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A Comparative Study on the Effectiveness of Garlic with Clofibrate in the Treatment of Hyperlipidemia

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In this study, the effectiveness of standardised garlic tablets (Kwai) was compared with clofibrate in the treatment of hyperlipidaemia. A total of 20 patients with total cholesterol and triglyceride values above 200 and 280 mg dL⁻¹, respectively, voluntarily took part in this study. Patients were randomly allocated to take a total of nine 100 mg standardised garlic tablets daily in three divided doses, or two capsules of 500 mg clofibrate a day at 12 h intervals. The serum triglyceride and cholesterol were measured on weeks 4 and 8 of treatment. The results showed that garlic tablets were superior to clofibrate in reducing the extent and the rate of both triglyceride and cholesterol levels. Garlic tablets and clofibrate capsules reduced the total cholesterol levels by an average of 9.8, 17.5, 3 and 7.2%, respectively after 4 and 8 weeks. While the triglyceride levels were reduced by 34.8 and 43.7% in the garlic-treatment group compared with 21.3 and 25.5% in the clofibrate-treated group for the corresponding periods. The safer profile associated with garlic tablets suggests that this natural source is a better alternative to clofibrate in the treatment of hyperlipidaemia.

Key words: Hyperlipidaemia, garlic, clofibrate, human subjects

INTRODUCTION

Hyperlipidemia is a disease that is commonly classified as an increase in serum triglycerides several classes of lipid-lowering drugs have been developed and used clinically to reduce the serum lipid levels. One of the commonly used group of drugs in the treatment of these type of patients is the use of derivatives of fibric acid. Clofibrate, a member of this group, is available in the Iranian pharmaceutical market. It is known to act via activation of lipoprotein lipase. However, prolonged use of this drug has been associated with several side effects, including increase in the formation of stones in the gallbladder, reduction in urine out put and reduced sexual activity (Inuzuka *et al.*, 2003). On the other hand, interest in the use of natural products as an alternative method of treatment of a variety of diseases is growing both among the Iranian population and world wide as a whole With increase in the rate and prevalence of diseases associated with dysfunction in lipid metabolism, much interest was focused on alternative, safer drugs of natural origin, among which garlic (*Allium sativum*) has had a fair share. The Egyptians used garlic, an ancient folk medicine, many centuries ago (Rivlin, 2001). It is only since the middle of 20th century that workers have been prompted to test its antimicrobial and antifungal effects scientifically (Cavallitio and Bailey, 1944). There is growing evidence that garlic has several useful activities on the circulatory and respiratory systems (Tattelman, 2005). There are even claims of its anti-tumor activity (Li *et al.*, 2002). Garlic, both fresh and in powder form, from a variety of geographical regions, have different quantities of alliin (Banerjee and Maulik, 2002). One of the main constituents of garlic bulb, which is commonly used as a standardizing measurement of the quality of garlic, is its percentage of alliin contents Alliin is a precursor for the active compound allicin and ajoene. The former is formed when garlic is crushed before drying, which has only a half life of 4 days. However, if it is dried before crushing, it maintains its stability for several years (Lawson, 1998).

In order to evaluate the effectiveness of garlic in any study, it is prudently clear that we must initially be sure that a standardized product is used. For this purpose, we obtained standardized tablet preparation (Kwai, Lichtwer Pharma GmbH, Berlin) which contains a standardized amount of alliin of 1.3% in each tablet. Each 100 mg tablet constituted to an equivalence of 300 mg of fresh garlic, or 1.3 mg of alliin. The aim of this study was to evaluate and compare the effectiveness of this standardized garlic tablets with clofibrate in 20 Iranian subjects suffering from hyperlipidemia and having serum cholesterol and triglyceride levels above 200 mg dL⁻¹.

MATERIALS AND METHODS

A total of 20 subjects, having the set criteria of higher than 200 mg dL⁻¹ of serum cholesterol and triglyceride level, out of 37 recruited, voluntarily completed the study. The patients were randomly allocated into two groups of 10 patients (three females and seven males in each group). With mean age in each group of 41.8 (range 54-47 years), with an average weight of 74.1 kg for the garlic-treated group and 75.5 kg for the clofibrate-treated group. All the patients were those attending Iranian Oil Company Beheshti Hospital on regular basis for treatment and follow up of their hyperlipidemia. This was a suitable selection, since we has access to their previous medical records.

Treatment protocol

Garlic-treated group: All subjects were advised to discontinue their lipid lowering drugs 7 days prior to starting taking the garlic tablets. At the end of the seventh day, their total cholesterol and triglyceride levels were measured after a 14 h fasting period. This measurement was considered as the initial level of their cholesterol and triglyceride level before taking the garlic tablets.

Forty day supply (126 tablets) of garlic tablets were dispensed to each patient and advised to take 9 tablets (900 mg, equivalent to 2.7 g of fresh garlic) a day in three doses of 3 tablets with food. Serum cholesterol and triglyceride levels were measured, as previously advised, on weeks 4 and 8 after their visit for their check ups and supply of the garlic tablets.

Clofibrate-treated group: The same procedure of the initial and follow up measurements of cholesterol and triglyceride serum levels were performed. Each patient was advised to take two 500 mg clofibrate capsules (R.F. Scherer GmbH and Co., KG Eberbach, Barden, Germany) a day at 12 h intervals with food. At similar intervals, both serum cholesterol and triglyceride levels were measured. All the patients were instructed and encouraged to follow a low-fat diet regiment.

Ethical considerations: This study was undertaken as a project and the research committee of School of Pharmacy, Ahwaz University of Medical Sciences, had given its ethical approval for its implementation. All patients were interviewed and supplied verbal information on the aims and the protocols of the study. A written consent and their rights to withdraw from the study whenever wished were considered an essential part of the study.

Statistical analysis: The data were statistically analyzed using computer aided Microsoft Excel program, using analysis of variance (ANOVA), followed by Tukey method of analysis.

RESULTS

Cholesterol reduction: The results showed a significant reduction in the cholesterol level during the 8 week period of study in the garlic-treated group ($p < 0.01$), but no similar significant reduction was observed with the clofibrate-treated group (Fig. 1). The effectiveness of garlic tablets in reducing the cholesterol level was evident as early as week four of starting the treatment and was maintained along the time period of the study. The percentage of reduction, relative to the initial level of cholesterol level, after 4 and 8 weeks of treatment with garlic tablets was 9.8 and 17.5%, respectively, which showed a significant and progressive reduction. This rate of reduction was statistically significance from the clofibrate-treated group ($p < 0.01$), which showed a mere 3.0 and 7.2% reduction after 4 and 8 weeks of treatment, respectively (Fig. 1).

Triglyceride reduction: Both standardized garlic tablets and clofibrate capsules reduced significantly serum triglyceride level as early as 4 weeks after starting therapy ($p < 0.01$). However, the percentage of reduction in the garlic-treated group was significantly greater than those on the clofibrate-treated group ($p < 0.01$). The percentage reduction after 4 weeks of treatment in the garlic-treated group was 35%, while this was 21.3% in the clofibrate-treated group. After 8 weeks of treatment, the percentage reduction relative to onset of treatment with the garlic treated group was 43.7%. While the corresponding value for the clofibrate-treatment was 25.5% ($p < 0.01$). The higher the initial triglyceride level, the greater the degree of reduction in both groups. The patients on the garlic-treatment regiment with initial high triglyceride above 450 mg dL^{-1} , the extent of reduction was up to 65%, while those who had moderate increase, between $250\text{-}450 \text{ mg dL}^{-1}$, in serum triglyceride, this reduction was 31%. While the corresponding data for the patients on clofibrate-treatment were 53 and 22% (Fig. 2).

Side effects: The major side effect experienced in one patient in the garlic-treated group was a characteristic garlic odor, which is attributed to its odoriferous sulfur-containing constituents. In addition mild gastrointestinal effects were experienced by some patients. None left this study for these reasons. One interesting observation, which deserves further investigation, was found in

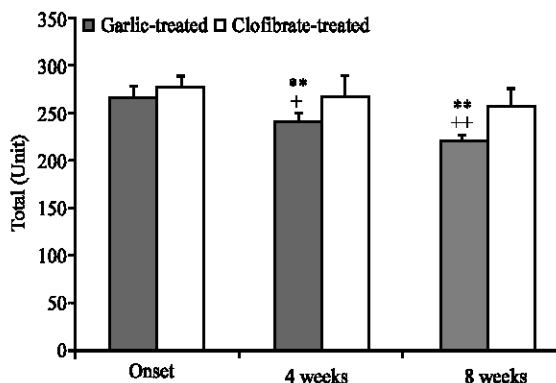


Fig. 1: Total serum cholesterol values during treatment with garlic tablets versus clofibrate. **: $p < 0.01$ among the garlic-treated group relative to the onset of treatment. ++: $p < 0.01$, between garlic and clofibrate-treated groups

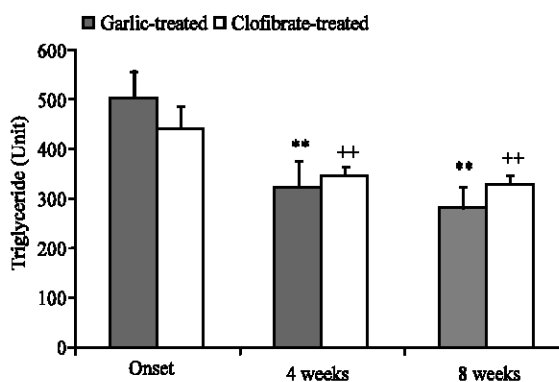


Fig. 2: Triglyceride serum values during treatment with garlic and clofibrate. **: $p < 0.01$ and ++: $p < 0.01$ relative to onset of treatment in garlic and clofibrate-treated groups, respectively

a patient in the garlic group who was a non-insulin dependent diabetic. He experienced a greater reduction in his blood glucose level relative to those previously measured with his oral hypoglycemic treatment alone. No change in the weight of patients in both groups were found during the treatment period. While the major side effects in the clofibrate-treated group were gastrointestinal side effects, all the 17 patients who did not complete the study did not do it due to the side effects associated with both treatment groups but did it owing to personal reasons, or they were simply excluded because of non compliance to their visiting schedule to the clinic for their routine tests and supply of drugs.

DISCUSSION

Though many clinical trials showed a positive effect of garlic on lowering cholesterol and triglyceride in the blood, however a number of negative studies have cast doubt on the cardiovascular efficacy of garlic (Gardner *et al.*, 2007; Kojuri *et al.*, 2007; Neil *et al.*, 1996; Stevinson *et al.*, 2000). Despite these controversies epidemiological studies shows that an inverse correlation between garlic consumption and reduced risk of cardiovascular disease progression existed (Silgay and Neil, 1994; Warshafsky *et al.*, 1993; Banerjee and Maulik, 2002). The results from our study demonstrated that not only standardized garlic tablets were more effective than clofibrate in reducing serum triglyceride level, but also reduced the total cholesterol level, on which clofibrate had a small and insignificant effect during this period of study.

Previous studies comparing the effectiveness of standardized garlic tablets with bezafibrate in human volunteers, showed that both treatments have similar and equipotent action in reducing total cholesterol and triglyceride levels (Holzgartner *et al.*, 1992). However, the garlic treated group showed a lower blood pressure level, while those on bezafibrate did not the same. Kojuri *et al.* (2007) also compared the effect of anethum and garlic on blood lipid in hyperlipidemic patients and showed that anethum had no significant effect on lipid profile, but garlic tablets significantly reduced blood cholesterol and LDL and increased HDL.

In this pilot open clinical trial study, we have shown that garlic was an effective medicinal plant in lowering the both triglyceride and cholesterol levels. However, a wider spectrum of activities of garlic could have been measured which would have given us a better view of its role in the metabolism of other lipids. Parameters such as LDL, HDL, blood glucose levels together with changes in blood pressure are possible choices for such evaluations.

The cholesterol lowering action of garlic has not been fully studied. Animals investigations, however, have revealed that garlic supplementation in the diet depressed the hepatic activities of lipogenic and cholesterogenic enzymes such as malic enzyme, fatty acid synthase, glucose-6 phosphate dehydrogenase (Chi, 1982; Chi *et al.*, 1982; Qureshi *et al.*, 1983a) and 3-hydroxy-3- methyl-glutaryl-CoA (HMG-CoA) reductase (Qureshi *et al.*, 1983b, 1987). It is, therefore, reasonable to assume that the hypocholesterolemic effect of garlic could partly be due to impaired cholesterol synthesis. It has also been shown that garlic extracts contained various sulfur compounds effectively decreased the plasma

concentration of cholesterol, resulting possibly from an inhibition of hepatic cholesterol synthesis (Yeh and Yeh, 1994).

Effectiveness of garlic preparations available in the Iranian market need to be assessed similarly, both in terms of its alliin contents and its lipid lowering properties. Such studies are of importance economically and to facilitate its wider use by the provision of a scientifically based evidence of effectiveness in the treatment of diseases associated disorders in lipid metabolism. Furthermore, considering the low side effect profile of garlic, it seems that this ancient folk medicine may have a role to play in the treatment of one of the most common underlying cause of morbidity and mortality in the 21st century.

The role of garlic in the prevention and treatment of atherosclerosis remains to be seen, but these studies with standardized garlic tablets are encouraging and reports of chronic use and trials in this Disease process is eagerly awaited.

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