7 (*P*<0.0001) and triglyceride levels from 96±25 mg/dl to 71±19 (*P*=0.009). Allicin had no effect on plasma cholesterol, insulin and adiponectin levels [22].

The study was to find out the effect of *Allium sativum* on experimentally induced hyperlipidemia in guinea pigs. For this, Twenty-five guinea pigs were fed cholesterol (0.5 g/Kg

body weight/day) for an initial period of 4 weeks. Cholesterol was then discontinued and the animals were divided into 3 groups. Group-I (control, n=7) was now fed normal diet with 1 ml normal saline. Group-II (n=9) was given 1 ml of aqueous extract with normal diet, and Group-III (n=9) was fed normal diet with 1 ml of alcoholic extract of garlic daily for 4 weeks. The garlic contents of both extracts were 2 g/ml. Fasting blood samples were collected at the end of 4 weeks after induced hyperlipidemia and finally at the end of the study (i. e. 8 weeks) for estimation of total serum cholesterol, serum triglyceride, HDLc, LDLc, VLDLc and atherogenic index was calculated in all 3 groups. The results showed that the aqueous and alcoholic extracts of garlic had a significant hypolipidemic activity as they reduced significantly serum cholesterol, serum triglyceride, LDLc, VLDLc and atheriogenic index in hyperlipidemic guinea pigs (p<0.001) as compared to control group. The significant rise in HDLc was observed in group II but not in group I and III animals. On comparison between the two extracts, aqueous extract of garlic was found to be more potent hypolipidemic agent than to the alcoholic extract [23].

The principle sulphur compound present in garlic extract and garlic oil is Diallyldisulphide (DADS) an unsaturated aliphatic disulphide, which is thought to be mainly responsible for garlic beneficial effects. The present work was under taken to assess usefulness and toxic effects of the garlic extracts in high lipid diet (HLD) fed rats. It is evident from results that garlic aqueous extracts have hypolipidemic effects in plasma and fatty changes in liver in high lipid diet rats. These hypolipidemic effects of garlic aqueous extracts may be due to its principle sulfur compound DADS [24].

The randomized, double-blind, placebo-controlled intervention study, the researchers showed that aged garlic extract (AGE) supplementation was effective in lowering plasma concentration of total cholesterol by 7% and LDL cholesterol by 10% in hypercholesterolemic men compared with subjects consuming a placebo. Supplementation of AGE in animal diets similarly reduced plasma concentrations of total cholesterol and triacylglycerol by 15 and 30%, respectively. In subsequent experiments using cultured rat hepatocytes, they found 44-87% inhibition of cholesterol synthesis by the water-extractable fraction (WEF), methanol-extractable fraction (MEF) and petroleum ether-extractable fraction (PEF) of fresh garlic, and Kyolic (liquid form of AGE). These observations suggested that hydrophilic and hydrophobic compounds of garlic are inhibitory to cholesterol synthesis. The results of the studies indicate that the cholesterol-lowering effects of garlic extract, such as AGE, stem in part from inhibition of hepatic cholesterol synthesis by water-soluble sulfur compounds, especially SAC(*S*-allylcysteine) [25].

Numerous *in vitro* studies have confirmed the ability of garlic to reduce serum total cholesterol, LDL and LDL oxidation, platelet aggregation, hypertension. Garlic has been shown to inhibit enzymes involved in lipid synthesis, decrease platelet aggregation, prevent lipid peroxidation of oxidized erythrocytes and LDL, increase antioxidant status, and inhibit angiotension-converting enzyme. These findings have also been addressed in clinical trials. The studies point to the fact that garlic reduces cholesterol, inhibits platelet aggregation, reduces blood pressure, and increases antioxidant status. Since 1993, 44% of clinical trials have indicated a reduction in total cholesterol, and the most profound effect has been observed in garlic's ability to reduce the ability of platelets to aggregate. Mixed results have been obtained in the area of blood pressure and oxidative-stress reduction. The findings are limited because very few trials have addressed these issues. The negative results obtained in some clinical trials may also have resulted from usage of different garlic preparations, unknown active constituents and their bioavailability, inadequate randomization, selection of inappropriate subjects, and short duration of trials [26].

The study shown that, Garlic consumption helps in fat metabolism, lowering blood cholesterol levels. Increases "good" cholesterol HDL and lowers,, bad" LDL cholesterol and triglycerides, protects blood vessels and the heart. Significantly reduces the activity of the enzyme-HMG-CoA reductase and may have an effect on the level of cholesterol hydroxylase and other enzymes-fatty acid synthase and enzymes taking part in pentose-phosphate metabolism. *In vitro* studies have shown that garlic has specific anti-atherosclerotic effects, by reducing the mRNA expression of inducible nitric oxide synthase (iNOS) and inhibition of oxidized low-density lipoprotein (LDL) induced by lactate dehydrogenase (LDH) and inhibition of oxidized LDL induced by depletion of glutathione [27].

The study was stated that, a very small Indian study of 32 hypercholestermic subjects paired fish oil with garlic ingestion. A significant reduction for the test group in all the lipid parameters (save high-density lipoprotein, which was increased) was found. After 60 days of supplementation, total cholesterol, low-density lipoprotein, serum triglyceride, very low-density lipoprotein, and total cholesterol were reduced by 20%, 21%, 37%, 36.7%, and 23.4%. The protective high-density lipoprotein increased by 5.1%. The potential of garlic may be enhanced by the concomitant intake of other anti-oxidants, such as lycopene and vitamin E [28].

The study was found that the patients, who used garlic, had a significant reduction in both total cholesterol (TC) and triglycerides (TG) (the main contributing factors to arteriosclerosis) in comparisons to the control group. The administration of garlic (1000 mg) lowers the levels of low density lipoproteins cholesterol (LDL-C) and raise the concentrations of high density lipoproteins cholesterol (HDL-C) and so for the very low density lipoproteins cholesterol (VLDL-C) if compared with that of the control group. So, it may be concluded that, Garlic may play an important role in the treatment of dyslipidemic patient [29].

Mechanism of action of garlic in hyperlipidemia

Mechanism of action of garlic are (i) depressed activity of hepatic lipogenesis and cholesterolegenic enzyme such as malic enzyme, fatty acid synthetase, glucose 6-phosphate dehydrogenase and 3hydroxy,3-methyl glutaryl CoA (HMG-CoA) reductase [30]. (ii) Inhanced excreation of acidic and neutral steroid into bile after garlic feeding [31] and increased loss of bile salt in faeces and mobilization of tissue lipid into circulation as garlic has a profound effect in post-prandial hyperlipidemia [32]. (iii) Suppressed LDL oxidation by garlic preparation, especially by aged garlic extract (AGE) and aqueous garlic extract [33], thus having anti-atherogenic effect [34-35]. Allicin present in garlic has been identified as the active compound responsible for anti-atherosclerotic effects. Recent *in vitro* studies revealed that water soluble organosulfur compounds especially S-allyl cysteine (SAC) present in aged garlic extract and diallyldisulphide (DADS) present in garlic oil are also potent inhibitors of cholesterol synthesis [30, 36]. Aged garlic extract and its constituents S-allyl cysteine have been found to protect vascular endothelial cell against injury caused by oxidized LDL [37]. (iv) Garlic is a potential

stimulant of lipase enzyme thereby, decreasing blood triglyceride level [38-40].

Conclusions

Hyperlipidemia is a medical condition characterized by an elevation of any or all lipid profile or lipoproteins in the blood. Although elevated low density lipoprotein cholesterol (LDL) is thought to be the best indicator of atherosclerosis risk, dyslipidemia can also describe elevated total cholesterol (TC) or triglycerides (TG), or low levels of high density lipoprotein cholesterol (HDL). On the basis of the clinical trials so far done, it can be concluded that Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol. Controlled clinical trials of longer duration are needed to assess the long term benefit of garlic on vascular and circulatory disease processes.

References

1. Mahmood ZA, Ahmed SW, Sualeh M, Mahmood SBZ. Hyperlipidemia development and consequences. Med Channel. 2009; 5:14-17.
2. Ducharme N, Radhamma R. Hyperlipidemia in the elderly. Clin Geriatr Med. 2008; 24:471-87.
3. Reiner Z, Tedeschi-Reiner E. Atherosclerosis-a paradox of Eastern European countries. Atherosclerosis. 2006; 7:461.
4. Simons LA. Additive effect of plant sterol-ester margarine and cerivastatin in lowering low density lipoprotein cholesterol in primary hypercholesterolemia. Am J Cardiol. 2002; 90:737.
5. Yokozawa T, Ishida A, Cho EJ, Nakagawa T. The effects of Coptidis rhizoma extract on a hypercholesterolemic animal model. Phytomedicine. 2003; 10:17.
6. Ibrahim SRM, Mohamed GA, Banjar ZM, Kamal HKM. Natural antihyperlipidemic agents: Current status and future perspectives. Phytopharmacology 2013; 4(3):492-531.
7. Aviello G, Abenavoli L, Borrelli F, Capasso R, Izzo AA, Lembo F *et al*. Garlic: empiricism or science? Nat Prod Commun. 2009; 4(12):1785-96.
8. Mikaili P, Maadirad S, Moloudizargari M, Aghajanshakeri S, Sarahroodi S. Therapeutic Uses and Pharmacological Properties of Garlic, Shallot, and Their Biologically Active Compounds. Iran J Basic Med Sci. 2013; 16(10):1031-48.
9. Ginter E, Simko V. Garlic (*Allium sativum* L.) and cardiovascular diseases. Bratisl Lek Listy. 2010; 111(8):452-6.
10. Thomson M, Ali M. Garlic (*Allium sativum*): A review of its potential use as an anti-cancer agent. Curr Cancer Drug Targets. 2003; 3(1):67-81.
11. Padiya R, Banerjee SK. Garlic as an anti-diabetic agent: recent progress and patent reviews. Recent Pat Food Nutr Agric. 2013; 5(2):105-27.
12. Dennehy CE, Tsourounis C. Botanicals (Herbal Medications) and nutritional supplements. In Katzung BG, editor. Basic and clinical pharmacology. 12th ed. USA: McGraw-Hills Companies. 2012; 11:25-37.
13. Chan JY, Yuen AC, Chan RY, Chan SW. A review of the cardiovascular benefits and antioxidant properties of allicin. Phytother Res. 2013; 27(5):637-46.
14. Chia-Wen al. Bio Medicine. 2012; 2:17-29.
15. WHO. Monographs on selected medicinal plants, by WHO. 1999; 1:16-32.
16. Cunha al. American journal of Botany, 2012, 17-19.
17. Tapiero H. Biomedicine & Pharmacotherapy journal, 2004, 183-193.
18. Yin Mc, Meat Science. 2003; 63:23-28.
19. Ashraf R, Aamir K, Shaikh AR, Ahmed T. Effects of garlic on dyslipidemia in patients with type 2 diabetes mellitus. J Ayub Med Coll Abbottabad, 2005, 17(3).
20. Ajayi OB, Ajayi DD. Effect of dry garlic powder on plasma lipid profile and enzyme activities in some tissues of hypercholesterolemic rats. Advances in Biochemistry. 2014; 2(3):45-49
21. Kannar D, Wattanapenpaiboon N, Gayle Savige S, Mark L Wahlqvist. Hypocholesterolemic Effect of an Enteric-Coated Garlic Supplement. Journal of the American College of Nutrition. 2001; 20(3):225-231.
22. Elkayam A, Peleg E, Grossman E, Shabtay Z, Sharabi Y. Effects of allicin on cardiovascular risk factors in spontaneously hypertensive rats. IMAJ, 2013, 15.
23. Choudhary PR, Shekhawat JS, Sharma MS, Dashora J. Effect of *Allium sativum* on experimentally induced hyperlipidemia in guinea pigs. Pak J Physiol. 2013, 9(2).
24. Murthy S, Kanthaiah Govindaswamy. Hypolipidemic effects of garlic extracts in high fat high cholesterol diet fed rats. Journal of Evolution of Medical and Dental Sciences. 2014; 3:06-10.
25. Yu-Yan Yeh, Lijuan Liu. Cholesterol-Lowering Effect of Garlic Extracts and Organosulfur Compounds: Human and Animal Studies. In the Journal of Nutrition, 2016, 13.
26. Rahman K, Gordon M. Lowe. Garlic and Cardiovascular Disease: A Critical Review. In the Journal of Nutrition, 2016, 13.
27. Majewski M. *Allium sativum*: facts and myths regarding human health. Rocz Panstw Zakl Hig. 2014; 65(1):1-8.
28. Peter B, Bongiorno Patrick M. Fratellone, Pina LoGiudice. Potential Health Benifits of Garlic (*Allium sativum*): A Narrative Review. Journal of Complementary and Integrative Medicine, 2008, 5, 1.
29. Hussien ZM. Effect of Garlic on Dyslipidemic Patients with Diabetes Mellitus. Diyala Journal of Medicine, 2014, 6, 1.
30. Yu-Yan-Yeh, Liu L. Cholesterol lowering effect of garlic extract and organo sulfur compounds; Human and animal studies. J Nutr. 2001; 131:989S-993S.
31. Chi MS, Koh ET, Stewart TJ. Effects of garlic products on lipid metabolism in cholesterol fed rats (41494). Proc Soc Exper Biol Med. 1982; 171:174-178.
32. Khoo YSK, Aziz Z. Garlic supplementation and serum cholesterol: A meta analysis, Journal of clinical pharmacy and therapeutics. 2009; 34(2):133-145.
33. Mccrindle BW, Helden E, Conner WT. Garlic extract therapy in children with hypercholesterolemia. Arch Pediatr Adolesc Med. 1998; 152:1089-1094.
34. Bordia A, Verma SK, Srivastava KC. Effects of garlic (*Allium sativum*) on blood lipids, blood sugar, Fibrinoghen and fibrinolitic activity in patients with coronary artery disease. Prostaglandin Leukot Essent Fatty Acids. 1998; 58(4):257-263.
35. Bordia A, Verma SK, Shrivastava KC. Effect of garlic (*Allium sativum*)on blood lipids, blood sugar, fibrinogen and fibrinolytic activity in patients with coronary artery disease. Prostaglandins Leukot Essent Fatty Acid. 1998; 58(4):257-263.
36. Gebhardt R, Beck H. Differential inhibitory effect of garlic derived organo sulfur compounds on cholesterol biosynthesis in primary rat hepatocyte culture. Lipids. 1996; 31:1269-1276.

37. Ide N, Lau BH. Garlic compounds protect vascular endothelial cells from oxidized low density lipoprotein induced injury. J Pharm Pharmacol. 1997; 49(9):908-911.
38. Bordia AK, Sandhya SK, Rathore AS, Bihu N. Essential oil of garlic on blood lipids and fibrinolytic activity in patients with coronary artery disease. J Assoc. Phys Ind. 1978; 26:327-333.
39. Bordia AK, Sharma KD, Parmar VK, Varma SK. Protective effect of garlic oil on the changes produced by 3 weeks of fatty diet on serum cholesterol, serum triglycerides, fibrinolytic activity and platelets adhesiveness in man. Ind Heart J. 1982; 34:86.
40. Chutani SK, Bordia A. The effect of fried versus raw garlic on fibrinolytic activity in man. Atherosclerosis. 1988; 38:417-421.