Time Tested Safe and Effect Oriented Drugs in Unani Medicine for Dyslipidem-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 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 hour to unfold Unani drugs to provide promised cure and safe medication 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’hazam (Dyspepsia), Ifrat naum (Excessive sleep), Ifrat sakun (Excessive rest), Qillate harkat e-badani (Sedentary life style), Martoob wa ghazl Ghiza (Meat, fatty/oily and sweets), Mizaj Barid (Cold Temperament), Ghalbe Balgham (Dominance of Phlegm), Ifrate Sharab bade Ghiz’a (Excessive Alcohol after meal), Virusat and Khilqua (Hereditary and Congenital), Hawa-e-Ghaliz (Polluted air), Aa’be Ghazl (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 tubyi tanasab (normal proportion), shaham and sameen increases in the body above normal limit. It may also increases due to maddi ashya (material) like mayest (water) 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 ghaareziya (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]. Janulis 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 Intima (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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Usool-e-ilaj (Principle of treatment)

Ilaj of Siman-e-mufrit is twofold; Umoomo Ilaj (General treatment) and Tahaffuzi tadabeer (preventive measures). Umoomo Ilaj consists of correction of altered akhlat (humors) 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 sarjia (swift exercise), Da’l k khashin (rough massage), Hammam yabis (dry bath), Tadeela mizaj (moderation of temperament), Taqeele 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/dyslipidemia 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 (Regimen) [16].

- Ilaj Bil Ghiza (Diet therapy)
- Ilaj Bil Tadbeer (Regimental Therapies) wa Nafisyati Ilaj (Psychotherapy)
- Ilaj Bil Dawaa (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. Filitil Daraz (Piper longum), Zeera (Cuminum cumini), Lehsun (Allium sativum), Rai (Brassica nigra), because they have mulattij 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 (Regimenal 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-Roghun Shhibat (Anebhum graeolvens), Roghan Qust (Sausarea lappa), Taareeq (Diaphoretic), Hammame Yabis (Dry bath), Dalk ma’ Muhallil Roghaniyat (Massage with dissolvent oil), Fasad (Venesection), Hijama Bish Shart (Wet cupping) Qai (Emesis), Jama druhaft poshidan (wearing of firm cloth), Khwabidan dar Sakht Bister (Sleep in hard bed) [4,14,16,18-22].

Nafisyati ilaj (Psychotherapy)

Jalunus (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 (Qaanun) for Ilaj Bil Dawaa i.e. (i) Dawa ki kaiyiyat (quality of drugs) (ii) Dawa ki kamiyiyat (quantity of the drug) and (iii) Awqate Dawaa (Timing of Drug) [16]. In classical text, Unani atibba (Unani Physicians) prescribe treatment for siman-e-mufrit with both Mufrad dawa (single drugs) and Murakakab 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 Safqoof Muazzizz, Quis Muazzizz, Arque Zeera, Lipotab, Irripil Sahgher, Jawarish Jalinus, Jawarish Bisbasa, Majoon Sheer, Quis Tabalbeer, Habbe Muqal, Majoon Muqal [24-30], and single drugs which possess antidysslipidemic activity like Lahnus (Allium sativum), Arjun (Terminalia arjuna), Badranboya (Mellissa officinalis), Tahlab (Spiralina platensice), Kalonji (Nigella sativa), Mehti (Trigonella foenum-graceum), Muqal (Comimplora mukul), Luk (Laccifer lacca), Zanjheel (Zingiber officinalis), Haldi (Curcuma longa), Afisanteen (Artemisia absinthium), Kundrucka (Coccinia indica), Abrehsem (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 bellierica), Amla (Emblica officinalis), Saad Koof (Cyphers rotundus), Rihan (Oximum sanctum), Ushba Magribi (Hindesmus indicus), Gilo (Tinospora cordfolia), Darchhini (Cinnamomum zeylancum), Badam (Prunus amygdalus, Narjeel (Cocos nucifera), Zaitoon (Oleum europaeum), Pau nut (Arachis hypogaea), Jaupalh (Myristica fragrans), Kachmar (Bauhinia variegatea), Sharfla (Antoona squamosa), Bael (Aegle marmelos), Sibr (Aloe vera), Kasondhi (Cassia occidentalis), Kishneez (Coriandrum sativum), Amrud (Psidium gujaava), Sumbulutib (Nardostachys jatamansi), Karafs (Apisum graveolans), Kharkhush (Trubulis terrestris), Kachnar (Bauhinia variegatea), Amalats (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 constitutes of herbal source which act as antidysslipidemic agents are mainly due to presence of Sterols and triterpenoids, Polyphenolic compounds, Alkaloids, Amino acid [41]. Some of the herbs possessing antidysslipidemic activity are enumerated with its validation through in vivo and in vitro studies.

Lahnus (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, anti diabetic, and anti 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 flavonoids, glycosides and tannins which possess unique properties of antioxidant, immunomodulator, anti-inflammatory, anti-dyslipidemic, cardiotonic activity [50]. A clinical study reported arjun bark as a hypolipidemic, hypcholesterolemic 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], antiobiotic 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 (Melissa 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 antidiylipidemic 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-1α 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 hypcholesterolemic 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 hypercholesterolaemia 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-Burcaceae. 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 gugulipid 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 gugulipid [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 imperator 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].

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 Tibibe Nabvi Prophet Muhammad (saw) has told that Shoneez has cure for all diseases except death. It is reported that clinical trial in 20 patients with all diabetic patients showed significant results [79]. Kalonji exhibited antiatherogenic effect by declining low density lipoprotein cholesterol level; it also increases high density liprotein 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 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 up to 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 antidysslipidemic 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 Sharre Asbap and Tibbe Akkar as

- Zeeta Tanaffus (Dyspnoea)-Due to vasoconstriction and Rooh is not provided to all organs
- Ghashi and Sakta (Syncope and Apoplexy)-Due to Inttilai Akhat in dimagh and qalb (brain and heart)
- Jiryan-ud-dam (Haemorrhage of vessels or in the body)
- Khafqan, Tap, Qai (Palpitation, fever and vomiting)
- Agr (Infertility)-Both in men and women as mani is not formed completely (oligospermia), abortion may occur in women if they conceive
- Fali (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 mazmin (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 drugs in Unani medicine corroborated with scientific studies in the management of dyslipidaemia.

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