

Time Tested Safe and Effect Oriented Drugs in Unani Medicine for Dyslipidemia-A Review

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Abstract

Dyslipidemia is a pathological condition in which lipid levels are deranged. It is a major health problem leading to dreadful complications such as *Waja'al-Qalb* (angina pectoris), *Khafaqan* (palpitation) *Iflas al Qalb* (myocardial infarction), *Siman-e-Mufrit* (obesity), *Ziabetus Shakri* (diabetes), *Sartan* (cancer) and abrupt death etc. Overall prevalence of metabolic syndrome which includes dyslipidemia in south Asians varies from 20% to 32% and 11% to 41% among Indians which pose great challenge on the economic implications and health care burden on the society. Many synthetic anti-dyslipidemia drugs like statins, fibrates, cholesterol absorption inhibitors, nicotinic acid are the corner stone of management at present, but these drugs are loaded with adverse effects and prolong use remains an impediment. In view of this, a recent trend has been developed and scientists are turning their attention towards the alternative medicine to overcome such dreaded ailments. In Unani Medicine many drugs have been used for the treatment of *Siman-e-mufrit* (obesity) which closely resembles to dyslipidemia in several aspects and many of these drugs have already been reported for their anti-dyslipidemia and other activities, among a huge list of such drugs a few have been reviewed in this paper.

Keywords: Dyslipidemia; Obesity; *Siman-e-mufrit*; Unani medicine

Introduction

Non communicable diseases (NCD) remain the leading cause of mortality worldwide [1]. An array of adverse life style changing factors such as nutritional imbalance, physical inactivity, stress, and increased consumption of alcohol and tobacco is said to be responsible for metabolic syndrome which include Dyslipidemia and obesity due to neo globalization, rampant urbanization and mechanization [2]. Dyslipidemia is a pathological condition in the plasma cholesterol triglyceride levels are increased above the normal range [3]. It is a major health problem leading to its dreadful complications such as *Waja'al-Qalb* (angina pectoris), *Khafaqan* (palpitation) *Iflas al Qalb* (myocardial infarction), *Siman-e-mufrit* (obesity), *Ziabetus* (diabetes), *Sartan* (cancer) etc. [4]. Overall prevalence of metabolic syndrome in south Asians varies from 20% to 32% and 11% to 41% among Indians, which pose great challenge on the economic implications and health care burden on the society [2]. Unsuccessful life style modification and pharmacological intervention with statins remains the mainstay of management. However severe adverse effects of statins result in its discontinuation posing much higher risk [5]. In view of this, a recent trend has developed and scientists are turning their attention towards the indigenous system of medicine to overcome the present day diseases [6]. In Unani Medicine many drugs have been used for the treatment of *Siman-e-mufrit* (obesity) which closely resembles to Dyslipidemia in various aspects and many of these drugs have already been reported for their anti-dyslipidemic activity [7]. However, a large proportion of Unani drugs remain still unexplored. It is the need of the hour to unfold Unani drugs to provide promised cure and safe medicament to the mankind. Hence strenuous attempt has been made to bring to medical domain certain single and compound formulations used in Unani system of medicine corroborated with scientific studies.

Asbaab (Etiology)

Its etiology is attributed to:-

Su'ehazam (Dyspepsia), *Ifrat naum* (Excessive sleep), *Ifrat sakun* (Excessive rest), *Qillate harkat- e-badani* (Sedentary life style), *Martoob wa ghaliz Ghiz'a* (Meat, fatty/oily and sweets), *Mizaj Barid* (Cold Temperament), *Ghalbae Balgham* (Dominance of Phlegm),

Ifrate Sharab bade Ghiz'a (Excessive Alcohol after meal), *Virasat and Khilqui* (Hereditary and Congenital), *Hawa-e-Ghaliz* (Polluted air), *Aa'be Ghaliz* (Contaminated water), *Farhat* (Excessive gratification), *Naghma* (Music), *Narm wa mulaim bister* (Soft couch) [8,9].

Mahiyat-e- marz (Pathology)

When *miqdar* (quantity) of *ratoobat* (moisture) and *baroodat* (coldness) escalates more than *tabyi tanasub* (normal proportion), *shaham* and *sameen* increases in the body above normal limit. It may also increase due to *maddi ashya* (material) like *mayeat* (watery) and *dasumat* (lipid) in the blood, which is more *ratab* (moist) than *dam* (blood), so it solidify in the body. Hence, *barid ratab* (cold and moist) people are more prone for *Siman-e-mufrit* (obesity) [10]. *Siman-e-mufrit* causes narrowing of vessels [11], so vessels transport less amount of *ruh* (oxygen) to the *ansaja* (tissues) which lead to decrease *hararate ghareeziya* (innate body heat) of the body and may result imbalance of *akhlat* and *mizaj* (humor and temperament) and leads to various *awarizaat* (complications) [12,13]. Jalinus has described the pathophysiology of *Siman-e-mufrit* closely in the same way as in modern pathology texts. According to the Greek Philosopher and Physician the *Siman-e-mufrit* reduces the diameter of vessels due to pressure and it produces the *Imtela* (plethora) as well as prevents *Tarveeh* (gaseous exchange) [11].

Alamaat-e-marz (Clinical features)

Excessive *Farbahi* (body weight), *Aiy'a* (Fatigue), *Bati ul Harkat*

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(Slow movements), *Waja ul Mufasil* (Pain in joints), *Zoafe Badan* (Weakness), *Usr al-Tanaffus* (Dyspnoea), *Khafqaan* (Palpitation) [14]

Usool-e-ilaj (Principle of treatment)

Ilaj of *Siman-e-mufrit* is twofold; *Umoomi Ilaj* (General treatment) and *Tahaffuzi tadabeer* (preventive measures). *Umoomi Ilaj* consists of correction of altered *akhlat* (humours) and correction of the *Su-e-Mizaj maddi*. Whereas, preventive measures includes various types of management including dietary (avoid oily/fatty and spicy food), *Riyazt sariya* (swift exercise), *Dalk khashin* (rough massage), *Hammam yabis* (dry bath), *Tadeela mizaj* (moderation of temperament), *Taqlele ghiza* (low intake of diet), *Harkate badani/Riyazat* (body movement & exercise), *Muddiraat* (diuretics), *Istefragh* (evacuation) [15].

Ilaj (Treatment)

The change in eating practices is the best way to treat *Siman-e-mufrit/dyslipidaemia* as it involves using a series of natural resources that help prevent and combat this disease. Unani medicine has a long successful record of treating obese people without any side effect; the most peculiar aspect of Unani system is its approach towards the body system by regulation of *Ghiza* (Diet), *Dawa* (Medicine) and *Tadbeer* (Regimens) [16].

- *Ilaj Bil Ghiza* (Diet therapy)
- *Ilaj Bil Tadbeer* (Regimental Therapies) wa *Nafsiyati Ilaj* (Psychotherapy)
- *Ilaj Bil Dawa* (Pharmacotherapy)

Ilaj bil ghiza (Diet therapy)

The regime for *Siman-e-mufrit* is to procure a “rapid passage” of the food from the stomach and intestine in order to prevent completion of absorption by the mesenteric vessels. Foods which are bulky (fibre containing like cabbage, bean, carrot, spinach, maize, bare, cucumber, water melon, lady finger, radish etc.) but low in nutrition/calorie may be used [17]. Use of dry diet like wheat (*Khushk roti*), Barley, use of vinegar and vinegar containing food, avoid from fatty (*roghani*), fried diet, beef soup [18]. Ismail Jurjani described the management of *farbahi* (obesity) in his book *Zakhirah Khwarzam Shahi* that, all those *ghiza* (food) which increases the formation of *Dam* (blood) should be reduced and hot spices should be added in *ghiza* (food) e.g. *Filfil Daraz* (*Piper longum*), *Zeera* (*Cuminum cyminum*), *Lehsun* (*Allium sativum*), *Rai* (*Brassica nigra*), because they have *mulattif* property, intake of *ghiza* once a day in winter season and daily use of hot water and to avoid cold drink [19].

Ilaj bil tadbeer (Regimental therapies)

Unani physicians used corporal means to restore health. But for some specific and complicated diseases, special techniques are prescribed, such techniques can be used as an adjuvant, that can be used as adjuvant along with either diet therapy or /and pharmacotherapy. Moreover, these techniques are various forms of rejuvenators and detoxifiers most of them are drugless regimens/therapies. They are not only curative but are also widely used for the prevention of diseases. *Riyazat saria* (rapid exercise), *Dalk khashin/sakht maalish* (Rough massage-oil with-Roghan Shibbat (*Anethum graveolens*), Roghan Qust (*Saussurea lappa*), *Taareeq* (*Diaphoretic*), *Hammame Yabis* (Dry bath), *Dalk m'a Muhallil Roghaniyat* (Massage with dissolvent oil), *Fasd* (Venesection), *Hijama Bish Shart* (Wet cupping) *Qai* (Emesis), *Jama drusht poshidan* (wearing of firm cloth), *Khwabidan dar Sakht Bister* (Sleep in hard bed) [4,14,16,18-22].

Nafsiyati ilaj (Psychotherapy)

Jalinus (Galen) espoused that drawn out thinking (Free association) and mental fatigue would lean the obese person. Over excitability of brain, insomnia, depression, pressurized situations are other conditions which can reduce obesity [23].

Ilaj bil dawa (Pharmacotherapy)

There are three principles (*Qanun*) for *Ilaj Bil Dawa* i.e. (i) *Dawa ki kaifiyat* (quality of drugs) (ii) *Dawa ki kamiyat* (quantity of the drug) and (iii) *Awqate Dawa* (Timing of Drug) [16]. In classical text, Unani *atibba* (Unani Physicians) prescribe treatment for *siman-e-mufrit* with both *Mufrad dawa* (single drugs) and *Murakkab dawa* (compound formulations). While treating emphasis is laid on temperamental contradictory state between the patients and drug *Ilaj bil Zid* (principle of contradiction), there are large number of medicinal plants used in Unani Medicine, single drugs or their combination are preferred over compound formulations such as *Safoof Muhazzil*, *Qurs Muhazzil*, *Arque Zeera*, *Lipotab*, *Itriphal Sagheer*, *Jawarish Jalinus*, *Jawarish Bisbasa*, *Majoon Sheer*, *Qurs Tabasheer*, *Habbe Muql*, *Majoon Muql* [24-30], and single drugs which possess antidyslipidemic activity like *Lahsun* (*Allium sativum*), *Arjun* (*Terminalia arjuna*), *Badranjboya* (*Mellisa officinalis*), *Tahlab* (*Spirulina platensis*), *Kalonji* (*Nigella sativa*), *Mehti* (*Trigonella foenum-graecum*), *Muql* (*Commiphora mukul*), *Luk* (*Laccifer lacca*), *Zanjbeel* (*Zingiber officinalis*), *Haldi* (*Curcuma longa*), *Afsanteen* (*Artemisia absinthium*), *Kundru* (*Coccinia indica*), *Abresham* (*Bombyx mori*), *Turanj* (*Citrus medica*), *Soya* (*Anethum graveolens*), *Unnab* (*Ziziphus jujuba*), *Dammulakhwain* (*Pterocarpus marsupium*), *Aam* (*Mangifera indica*), *Darhald* (*Berberis aristata*), *Halela* (*Terminalia chebula*), *Balela* (*Terminalia bellerica*), *Amla* (*Emblia officinalis*), *Saad Kofi* (*Cyperus rotundus*), *Rihan* (*Ocimum sanctum*), *Ushba Magribi* (*Hemidesmus indicus*), *Gilo* (*Tinospora cordifolia*), *Darchini* (*Cinnamomum zeylanicum*), *Badam* (*Prunus amygdalus*), *Narjeel* (*Cocos nucifera*), *Zaitoon* (*Oleum europium*), *Pea nut* (*Arachis hypogaea*), *Jaiphal* (*Myristica fragrans*), *Kachnar* (*Bauhinia variegata*), *Sharifa* (*Annona squamosa*), *Bael* (*Aegle marmelos*), *Sibr* (*Aloe vera*), *Kasondhi* (*Cassia occidentalis*), *Kishneez* (*Coriandrum sativum*), *Amrud* (*Psidium guajava*), *Sumbuluttib* (*Nardostachys jatamansi*), *Karafs* (*Apium graveolans*), *Kharkhask* (*Tribulus terrestris*), *Kachnar* (*Bauhinia variegata*), *Amaltas* (*Cassia fistula*) etc. [31-40].

The medicines administered are such that synchronize well with the temperament of the patient, thus accelerating the route of recovery and also knock out the hazard of drug reaction. The major chemical constituents of herbal source which act as antidyslipidemic agents are mainly due to presence of Sterols and triterpenoids, Polyphenolic compounds, Alkaloids, Amino acid [41]. Some of the herbs possessing antidyslipidemic activity are enumerated with its validation through in vivo and in vitro studies.

Lahsun (Allium sativum)

Family-Liliaceae *A. sativum* commonly known Garlic is used as a spice and medicinal herb [42]. It has been reported to possess immunomodulatory, antioxidant hepato-protective, antidiabetic, and ant carcinogenic, anti-dyslipidemic activity [43-46]. Garlic extract have been revealed beneficial effects in prevention of cardiovascular diseases [47]. Another study reported that, high hydrostatic pressure extract of garlic increase the HDL-C level and regulation of hepatic apolipoproteins A-1 (apoA-1) gene expression [48].

Chal arjun (Terminalia arjuna)

Family-Combretaceae *T. Arjuna* has been used by ancient

physicians in *Amraze Qalb* (cardiovascular disease) [49]. The bark contains flavanoids, glycosides and tannins which possess unique properties of antioxidant, immunomodulator, anti-inflammatory, anti-dyslipidemic, cardiotoxic activity [50]. A Clinical study reported arjun bark as a hypolipidemic, hypocholesterolemic and oxidative stress inhibitory agent [51]. 50% ethanolic extract of *T.arjuna* bark at doses of 500 mg/kg body weight exhibited hypoglycemic and hypolipidemic effect in the alloxan induced diabetic rats [52], antifibrotic activity [53]. Methanolic extract of *T. arjuna* leaves acts as hypolipidemic activity in rat models [54,55]. Another study reported that arjun bark shows symptomatic relief from ischaemic cardiomyopathy and coronary heart failure patients [56].

Badranjboya (*Mellisa officinalis*)

Family-Lamiaceae Badranjboya is also known as lemon balm. It is reported that extract obtained from leaves of *badranjboya* contain essential oil which shows antidyplipidemic activity in cholesterol fed rabbits [57]. Essential oil of *M. officinalis* reduces Plasma triglycerides in human subjects [58]. Another study reported that aqueous extract of *M. officinalis* when given orally at the doses of 2 gm/kg body weight in rats, it was found that total lipid, total cholesterol, alanine aminotransaminase, aspartate amino transaminase and alkaline phosphatase in blood serum were reduced [59]. When *M. officinalis* given as a test drug and Atorvastatin as control drug in rats model showed more significance in test group of hyperlipidemic rats [60]. *Badranjboya* has been usually used for different medicinal purposes as tonic, strengthening the memory, carminative, antispasmodic, diaphoretic, surgical dressing for wounds, sedative-hypnotic, migraine, arthritis and neurotropic agent but in contemporary pharmacology is worth in the management of mild to moderate Alzheimer's, antitumor and antioxidant activities [61]. *M. officinalis* has revealed beneficial effect on ischemic injury interceded by the inhibition of HIF-1 α and oxidative stress, followed by the cessation of apoptosis [62].

Tahlab (*Spirulina platensis*)

Family-Algae Tahlab is commonly known as blue green algae and it is used as a food since Aztec civilisation. The hypocholesterolemic effect of Spirulina in humans has been reported widely [63]. Spirulina was administered for 90 days at the dose of 500 mg/day in two times in capsule form exhibited hypolipidemic activity in NIDDM patients [64]. The hypolipidemic outcome of Spirulina was also established in ischaemic heart disease patients with hypercholesterolemia condition [65]. Oral intake of Spirulina at a dose of 8 g per day for the period of 12 weeks duration significantly decreased total serum cholesterol, LDL fraction and triglyceride levels in hypercholesterolemia patients [66]. Spirulina supplementation at the dose of 2 g per day for 2 months showed significant reduce in total serum cholesterol, triglycerides and free fatty acid levels in lipidemia with type 2 diabetes patients [67].

Muql (*Commiphora mukul*)

Family-Buraceae Muql is an Oleogum resin known as gugul which is obtained from *C. mukul*. There are many chemical constituents reported in gugul but guggulsterone and guggulipid is the bioactive constituents which is responsible for the therapeutic effects and a number of clinical trials carried out to evaluate the hypolipidemic effect of guggulipid [68]. Guggulsterone acts as antagonist of the bile acid receptor in human [69]. Guggulsterone regulates the expression of human bile salt export pump [70]. One of the study revealed that Gugul contains two stereoisomers E- and Z-guggulsterone as active constituents in this resin, and it is believed to be the rival ligands for the bile acid receptor farnesoid X receptor, which is an imperative regulator

of cholesterol homeostasis, it suggests some hypolipidemic action of these phytosteroids [71]. Resinoids of gugul showed antihyperlipidemic activity in wistar *albino* rats [72]. Oral administration of Commiphora mukul ethanol extract gum resin at a dose of 200 mg/kg for 60 days in rats has showed antihyperglycemic and antioxidant activities [73,74] cardio protective effect [75].

Haldi (*Curcuma longa*)

Family-Zingiberaceae Haldi is used as spice and medicinal purpose from centuries. Curcumin is the active principle of *haldi* which showed hypolipidemic action in streptozotocin induced diabetic rats [76]. Clinical study reported that Turmeric (*Curcuma longa* L.) and Garlic (*Allium sativum* L.) extracts act as antihyperglycemic and antihyperlipidemic agent in Type-2 diabetes-dyslipidemia patients [77]. Aqueous extract of turmeric at the dose of 1.4 gm/day in the form of capsule for three months has shown lipid lowering properties among overweight hyperlipidemic subjects [78].

Kalonji (*Nigella sativa*)

Family: Ranunculaceae Kalonji is also known as *Shoneez* (Black seed), according to Tibbe Nabvi Prophet Muhammed (saw) has told that *Shoneez* has cure for all diseases except death. It is reported that clinical trial in 20 patients with *Safoofe Kalonji* at the dose of 1 gm twice a day for 60 days given to dyslipidemia patients showed significant results [79]. Kalonji exhibited antiatherogenic effect by declining low density lipoprotein cholesterol level; it also increases high density lipoprotein level [80]. Another study reported that at the dose of 500 mg *Nigella sativa* seed powder along with statin (10-20 mg), and controlled group with statin (10-20 mg) alone, study outcomes revealed that Kalonji with statin shows significant ($P<0.05$) decline in cholesterol, LDL, VLDL and triglycerides, and significant increase of HDL. [81]. *N. sativa* seeds in the diet have favourable outcome on lipid profile by lowering the triglyceride, total cholesterol, LDL and increasing the HDL cholesterol in albino rats [82]. Another study clearly revealed that *N. sativa* seed possess significant anti-metabolic syndrome effect; it has slightly anorexic effect which exerted advantageous achievement on serum lipids and weight gain [83]. When *N. sativa* oil given to diabetic and dyslipidemic patients, it showed significant result and found to be effective as adjuvant therapy in patients with insulin resistance [84]. *N. sativa* has effect on dyslipidemia, and hyperglycemia so it has shielding effect on cardiovascular system [85,86]. *N. sativa* seed extract could be a nutritional supplement, due to their antioxidant activity so it is beneficial therapy for diabetic patients and avert diabetic complications due to lipid peroxidation and free radical oxidant [87], anticancer effect [88], antidiabetic, antioxidant and immunomodulatory effect [89].

Tukhm Soya (*Anethum graveolens*)

Family-Apiaceae Tukhm soya is also known as Dill seed and which is used as food spice and medicinal purpose. Oral administration of *Anethum graveolens* leave powder in capsule form has shown to possess hypolipidemic activity in hyperlipidemic patients, at the dose of 500 mg twice daily upto four weeks [34]. Another clinical study in metabolic syndrome patients were treated with 12 weeks of dill extract in a dose of 600 mg in capsule form had advantageous effect in reducing triglyceride from baseline values [35]. In an experimental study with *Anethum graveolens* essential oil at the doses of 45, 90 and 180 mg/kg for two weeks drastically reduced total cholesterol, triglyceride and low density lipoprotein cholesterol in wistar rats [36]. It is reported that when dill extract given to rats at the dose 300 mg/kg for 45 days in paracetamol induced liver injury, has significantly showed antioxidant and hypolipidemic activity [37].

Tukhm Methi (*Trigonellafoenum-graecum*):

Family- Fabaceae Tukhm methi is also known as fenugreek seeds. A clinical study reported that powder of methi given orally in dyslipidemic patients at the dose of 25 and 50 gm twice a day for 20 weeks before food exerts hypolipidemic effect in hypercholesterolemia patients [90]. Alcoholic extracts of methi seeds at a dose of 200 mg/kg body weight in triton-induced and high-fat diet-induced hyperlipidemia rats shown antidyslipidemic effect [91].

Complications (*Awarizat*)

Many *awarizat* (complications) of *Siman-e-mufrit* (dyslipidemia) have been described by several Unani physicians in their classical literature viz Nafeesi and Akbar Arzani have categorized the complications into seven headings in their books *Sharreh Asbab* and *Tibbe Akbar* as

- *Zeeqe Tanaffus* (Dyspnoea)-Due to vasoconstriction and *Rooh* is not provided to all organs
- *Ghashi* and *Sakta* (Syncope and Apoplexy)-Due to *Imtilai Akhlat in dimagh and qalb* (brain and heart)
- *Jiryan-ud-dam* (Haemorrhage of vessels or in the body)
- *Khafqan, Tap, Qai* (Palpitation, fever and vomiting)
- *Aqr* (Infertility)-Both in men and women as *mani* is not formed completely (oligospermia), abortion may occur in women if they conceive
- *Falij* (Paralysis)
- *Zarb wa Ishal* - In obese person effect of drug are least, as the delivery of drug is not occur perfectly and Hence, these people more prone to *amraz muzmina* (chronic diseases) [14,92,93].

Conclusion

Non communicable diseases remain the leading cause of mortality worldwide. An array of adverse life style changing factors such as nutritional imbalance, physical inactivity, stress, and increased consumption of alcohol and tobacco is said to be responsible for metabolic syndrome which include dyslipidaemia due to neo globalization, rampant urbanization and mechanization. This dismal scenario warranted to put forward the safe, time tested and effective natural hypolipidemic agents enshrined in classical Unani texts. The comprehensive approach espoused by Unani scholars in the management of *Siman-e-mufrit* had resulted in overall improvement and patient satisfaction during their era. Hence strenuous attempt has been made through this review to bring to medical domain certain single and compound formulations used in Unani system of medicine corroborated with scientific studies in the management of dyslipidaemia.

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