Clinical evaluation of the efficacy of a combination of zanjabeel (Zingiber officinale) and amla (Emblica officinalis) in hyperlipidaemia

Rihana Kamal* & Shagufta Aleem
Department of Moalijat, AK Tibbiya College, Aligarh Muslim University, Aligarh 202 001, Uttar Pradesh

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In Unani System of Medicine, many drugs (single drugs as well compound formulations) are used for the purpose of reducing body weight and treating the obesity (Muhazzil). Indian gooseberry (amla) & ginger (Zanjabeel) are among these medicines. Since these drugs are useful in obesity, these can also be proved beneficial in lowering increased concentration of plasma lipids or treating hyperlipidaemia. Their efficacy has also been proved pharmacologically and these are documented as good hypolipidaemic as well as antioxidant natural agents. The combination of drugs was found to be significant in lowering the level of serum total cholesterol, serum tryglycerides, serum LDL-cholesterol, serum VLDL-cholesterol and in increasing the level of serum HDL-cholesterol in patients of primary hyperlipidaemia.

Keywords: Unani medicine, Hyperlipidaemia, Atherosclerosis, Amla, Ginger

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Hyperlipidaemia is a major health problem throughout the world because of its important and vital role in the pathogenesis of atherosclerosis. Atherosclerosis is responsible for the majority of the cases of coronary artery disease, cerebral stokes and essential hypertension. The concept of hyperlipidaemia is based on the biochemical changes in the blood, i.e. disturbed lipid metabolism and as a result thereof increased concentration of lipids in the blood. The Ancient Unani scholars like Hippocrates, Galen, Rhazes and Avicenna have described the condition, Saman-e-mufrat (obesity), in their treatises and have mentioned the etiological factors, clinical features and complications of it. They have narrated possible complications of obesity, like paralysis, stroke, narrowing of blood vessels, hemorrhages and sudden death in their compositions; most of these are very much similar to that of hyperlipidaemia. As far as the presence of fat (lipids) is concerned in blood, some ancient renowned Unani physicians have reported its presence in blood, produced from Dosoomat of blood or when the oily substance of blood reaches the different organs of body, it start to deposit in them and takes the form of fat (Shaham). Dosoomat or the oily substance present in blood could well have been the lipids but as the facilities of biochemical analysis of blood were not available at that time, they were unable to describe it as per modern parameters.

In present scientific era, both obesity and hyperlipidaemia are considered as two different diseases, but that there is an established link between these two diseases. The hyperlipidaemia means a higher than average amount of lipids in blood and can be defined as serum cholesterol and/or triglycerides, which are above 95th percentile of the level found in comparable healthy population. The definition of hyperlipidaemia is arbitrary, because the lipids and lipoprotein concentrations that are normal in a statistical sense are not necessarily healthy. The results of LRC–CPPT (lipid research clinic – coronary primary prevention trial) showed that the use of 95th percentile to define hyperlipidaemia is inappropriate. Now higher serum cholesterol cut-off values have been revised downward from 6.5 mmol/l (250 mg/dl) to 5.0 mmol/l (194 mg/dl). Also the cut point for normal triglycerides level has been lowered to 150 mg/dl (from 200 mg/dl in previous guidelines). Hyperlipidaemia can be designated as primary or secondary. Secondary hyperlipidaemia is the complication of a more generalized metabolic disturbance such as diabetes mellitus and hypothyroidism, etc. or due to excessive intake of excessive alcohol and some drugs like oral contraceptive pills (OCPs), thiazid diuretics and β-blockers. Primary hyperlipidaemia is a disorders of

*Corresponding author
lipid metabolism caused by inherited single gene defect (monogenic hyperlipidaemia) or appear to be caused by combination of multiple subtle genetic factors that act together with environmental insults (multifactorial or polygenic hyperlipidaemia)\(^1\).

To overcome the problem of hyperlipidaemia, day-by-day several synthetic drugs of better efficacy are being introduced in the modern system of medicine. But apart from being effective most of these medications induce adverse side effects\(^1\). Therefore, these potential agents could not be used for long time but hyperlipidaemia requires long term treatment, so it is important to choose lipid lowering medications that do not adversely affect their efficacy profile, or reinforce their potential negative side effects. Therefore, search for safe and effective lipid lowering drugs was the main motivating factor behind the study. In ancient Unani literature, there is description of many drugs (single drugs as well compound formulations) used for the purpose of reducing body weight and treating the obesity (Muhammad). Indian gooseberry (amla) & ginger (Zanjabeel) are among these medicine\(^12,13\). As these drugs are useful in obesity, they can also be proved beneficial in lowering increased concentration of plasma lipids or treating hyperlipidaemia. Their efficacy has also been proved pharmacologically and these are documented as good hypolipidaemic as well as antioxidant natural agents.

**Methodology**

To evaluate the efficacy of mentioned combination of drugs, 60 cases of primary hyperlipidaemia between the age group of 15-65 yrs of either sex were selected from Ajmal Khan Tibiya College Hospital, AMU, Aligarh. Out of these, test drugs combination was given to 40 patients (test group) and to 20 patients no drug was given (control group). Patients having Zanthoma Xanthelesma premature arcus cornes, symptoms of Ischaemic heart disease (IHD), patient having obesity and overweight, patient having family history of hyperlipidaemia and IHD, pregnant women, patients taking any medicine which increase the level of lipids such as oral contraceptive pills Ps, \(\beta\)-blockers and thiazide diuretic, etc. were excluded. Only those patients were selected whose have left the use of hypolipidaemic drugs at least six weeks prior to sampling and the subject having been following their habitual diets for at least two weeks. There has been no major or minor illness, operation or injury for at least 3-4 weeks and no minor illness in the preceding weeks. Patients selected for lipid profile were asked to attend the PG Laboratory, Department of Molejat in a 12-14 hrs fasting state (water permitted). The samples were obtained in plain vials and centrifuged to obtain serum and lipids profile was done to estimate serum lipids & lipoproteins. Serum total cholesterol, serum tryglycerides and serum high density lipoprotein (HDL cholesterol) were estimated. Very low density lipoprotein (VLDL cholesterol) – was estimated by the following calculation\(^14,15\).

\[
\text{VLDL (mg/dl)} = \frac{\text{Triglycerides (ml/dl)}}{5}
\]

Low density lipoprotein (LDL-cholesterol)– was calculated by applying Freidwald equation as follows: LDL-cholesterol (mg/dl) = Total cholesterol (mg/dl)– (VLDL+HDL) mg/dl. In patients having increased concentration of plasma lipids, serum amalase, liver functions test, renal function test and blood sugar (random) were done at the beginning of the study to exclude the causes of secondary hyperlipidaemia. Renal function test and liver function test were also repeated at end of the study to access a safety profile of test drugs. Zanjabeel and amla were given @10 gm/days, and 3 gm/day, respectively to all the 40 cases of test group irrespective of the age, sex and blood lipids level. Both the drugs were given in powdered form in two divided dosage, before meal orally. The patients were informed of the duration of the study, expected advantages and disadvantages of the drugs. No concomitant treatment was allowed. Duration of the study was 60 days; follow up of all the cases was done as regular interval of 20 days. The data of both the test and control groups were tabulated and statistically analyzed by calculating the mean and standard deviation followed by applying unpaired t’ test to the observations recorded at the end of the study (60 days).

**Results and discussion**

In patients of primary hyperlipidaemia however, the genetic defect was present from birth but elevation in plasma lipids appeared after attaining the age of 20 yrs\(^16\). The observation was also in accordance with the description as the maximum number of cases i.e. 43 were of the age between 26-45 yrs (Table 1). The higher number of female patients may be due to the lack of physical exercised among them\(^17,18\). The reason behind predominance of Muslims (Table 2)
may either be due to the use of excessive meat in their diet, which contains most of its fat in the form of saturated fats, which increases the concentration of plasma lipids \(^1\,^9\,^{16}\). The maximum number of patients (43) were housewives and from business class (Table 3). This may also be due to the lack of physical exercise among the patients of these occupations \(^19\). According to their type of food, as many as 52 cases were non-vegetarian, which may be because of the use of excessive meat full of saturated fats and deficient in dietary fibers (Table 3). Saturated fats increases the level of blood lipids \(^1\,^9\,^{16}\). The family history of hyperlipidaemia was found to be positive in 28 cases and of IHD in 36 cases (Table 2) suggesting the role of heredity in pathogenesis of primary hyperlipidaemia \(^1\,^{20}\).

After the completion of sixty days of treatment, the drug combination exhibited significant decrease in the level of serum total cholesterol (Fig. 1) and serum triglycerides (Fig. 2). This effect may be due to the presence of some chemical constituents in ginger, which inhibit the absorption of dietary fat by inhibiting its hydrolysis, it also stimulate the activity of hepatic

<p>| Table 1—Distribution of patients according to age and sex Total No of patients = 60 |</p>
<table>
<thead>
<tr>
<th>Age groups</th>
<th>Males</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-25</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>26-35</td>
<td>7</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>36-45</td>
<td>10</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>46-55</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>56-65</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

<p>| Table 2—Distribution according to the religion, family history of hyperlypidaemia and ischaemic heart disease; Total No of patients = 60 |</p>
<table>
<thead>
<tr>
<th>Religion</th>
<th>family history of hyperlypidaemia</th>
<th>Family history of ischaemic heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muslim</td>
<td>Positive – 28</td>
<td>Positive – 36</td>
</tr>
<tr>
<td>Non-muslim</td>
<td>Negative – 32</td>
<td>Negative – 24</td>
</tr>
</tbody>
</table>

<p>| Table 3—Distribution according to The Occupation, Physical Exercise And Diet Total No Of Patients = 60 |</p>
<table>
<thead>
<tr>
<th>Occupation</th>
<th>Physical Exercise</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Service</td>
<td>Heavy – 07</td>
<td>Vegetarian – 52</td>
</tr>
<tr>
<td>Business</td>
<td>Moderate – 25</td>
<td>Non-vegetarian – 08</td>
</tr>
<tr>
<td>Student</td>
<td>Sedentary – 28</td>
<td>—</td>
</tr>
<tr>
<td>House Wives</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Fig.1 Effect of drugs on serum total cholesterol

Fig.2 Effect of drugs on serum triglycerides

Fig.3 Effect of drugs on serum HDL-cholesterol

Fig.4 Effect of drugs on serum LDL-cholesterol

Fig.5 Effect of drugs on serum VLDL-cholesterol

Fig.6 Effect of drugs on body weight
enzyme cholesterol 7-alpha hydroxylase, which in turn stimulate the excretion of cholesterol from the body\textsuperscript{21,22}. Flavonoids of \textit{aila} were found to decrease the activity of enzyme HMG-Co A reductase and increase the degradation and elimination of cholesterol from the body\textsuperscript{13,14,18,23}. The significant effect of test drugs in decreasing the level of LDL cholesterol (Fig.3) and VLDL cholesterol (Fig.4) most likely be attributed to the serum cholesterol and triglyceride and lowering effect of test drugs as LDL and VLDL cholesterol are the major careers of cholesterol and triglycerides in blood, respectively\textsuperscript{15,24}. HDL cholesterol is considered as protective against atherosclerosis because it moves cholesterol from peripheral tissues to the liver (reverse cholesterol or good transport of plasma cholesterol)\textsuperscript{14,15,25}. The effect of test drugs in increasing the level of HDL cholesterol is also significant (Fig.5). Most probably this may be due to the reduction in body weight and serum triglycerides both of which are inversely related to the level of HDL cholesterol and in blood\textsuperscript{9,18,26}. The effect of drugs in reducing the body weight (Fig.6) is highly significance as this may most likely be due to the inhibitory action of ginger on absorption dietary fats by inhibiting its hydrolysis and as a result may decrease the adipost tissue weight\textsuperscript{21}.

Conclusion

It may be concluded that the effect of the test combination of drugs in lowering the level of serum total cholesterol, serum tryglycerides, serum LDL-cholesterol, serum VLDL-cholesterol and in increasing the level of serum HDL-cholesterol is significant in patients of primary hyperlipidaemia. The drugs were well tolerated and there were negligible or no side effect, therefore those can be used for a long time in patients of primary hyperlipidaemia and may prove beneficial in primary as well as secondary prevention of atherosclerotic diseases. Further studies at advanced level and the search for better drug combinations need to be carried forward.

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