

## REVIEW ARTICLE

# A Comprehensive Review on *Trigonella foenum-graecum* L. with Special Reference to Unani Medicine

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**Abstract:** *Trigonella foenum-graecum* L., commonly known as *Hulba* or *Methi* in Unani medicine, is an annual self-pollinating plant belonging to the *Leguminosae* family. It has been utilized for centuries to treat a wide range of diseases, and modern research has supported its traditional medicinal claims. In this study, the authors have conducted manual and online searches to gather and summarize the scientific literature on *Hulba*. This article seeks to underscore the potential of *Hulba* in addressing a variety of health conditions as identified by esteemed classical Unani scholars, as well as to investigate its phytochemistry and pharmacological properties in contemporary medicine. The authors have utilized electronic databases, such as PubMed, Science Direct, DOAJ, Google Scholar, and Ayush Research Portal to filter published material. According to the gathered literature, Unani physicians have consistently recommended *Hulba* seeds for a variety of ailments, such as indigestion, flatulence, colitis, arthritis, backache, paralysis, headaches, common cold, cough, bronchial asthma, diabetes mellitus, vitiligo, and pityriasis. Additionally, the seeds and green leaves of *Hulba* contain several chemical constituents, such as alkaloids, flavonoids, steroids, saponins, and amino acids. Furthermore, several pharmacological studies have demonstrated that *Hulba* possesses various properties, including antidiabetic, antispasmodic, hypolipidemic, immunological, antibacterial, anthelmintic, anti-inflammatory, analgesic, and antioxidant activities. Based on the available evidence, it can be concluded that *Hulba* has been effectively used in Unani medicine for treating a wide range of diseases. Unani scholars have extensively documented its pharmacological properties, which have been supported by modern research studies. However, further research is necessary to validate some of the claims made in traditional medicine using scientific parameters.

**Keywords:** *Trigonella*, phytochemistry, traditional medicine, ethnopharmacology, *Hulba*, hypolipidemic.

## 1. INTRODUCTION

*Trigonella foenum-graecum* L. is native to the countries along the Mediterranean's eastern coastlines, including central Asia. It was cultivated in ancient Greece and Italy for spring fodder and therapeutic purposes [1, 2]. It is one of the world's oldest medicinal plants, with origins in ancient "Egypt and Greece". Desiccated seeds of *Trigonella foenum-graecum* were recovered in the tomb of Tutankhamen, as well as charred *T. foenum-graecum* seeds from "Tall Hala" Iraq (Radiocarbon dating to 4000 BC) and Bronze Age level of Lachish [3]. It is a plant that has traditionally been used to increase milk production in breastfeeding mothers since

Biblical times. "A *Trigonella foenum-graecum* skin preparation is listed on the *Ebers papyrus* from 1500 BC Egypt" [4]. According to Hidvegi *et al.* (1984), detailed information on the plant is given in the famous Herbarium compiled by Melius (1578) [5]. *Hulba* was first used in Chinese medicine under the Song dynasty in AD 1057 [3]. It is widely used to make an infusion that is drunk hot to loosen and evacuate excess phlegm in Western herbal medicine. It becomes a valuable tonic if taken as a decoction or powder [3]. It is primarily used as a tonic in Chinese medicine to treat chronic fatigue and sexual ailment [6].

*Trigonella foenum-graecum* L., commonly known as *Hulba* or *Methi*, is a well-known herb used in the Unani system of medicine [7]. Unani medicine is a traditional system of medicine that originated in ancient Greece and was later developed and refined by Arab and Persian physicians during the Islamic Golden Age. It is based on the concept of the

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four humors and emphasizes the importance of a healthy lifestyle, including a balanced diet, regular exercise, and stress management, as well as the use of natural remedies, such as herbs and minerals [8, 9].

According to Unani medicine, the human body is made up of seven main principles, namely, elements (*Arkān*), temperament (*Mizāj*), humours (*Akhlāt*), organ (*A'ḍā'*), pneuma (*Arwāh*), faculties (*Quwwā*), and functions (*A'f'āl'*), collectively called as *Umūr-i Ṭabī'iyya*. The absence or derangement of any of these components can threaten the very existence of health and lead to disease [8]. The Unani system of medicine is founded on scientific and holistic conceptions of health and healing. Its fundamental principles, diagnoses, and treatment modalities are all based on these concepts. Unlike a reductionist approach to health and disease, the Unani system of medicine considers the whole individual [9]. The demand for Unani medicine is increasing continuously due to its efficacy and minimal adverse effects [8, 10]. Since ancient times, many single and compound drugs have been used to alleviate diverse pathological states [11]. *Hulba* has been regarded as a soothing plant by Hippocrates, who used it to treat coughs, lung congestion, and upper respiratory ailments. Dioscorides, a renowned Greek physician from Anazarbus in Cilicia and considered the father of pharmacology, recommended it for all forms of gynecological problems. He also noted in his famous book *De-Materia Medica* that *Hulba* is an effective ingredient in ointments [3]. The seed is also valuable in Islamic medicine [12]. Avicenna, a prominent Unani physician, also described its beneficial effect on various ailments [3].

The study delves into the potential medicinal benefits of *hulba*. The authors aim to explore and analyze the traditional knowledge surrounding *hulba* and its use in treating various disorders. This literary research is geared towards providing valuable insights into *hulba*'s therapeutic properties for the scientific community's perusal. In addition to reviewing the traditional uses of *Hulba* in Unani medicine, the review also examines the scientific literature on the phytochemistry and pharmacological activities of the drug. Moreover, *Hulba* has been the subject of numerous articles, including several comprehensive reviews recently published by Visuvanathan *et al.* [13], Singh *et al.* [14], Yadav *et al.* [15], Yao *et al.* [16], Sun *et al.* [2], Ouzir *et al.* [17], and Syed *et al.* [18]. These reviews have primarily focused on the pharmacological effects and medicinal use of *Hulba*. Some have also delved into the nutritional and toxicological properties of the plant, as well as its historical use. However, there is a lack of detailed reviews on the chemical constituents of *Hulba*. To address this gap in knowledge, the authors have attempted to incorporate as much phytochemistry of *Hulba* as possible in this study.

## 2. METHODOLOGY

The authors painstakingly searched for *Hulba* both in ancient and modern literature to compile and contextualize the facts and figures relating to its morphology, *Mizāj* (temperament), pharmacological characteristics, and medicinal benefits. Aside from that, the terms '*Hulbah*', '*Methi*', '*Trigonella foenum-graecum*', and '*Hulba*' were searched in electronic databases, like PubMed, ScienceDirect, DOAJ (The Directo-

ry of Open Access Journals), Semantic Scholar, Google Scholar, and Ayush Research Portal. The additional terms used with Boolean operators, 'AND' or 'OR' were Unani medicine, *in vitro* study, *in vivo* study, pre-clinical study, clinical trial, pharmacology, pharmacognosy, and phytochemistry. Unani words and transliterations were based on the most recent standard Unani terminology. 'World Flora Online' (<http://www.worldfloraonline.org>) was used to verify the taxonomic details and synonyms.

Based on the data reviewed, this paper divides the information into two sections: (1) a description of *Hulba* in Unani medicine, and (2) a description of *Hulba* in scientific literature.

## 2.1. Description of *Hulba* in Unani Medicine

### 2.1.1. Vernacular Names

The vernacular names of *Hulba* are as follows: Algerian: Holba [19]; Arabic: *Hulba* [12]; Bengali: Heanu graeb, Methi [12, 20]; Burman: Penantazi; Canaries: Mente, Menthya; Catalan: Cenigrech, Fenugrech; Ceylon: Mathi, Uluvaarisi, Vendayam; Chinese: Hu Lu Pa [19]; Dutch: Fenegriek [3]; Egyptian: Helbek [19]; English: Fenugreek [21], Greek Hayes [22]; French: Senegre [23]; German: Griechischten [3]; Gujarati: Bhzjim Methi, Methini [20]; Hindi: Methi, muthi [20, 24]; Italian: Fiengreco, Fienogreco [23]; Languedoc: Fenigre, Senegre [19, 25]; Malayalam: Ventayam, ventham, Ulva [26]; Malta: Fenugreek, helba, fienu; Mundari: Asaraara [19]; Persian: Shamblylh, Shamlit; Panjabi: Methi, Methun, Methri [3, 19]; Sanskrit: Bahuparni, Chandrika [19]; Spanish: Alolva, Fenogreco [27]; Tamil: Vendayam, Ventayam; Telugu: Menthkura, Mentula [12]; and Urdu: Methi [28].

### 2.1.2. Unani Description

The drug is described in Unani literature under the Arabic term *Hulba* that is about half a meter tall having blackish-green leaves and white-colored flowers [29]. The seeds are yellowish-orange in color with a sharp aroma and are slightly bitter [30]. The reported shelf life of dried leaves and seeds is 1-2 years and 2-3 years, respectively [31]. The plant is consumed as food in India and the subcontinent, while the seeds are consumed as a spice [29]. In USM, its leaves and seeds are described to have medicinal properties. Additionally, the mucilage of seeds is reported to possess remarkable therapeutic capabilities [32].

## 2.2. Temperament (*Mizāj*)

*Mizāj* (temperament) is an important concept of USM. According to USM, all entities of this universe are comprised of a mixture of elements resulting in qualitative characteristics and temperament, such as hot, cold, moist, or dry [33]. The drugs also have hot, cold, moist, or dry temperaments, which means that the drug has the properties to change the body's temperament accordingly. Further, a drug can be sub-classified in 1, 2, 3, or 4th degrees according to intensity of action [29].

All Unani scholars have regarded the seeds and leaves of *Hulba* as having a *Hār* (hot) and *Yābis* (dry) temperament, but there is a variation in degrees, *i.e.*, *Hār<sup>2</sup> Yābis<sup>2</sup>* [34, 35],

*Hār<sup>2</sup> Yābis<sup>1</sup>* [36], *Hār<sup>1</sup> Yābis<sup>1</sup>* [37], *Hār<sup>1</sup> Yābis<sup>2</sup>* [38], and *Hār Yābis<sup>3</sup>* [27] for seeds, and *Hār<sup>2</sup> Yābis<sup>2</sup>* [29] for leaves.

### 2.3. Pharmacological Actions (*Af'āl*) and Therapeutic Uses (*Mawāq-i Isti'mālāt*) of *Ḥulba*

*Hulba* is a wonder drug with a wide variety of pharmacological effects. The pharmacological actions and therapeutic uses of *Ḥulba* are listed in Tables 1 and 2, respectively.

### 2.4. Parts used (*Ajza-i Musta'mila*) and Recommended Dose (*Miqdār-i Khurāk*)

*Tukhm* (seed) and *Barg* (leaf) are used medicinally [7, 47]. The pharmacological actions and uses of both parts are almost similar (Tables 1 and 2). Regarding dose, different scholars have advocated different doses of the parts of *Ḥulba*, which range from 2 g to 7 g for seed [19, 34, 38, 40] and 35 g for leaves and branches (1).

**Table 1. Pharmacological actions of *Ḥulba* in Unani medicine.**

Pharmacological Action	Description	References
<i>Mundij</i>	Concoctive: An agent which matures and prepares the morbid humours for evacuation from the body	[29, 37, 39-41]
<i>Musakkin-i Alam</i>	Analgesic	[36, 42]
<i>Jāli</i>	Detergent: a substance that cleanses the skin's surface	[40, 41, 43]
<i>Kāsir-i Riyāh</i>	Carminative	[40, 42]
<i>Muhallil-i Waram</i>	Anti-inflammatory	[40, 42]
<i>Mudirr-i Bawl</i>	Diuretic	[39, 40]
<i>Mudirr-i Laban</i>	Galactagogue	[40]
<i>Muharrrik-i A'sāb</i>	Nervine stimulant	[39]
<i>Naf-'i Surfa</i>	Anti-tussive	[39, 44]
<i>Naf-'i Dard-i Jigar</i>	Liver pain reliever	[37]
<i>Naf-'i Dard-i Mathāna</i>	Urinary bladder pain reliever	[19]
<i>Naf-'i Taqtir al-Bawl</i>	Beneficial in relieving urine incontinence	[19]
<i>Muzayyad-i Dam</i>	Hematinic: an agent helpful in the proper formation of blood	[19]
<i>Munaffith-i Balgham</i>	Expectorant	[39]
<i>Qātil-i Dīdān-i-Am 'ā'</i>	Anthelmintic	[39, 44]
<i>Mudirr-i Hayḍ</i>	Emmenagogue	[34, 40, 42]
<i>Naf-'i Nigris</i>	Beneficial in gout	[39]
<i>Mulayyīn</i>	Laxative	[39, 40]
<i>Mulaṭṭif</i>	Demulcent: an agent which liquefies thick and viscous matter	[39]
<i>Muṣaffi-i-Dam</i>	Blood purifier	[34]
<i>Naf-'i Dam'a Chashm</i>	Anti-lacrimation	[40]
<i>Muqawwī-i Badan</i>	General body tonic	[30, 42]
<i>Muqawwī-i Mi'da</i>	Stomachic	[7, 39-41, 43]
<i>Muqawwī-i Bāh</i>	Aphrodisiac	[30, 40]
<i>Muhassin-i Lone</i>	Skin fairer	[39]
<i>Naf-'i Dīq al-Nafas</i>	Anti-asthmatic	[19]
<i>Taṣfiya-i Ṣawt</i>	Voice clearer	[19]
<i>Mushtahi</i>	Appetizer	[39]
<i>Ḥābis-i-Dam</i>	Hemostyptic: The substance that stops bleeding by altering the blood's consistency due to its temperamental coldness by directing blood away from the bleeding site and into the blood vessel by constricting the vessels locally or by blocking the opening of the vessels with its mucilage	[19]

(Table 1) Contd...

Pharmacological Action	Description	References
<i>Mushil</i>	Purgative: It is purgative when used with honey and black mustard. In contrast, when consumed with roti or on a full stomach, its purgative action is decreased, and constipation and anaphrodisia may ensue.	[40]
<i>Muqawwī-i Sha'r</i>	Hair tonic	[39]
<i>Muqawwī-i Mi'da</i>	Stomachic: an agent that strengthens the stomach and improves its function	[40, 41]
<i>Dāfi 'Amrāḍ Bārīda</i>	Beneficial in the diseases developed by the excess coldness of temperament	[7, 39-41, 43]
<i>Munāsh-i Fam</i>	Mouth freshener	[39, 40]
<i>Mu'aṭṭar</i>	Aromatic	[39, 40]
<i>Dāfi 'Hudār</i>	Anti-rheumatic	[39, 40]

Table 2. Therapeutic applications of *Hulba* leaves and seeds in Unani medicine.

Mawāq-i Isti'mālāt (Therapeutic Uses)	Description	References
<i>Dhayābīṭus Sukkari</i>	Diabetes mellitus	[39, 45]
<i>Naḥkh-I Shikam</i>	Flatulence	[39]
<i>Du'f-I Mi'da</i>	Indigestion	[39]
<i>Qūlanj</i>	Colic	[39, 45]
<i>Waram-i Am 'ā'</i>	Swelling/inflammation of the intestine	[39]
<i>Amrāḍ-i Bārīda</i>	Cold temperamental diseases	[40]
<i>Ṣar'</i>	Epilepsy	[40]
<i>Ṣudā'</i>	Headache	[40]
<i>Fālij</i>	Hemiplegia	[40]
<i>Laqwa</i>	Facial palsy	[40]
<i>Waram-i Ṭihāl</i>	Spleen inflammation	[40]
<i>Dard-i Raḥim</i>	Uterine pain	[40]
<i>Waja' al-zahr</i>	Backache	[40]
<i>Burūdat-i Mathāna</i>	Coldness of bladder	[40]
<i>Waja' al-Mafāṣil</i>	Polyarthritis	[40]
<i>Du'f al-A 'ṣāb</i>	Nervine debility	[40]
<i>Bawāsīr-i Bādi</i>	Non-bleeding piles	[39]
<i>Su'āl</i>	Coughing	[39]
<i>Waja' al-Jigar</i>	Liver pain	[39]
<i>Taqīr al-Bawl</i>	Dribbling of urine	[39]
<i>Iḥtibās al-Ṭamth</i>	Amenorrhea due to morbid matters from the uterus	[7,40]
<i>Awram Bātina</i>	Internal inflammation	[7,40]
<i>Awram Zāhira</i>	External inflammation	[7,40]
<i>'Izam-i Aḥshā</i>	Organomegaly	[7, 40]
<i>Fasād-i Lawn</i>	Pigmentary disorders	[7, 40]

(Table 2) Contd...

Mawāq-i Isti'māl (Therapeutic Uses)	Description	References
Dark complexion	<i>Tilā'</i> (liniment) is used alone or in combination with other appropriate drugs to improve the complexion of the face	[39]
<i>Dam'a</i>	Epiphora	[39]
<i>Ṭarfa</i>	A red spot on the palpebral conjunctiva caused by eye vessel rupture following injury or congestion	[39]
<i>Āshūb-i Chashm</i>	Conjunctivitis as <i>Quṭūr</i>	[39]
<i>Ghalīz Akhlāt of Ri'a</i>	Morbid matter of lungs	[39]
<i>Ḍ'uf al-Bāh</i>	Anaphrodisia/ loss of libido <i>Tarfa</i>	[40]
<i>Waja' al-Raḥim</i>	Pain in the uterus	[40]
<i>Ḥazāz-o-Ibriyya/ Baḥā</i>	Dandruff	[40]
<i>Baraṣ wa Bahaq</i>	Vitiligo and pityriasis	[7, 40]
<i>Qabḍ</i>	Constipation	[39]
<i>Su'āl</i>	Cough	[39]
<i>Nazla</i>	Catarrh	[39]
<i>Ḍīq al-Nafas</i>	Bronchial asthma	[19]
<i>Bawāsīr</i>	Hemorrhoids	[39]
<i>Awrām-i Bātina</i>	Visceral organ inflammation	[39]
<i>Waja' al-Raḥim</i>	Spasmodic pain in the uterus and the hardness of the uterus	[40, 46]
<i>Waja' al-Udhun</i>	Otalgia	[7]
<i>Fasād al-Dam</i>	Chronic abnormality of blood that affects the nutrition of the skin and produces various changes in it, e.g., pigmentation, discolouration, melasma, etc.	[7]

## 2.5. Adverse Effects (Muḍīr Atharāt), Correctives (Muṣliḥ), and Substitute (Badal) of Ḥulba

According to Unani scholars, *Ḥulba* is contraindicated for *Hār Mizāj* (hot-tempered) persons as the drug already has *Hār* (hot) and *Yābis* (dry) temperament, which may lead to excessive heat in the body causing certain adverse effects. Also, its large doses may cause internal bleeding, facial swelling, allergy, chest pain, and difficulty in breathing and swallowing [29, 48]. Its adverse effects may be corrected by certain drugs, like *Kāsni* (*Cichorium intybus*), *Pālak* (*Spina-cia oleraceae*), *Kulḥā* (*Portulaca oleracea*), *Gajar* (*Daucus carota*) [19, 29, 38, 42] and *Anisūn* (*Pimpinella anisum*) [20]. The eminent Unani physicians have suggested that *Alsi* (*Linum usitatissimum*) and *Nākhuna* (*Trigonella uncata*) may be used as a substitute for *Ḥulba* [7, 32].

## 2.6. Unani Compound Formulations (Murakkabāt) of Ḥulba

*Tiryaq-i Dīq al-Nafas*, *Roghan-i Shifa*, *Marham Dākhi-lyūn*, *Dawa al-Misk*, *Qairūti Arad Kirsana*, *Zimad-i Khanāzīr*, *Habb-i Khubth al-Hadīd*, and *La'ūq Habb-ul-Sanobar* are some of the Unani compound formulations [27, 38, 49].

## 3. DESCRIPTION OF ḤULBA IN THE SCIENTIFIC LITERATURE

### 3.1. Synonyms

*Foenum-graecum officinale* var. *tibetanum* Alef. and *Trigonella tibetana* (Alef.) Vassilecz [50].

### 3.2. Botanical Description

*Ḥulba* (*Trigonella foenum-graecum* L.) is an annual plant of clade: Angiosperms; order: *Fabales* Bromhead; family: *Fabaceae* Juss., and genus: *Trigonella*, which completes its life cycle in one year [50]. *Trigonella foenum-graecum* L. is derived from the Latin *Trigonella* and *faenu-graecum*. The terms *trigonella* and *faenu-graecum* mean "small triangle" and "Greek hay," respectively. The flower of *Trigonella foenum-graecum* L. is triangle-shaped and pale yellow [25, 51].

### 3.3. Cultivation

*Ḥulba* is native to northern India, including Panjab, Kashmir, and Upper Gangetic plains extending through Asia and the Middle East, Africa Europe, North America, South America, and Oceania [52-54]. For the cultivation of *Ḥulba*, organic matter-rich, well-drained loamy soil is considered the best. The plant is best cultivated in June-July and Octo-

ber-November seasons with a cool and dry frost-free climate [55]. The field is prepared to a fine tilth and the seeds are sown at 20 X 15 cm space followed by the first irrigation. Further irrigations are given on the 3<sup>rd</sup> day and at 7 – 10 days intervals subsequently. After cultivation, care, including plant thinning, pinching, and weeding, is also necessary after 20 - 25 days of sowing [56].

### 3.4. Macroscopic Description

The plant is 30-60 cm tall. The leaves are pinnate and trifoliate, and stipules are not toothed, while the leaflets are 2-2.5 cm long, oblanceolate-oblong dentate. The flowers are white or yellowish-white in color, 1-2, axillary and sessile. The other features of the plant are as follows: calyx: teeth linear; corolla: much exerted, pods: 5-7.5 cm long, with a long persistent beak, often falcate, 10-20 seeded, without transverse reticulation; and seeds: green-brown, 2.5-5x2.0-3.5 mm long [19, 21].

### 3.5. Microscopic Description

#### 3.5.1. Transverse Section of Leaf

The leaf of *Hulba* has a unique dorsiventral transverse segment. The upper epidermis, mesophyll layer, and lower epidermis are visible in the lamina part. A single layer of tubular cells is present in the upper and lower epidermis. An adaxial palisade zone and an abaxial spongy parenchyma region divide the mesophyll tissue. Stomata interrupt the epidermis on both sides. The vascular stand of the midrib is tiny, simple, and collateral. The xylem pieces have thick walls, are angular, and are closely packed in a row. Underneath the xylem, the phloem forms a narrow arc [57].

#### 3.5.2. Transverse Section of the Petiole

The petiole does have a plano-convex form in the cross-section. The epidermis is a single layer of densely packed barrel-shaped cells that are shielded by the cuticle. Following the epidermis, a collenchymatous hypodermis with three to four layers is present. Ground tissue lies beneath the hypodermis and is composed of parenchymatous cells with no intercellular spaces. On either side of the main vascular bundle, the vascular bundles are smaller. The xylem is located on the upper side of the plant, whereas the phloem is located on the lower side [58].

#### 3.5.3. Transverse Section of Stem

Stomata and simple trichomes can be located on the surface of the plant. The stem has an uneven pattern in the cross-section view. 4-5 layers of the parenchymatous cortex follow the epidermis. The endodermis is a layer of tissue that lies beneath the cortex and separates it from the vascular tissues below it. A tiny phloem zone and a relatively large xylem zone form the vascular cylinder. The pith is parenchymatous and has a large width [58].

#### 3.5.4. Powder Microscopy

Microscopy reveals simple trichomes, stomata, leaf segments with vein islets, spiral, and pitted thickenings of the vessel [58].

### 3.6. Phytochemistry

#### 3.6.1. Chemical Constituents

The alkaloids [59], amino acids [60], saponins, steroids, sapogenin, flavonoids, lipids, fatty acids [25, 61, 62], and other important chemical constituents [59, 62] present in *Hulba* are illustrated in Figs. (1-3).

#### 3.6.2. Pharmacological Activities of *Hulba*

There is an abundance of scientific evidence regarding the pharmacological effects of *Hulba*. The majority of these effects are summarised in the sections below (Fig. 4).

### 3.7. Anti-diabetic Activity

*Hulba* is one of the oldest plants documented in the Unani and other traditional medical systems [4]. A huge number of preclinical studies are available concluding the antidiabetic effect of *Hulba* seeds powder, leaves extracts, etc., and its bioactive compounds, *trigonelline*, *diosgenin*, *4-hydroxy isoleucine*, *galactomannan*, and *quercetin*. These active ingredients have been shown to have hypoglycemic, hypolipidemic, insulinotropic, antioxidant, and anti-inflammatory properties. The inherent mechanism of action is potentiation of insulin secretion, increasing surface GLUT4 level in skeletal muscle cells *via* phosphatidylinositol-3- kinase-dependent pathway, insulin sensitivity restoration through IRS-1 function regulation, lipid modulation, and stimulation of lipolysis [63-65] (Fig. 5). Despite the fact that there are limited clinical researches on the anti-diabetic impact of *Hulba*, it is reasonable to conclude that *Hulba* has significant therapeutic potential for type 2 DM.

### 3.8. Antioxidant Activity

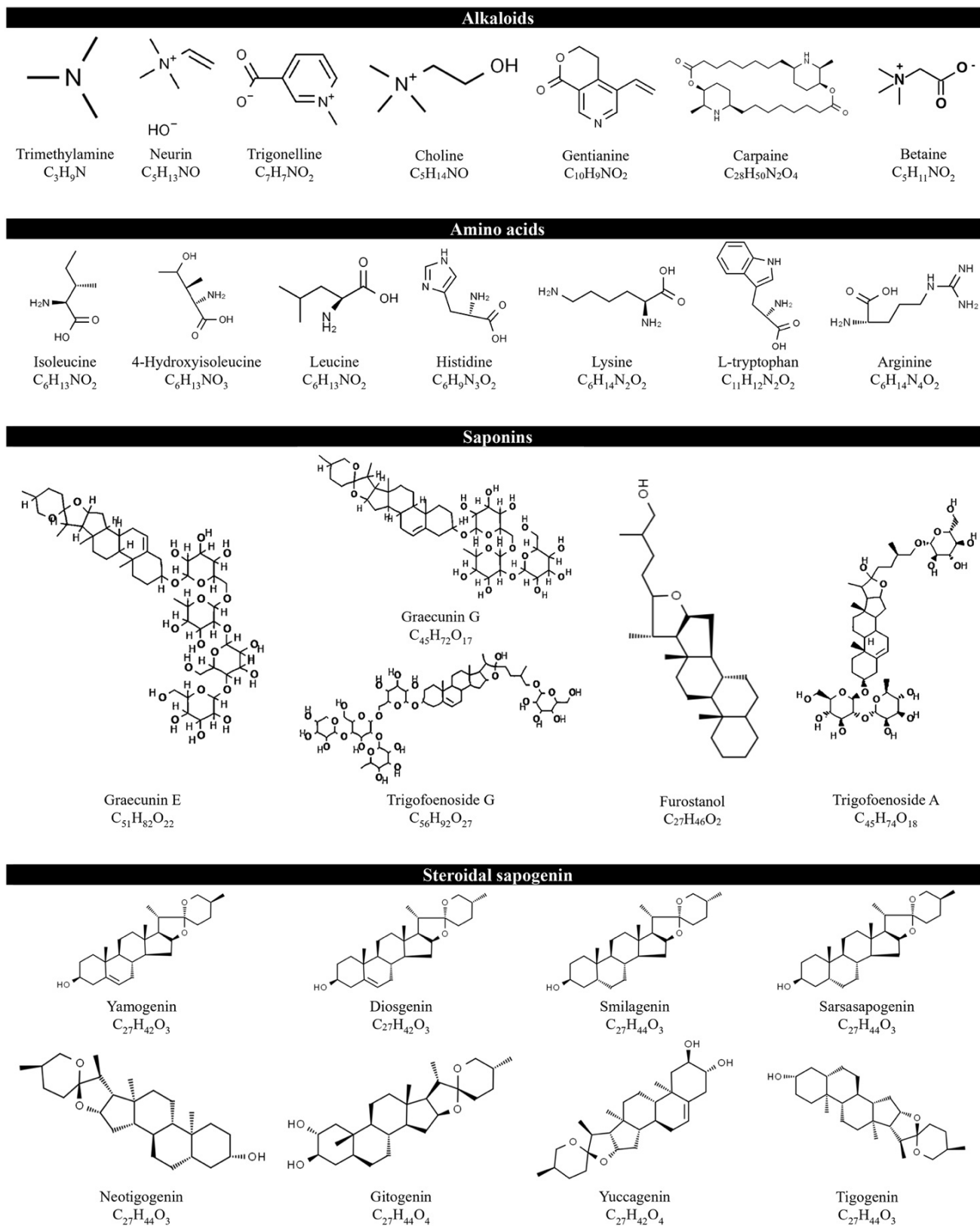
Researchers have attributed the antioxidant property of *Hulba* to its polyphenols and flavonoids. Many studies on aqueous and hexane extracts, 80% methanol extracts, ethyl acetate extracts, ethanol extracts, and dried extracts of *Hulba* seed in diverse animal models have revealed *Hulba* seed to exhibit high antioxidant activity (Fig. 6) [66-73].

### 3.9. Hypolipidemic Activity

Numerous preclinical and clinical studies have indicated the parts of *Hulba* to have hypolipidemic activity and to lower cholesterol and triglyceride levels, which has been attributed primarily to the saponins found in the seeds of *Hulba*. The underlying mechanism of action is considered as the lowering of cholesterol accumulation in the liver and rapid excretion, oxidative stress reduction, and lipid deposition reduction. The biochemical compounds, *diosgenin* and *4-hydroxy isoleucine*, have also been reported to exhibit lipid metabolism regulation in experimental studies [63, 64, 74].

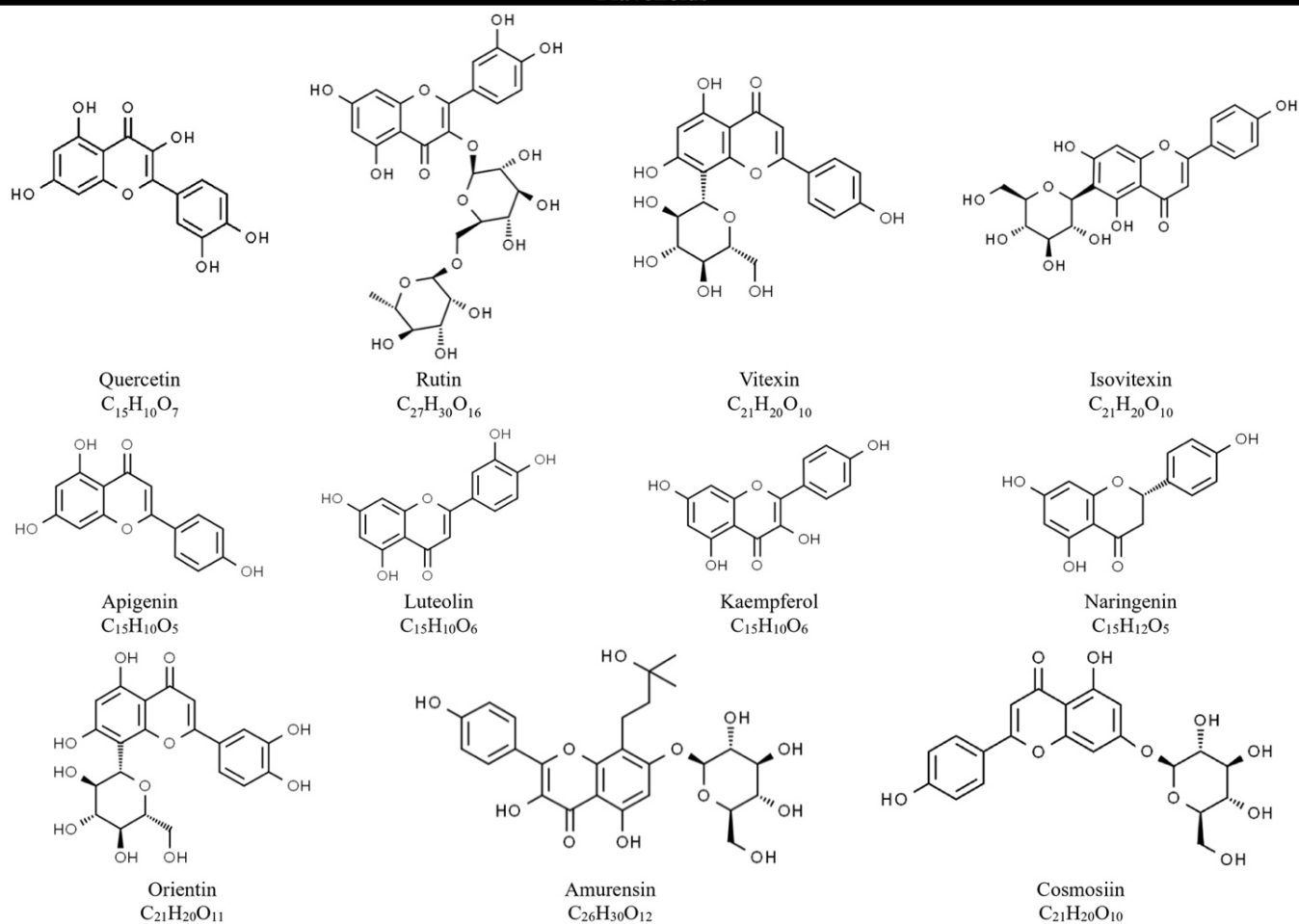
### 3.10. Anti-cancerous Activity

Several *in vitro* studies on crude extracts, aqueous extracts, methanol extracts, chloroform fractions of the methanol extract, ethanol extract of defatted *Hulba* seeds, alcoholic whole-plant extracts, and chloroform-based *Hulba* seed extracts have concluded anti-cancerous activities on breast,

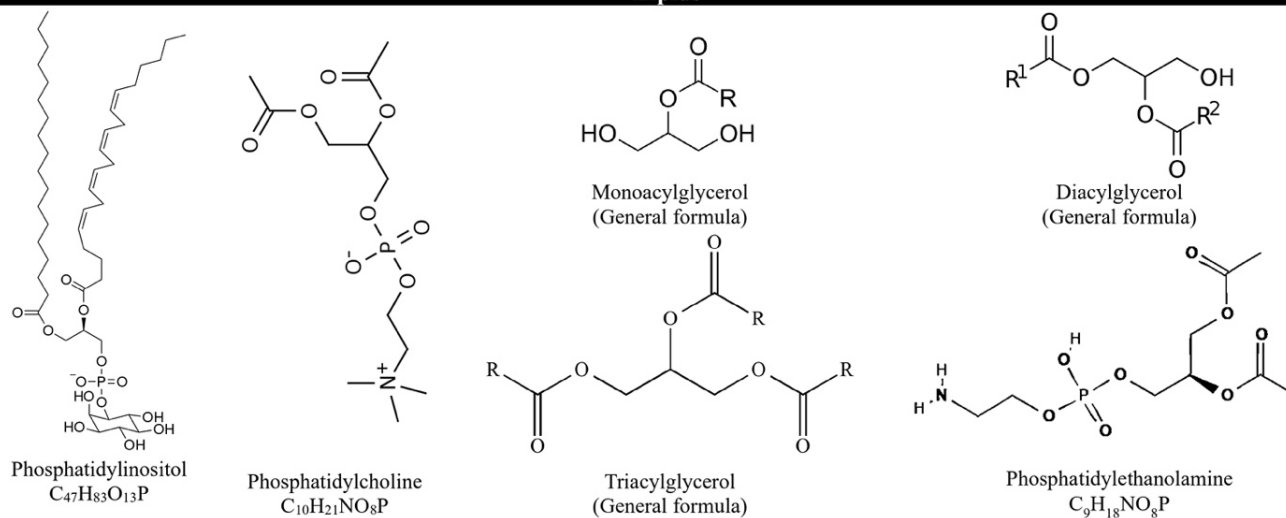


**Fig. (1).** The chemical structure and molecular formulae of alkaloids, amino acids, saponins, and steroidal saponin inherent in Hulba (chemical information and structures were taken from PubChem and ChemSpider).

### Flavonoids

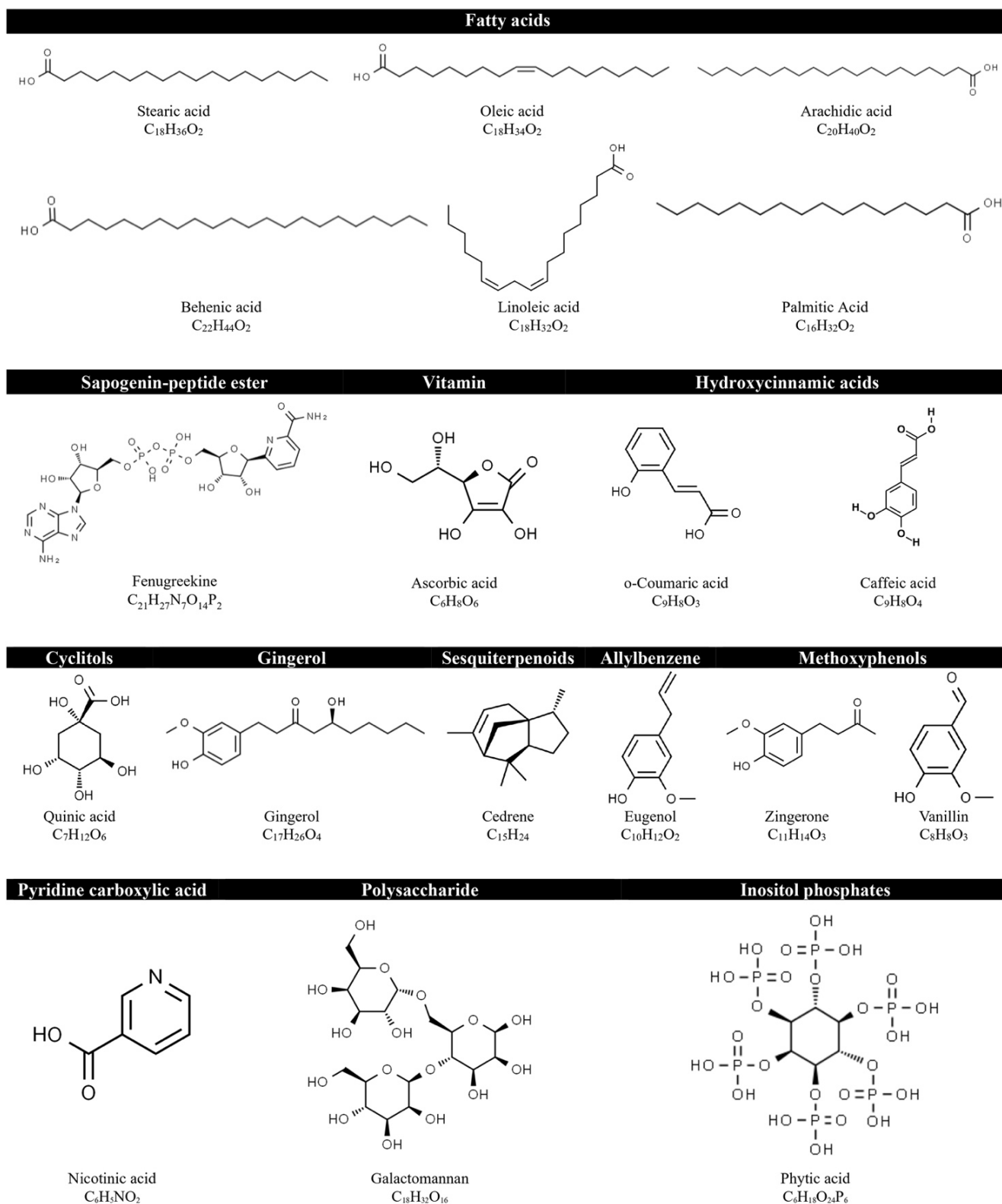


### Lipids



**Fig. (2).** The chemical structure and molecular formulae of flavonoids and lipids inherent in *Hulba* (chemical information and structures were taken from PubChem and ChemSpider).





**Fig. (3).** The chemical structure and molecular formulae of fatty acids, sapogenin-peptide ester, vitamin, hydroxycinnamic acids, cyclitols, gingerol sesquiterpenoids, allylbenzene, methoxyphenols, pyridine carboxylic acid, polysaccharide, and inositol phosphates inherent in Hulba (chemical information and structures were taken from PubChem and ChemSpider).

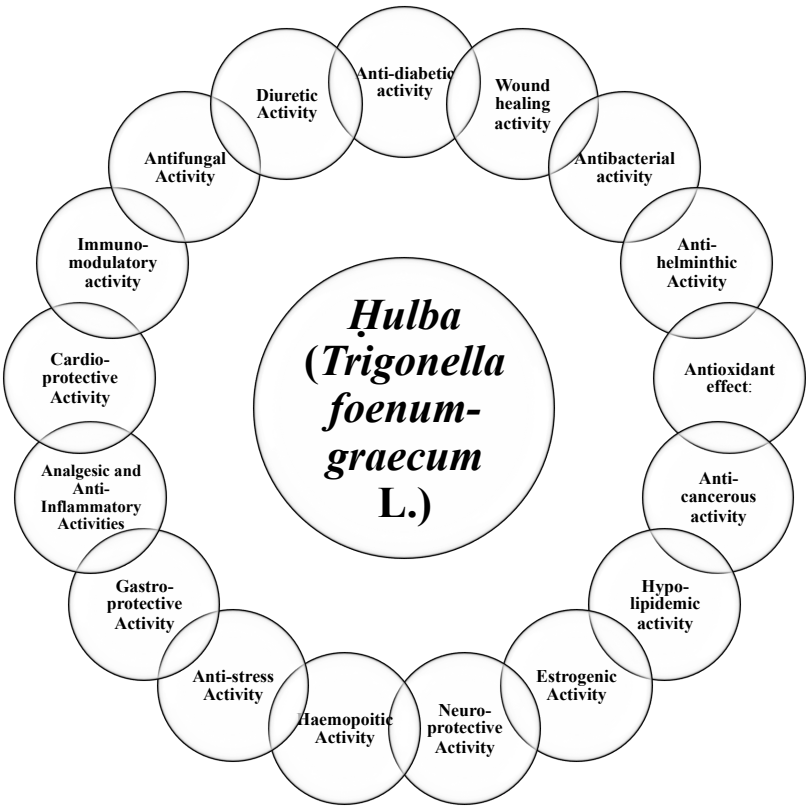


Fig. (4). Pharmacological activities of *Hulba* (*Trigonella foenum-graecum* L.).

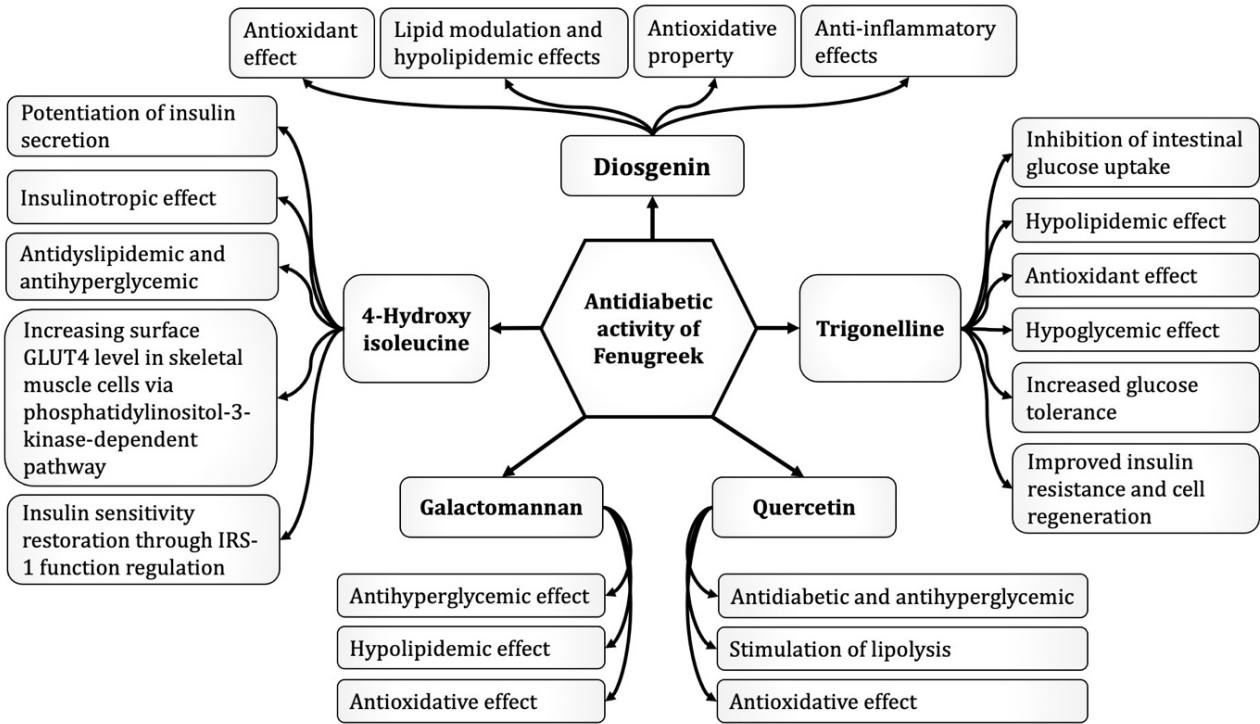


Fig. (5). Antidiabetic activity of bioactive constituents of *Hulba*.

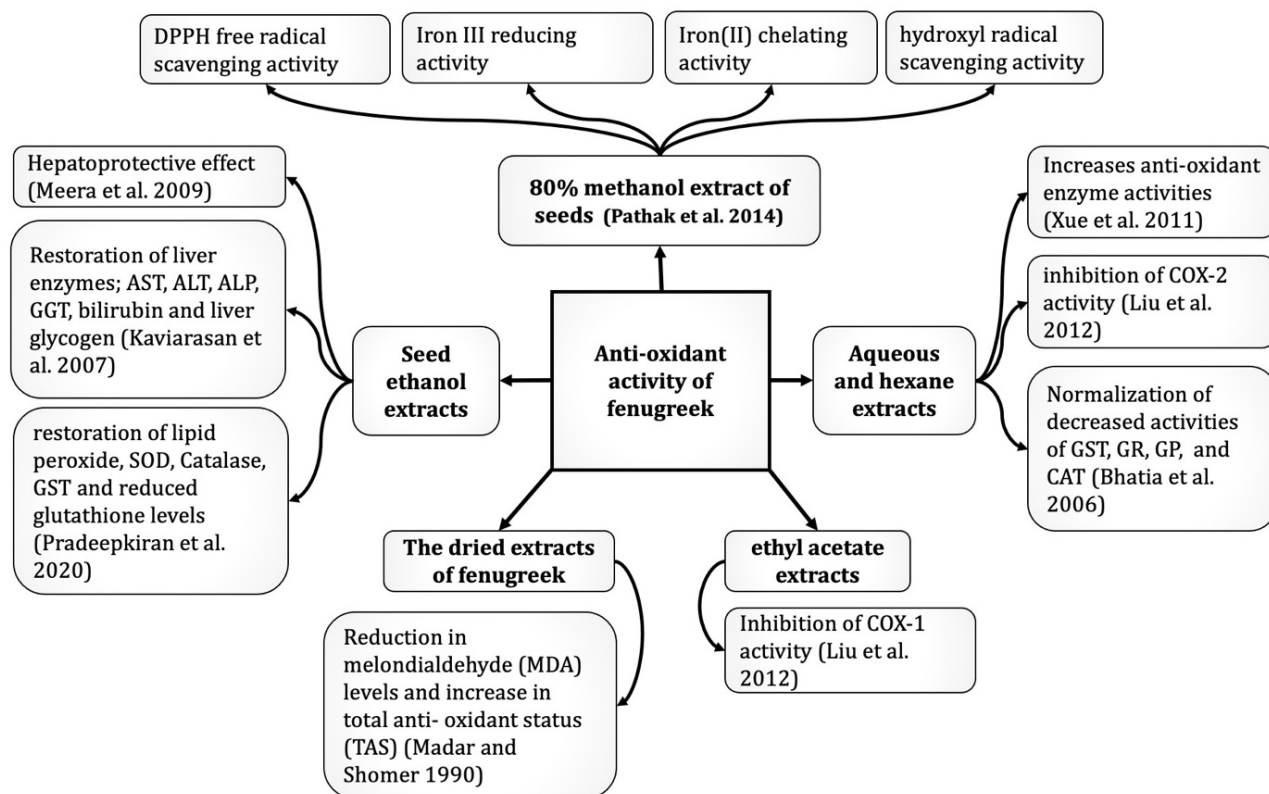


Fig. (6). Antioxidant activity of *Hulba* with the postulated mechanism of action.

liver, prostate, and colon cell lines. The reported mechanisms of action are increased apoptosis in cancer cell lines *via* caspase 3, 8, 9, p53 protein, Bax, PCNA, Fas, and FADD expression, inhibition of NF- $\kappa$ B and Akt, downregulation of c-Src, JAK1, and JAK2, and increased GPx, GST, SOD, and catalase activities in the liver [64, 75].

### 3.11. Antimicrobial Activity

Multiple research studies have demonstrated *Hulba* extract to have antimicrobial activity against *Helicobacter pylori* [76-78]. It is tested for its antimicrobial activity against a wide range of microorganisms, such as bacteria, viruses, and fungi [79-82].

### 3.12. Antifungal Activity

Multiple *Hulba* plant components were studied for antifungal activity by Haouala *et al.*, who discovered significant antifungal activity against *Pythium aphanidermatum*, *Botrytis cinerea*, *Alternaria* sp., *Fusarium graminearum*, and *Rhizoctinia solani* [83].

Montagner *et al.* reported the antifungal activity of coumarin, a biochemical compound found in *Hulba* [84]. Dharajiya *et al.* concluded the potent antifungal activity of methanol and ethyl acetate extracts of *Hulba* leaves against *Trichoderma viridae* [85].

### 3.13. Immunomodulatory Activity

Rehman *et al.* evaluated the modulatory effect of aqueous extracts of Fenugreek seeds in mice immunosuppressed by deltamethrin. There was a significant ( $p < 0.01$ ) increase in

plaque-forming cells and quantitative hemolysis of SRBC [86].

Male Swiss albino mice were given three doses (50, 100, and 250 mg/kg body weight per os) of an aqueous extract of *Hulba* seeds over a ten-day period. The dose of 100 mg/kg resulted in a significant increase in humoral immunity, but no significant increase in lymphoid organ cellularity at any dose [87]. Ramadan *et al.* demonstrated Egyptian *Hulba* seed powder to have a significant immunomodulatory effect on rats treated with cyclophosphamide [88].

### 3.14. Cardio-protective Activity

Murugesan *et al.* discovered that *Hulba* seeds suspension (made in 0.5 percent carboxymethyl cellulose) can prevent male albino Wistar rats from isoproterenol-induced myocardial infarction. The medication significantly decreased the levels of reactive thiobarbituric acid compounds in an animal model and increased the activity of both enzymatic and non-enzymatic antioxidants [89].

### 3.15. Analgesic and Antipyretic Activities

Many studies on *Hulba* leaf and seed extracts have demonstrated significant peripheral and central analgesic activity in hot plate-induced pain, acetic acid writhing, sciatic nerve partial ligation-induced neuropathic pain, and sciatic nerve crush injury-induced pain in rats and mice [64]. Additionally, one study proposed that the central antinociceptive activity of leaf extracts is mediated by the serotonergic system [90]. Along with analgesic activity, sprouts of *Hulba* seeds have been found to have antipyretic activity in mice

subjected to Brewer's yeast-induced pyrexia [91]. The studies have also suggested the anti-nociceptive activity due to the anti-inflammatory effects of *Hulba*, which has been attributed to flavonoids present in them [92].

### 3.16. Anti-inflammatory Activity

Numerous studies on animal models using alcohol extracts, aqueous extracts, ethanol extracts, petroleum ether extracts, and pure mucilage from ether extracts of *Hulba* have demonstrated potent anti-inflammatory activity. The activity has been reported to be induced by inhibiting COX2, suppressing TNF-, IL-1, IL-2, and IL-6 levels, and by lowering serum SGOT, SGPT, CRP, nitrites, MPO, PBMN, and 5-LOX levels [64].

### 3.17. Gastro-protective Activity

Pandian *et al.* demonstrated the soluble gel fraction of *Hulba* seeds to have anti-ulcer activity in rats with ethanol-induced gastric ulcers. They also reported that the fraction has prevented lesion formation more effectively than omeprazole. The water-soluble mucilage and flavonoid/phenolic glycosides in *Hulba* are thought to be responsible for its gastroprotective properties [93]. Kheirandish *et al.* discovered that an aqueous extract of *Hulba* seeds prevented the development of reflux esophagitis in male albino Wistar rats [94].

### 3.18. Anthelmintic Activity

Khadse *et al.* discovered crude extracts of *Hulba* seeds to have *in vitro* anthelmintic activity against *Pheritima posthuma* [95]. Buchineni *et al.* found the significant anthelmintic activity of aqueous extracts of *Hulba* leaves against Indian earthworms; however, in comparison to albendazole, the activity of *Hulba* leaves extracts was lesser [96].

### 3.19. Diuretic Activity

Al-Atwi found a significant increase in urine, sodium, potassium, and chloride excretion in the animal model (male albino rabbit) after administration of *Hulba* extract [97]. Rohini *et al.* found promising diuretic effect of aqueous and benzene extracts of *Hulba* seed in the male Wistar rat model [98]. In contrast, Nawasany *et al.* discovered the methanol extract of *Hulba* to be ineffective as a diuretic in patients with cirrhotic ascites, but it was found to be safe and well tolerated [99].

### 3.20. Anti-stress Activity

Pawar and Hugar investigated the anti-stress activity of the methanolic extract of *Hulba seeds* against anoxia and immobilization stress models. The authors had taken *Withania somnifera* as a reference standard for this study [100].

### 3.21. Estrogenic Activity

Sreeja *et al.* investigated the *in vitro* estrogenic effects of chloroform extracts of *Hulba* seeds in MCF-7 human breast cancer cells. The study's findings revealed that estrogen receptor binding stimulated MCF-7 cell growth. The extracts also acted as an agonist for estrogen receptor-mediated tran-

scription *via* estrogen receptor elements. Ultimately, the study concluded the estrogenic activities of *Hulba* seeds [101].

### 3.22. Hemopoietic Activity

Doshi *et al.* evaluated the efficacy of *Hulba* on hemoglobin levels in females 20-22 years of age in an RCT. The study postulated the hemopoietic activity of *Hulba* by its restorative and nutritive properties [102].

### 3.23. Neuroprotective Activity

The effect of *Hulba* seed extract treatment on the function of the sciatic nerves of neuropathic mice was examined. The results indicated that pyridoxine intoxication caused neuropathy in mice. The animals were then given 0.2, 2, and 20 mg/kg of hydro-alcoholic extract of *Hulba* seeds, which exhibited an anti-neuropathic effect and restored nerve fibre function. Furthermore, electrophysiological recordings revealed that animals treated with 20 mg/kg extracts healed the fastest [103]. Gaur *et al.* conducted another investigation in animal models of Parkinson's disease to identify and assess standardized hydroalcoholic extracts of *Hulba* seeds. The study found *Hulba*'s neuroprotective effects to be responsible for the reversal of motor symptoms in animal models of Parkinson's disease [104].

### 3.24. Wound Healing Activity

Sumitra *et al.* discovered that an aqueous suspension of *Hulba* seeds can help heal wounds. In rat wound models, the suspension greatly increased collagen maturation [105]. Taranalli and Kuppast found the aqueous suspension and *Hulba* seed extracts to have wound-healing properties [106].

## CONCLUSION

This review has explored *Hulba* in traditional Unani medicine and presented scientific reports. Based on the information gathered from multiple sources, it can be ascertained that *Hulba* is a medicinal plant that has been used as a herbal remedy in many traditional medical systems for centuries. It has a long history of use in both culinary and medicinal applications for the prevention and treatment of a variety of diseases through its anti-inflammatory, antioxidant, hepatoprotective, cardioprotective, neuroprotective, nephroprotective, immunomodulatory, and antimicrobial properties. A large amount of pharmacological research has been published in reputable journals to support these activities. Clinical trial data on *Hulba*, on the other hand, are scant in comparison to preclinical evidence. As a result, well-designed clinical trials are required to back up the claims. Moreover, there is a wealth of research on *Hulba* and its pharmacological properties, but there remains a notable dearth of comprehensive chemical analyses of its constituents. To bridge this gap in knowledge, it would be beneficial to conduct a thorough examination of each chemical constituent of *Hulba* through a comprehensive study that incorporates *in vitro*, *in vivo*, *in silico*, and clinical research. Such an approach would allow for a more complete understanding of the individual compounds that make up *Hulba* and their potential biological activities. Moreover, future research on *Trigonella foenum-graecum* L. should focus on the merging

of Unani and contemporary principles. Furthermore, pharmacological and clinical investigations on the tested prescriptions proposed by Unani academics appear to be necessary to determine efficacy and safety using recognized scientific parameters.

## LIST OF ABBREVIATIONS

COX	=	Cyclooxygenase
CRP	=	C-Reactive Protein
DM	=	Diabetes Mellitus
DOAJ	=	The Directory of Open Access Journals
FADD	=	Fas-Associated Protein with Death Domain
GLUT4	=	Glucose Transporter Type 4
GPx	=	Glutathione Peroxidase
GST	=	Glutathione S-Transferase
IL	=	Interleukin
IRS-1	=	Insulin Receptor Substrate-1
JAK	=	Janus Kinase
LOX	=	Lipoxygenase
MPO	=	Myeloperoxidase
NFκB	=	Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B-Cell
PBMN	=	Peripheral Blood Mononuclear Cells
PCNA	=	Proliferating-Cell Nuclear Antigen
RCT	=	Randomized Control Trial
SGOT	=	Serum Glutamic Oxaloacetic Transaminase
SGPT	=	Serum Glutamic Pyruvic Transaminase
SOD	=	Superoxide Dismutase
TNF	=	Tumor Necrosis Factor
USM	=	Unani System of Medicine.

## CONSENT FOR PUBLICATION

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## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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