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**METABOLIC SYNDROME AND THERAPEUTIC EFFECTS OF  
UNANI PHARMACOPOEIAL HERBAL DRUGS IN ITS  
MANAGEMENT: A SYSTEMATIC REVIEW**

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**ABSTRACT**

**Introduction**

Metabolic syndrome is a multi-faceted global health challenge characterized by a cluster of interconnected risk factors that increase the likelihood of cardiovascular diseases, diabetes, and related disorders. This systematic review critically evaluates the existing literature on the therapeutic effects and possible mechanism of action of Unani single drugs, Darchini (*Cinnamomum Zeylanicum*), Hulba (*Trigonella foenum*), and Jaiphal (*Myristica fragrans*) in managing various components of metabolic syndrome, such as obesity, insulin resistance, dyslipidemia, and hypertension.

**Results:**

The findings indicate that Darchini, Hulba, and Jaiphal, either individually or in combination, exhibit promising anti-inflammatory, antioxidant, hypolipidemic, and hypoglycemic properties. These herbs were found to improve insulin sensitivity, lipid metabolism, reduce adiposity, and help regulate blood pressure. The review also highlights the potential mechanisms of action, which include the modulation of insulin signalling pathways, adipokine secretion, and lipid metabolism.

**Conclusion:**

This review enhances the understanding of Unani medicine as a potential therapeutic approach for metabolic syndrome. It underscores the promising effects of Darchini, Hulba, and Jaiphal and provides insights for future research and clinical applications, including safety considerations and potential adverse effects.

**Keywords: Cinnamon; Fenugreek; Nutmeg; Metabolic Syndrome; Insulin resistance; Syndrome**

**1. INTRODUCTION**

Metabolic Syndrome also known as Syndrome X or Insulin Resistance Syndrome consists of a constellation of metabolic abnormalities that confer an increased risk of cardiovascular disease and Diabetes mellitus.<sup>1</sup> This is characterized by the presence of abdominal obesity, atherogenic dyslipidemia, high fasting glucose, and high blood pressure. Other comorbidities are non-alcoholic steatohepatitis (NASH), and reproductive/sexual disorders including polycystic ovarian syndrome, and erectile dysfunctions. The metabolic syndrome is also associated with proinflammatory and prothrombotic states causing increased risk of type 2 diabetes, cardiovascular disease and mortality from all associated factors.<sup>2,3</sup> The conventional treatment of metabolic syndrome includes dietary and lifestyle modifications and the use of synthetic drugs like statins, fibrates, Beta-blockers, and glibenclamide. However, these drugs are poorly tolerated by patients, inconclusive in effectiveness, and associated with considerable side effects<sup>4</sup>

In Unani system of medicine, comprehensive management of the discrete entities of Metabolic syndrome is based on a holistic approach and includes a combination of lifestyle modifications, *Ilaj bil Ghiza* (Diet therapy), *Ilaj bil Dawa* (Pharmacotherapy), and *Ilaj bil Tadbeer* (Regimenal therapy). Pharmacotherapy (*Ilaj bil Dawa*) for metabolic syndrome can be comprised of herbal drugs that often have a wide range of biologically active compounds that can have a synergistic effect or work together to enhance each other's effectiveness providing more benefit than a single chemical substance<sup>5</sup>. The clinical manifestations of metabolic syndrome may be correlated with signs and symptoms of *Sue Mizaj Barid Maddi* (abnormal cold temperament of the body). Based on the *Ilaj Bil Zid* principle (treatment with drugs of opposite temperament), the Unani herbal drugs possessing hot and dry (*Haar Yabis*) temperament may be useful for treating or preventing metabolic syndrome. On the basis of having hot and dry temperament, the Unani Pharmacopoeial herbal drugs

Darchini (*Cinnamomum zeylanicum*), Hulba (*Trigonella foenum*), and Jaiphal (*Myristica fragrans*) were selected for the study. The purpose of this study was to critically evaluate the existing literature on the therapeutic potential of these Unani herbal drugs to provide insights into their efficacy and scientific mechanisms of action in addressing the key risk factors and management of various components of metabolic syndrome, such as obesity, insulin resistance, dyslipidaemia, and hypertension.

## 2. Methodology

An extensive article search was carried out through five online major scientific databases namely, PubMed, Science Direct, Scopus, Web of Science and Google Scholar to identify relevant studies published up to the present date. The search strategy included the keyword 'metabolic syndrome' herbal drugs and clinical/pharmacological effects. The review includes randomized

controlled trials, observational studies, and preclinical investigations focusing on the effects of managing metabolic syndrome. Methodological quality and risk of bias assessments were performed to ensure the validity of the included studies.

## 3. Diagnostic criteria:

According to the National Cholesterol Education Program and Adult Treatment Panel III (NCEP: ATP III) definition, metabolic syndrome is present if three or more of the following five criteria are met:

1. Central Obesity: Waist circumference >102 cm or >40 inches for males and >88cm or >35inches for females.
2. Hypertriglyceridemia: Triglyceride level > 150 mg/dl.
3. Low HDL: <40 mg/dl for men and <50 mg/dl for women.
4. Hypertension: Blood Pressure >130/85 mmHg.
5. Fasting Blood Sugar >100 mg/dl. <sup>1</sup>

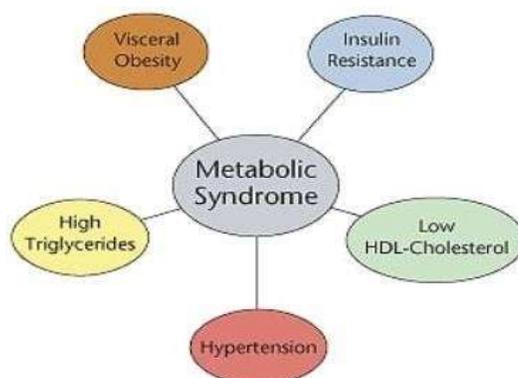


Figure 1: Individual components of Metabolic Syndrome

#### 4. Epidemiology

Globally, the Metabolic Syndrome varies and often corresponds with the prevalence of obesity. The distribution of adipose tissue between subcutaneous (SC) and visceral depots varies significantly for any given waist circumference, with intra-abdominal circumference (visceral adipose tissue) having the strongest correlation with insulin resistance, diabetes risk, and cardiovascular disease (CVD). Thus, there is a lesser vs greater risk at the same waist circumference within and between populations. The prevalence also varies greatly according to some factors such as age, gender, race/ethnicity, and diagnostic criteria used. About 25% of people in Europe and at least a fifth of the population in the USA suffer from metabolic syndrome.<sup>6</sup> Metabolic syndrome is less common in Southeast Asia. Metabolic syndrome and insulin resistance are very common in India. According to some recent studies, the age-adjusted prevalence of metabolic syndrome was found to be around 25% in the urban Indian population (almost 31% in women and 18.5% in males).<sup>7</sup> A recent meta-analysis of 111 Indian studies reported a pooled prevalence of 30% among Indian adults (> 18 years).<sup>8</sup>

#### 5. Etiology and pathogenesis

Both Genetic and acquired variables play a role in the pathophysiology of Metabolic Syndrome, contributing to the final pathway

of inflammation that ultimately leads to cardiovascular disease. The fact that the geographic distribution of Metabolic Syndrome varies greatly and that there has been a recent "catch-up" in the developing world highlights the significance of lifestyle and environmental variables, such as consumption of extra calories and lack of physical activity being key factors. It has been shown that visceral adiposity is the main initiator of most of the metabolic syndrome pathways, highlighting the significance of a high caloric intake as a major contributing factor. Insulin resistance, neuro-hormonal activation, and chronic inflammation seem to be the primary key players in the onset, development, progression, and transition of Metabolic syndrome to CVD.<sup>6</sup>

Chronic inflammation is known to be associated with visceral obesity and insulin resistance which is characterized by the production of abnormal adipocytokines such as tumour necrosis factor  $\alpha$ , interleukin-1 (IL-1), IL-6, leptin, and adiponectin. The interaction between components of the clinical phenotype of the syndrome with its biological phenotype (insulin resistance, dyslipidemia, etc.) contributes to the development of a pro-inflammatory state and further, a chronic, subclinical vascular inflammation which modulates and results in atherosclerotic process. For such a

population, lifestyle modification remains the primary intervention of choice.<sup>9</sup>

## 6. Complications

Complications of metabolic syndrome arise due to the combined effect of high blood pressure, insulin resistance, dyslipidemia (abnormal cholesterol levels), and obesity. Here are the major complications associated with metabolic syndrome.

### 6.1. Cardiovascular Disease<sup>10-12</sup>

#### 6.1.1. Atherosclerosis and Hypertension

Plaque build-up in arteries leads to narrowed and hardened arteries, increasing the risk of heart attacks and strokes.

#### 6.1.2. Coronary Artery Disease

Metabolic syndrome contributes to the narrowing of the coronary arteries, leading to reduced blood flow to the heart muscle.

#### 6.1.3. Heart Attack

Increased risk due to atherosclerosis and coronary artery disease.

#### 6.1.4. Stroke

Increased likelihood due to atherosclerosis affecting the blood vessels supplying the brain.

### 6.2. Type 2 Diabetes<sup>12</sup>

Insulin resistance, a hallmark of metabolic syndrome, results in the inability of cells to use insulin effectively, leading to elevated blood sugar levels and, ultimately, type 2 Diabetes.

### 6.3. Non-Alcoholic Fatty Liver Disease (NAFLD)<sup>13,14</sup>

Metabolic syndrome is closely associated

with NAFLD, which can progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and liver failure if untreated.

### 6.4. Chronic Kidney Disease (CKD)<sup>15,16</sup>

The combination of hypertension, insulin resistance, and inflammation linked to metabolic syndrome increases the risk of developing chronic kidney disease.

### 6.5. Sleep Apnea<sup>17,18</sup>

Obesity and insulin resistance in metabolic syndrome contribute to sleep apnea, a condition in which breathing repeatedly stops and starts during sleep.

### 6.6. Polycystic Ovary Syndrome (PCOS)<sup>19</sup>

Women with metabolic syndrome are at increased risk of PCOS, a hormonal disorder characterized by irregular menstrual cycles, excessive androgen levels, and cysts in the ovaries.

### 6.7. Cancer<sup>20,21</sup>

Obesity and insulin resistance associated with metabolic syndrome increase the risk for certain cancers, including colorectal, breast, and pancreatic cancer.

### 6.8. Dementia<sup>22-24</sup>

Metabolic syndrome can increase the risk of dementia through insulin resistance, vascular damage, chronic inflammation, oxidative stress, and obesity-related mechanisms. These pathways collectively contribute to cognitive decline and neurodegeneration. Early intervention in managing metabolic syndrome is crucial to

potentially reduce the risk of developing dementia later in life.

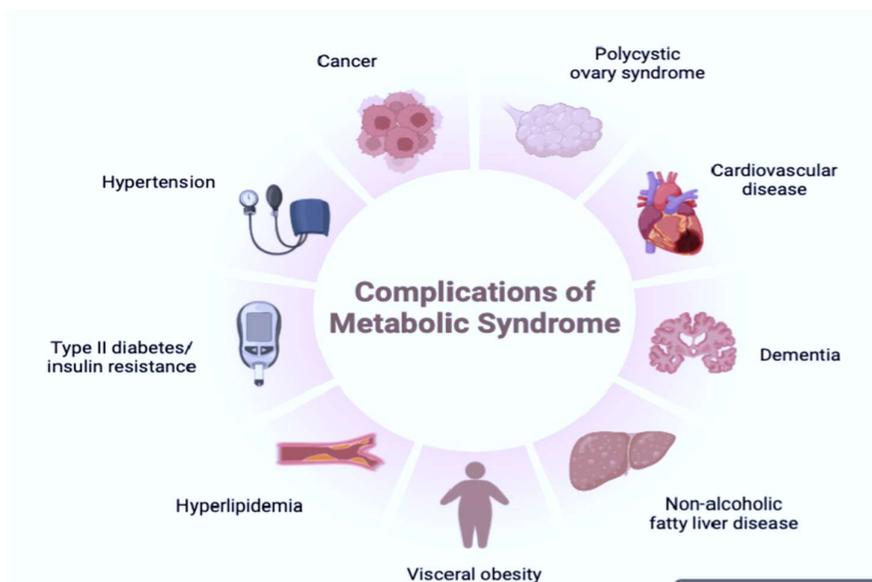


Figure 2: Complications of Metabolic Syndrome

## 7. Management

Management of Metabolic Syndrome involves a dual approach that combines lifestyle changes and pharmacological interventions to decrease CVD.

### 7.1. Lifestyle modification

Lifestyle modification is extremely, incredibly important in the management of the underlying risk factors. Modern lifestyle modification therapy combines dietary and exercise guidelines with behavioral techniques.

Weight reduction and maintenance of ideal body weight are essential preventive and management strategies as Central obesity is the driving force behind the Metabolic Syndrome.

Dietary modification can also regulate other Metabolic Syndrome components:

low intake of saturated fats, trans fats,

cholesterol, sodium, and simple sugars is known to help with dyslipidemia, hyperglycemia and hypertension.

Exercise increases calorie consumption, helping with weight loss and bringing down the overall CVD risk. Moderate-intensity exercise for around 30-60 minutes and conscious efforts to alter a sedentary lifestyle are beneficial for the management of Metabolic Syndrome.<sup>1,6</sup>

### 7.2. Pharmacotherapy

Another strategy for preventing CVD is Pharmacotherapy. Pharmaceutical therapy is aimed at treating the individual components of Metabolic Syndrome such as dyslipidemia with statins, decreasing prothrombotic risk with antiplatelet drugs, and the use of insulin sensitizers to decrease the risk of diabetes. There is no single drug therapy for Metabolic Syndrome and

currently available pharmacotherapy and associated comorbidities necessitate prolonged use of multiple medications, which is challenging for patients due to polypharmacy and reduced compliance.

In addition to this, the long-term use of these drugs results in the development of several side effects like dizziness, dry cough, peripheral neuropathy, myalgias and myositis, aplastic and haemolytic anaemias, sexual dysfunction, nausea, diarrhoea, lactic acidosis etc. Thus, there is a surge of interest in the use of naturally occurring compounds in lowering the risk and progression of Metabolic Syndrome.<sup>6</sup>

### **8. Metabolic syndrome in Unani system of medicine**

The term "Metabolic syndrome" dates back to at least the late 1950s, but it became popular in the late 1970s to describe various associations of risk factors with diabetes that had been noted as early as the 1920s, so there is no description of metabolic syndrome in Unani classical textbooks, but the idea of its distinct entities and their treatment has been clearly stated. Metabolic syndrome may be correlated with *Sue Mizaj Barid Maddi* (Abnormal cold temperament of the body) in classical literature of Unani medicine. Obesity is the driving force behind the metabolic syndrome. Obesity develops as a result of diminished *Hararat-e-ghariziya* (innate heat), generally by birth, and as a result of *Barid Mizaj*.<sup>25</sup> *Shaham* (fat) is

*Barid ratab*. Thus, excess of *Ratubat* and *Barudat* cause excess of *Shaham*; *Ratubat* being the *Sabab-e-Maddi* (material cause) and *Burudat*, the *Sabab-e-faili* (active cause). This is why *Barid Ratab* body has excess *Shaham* and *Har Yabis* lacks it.<sup>26</sup>

In the Unani system of medicine, obesity is referred to as *Saman-e-Mufrat*. *Imtila* is a term used by Unani academics to describe a disease in the body that creates symptoms owing to the buildup of normal and/or abnormal (*akhlal*) fluids. *Imtila*'s clinical characteristics, as outlined in Unani ancient literature, are comparable to those noticed in hypertension patients on deep analysis. As a result, we may reasonably conclude that the terms *Imtila* and Hypertension significantly overlap. In Unani Medicine, the term '*Zaghat-ud-dam-Qawi*' for 'Hypertension' was later devised. Dyslipidemia, as such, is not addressed in the Unani literature, however it could be viewed as an anomaly of the entire *Hazm-e-kabidi* (Hepatic digestion). *Dam-e-Balghami* (Phlegmatic blood) produced as a result of the liver's insufficiency of *Quwwat-e-Hazma* (digestive faculty) may lead to the formation of unripe blood containing more *Balgham*, resulting in dyslipidemia.<sup>27</sup>

#### **8.1. Management of Metabolic syndrome in Unani system of medicine**

As mentioned earlier, Metabolic Syndrome is not mentioned by any particular name in the classical Unani literature. However, the

various components constituting it are mentioned in detail. In Unani system of medicine, comprehensive management of the discrete entities of Metabolic syndrome is based on a holistic approach and includes a combination of:

Lifestyle modifications like increasing physical activity and exercise etc.,

*Ilaj bil Ghiza* (Diet therapy) like *Taqilil-e-Ghiza* (Reduction in the quantity of foods) and use of *Aghziya Hirrifā* (Dry diets) etc.,

*Ilaj bil Tadabeer* (Regimenal therapies) like *Hammam Yabis* (dry bath), *Ishaal* (purgation), *Idrar* (diuresis) and *Ta'riq* (Diaphoresis) etc.,

*Ilaj bid Dawa* (Pharmacotherapy)- both Single as well as compound Unani drugs having *Muddir* (Diuretic), *Mussakin* (Sedative), *Mufattit-e-Urooq* (Vasodilators), *Dafe' Ziabetes* (Anti-diabetic), *Mussafi-e-Dam* (Blood purifier), *Muqawi-e-Jigar* (Liver tonic), *Dafe' Shahm* (Hypolipidaemic) activities are available to address the various components of metabolic syndrome.<sup>28,29</sup>

#### 8.1.1. Effects of *Cinnamomum zeylanicum* in the Management of Metabolic Syndrome:

Cinnamon, known as Darchini in Unani medicine is derived from the bark

of *Cinnamomum zeylanicum*. It has been widely recognized in Unani medicine for its diverse therapeutic benefits. Darchini is classified as having a hot and dry temperament (*Mizaj*), making it effective in treating various ailments related to digestion, circulation, and the nervous system. It is a widely used herb in Unani medicine due to its carminative, antiseptic, liver tonic, nervine tonic, and astringent properties.<sup>30</sup> Unani scholars such as Ibn Sina and Al-Razi have documented its efficacy in treating ailments related to the gastrointestinal, cardiovascular, and respiratory systems.<sup>31,32</sup>

Darchini plays a multifaceted role in managing metabolic syndrome by addressing key components such as obesity, hyperglycemia, dyslipidemia, and hypertension. Its mechanisms include reducing appetite and body fat, improving glucose metabolism, lowering cholesterol, and enhancing cardiovascular health. Additionally, Darchini's antioxidant and anti-inflammatory properties further support its protective effects against oxidative stress and inflammation, making it a valuable tool in managing and preventing metabolic syndrome and its complications (**Table 1**).

Table 1: Key mechanisms of Darchini to counter the individual components of MetS

Component	Darchini's Effect	Mechanism	References
Obesity	Reduces hunger, calorie intake, body weight, and visceral fat, enhances fat metabolism.	- Cinnamaldehyde: Decreases ghrelin secretion, reducing appetite and calorie intake. - Darchini Polyphenols: Reduce body weight and visceral fat.	33-35
Hyperglycemia	Improves glucose metabolism and insulin sensitivity.	- Methyl Hydroxy Chalcone Polymer (MHCP): Mimics insulin, stimulates glucose oxidation. - Procyanidin Type-A Polymers: Enhance glucose uptake, increase glycogen synthesis, and reduce glucose absorption. - Cinnamtannin B-1: Activates insulin receptors, increasing insulin sensitivity. - Cinnamaldehyde: Increases GLUT4 receptor expression.	36-39
Dyslipidemia	Lowers blood triglycerides and cholesterol levels, increases HDL cholesterol, improving lipid profiles.	- Inhibition of HMG Co-A Reductase: Reduces cholesterol synthesis. - Reduction of Oxidative Stress: Inhibits 5-lipoxygenase, decreasing lipid peroxidation. - Lipolytic Activity: Enhances hepatic antioxidant enzyme activity.	36,38,39
Hypertension	Reduces blood pressure and supports cardiovascular health.	- Cinnamaldehyde: Relaxes coronary arteries by inhibiting Ca <sup>2+</sup> influx and reducing Ca <sup>2+</sup> sensitivity in vascular smooth muscle cells. - Micelles Containing Cinnamaldehyde: Induce endothelium-dependent relaxation by releasing NO and H <sub>2</sub> O.	39,40
Oxidative Stress	Reduces oxidative stress and damage.	- Antioxidant Activity: Darchini's polyphenols neutralize free radicals by acting as electron donors and reduce oxidative stress, protecting cells from damage. - Enhanced Hepatic Antioxidant Enzyme Activity: Improves antioxidant defenses in the liver.	41-43
Inflammation	Reduces inflammation and associated complications.	- Anti-inflammatory Compounds: Darchini inhibits the production of inflammatory cytokines, reducing systemic inflammation and mitigating complications associated with metabolic syndrome.	44,45
Cardio-protection	Supports heart health and reduces cardiovascular risk.	- Cardio-protective Effects: Darchini's antioxidant and anti-inflammatory properties help reduce the risk of cardiovascular diseases. - Improved Lipid Profile: Reduces cholesterol and triglyceride levels, contributing to heart health.	46,47

### 8.1.2. Effects of Hulba (*Trigonella foenum*) in the Management of Metabolic Syndrome:

Hulba (*Trigonella foenum*), commonly known as fenugreek, has been extensively used in Unani medicine for its therapeutic benefits. Hulba (*Trigonella foenum*) is an annual herb belonging to the Fabaceae family. It is an herbaceous plant that grows up to 60 cm in height. It has trifoliate leaves,

yellowish-white flowers, and slender, elongated pods containing small, hard, brownish seeds. The seeds have a distinct bitter taste and strong aroma due to the presence of volatile oils and saponins. Hulba boasts a diverse range of pharmacological activities, enhancing its therapeutic value. Its notable properties include anti-inflammatory, antioxidant, hypoglycemic, hypolipidemic, analgesic, gastroprotective,

lactogenic, anti-obesity, anticancer, and antimicrobial effects.<sup>48-54</sup>

In addition to these, traditional Unani medicine recognizes Hulba for its diuretic, expectorant, blood-purifying, nerve-tonic, emmenagogue, laxative, carminative, hair tonic, general body tonic, and aphrodisiac qualities, highlighting its extensive use in promoting overall health and well-being<sup>55-57</sup>.

Hulba offers comprehensive benefits for managing metabolic syndrome by targeting key components such as obesity, hyperglycemia, dyslipidemia, and hypertension. It aids weight loss through soluble fibre, enhances insulin sensitivity, lowers cholesterol, and manages blood pressure. Additionally, its antioxidant and anti-inflammatory properties contribute to reducing oxidative stress, inflammation, and cardiovascular risk (**Table 2**).

Component	Hulba's Effect	Mechanism	References
Obesity	Aids in weight loss and reduces body fat.	<ul style="list-style-type: none"> <li>- Galactomannan: Soluble fibre that forms a viscous gel in the intestine, inhibiting glucose and lipid absorption, delaying gastric emptying, and increasing satiety.</li> <li>- Suppression of Appetite: Reduces hunger and calorie intake by affecting appetite-regulating hormones.</li> </ul>	51,58-60
Hyperglycemia	Improves glucose control and insulin sensitivity.	<ul style="list-style-type: none"> <li>- 4-Hydroxyisoleucine (4-OHIlc): Enhances glucose-induced insulin release, improving insulin sensitivity.</li> <li>- Hulba seeds being rich in soluble fibre, help lower blood sugar by slowing down carbohydrate digestion and absorption.</li> <li>- Reduction in Diabetes Incidence: Long-term intervention shows a significant reduction in diabetes incidence in Hulba-treated individuals.</li> </ul>	61,62
Dyslipidemia	Lowers cholesterol and triglyceride levels.	<ul style="list-style-type: none"> <li>- Saponins: Reduce triglycerides, LDL, and total cholesterol by increasing biliary cholesterol excretion.</li> <li>- Cholesterol Metabolism: Accelerates cholesterol metabolism, inhibits cholesterol synthesis, and facilitates reverse cholesterol transport.</li> </ul>	63,64
Hypertension	Helps in managing blood pressure.	<ul style="list-style-type: none"> <li>- Dietary Fiber: Forms a viscous gel in the intestines, aiding in cholesterol regulation and reducing blood pressure.</li> <li>- Antihypertensive Activity: Exhibits significant reduction in blood pressure in animal models, potentially through 5-HT2B receptor antagonism.</li> </ul>	65-67
Oxidative Stress	Reduces oxidative damage and protects against cellular damage.	<ul style="list-style-type: none"> <li>- Antioxidant Properties: These are due to their polyphenolic compounds, flavonoids, and vitamins (C and A), which scavenge free radicals, reduce oxidative stress, and inhibit lipid peroxidation.</li> <li>- Enhancement of Antioxidant Enzyme Activity: like superoxide dismutase (SOD), catalase, and glutathione peroxidase, providing additional antioxidant effects.</li> </ul>	52,68
Inflammation	Reduces inflammation and related complications.	<ul style="list-style-type: none"> <li>- Anti-inflammatory Compounds; such as flavonoids, alkaloids, and saponins, inhibit pro-inflammatory cytokines (TNF-<math>\alpha</math>, IL-6)</li> </ul>	69-71

complications	Supports heart health and reduces cardiovascular risk.	<p>and enzymes (e.g., COX-2) by modulating signalling pathways such as NF-<math>\kappa</math>B.</p> <p>- Linoleic and Linolenic acids present in Hulba exert significant anti-inflammatory and anti-arthritic activities as evidenced in many studies. They cause significant reductions in the elevated SGPT and ALP activities in the serum and liver of rats.</p> <p>The cardioprotective effects come from its flavonoids, saponins, and fibre, which</p> <ul style="list-style-type: none"> <li>- Improve lipid profile by reducing cholesterol and triglyceride levels</li> <li>- enhance antioxidant and anti-inflammatory activity, and</li> <li>- improve vasodilation by enhancing nitric oxide production.</li> </ul>	64,69,72
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### 8.1.3. Effects of Jaiphal (*Myristica fragrans*) in the Management of Metabolic Syndrome:

Jaiphal (*Myristica fragrans*), commonly known as nutmeg, is a significant medicinal spice in Unani medicine. Jaiphal, or nutmeg, is an evergreen tree belonging to the *Myristicaceae* family. It is native to the Moluccas (Indonesia) and is now cultivated in various tropical regions. Jaiphal (*Myristica fragrans*) is a medium-sized evergreen tree that grows up to 15 meters in height. The plant bears yellowish flowers and produces a fleshy fruit, which contains a seed (nutmeg) and an aril (mace). The seed is oval-shaped, brown, and has a hard, wrinkled surface. The dried kernel of the seed is commonly used as a spice and in medicinal formulations.<sup>73</sup>

In Unani medicine, Jaiphal has been extensively used for various ailments,

including digestive issues, neurological disorders, and sexual debility. Scientific studies have provided evidence supporting many of these traditional uses, highlighting its pharmacological significance.

*Myristica fragrans* (Jaiphal) counters metabolic syndrome through multiple mechanisms, including anti-adipogenic, anti-inflammatory, antioxidant and anti-diabetic effects. It regulates blood glucose, enhances lipid metabolism, and provides cardio-protective benefits by reducing blood pressure and arterial stiffness. It reduces oxidative stress, modulates inflammatory pathways, and improves insulin sensitivity, thereby aiding glucose regulation and protecting against diabetes-related complications commonly linked to metabolic syndrome.

Table 3: Key mechanisms of Myristica to counter the components of MetS			
Component	Jaiphal's Effect	Mechanism	References
Obesity	Aids in weight loss, reduces adipose tissue growth, and inhibits fat accumulation.	<ul style="list-style-type: none"> <li>- Tetrahydrofuran (THF), lignans, flavonoids, saponins, and tannins show anti-adipogenic and cholesterol-lowering activities.</li> <li>- Nectandrin B (NecB) activates AMP-activated Protein Kinase (AMPK), regulating food intake and energy metabolism.</li> <li>- Saponins inhibit pancreatic lipase, reducing fat absorption.</li> <li>- Potent anti-adipogenic effect on differentiating 3T3-L1 preadipocytes, and this effect is achieved by downregulating STAT3 (signal transducer and activator of transcription 3) phosphorylation and Fatty acid synthase expression.</li> </ul>	74-79
Hyperglycemia	Improves insulin sensitivity and glycemic control, reduces postprandial glucose spikes.	<ul style="list-style-type: none"> <li>- Inhibits intestinal <math>\alpha</math>-amylase and <math>\alpha</math>-glucosidase, reducing carbohydrate digestion and glucose absorption.</li> <li>- Macelignan (Fragrin A) acts as a Peroxisome proliferator-activated receptor (PPAR)-<math>\alpha</math>/gamma dual agonist, enhancing lipid metabolism and insulin sensitivity synergistically.</li> <li>- Macelignan boosts adiponectin production, reduces insulin resistance, and lowers ER stress and JNK (Jun N-terminal kinase) phosphorylation, aiding type 2 diabetes treatment.</li> <li>- Reduces advanced glycation end products (AGEs)</li> </ul>	80-86
Dyslipidemia	Lowers cholesterol and triglycerides, improves lipid metabolism and clearance.	<ul style="list-style-type: none"> <li>- Reduces LDL cholesterol and serum triglycerides while elevating HDL levels.</li> <li>- Inhibits HMG-CoA reductase, the enzyme involved in cholesterol synthesis.</li> <li>- The lignan Nectandrin B (NecB) activates AMPK to regulate lipid metabolism.</li> <li>- Macelignan enhances insulin sensitivity and corrects lipid metabolic abnormalities by activating PPAR<math>\alpha</math>/<math>\gamma</math> and reducing ER stress.</li> </ul>	75,77,81,87,88
Hypertension	Indirectly helps in lowering blood pressure and improves cardiovascular health.	<ul style="list-style-type: none"> <li>- Anti-inflammatory and antioxidant actions reduce oxidative stress and inflammation, improving blood vessel function.</li> <li>- Inhibits angiotensin-converting enzyme (ACE), promoting vasodilation.</li> <li>- Jaiphal phenolics enhance endothelial function and reduce arterial stiffness.</li> <li>- Weight loss and lipid-lowering effects contribute to better blood pressure control.</li> </ul>	87,89-92
Oxidative stress & Inflammation	Reduces oxidative stress and inflammation, improving metabolic health.	<ul style="list-style-type: none"> <li>- Myristicin, macelignan, and elemicin scavenge free radicals and reduce oxidative stress, preventing insulin resistance.</li> <li>- Inhibits pro-inflammatory cytokines (TNF-<math>\alpha</math>, IL-6), which are elevated in obesity and metabolic disorders, thus improving insulin sensitivity.</li> </ul>	89,90,93
Cardio-protection	Protects heart health and reduces cardiovascular risk.	<ul style="list-style-type: none"> <li>- Inhibits angiotensin-converting enzyme (ACE), promoting vasodilation.</li> <li>- Improves endothelial function and reduces arterial stiffness, key factors in maintaining healthy blood pressure.</li> <li>- Antioxidant and anti-inflammatory properties reduce the risk of atherosclerosis and other cardiovascular conditions.</li> </ul>	91,92,94,95

## 9. CONCLUSION

Metabolic Syndrome is a global epidemic and an established risk factor for atherosclerotic and non- atherosclerotic

CVD. Various stimuli culminating in a state of chronic inflammation seem to be the main pathophysiological drivers for Metabolic Syndrome. Existing Allopathic therapies to

tackle various components of Metabolic Syndrome are limited by various factors as described above. This review article expressed the main aspects of metabolic syndrome and protective mechanisms of the active ingredients of Darchini, Hulba and Jaiphal in reducing and ameliorating complications of metabolic syndrome. It has been concluded these drugs have potential therapeutic use in metabolic syndrome and can prevent morbidity and mortality due to cardiovascular diseases. Another advantage of these natural drugs is that they are readily available and have minimal side effects. Further research studies involving large number of subjects need to be carried out to explore and establish the role of other Unani drugs against Metabolic Syndrome mentioned in the classical Unani literature.

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