*Int. J. Biol. Res*., **4(1): 28-33, 2016.**

# CARDIOPROTECTIVE EFFECTS OF HERBAL MIXTURE (GINGER, GARLIC, LEMON, APPLE CIDER VINEGAR & HONEY) IN EXPERIMENTAL ANIMAL MODELS OF HYPERLIPIDEMIA

**NASEEM, E., M. SHAMIM* AND N.I. KHAN**

*Pathophysiology Research Unit, Department of Physiology*
*University of Karachi, Karachi, Pakistan*
***Corresponding author's email: mufzalashamim@yahoo.com***

**ABSTRACT**

Results of present study showed that oral administration of herbal extract caused significant reduction in plasma triglyceride (TG) and very low density lipoprotein VLDL levels (TG- $p<0.05$; VLDL- $p<0.01$), plasma total cholesterol (TC) levels also decreased ($p>0.05$) whereas plasma high density lipoprotein (HDL) and plasma low density lipoprotein (LDL) levels were increased ($p>0.05$). Significant reduction in plasma AIP ($p<0.01$) observed. Plasma GSH increased ($p<0.05$) whereas plasma ALT and glucose levels were also changed but non-significantly. Results conclude that dietary herbal extract has cardio protective and anti-atherogenic effects devoid of any known side-effects in experimental animal models.

**KEY WORDS:** Coronary heart disease, Hyperlipidemia, Cardio-protective effect, Atherosclerosis, Anti-oxidant effect.

## INTRODUCTION

Coronary heart disease (CHD) and stroke are the major worldwide cause of death. In 2012 CHD accounts for 17.5 million deaths representing 31% of total deaths all over the world and it is estimated up to 26% abide 2030 (WHO Report, 2008; Takata *et al.*, 2016). It was explored that the rate of mortality was predicted to turn down in the established countries from the year 1970 to 2015, whereas it was expected to approximately become twice in establishing countries (Bhagat *et al*., 2010; Ghosh *et al*., 2010). People belonging to Indo-Asian races are considered to be at higher risk in the whole world (Gupta *et al*., 2006; Jafar *et al*., 2008; Joshi *et al*., 2007) and therefore, it is not astonishing that CHD is the primary source of death in India and Pakistan (Lopez *et al*., 2006; Jafar *et al*., 2008). According to several studies occurrence of CHD increased to 2.5 folds from 1970 to 1990, comprise of 3.6% in 1970 and reached to 9.5% in 1990 in citizens of urban India, having age>35 years (Gupta and Gupta VP, 1996; Jafar *et al*., 2008). Study of Al-Mamaric reported that heart diseases associated with coronary arteries are ensured to be a consistent indicator of more prevalence of the phenomenon of atherosclerosis (Griffin, 1999; Al-Mamari, 2009).

Recent researches have reported that atheroma advancement and susceptibility are produced or augmented due to fibro inflammatory plaque cells and fat constituents (Mizuno *et al*., 2011). Dietary therapies are usually considered as first line of defense in treating diseases. Dietary therapies mostly are based on the use of herbs in the daily diet or marketed herbal products. Various studies are confirming beneficial effects of herbs in the treatment of cardiovascular diseases. Many traditional herbs, spice and fruits such as garlic, ginger, kalonji (balck seed), saffron, fenugreek, pomegranate, oranges, grapefruit etc, have been identified with beneficial cardiovascular effects.

In present study, cardio-protective effects of some of these herbs (apple cider vinegar, honey, garlic, ginger and lemon) were investigated in experimental animal models of hyperlipidemia.

## MATERIAL AND METHOD:

Total of 24 New Zealand white rabbits of either sex were selected for the study. Animals were 15-20 weeks old at the start of experiment, and had a mean body weight of 1-1.8 kg.

**Experimental protocol*:*** Initially all the rabbits were kept for acclimatization (1 week). Their body weights and other physical conditions were closely monitored throughout the study. After 12 hours of fast, blood was drawn from the central ear artery and plasma base line values for all parameters were checked. Rabbits were then randomly divided into three groups. Group I (n=8) animals were fed normal rabbit chow and served as control. Group II (n=8) and group III (n=8) animals received an atherogenic diet (1 g butter fat/ 100g of daily diet) for 4 weeks (Moghadasian *et al.*, 2001). Food and water were provided *ad libitum* during the study period. After 4 weeks group III animals were maintained on atherogenic diet and in addition received 1 gram of herbal extract per 100 g of daily diet, orally for 24 days (modified from Anonymous, 2012). Blood samples were collected from all the animals after every dietary modification. Body weight, plasma lipid profile (TG, TC, LDL, HDL, VLDL), AIP glucose, ALT and GSH were measured.

**Preparation of herbal extract:** Herbal extract was prepared by combining equal quantities (40ml each) of garlic juice, ginger juice, lemon juice and apple cider vinegar. The mixture then boiled for about 15 minutes. When reduced to one-fourth of the original quantity, it was allowed to cool. After cooling, 120 ml of honey was added in the mixture and it was then stored in an air tight jar at room temperature (modified from Anonymous, 2012).

**Biochemical analysis:** Plasma total cholesterol and plasma triglyceride concentration was determined by CHOD-PAP enzymatic endpoint and GPO-PAP enzymatic endpoint method respectively by using enzymatic kit (Global, UK). Plasma high density lipoprotein cholesterol was determined by Phosphotungstic precipitation method using enzymatic kit (Global, UK). Low density lipoprotein cholesterol concentration determined by using Friedewald's formula (Friedewald *et al*., 1972). Plasma very low density lipoprotein level was calculated by formula as described by Bairaktari *et al*. (2005). Atherogenic index of plasma was calculated using formula as described by Umeshchandra *et al*. (2012). Plasma glucose concentration was determined by Enzymatic-Colorimetric, GOD-PAP in vitro method using enzymatic kit (Global, UK). Plasma ALT was estimated by using enzymatic kit (Randox, UK). Recommended procedure was used to measure plasma glutathione (GSH) levels (Carlberg and Mannervik, 1985).

**Statistical analysis:** The data expressed as mean ± S.E.M. and were analyzed by t-test. A value of $P<0.05$ was chosen as the criteria of statistical significance.

## RESULT

**Pathogenesis of hypercholesterolemia:** The plasma levels of total cholesterol (TC), triglyceride (TG), HDL-C, LDL-C and body weight in rabbits fed on normal chow diet (group I) remain stable throughout the experimental period (Table 1). With hypercholesterolemic diet body weight increases ($p>0.05$), there was significant rise in TC, TG, VLDL and AIP ($P<0.05$) HDL and LDL levels were also increased but non-significantly ($p>0.05$). Plasma glucose and ALT levels were increased and plasma GSH decreased in hyperlipidemic animals as compared to control group.

**Table 1. Effect of herbal extract on plasma lipid profile, AIP, glucose, ALT and GSH levels in hyperlipidemic animal models.**

| Experimental groups | BW (g) | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | LDL (mg/dl) | VLDL (mg/dl) | AIP - | Glucose (mg/dl) | ALT (U/L) | GSH (nmol/g of Hb) |
|---|---|---|---|---|---|---|---|---|---|---|
| Control group | 1206.33 | 127.026 | 143.968 | 49.828 | 61.143 | 28.793 | 0.477 | 161.215 | 1.83 | 0.222 |
| | ±124.74 | ±11.069 | ±38.312 | ±9.56 | ±6.568 | ±18.768 | ±0.163 | ±29.872 | ±0.36 | ±0.023 |
| Hyperlipidemic group | 3210.33 | 213.033** | 240.963 | 50.275 | 114.565 | 48.192* | 0.703** | 256.703* | 1.41* | 0.04*** |
| | ±2027.68 | ±23.083 | ±15.406 | ±8.055 | ±18.376 | ±7.547 | ±0.157 | ±25.399 | ±0.06 | ±0.013 |
| Herbal extract treated group | 1040.83 | 209.75 | 167.625** | 71.683* | 104.541 | 33.525*** | 0.39*** | 154.076 | 1.55 | 0.225* |
| | ±69.09 | ±30.962 | ±20.723 | ±11.988 | ±34.22 | ±10.152 | ±0.332 | ±64.434 | ±0.13 | ±0.072 |
| | ±69.09 | ±30.962 | ±20.723 | ±11.988 | ±34.22 | ±10.152 | ±0.332 | ±64.434 | ±0.13 | ±0.072 |

***** Significant *p*-value, ****** Moderately significant *p*-value, ******* Highly significant *p*-value

**Effect of herbal extract on hyperlipidemic animal models:** Per day oral administration of herbal extract with the ratio of 1gm of mixture/100gm of daily diet for 15 days in hyperlipidemic animals produced substantial effects on lipid profile, AIP, plasma glucose, ALT and GSH. Plasma TG decreased to 27.15% ($p<0.05$), TC lowers to 24.45% ($p>0.05$), VLDL significantly reduced to 43.7% ($p<0.01$), HDL-C increased (29.86%), LDL-C also increased (10.6%) but non-significantly ($p>0.05$), whereas plasma AIP decreased to 80.25% ($p<0.01$). Plasma glucose level was also reduced ($p>0.05$), plasma ALT and GSH levels were increased but non-significantly (ALT-- $P>0.05$; GSH-- $P=0.05$) in extract treated group as compared to hyperlipidemic group (Table 1).

## DISCUSSION

Presently, CVD is the foremost reason of death for males and females all over the world (Ghosh *et al.*, 2010) and it is the primary cause of death in India and Pakistan (Jafar *et al.*, 2008). Hyperlipidemia, hypercholesterolemia and hyperlipoproteinemia are the underlying phenomena of CADs. To treat hyperlipidemia, statins are widely used as primary and secondary prevention of CHD. But these statins does not produce immense increase in HDL thus does not affect AIP (Evans *et al.*, 2003). Moreover these statins or pharmacological drugs produce some serious side effects on body. Therefore, non-pharmacological interventions (such as dietary modifications, life style changes as exercise, cessation of smoking and alcohol) are considered to be a cornerstone to treat primary cases of CHD (Natarajan *et al.*, 2010). Dietary therapies are usually considered as first line of defense in treating coronary artery diseases. Dietary

therapies mostly are based on the use of herbs in the daily diet with decreased daily intake of dietary fats (less than 7% of total calories consumed) and cholesterol (<200mg/day) together with increased physical activity and avoidance of sedentary life style. Since various research studies has revealed the beneficial effects of herbs or there extract in the treatment of CVDs (Brevoort, 1998; Eric *et al.*, 2002; Khan *et al.*, 2010).

The present study aims to investigate the hypolipidemic and cardio-protective effects of herbal extract (apple cider vinegar, honey, garlic, ginger, and lemon) in experimental hyperlipidemic animal models. Per day oral administration of herbal extract (1gm of mixture/100gm of daily diet) for 15 days in hyperlipidemic animals produce substantial effect on lipid profile (TG, TC, HDL, LDL, and VLDL), AIP, ALT, GSH and glucose. Herbal extract effectively reduce plasma TG to 27.15% ($p<0.05$), plasma TC to 24.45% ($p>0.05$) HDL-C increased by 29.86% and LDL-C non-significantly increased to 10.6%, VLDL and AIP both decreased significantly ($p<0.01$). Plasma GSH level increased significantly whereas changes in plasma glucose and ALT levels were also observed in hyperlipidemic animals (Table 1). Hence showing the cardio-protective and hypolipidemic effects of herbal extract.

**Hypolipidemic effects of herbal extract:** Elevated plasma TG levels can greatly increase the risk of atherosclerosis. Several studies described the beneficial hypolipidemic effects of natural honey which is rich source of antioxidants, nutritional and trace elements as described by Yaghoobi and colleagues, 70g of natural honey dissolved in 250ml of tap water significantly decrease plasma TG and other lipoproteins in hyperlipidemic individuals (Yaghoobi *et al.*, 2008). Consistent to these results, our study also showed the hypolipidemic effects of honey possibly because of trace elements (zinc & copper) and its antioxidant properties.

Apple cider vinegar also reported to produce hypolipidemic effects in various experimental studies. Acetic acid (key component of vinegar) decrease plasma TG levels by inhibiting hepatic lipogenesis along with increase in beta-oxidation of fatty acids in rats (Fushismi *et al*., 2006; Shishehbor *et al*., 2008). Acetic acid present in diet also blocks the expression of sterol regulatory element binding protein-1(SREBP-1) gene that decreases the action and levels of ATP citrate lyase (ATP-CL) and mRNA respectively which in turn decrease supply of acetyl CoA (essential component for fatty acid and cholesterol production) (Foufelle and Ferre., 2002; Fushimi *et al.*, 2006). The alterations in HDL and LDL levels may be due to effect of polyphenols present in vinegar that inhibits release of intestinal lipids (Vidal *et al*., 2005; Shishehbor *et al.*, 2008).

Hypolipidemic effects of garlic has been reported and confirmed by multiple research studies. Several experimental studies showed hypercholesteremic effects of garlic in animal models. Sobenin and colleagues reported per day consumption of *Alicor* (tablets containing 150 mg garlic powder) for 1 year significantly reduce plasma TC, LDL and TG in hyperlipidemia patients. This hypolipidemic effect of garlic is produced mainly by sulfur containing amino acid such as ajoene, S-allylcysteine, allicin, S-methylcysteine, sulfoxides, and diallyl disulfide that are adequately present in garlic (Sobenin *et al*., 2010).

Ginger, a well-known medicine and spice of Indo-Asian region also possess hypolipidemic effects. Alizadeh-Navaei (2008) reported that ginger capsules (3g/day) decrease TG and cholesterol levels in humans. It has been established that ginger and its extract decrease endogenous cholesterol synthesis, increase expression of LDL receptors for removal of LDL-C from plasma. Ginger increases the actions of pancreatic amylase and lipase and decrease intestinal lipid hydrolysis (Han *et al*., 2005; Alizadeh-Navaei *et al*., 2008).

Lemon, a rich source of vitamin C, citric acid, flavonoids & minerals. It has been using in traditional medicinal system since long ago because of its antioxidant, anti-bacterial, anti-hyperlipidemic, anti-carcinogenic, anti-inflammatory and several other properties. These highly beneficial effects of lemon are greatly because of *flavonoids* that are present in ample amount in lemon. A study of Khan *et al.*, demonstrates that per day administration of lemon juice (1mg/Kg of BW) effectively reduced plasma TG, TC and LDL cholesterol while increase HDL cholesterol levels of plasma hence significantly decreasing the atherogenic index of plasma in hyperlipidemic rabbits (Rice-Evans, 1997; Khan *et al*., 2010).

**Anti-oxidant effects of herbal extract:** A large number of diseases such as atherosclerosis, neurological disorders and cancer are related with free radicals formation which develop oxidative stress as one of the most important etiological factor.

Oxidative stress alone can exaggerate several disorders particularly including nervous system and cardiovascular disorders. Popular known antioxidants are vitamin E, C and phenolic compounds (exogenous) superoxide dismutase and glutathione reductase are examples of endogenous antioxidants, regulating oxidation effects on DNA, proteins and lipids (Gutteridge, 1995; Weinbrenner *et al*., 2003).

Present study shows that oral extract administration 6 times increased blood glutathione levels as compared to hyperlipidemic group. However GSH levels are maintained in treated group in contrast to control group. In consistent to our results, several studies also showed combine effect of honey, apple cider vinegar, garlic and ginger in preserving antioxidant status in treated animals.

Many research studies reported antioxidant effect of honey. Major antioxidant components of honey include glucose oxidase, ascorbic acid, catalase, flavonoids, carotenoid derivatives, phenolic acids. Bogdanov *et al*., reported that with daily serving of 1.2g of honey per Kg of body weight in humans increased body's antioxidant status by increasing blood ascorbate levels by 47%, uric acid-12%, carotene-3% and blood glutathione reductase concentration by 7% (Bogdanov *et al*., 2008).

Apple cider vinegar contain beta-carotene- a potent antioxidant phytochemical, therefore it reduce oxidative stress by scavenging reactive free radicals (Vardi *et al*., 2009).

Antioxidant property of garlic mainly is based on its active ingredients– allixin and selenium that not only scavenge free radicals but also increase the levels of cellular antioxidant enzymes i.e. super oxide dismutase, catalase and glutathione (Borek, 2001). It is also exhibited by Ide and colleague study that garlic contain an ingredient namely S-allylcysteine which prevent vascular intima from damage induced by oxidized LDL by restricting the removal of GSH from the cell and depleting peroxides (Ide and Lau, 2001).

Decreased oxidative response in macrophages have been reported with ginger extract consumption in apolipoprotein E-deficient mice and this is because the inert ingredients of ginger extract act inside the cell and within the cell membrane which influence cell receptors and enzyme functions. Oral ingestion of ginger extract down regulates the uptake of oxidized LDL, probably because of structural alteration of plasma membrane lipoprotein receptors (Fuhrman *et al*., 2000). The main constituents of ginger that have antioxidant properties are gingerols, shogaols and zingerone (Jafri *et al*., 2010).

Water soluble and fat soluble vitamins (Vitamin C and E), citrate, and flavanoids for *e.g*. hesperetin, eriocitrin and limonoids (Yu *et al*., 2005; Touhami *et al*., 2007) are responsible for antioxidant agents of lemon juice. Among all of these components vitamin C is found to be most effective in preventing oxidation of LDL as demonstrated by variety of experimental studies (Jilal and Grungy, 1991). Ascorbic acid scavenges free radicals (reactive oxygen and nitrogen species) efficiently and protects LDL from oxidation (DRI report, 2000).

**Anti-diabetic effects of extract:** Hyperglycemia is directly co-related with atherosclerosis as it is a major conventional risk factor of CAD. Present study shows remarkable reduction in blood glucose levels after oral administration of herbal extract, which lowered to 34% in treated animals.

Hypoglycemic effect of honey is because of the presence of two CHO i.e. glucose and fructose that produce synergistic effect in increasing assimilation of fructose in intestine and encouraging release of insulin, as a consequence more and more glucose enter into liver from blood and converted into glycogen (Erejuwa *et al*., 2012).

Apple vinegar also produces hypoglycemic effect by decreasing the levels of glycosylated hemoglobin in diabetic rats. This effect might be because of acetic acid action which is the major constituent of apple cider vinegar (Shishehbor *et al*., 2008).

Garlic extract also produces anti-diabetic effect in rats, reported by Jelodar *et al*. (2005) mainly because of allyle propyl disulphide and diallyle disulphide, abundantly present in garlic and also by enhancing response of insulin (Jelodar *et al*., 2005).

It has been established from various studies that ginger also possess hypoglycemic effects.

Per day administration of 500mg of ginger extract per Kg of body weight produced significant hypoglycemic effects in alloxan treated diabetic rats (Elshater *et al*., 2009; Jafri *et al*., 2010).

Hypoglycemic effect of lemon juice is mainly due to its acid content which considerably slows down gastric emptying hence lowers blood glucose levels (Anonymous, 2012).

**Hepato-protective effects of herbal extract:** Liver dysfunction is mainly indicated by the elevation of hepatocellular enzymes (ALT, AST, and ALP) and proteins in plasma. In present study we determine the levels of ALT after every dietary modification and with 15 days administration of extract it is found to be slightly elevated but non-significantly as compared to hyperlipidemic but still lower as compared to control group.

Hepato-protective effects of honey has been reported in many studies. Honey reduces oxidation in liver and improves hepatic enzyme function (AST, ALT and ALP) in trichlorfon treated mice (Erejuwa *et al*., 2012).

Garlic (20 mg/Kg/day for three months) has been shown to have hepatoprotective effect because it diminishes the leakage of hepatocellular enzymes (AST, ALT and ALP) in serum and restrict hepatic injury with accumulation of excessive matrix protein (liver fibrosis) in N-nitrosodiethylamine injected rats. All these effects are produced due to scavenging actions of garlic (Shaarawy *et al*., 2009).

Hepato-protective effect of ginger is reported by Sabina and colleagues in their study, which states that after administration of 30mg/Kg of body weight of 6-gingerol (active ingredient of ginger) in hepatotoxic (acetaminophen treated) mice, decrease the levels of hepatic transaminases via repairing and amelioration of liver parenchyma and hepatic cells. (Sabina *et al*., 2011).

Apple cider vinegar and lemon are known to reduce glycosylated Hb & oxidative stress respectively and this could be the reason of their hepato-protective effects as are reported in our study.

## CONCLUSION

Results of present study revealed the cardio-protective effects of herbal extract administration in experimental animal models of hyperlipidemia. Although, the changes in some blood parameters were not very much marked but they could be significant with prolonged duration of administration. This herbal extract can be used to treat primary cases of CHD however for secondary prevention trials its interaction with prescribed pharmacological agents should be checked or confirmed.

**REFERENCES**


Alizadeh-Navaei, R., F. Roozbeh, M. Saravi, M. Pouramir, F. Jalali and A.A. Moghadamnia. (2008). Investigation of the effect of ginger on the lipid levels. A double blind controlled clinical trial. *Saudi Med. J*., 29: 1280-4.

Al-Mamari, A. (2009). Atherosclerosis and Physical Activity. *OMJ*., 24: 173-178.

Anonymous. 2012. Natural remedies for heart diseases. www.earthclinic.com. (February 2012)

Bairaktari, E.T., K.I. Seferiadis and M.S. Elisaf. (2005). Evaluation of methods for the measurement of low density lipoprotein cholesterol. *J. Cardio. vasc. Pharmacol. Therap*., 10: 45-54.

Bhagat, M., S. Mukherjee, P. De, R. Goswami, S. Pal, M. Das and A. Ghosh. (2010). Clustering of cardiometabolic risk factors in Asian Indian women: Santiniketan Women Study. *Menopause*, 17: 359-64.

Bogdanov, S., T. Jurendic, R. Sieber and P. Gallmann. (2008). Honey for nutrition and health: A review. *Journal of the American College of Nutrition*, 27: 677-689.

Borek, C. (2001). Antioxidant health effects of aged garlic extract. *J. Nutr*., 131: 1010S-1015S.

Brevoort, P. (1998). The booming U.S. botanical market: A new overview. *Herbal Gram*., 44: 33-46.

Carlberg, I and B. Mannervik. (1985). Glutathione reductase assay. Methods in Enzymology. *Academic Press, Orlando FL*., 113: 484-90.

DRI Report. (2000). A report of the panel on dietary antioxidants & related compounds. Food & Nutrition board. Institute of medicine. National Academy Press, Washington D.C.

Elshater, A.A., M.M.A. Salman and M.M.A. Moussa. (2009). Effect of ginger extract consumption on levels of blood glucose, lipid profile and kidney functions in alloxan induced-diabetic rats. *Egypt. Acad. J. Biolog. Sci*., 2:153-162.

Erejuwa, O.O., S.A. Sulaiman and M.S. Wahab. (2012). Fructose might contribute to the hypoglycemic effect of honey. *Molecules*, 17: 1900-15.

Eric, H., C. Linda and S. Hollander. (2002). Treatment of Hyperlipidemia. *J. Fam. Pract*., 51: 370-376.

Evans, M., A. Roberts and A. Rees. (2003). Pharmacological management of hyperlipidaemia. *Br. J. Diabetes Vasc. Dis*., 3: 204-10.

Foufelle, F. and P. Ferre. (2002). New perspective in the regulation of hepatic glycolytic and lipogenic genes by insulin and glucose: A role for the transcription factor sterol regulatory element binding protein-1c. *Biochem. J*., 366: 377-391.

Friedwald, W.T, R.J. Levy and D.S. Fredrickson. (1972). Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin. Chem*., 18: 499-502.

Fuhrman, B., M. Rosenblar, T. Hayek, R. Coleman and M. Aviram. (2000). Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E deficient mice. *J. Nutr*., 130: 1124-1131.

Fushimi, T., K. Suruga, Y. Oshima, M. Fukiharu, Y. Tsukamoto and T. Goda. (2006). Dietary acetic acid reduces serum cholesterol and triacylglycerols in rats fed a cholesterol-rich diet. *British Journal of Nutrition*, 95: 916-924.

Ghosh, A., M. Bhagat, M. Das, S.K. Bala, R. Goswami and S. Pal. (2010). Prevalence of cardiovascular disease risk factors in people of Asian Indian origin: Age and sex variation. *J. Cardiovasc. Dis., Res*., 1: 81-5.

Griffin, B.A. (1999). Lipoprotein atherogenicity: an overview of current mechanisms. *Proc Nutr Soc*., 58: 163-169.

Gupta, M. Singh and S. Verma. (2006). South Asians and cardiovascular risk: what clinicians should know. *Circulation*, 113: 924-9.

Gupta, R. and V.R. Gupta. (1996). Meta-analysis of coronary heart disease prevalence in India. *Indian Heart J*., 48: 241-5.

Gutteridge, J.M. (1995). Lipid peroxidation and antioxidants as biomarkers of tissue damage. *Clin. Chem.*, 41: 1819-28.

Han, L.K., X.J. Gong, S. Kawano, M. Saito, Y. Kimura and H. Okuda. (2005). Antiobesity action of Zingiber Officinale Roscoe. *Yakugaku Zasshi (Japnese)*, 125: 213-217.

Ide, N. and B.H.S. Lau. (2001). Garlic compounds minimize intracellular oxidative stress and inhibit nuclear factor-κB activation. *Journal of Nutrition*, 131: 1020-1026.

Jafar, T.H., Z. Qadri and N. Chaturvedi. (2008). Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. *Heart*, 94: 408-413.

Jafri, S.A., S. Abass and M. Qasim. (2010). Hypoglycemic effect of ginger (*Zingiber officinale*) in alloxan induced diabetic rats (*Rattus norvagicus*). *Pak. Vet. J*., 31: 160-162.

Jelodar, G.A., M. Maleki, M.H. Motadayen and S. Sirus. (2005). Effect of fenugreek, onion and garlic on blood glucose and histopathology of pancreas of alloxan-induced diabetic rats. *Indian J. Med. Sci*., 59: 64-69.

Jilal, I. and S.M. Grungy. (1991). Preservation of the endogenous antioxidants in LDL by ascorbate but not probucol during oxidative modification. *J. Clin. Invest*., 87: 597-601.

Joshi, P., S. Islam, P. Pais, S. Reddy, P. Dorairaj, K. Kazmi, M.R. Pandey, S. Haque, S. Mendis, S. Rangarajan and S. Yusuf. (2007). Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA*., 297: 286-94.

Khan, Y., R.A. Khan, S. Afroz and A. Siddiq. (2010). Evaluation of hypolipidemic effect of citrus lemon. *Journal of Basic and Applied Sciences*, 6: 39-43.

Lopez, A.D., C.D. Mathers, M. Ezzati, D.T. Jamison and C.J. Murray. (2006). Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. *Lancet*., 367: 1747-57.

Mizuno, Y., R.F. Jacob and R.P. Mason. (2011). Inflammation and the development of atherosclerosis. Effects of lipid-lowering therapy- A review. *Journal of Atherosclerosis and Thrombosis*, 18: 351-5.

Moghadasian, M.H., J.J. Frohlich and B.M. McManus. (2001). Advances in experimental dyslipidemia and atherosclerosis. *Laboratory Investigation*, 81: 1173-8.

Natarajan, P., K.K. Ray and C.P. Cannon. (2010). High-density lipoprotein and coronary heart disease: Current and future therapies. *J. Am. Coll. Cardiol*., 55: 1283-99.

Rice-Evans, C.A., N.J. Miller and G. Paganda. (1997). Antioxidant properties of phenolic compounds. *Trends in Plant Science*, 2: 152-159.

Sabina, E.P., S.J. Pragasam, S. Kumar and M. Rasool. (2011). 6-Gingerol, an active ingredient of ginger, protects acetaminophen-induced hepatotoxicity in mice. *Journal of Chinese Integrative Medicine*, 9: 1264-9.

Shaarawy, S.M., A.A. Tohamy, S.M. Elgendy, Z.Y. Abd Elmageed, A. Bahnasy, M.S. Mohamed, E. Kandil and K. Matrougui. (2009). Protective effects of garlic and silymarin on NDEA-induced rats hepatotoxicity. *International Journal of Biological Sciences*, 5: 549-557.

Shishehbor, I.F., I.A. Mansoori, A.R. Sarkaki, M.T. Jalali and S.M. Latifi. (2008). Apple cider vinegar attenuates lipid profile in normal and diabetic rats. *Pakistan Journal of Biological Sciences ll*, 23: 2634-2638.

Sobenin, I.A., V.V. Pryanishnikov, L.M. Kunnova, Y.A. Rabinovich, D.M. Martirosyan and A.N. Orekhov. (2010). The effects of time-released garlic powder tablets on multifunctional cardiovascular risk in patients with coronary artery disease. *Lipids in Health and Disease*, 9: 119.

Takata, K., S. Imaizumi, B. Zhang, S. Miura and K. Saku. (2016). Stabilization of high-risk plaques. *Cardiovasc Diagn Ther*., 6: 304-21.

Touhami, M., A. Laroubi, K. Elhabazi, F. Loubna, I. Zrara, Y. Eljahiri, A. Oussama, F. Grases and A. Chait. (2007). Lemon juice has protective activity in a rat urolithiasis model. *BMC Urology*, 7: 18.

Umeshchandra, S., D.G. Umeshchandra and S.M. Awanti. (2012). Atherogenic Index of plasma (AIP) in post-menopausal women. *Research Journal of Pharmaceutical Biological And Chemical Sciences*, 3: 519-523.

Vardi, N., H. Parlakpinar, F. Ozturk, B. Ates, M. Gul, A. Cetin and A. Otlu. (2009). Potent protective effect of apricot and beta-carotene on methotrexate-induced intestinal oxidative damage in rats. *Food & Chemical Toxicology*, 46: 3015-3002.

Vidal, R., S. Hemandez-Vallejo and T. Pauquai. (2005). Apple procyanidins decrease cholesterol esterification and lipoprotein secretion in Caco-2/T C7 enterocytes. *J. Lipid Res*., 46: 258-268.

Weinbrenner, T., M. Cladellas, M. Isabel Covas, M. Fitó, M. Tomás, M. Sentí, J. Bruguera and J. Marrugat. (2003). High oxidative stress in patients with stable coronary heart disease. The SOLOS Study Investigators. *Atherosclerosis.* 168: 99-106.

WHO Report. (2008). Department of measurement & health information systems of the information, evidence and research cluster. Geneva: WHO Press; 2008. World Health Statistics; pp. 29-31.

Yaghoobi, N., N. Al-Waili, M. Ghayour-Mobarhan, S.M.R. Parizadeh, Z. Abasalti, Z. Yaghoobi, F. Yaghoobi, H. Esmaeili, S.M.R. Kazemi-Bajestani, R. Aghasizadeh, K.Y. Saloom and G.A.A. Ferns. (2008). Natural honey and cardiovascular risk factors; effects on blood glucose, cholesterol, triacylglycerole, CRP, and body weight compared with sucrose. *Scientific World Journal*, 8: 463-469.

Yu, J., L. Wang, R.L. Walzem, E.G. Miller, L.M. Pike and B.S. Patil. (2005). Antioxidant activity of citrus limonoids, flavonoids, and coumarins. *J. Agric. Food Chem*., 53: 2009-2014.

(Received January 2016; Accepted March 2016)