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Review Article

A Systematic Review of Barley (*Hordeum vulgare* Linn.) in Unani Medicine with Recent Advances

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Abstract

Objective: The present review article focuses on exploring the wide dimensions of barley including botanical description, nutritional composition, phytochemistry, experimental pharmacology, and clinical studies along with its traditional uses in Unani medicine.

Background: Barley (*Hordeum vulgare* L.) which is referred to as 'Jao' in the Unani system of medicine has a long history of utilization as a food and medicine. It belongs to family *Poaceae* and is considered as one of the founder crops of old-world agriculture.

Methodology: A manual literature survey of classical Unani texts was conducted to collect the information available on 'Jao'. Besides, a comprehensive search of electronic databases like PubMed, Google Scholar, and Science Direct, was carried out to collect all the available information regarding its phytochemical, pharmacological and clinical studies.

Result: In Unani medicine, barley is an important drug commonly used in many disorders of the respiratory system, gastrointestinal system, musculoskeletal system, skin, etc. It is used to treat obesity, diabetes, headache, pain and inflammation of the throat, acute swelling of joints and gout, chronic swellings, diarrhoea, fever, skin eruptions, hyperpigmentation of the skin, etc. Recent studies revealed that barley constitutes beta-glucan and a myriad of bioactive compounds that play numerous biological activities such as hypoglycemic, hypocholesterolemic, anti-inflammatory, antioxidant, anti-obesity, anticancer, and wound healing activities.

Conclusion: Barley is a potent drug that exhibits a wide range of health benefits, most of which have been confirmed via preclinical and clinical studies. This review may thus be helpful for the research community as well as common people to avail the benefits of this drug.

Keywords: Barley, Beta-glucan, *Hordeum vulgare*, *Jao*, Unani medicine

Introduction

Barley (*Hordeum vulgare* L.) which belongs to the genus *Hordeum* and family *Poaceae* is considered as one of the founder crops of old-world agriculture. The evolution of human civilization, agronomy, genetics and plant breeding all benefited from the cultivation of barley.¹ According to archaeological findings, barley was first domesticated in the Fertile Crescent about 10,000 years ago from its wild relative *Hordeum spontaneum*.^{2,3} Since then, it has been moulded by the hands of many cultures and has been carried to different parts of the world. It is the fourth most significant crop around the world cultivated in more than 100 countries to obtain its grain.⁴ The global production of barley in the crop year 2022/2023 amounted to about 151.62 million metric tons, increasing from around 145.37 million metric tons in 2021/2022.⁵ In India, barley occupied an average of 574-thousand-hectare area with 1,632 thousand tons production during the last 5 years from 2018-2023.⁶

Barley is a resilient crop that can thrive in a variety of conditions than any other cereal, including extremes of latitude, longitude and high altitude.⁷ Barley has an extensive distribution around the globe and occupies a wide range of ecologic niches. The Russian Federation, Australia, France, Germany, and Ukraine are the leading barley-producing countries in the world.⁸ In India, it is cultivated in the plains as well as in the hilly regions of the Himalayas, up to an elevation of around 4000 meters.⁹ The chief barley-growing states are Rajasthan, Bihar, Uttar Pradesh, Madhya Pradesh, Haryana, Punjab, Uttarakhand, Himachal Pradesh and Jammu and Kashmir.^{10,11,12} Barley has been extensively utilized for a variety of purposes including forage, malting, brewing, food and medicine.

Materials and Methods

A manual literature survey of classical Unani texts was conducted to collect the information available on 'Jao'.

Important textbooks of Unani medicine including *Al-Qanoon fit Tib* of Ibn Sina (980–1037 AD), *Al Jamai ul Mufradat Al Advia Wal Aghzia* of Ibn al Baitar (1197–1248 AD), *Muheet-e-Azam* of Hakeem Azam Khan (1806–1902 AD), *Khazainul Advia* of Najmul Ghani (19th century), *Kitab al-Mansoori* of Zakariya Razi (865–925 AD), *Kitab al-Mukhtar fit Tib* of Ibn Hubal Baghdadi (1121–1213 AD) etc., were reviewed. ‘Standard Unani Medical Terminology’ published by the Central Council for Research in Unani Medicine in collaboration with the World Health Organization was used to describe the appropriate Unani terminologies. Besides, a comprehensive search of electronic databases like PubMed, Google Scholar, and Science Direct, was carried out to collect all the available information regarding its general description, nutritional composition, phytochemistry, and pharmacological and clinical studies. Indian Medicinal Plants, Medicinal Plants of the World, Wealth of India, Unani Pharmacopoeia of India and different indexed journals were consulted for botanical description. The taxonomical classification was validated through the ‘United States Department of Agriculture’ (<http://www.plants.usda.gov>). The keywords used were ‘Unani Medicine’, ‘*Hordeum vulgare*’, ‘Jao’, ‘Barley’, ‘in vitro study’, ‘in vivo study’, ‘clinical trial’, ‘study on barley’, ‘phytochemistry of barley’, and ‘nutritional composition of barley’.

Result and Discussion

Taxonomical Classification¹³

Kingdom – *Plantae*

Subkingdom – *Tracheobionta*

Division – *Magnoliophyta*

Superdivision – *Spermatophyta*

Class – *Liliopsida*

Subclass – *Commelinidae*

Order – *Cyperales*

Family – *Poaceae*

Genus – *Hordeum* L.

Species – *Hordeum vulgare* L.

Botanical Description

1. Macroscopic Description

Hordeum vulgare L. is an annual, erect, stout and tufted herb, reaching a height of about 50-100 cm.^{9,14,15}

Roots - Roots are fibrous, 0.5 to 0.1 cm thick, cylindrical in shape, glabrous and greyish brown in color.¹⁶

Stem - The stem is cylindrical, 0.4 to 0.6 cm in thickness, slightly flattened and smooth.¹⁶ It consists of five to seven hollow internodes separated by solid nodes, from which the leaves arise.^{10,17}

Leaves - These are few, linear-lanceolate in shape, about 15-25 cm in length and yellowish grey in color.^{9,16} Although, the shape and size of leaves vary with variety, growing conditions, and position of the plant.¹⁷

Spike - The apex of the stem gives rise to a spike that holds the flowers and later the mature seed. Spike is terminal, linear-oblong, compressed, 5-6 cm long and heavily flowered. It consists of spikelets that are sessile and arranged in three on both sides of a flattened rachis. All spikelets are fertile in six-row type, while lateral ones are barren and occasionally rudimentary and only the central spikelet develops a seed in two-row type.⁹

Fruit - The fruit is caryopsis, elliptic, short pointed, grooved on the inner surface, smooth and free or adherent to lemma and palea.⁹ It is about 1 cm in length and 0.2-0.3 cm in width. It is dorsally compressed and flattened on the sides with a shallow longitudinal furrow. It is pale-greenish-yellow in color, sweetish-acrid in taste with no distinct odour.^{15,18}

2. Microscopic description

Root - Features include a single-layered epidermis that is covered by a striated cuticle. The cortex is made up of four to six layers of round to polygonal, thin-walled, parenchymatous cells with intercellular spaces. The vascular bundles are arranged in a discontinuous ring with the usual elements in each. Pith is very wide consisting of round to polygonal, thin-walled, parenchymatous cells with intercellular spaces.¹⁶

Stem - The stem displays a single-layered epidermis with a thick cuticle covering it. The hypodermis consists of five to six layered, round to polygonal, lignified, sclerenchymatous cells. The ground tissue is composed of five to seven-layered, round to polygonal, thin-walled, parenchymatous cells with intercellular spaces. The vascular bundles made up of typical elements are found scattered throughout the ground tissues.¹⁶

Leaf - It shows a single-layered epidermis that is covered by a thick cuticle on either surface. Few big or bulliform cells are present in the upper and lower epidermis. The vascular bundles are conjoint, collateral, and closed and each is covered by a bundle sheath. Paracytic stomata are found on both surfaces with stomatal numbers 9 to 17 per square mm on the lower surface and 5 to 8 per square mm on the upper surface. The stomatal index is 15 to 23 on the lower surface and 9 to 15 on the upper surface.¹⁶

Fruit - It has a single layer of epidermis with cells that are crescent-shaped, round to oval, and have wavy walls. This is followed by 2-3 layers of thick-walled sclerenchymatous fibers. Beneath the sclerenchyma are present irregular, square, or quadrilateral, spongy parenchymatous cells, with a few cell walls containing silica bodies through which the fibro-vascular bundles of the ribs run. More or less polygonal inner epidermal cells are next, with a few inner epidermal cells having unicellular claw-shaped hair and stomata. The pericarp is made up of cells with more or less compressed parenchymatous cells. The seed coat appears as a colorless line, the perisperm is composed of cells with somewhat wavy walls having narrow lumens. The endosperm is separated into two zones, containing 2-4 cells deep aleurone layers, and the remaining starch layers.^{15,18}

Description in Unani Classical Literature

In the Unani system of medicine, barley is referred to as 'Jao'- a Persian word. Two types of barley grains are mentioned in Unani literature, one is elongated with a thick outer hull while the other is shorter in length having a thin outer hull.¹⁹ Unani scholars mentioned certain characteristics of high-quality barley such as it should be ripe, receive a lot of rain, free from putrefaction, white in color, large in size and heavy in weight. It should not be unduly fresh or old. According to some scholars, fresh barley is superior since it gets bad or smells bad after a year.^{20,21,22} Barley and its various formulations including *Ma'ul Shaeer* (Barley water), *Ma'ul Shaeer Mohammas*, *Ma'ul Shaeer Mulham*, *Kashkush Shaeer* as well as its *Sattu* (flour of roasted barley grains) and *Roti* (Bread) are well described in Unani literature along with their health benefits, pharmacological actions and therapeutic indications in various ailments.

Therapeutic actions ^{15,19,20,22,23,24,25,26,27,28,29}

- *Jali* (Detergent)
- *Qabiz* (Astringent)
- *Mujaffif* (Desiccant)
- *Munziz* (Concoctive)
- *Ra'de* (Repellent)
- *Dafa-e-Humma* (Antipyretic)
- *Musakkin-e-Atash* (Thirst quencher)
- *Dafa-e-Su'al* (Antitussive)
- *Musakkin hiddat Dam wa Safra* (Blood and yellow bile calming agent)
- *Muwalid-e-Dam* (Hemopoietic)
- *Mudir-e-Baul* (Diuretic)
- *Munaqqi Gurda wa Masana* (Kidney and urinary bladder cleanser)
- *Mughazzi* (Nutritive)
- *Muhallil* (Resolvent)
- *Musakkin Alam* (Analgesic)
- *Muhazzil* (Antiobesity)

Therapeutic Uses

Table 1: Therapeutic Uses of Barley in Unani Medicine

Therapeutic uses	Formulation	Method of preparation and mode of application	Ref
<i>Suda</i> (Headache)	<i>Jao sattu</i> (Roasted barley flour) and <i>Aabe Pudina</i> (<i>Mentha arvensis</i> juice).	Both ingredients are mixed and applied on the forehead as a paste to relieve pain.	30
<i>Sahr</i> (Insomnia)	<i>Barge Bed</i> (<i>Salix caprea</i> leaf-12 gm), <i>Arade Jao</i> (Barley flour-56 gm), <i>Gule Khatmi</i> (<i>Althaea officinalis</i> flower), <i>Mako</i> (<i>Solanum nigrum</i>) each 10.5 gm, <i>Gule Banafsha</i> (<i>Viola odorata</i> flower) and <i>Gule Neelofar</i> (<i>Nymphaea alba</i> flower) each 7 gm.	All drugs are boiled in water and filtered to obtain a decoction. This decoction is used for footbath (<i>pashoya</i>).	31
<i>Ashobe Chashm</i> (Conjunctivitis)	<i>Behidana</i> (<i>Pyrus Cydonia</i> - 20 pieces), <i>Jao</i> (<i>Hordeum vulgare</i> - 20 grains), <i>Kishneez</i> (<i>Coriandrum sativum</i> - 10 pieces) and <i>Anzarut</i> (<i>Astragalus sarcocolla</i> - 35 gm).	All the drugs are boiled in water and the filtered liquid is used as eye drops (<i>qutoor</i>).	32
<i>Zufra</i> (Pterygium)	<i>Jao</i> (<i>Hordeum vulgare</i>) and <i>Zoofa</i> (<i>Hyssopus officinalis</i>).	Both the drugs are boiled in water to make a decoction. Hot fomentation is done on the affected eye with this decoction.	33
<i>Warme Halaq</i> (Pharyngitis)	Barley	Barley is crushed in water and the resulting milky water is used for gargling.	28
<i>Zaatul Janb</i> (Pleurisy)	<i>Gule Banafsha</i> (<i>Viola odorata</i> flower), <i>Gule Neelofa</i> (<i>Nymphaea alba</i> flower), <i>Babuna</i> (<i>Matricaria chamomilla</i>), <i>Nakhuna</i> (<i>Trigonella glabra</i>), <i>Tukhme Khatmi</i> (<i>Althaea officinalis</i> seed), <i>Gule Khatmi</i> (<i>Althaea officinalis</i> flower), <i>Jao muqashshar</i> (Dehusked barley) and <i>Khashkhash</i> (<i>Papaver somniferum</i>).	All drugs are boiled in water and the liquid is filtered. <i>Raughan Banafsha</i> (<i>Viola odorata</i> oil) is added to the filtrate and boiled again. When only oil is left, <i>Mom safaid</i> (Beeswax), <i>Safaidda Kashghari</i> (Zinc oxide) and <i>Kateera</i> (Gum Tragacanth) are added and the preparation is applied locally on the chest.	31
<i>Ishal</i> (Diarrhoea)	<i>Jao Sattu</i> (Roasted barley flour- 140 gm), <i>Tabasheer</i> (<i>Bambusa arundinacea</i> -10.5 gm) and <i>Samaghe Arabi</i> (<i>Acacia arabica</i> -10.5 gm).	Roasted barley flour is dissolved in a large quantity of water and boiled to make it slightly viscous. Then, it is filtered and the rest of the two drugs are added to it.	29

<i>Wajaul Meda</i> (Gastralgia)	<i>Arade Jao</i> (Barley flour) and <i>Arq Gulab</i> (<i>Rosa damascena</i> distillate).	Both the ingredients are mixed and applied locally to the site of pain.	34
<i>Hirqatul Meda</i> (Hyperacidity)	<i>Arade Jao</i> (Barley flour) and <i>chhachh</i> (Buttermilk).	Barley flour is mixed with sour buttermilk and kept overnight. The next morning, decanted water (<i>zulal</i>) is consumed.	19
<i>Warme Kabid</i> (Hepatitis)	<i>Tukhme Katan</i> (<i>Linum usitatissimum</i> seed), <i>Arade Jao</i> (Barley flour) and <i>Khajoor</i> (<i>Phoenix dactylifera</i>).	All drugs are mixed and applied as a paste (<i>zimad</i>) at the site of the liver.	35
<i>Salabate Tihal</i> (Chronic splenitis)	<i>Arade Jao</i> (Barley flour) and <i>Usarae Sudab</i> (<i>Ruta graveolens</i> extract).	Barley flour is mixed with <i>Ruta graveolens</i> extract and the preparation is locally applied.	35
<i>Nafakh</i> (Flatulence)	<i>Arade Jao</i> (Barley flour) and <i>Khardal</i> (<i>Brassica nigra</i>).	Both the ingredients are mixed well and applied to the abdomen to resolve flatulence.	20
	Barley husk	Hot fomentation with the husk of barley helps to relieve pain due to flatulence.	19
<i>Zaheer</i> (Dysentery)	<i>Ma'ul Shaeer</i> (Barley water) and <i>Arqe Mako</i> (<i>Solanum nigrum</i> distillate).	Both ingredients are mixed and used as an enema.	32
<i>Niqris</i> (Gout)	<i>Masoor</i> (Red lentil), <i>Sirka</i> (Vinegar) and <i>Arade Jao</i> (Barley flour).	Red lentil is cooked in vinegar and then barley flour is added. The preparation is mixed well to make a paste and applied at the site of pain.	36
<i>Wajaul Mafasil</i> (Arthritis)	<i>Tukhme Sambhalu</i> (<i>Vitex nugundo</i> seed), <i>Arade Jao</i> (Barley flour), <i>Bura Armani</i> (<i>Bole armenia</i>) and <i>Mom</i> (Beeswax).	All drugs are mixed to be applied locally as a paste.	36
<i>Kalaf</i> (Melasma)	<i>Arade Jao</i> (Barley flour), <i>Nashasta</i> (Starch), <i>Arade Nakhud</i> (Gram flour), <i>Kateera</i> (Gum tragacanth), <i>Baqila</i> (<i>Vicia faba</i>), <i>Zeera Siyah</i> (<i>Carum carvi</i>), <i>Post Bakayin</i> (<i>Melia azedarach</i> peel), <i>Badam</i> (<i>Prunus amygdalus</i>), each 10 gm and <i>Zafran</i> (<i>Crocus sativus</i>) 1 gm.	All the drugs are powdered. A small quantity of this powder is mixed with raw milk and applied to the face at night. After 3 hours, the face is washed with soap and lukewarm water and then, coconut oil is applied.	26
<i>Bafa</i> (Dandruff)	<i>Arade Nakhood</i> (Gram flour), <i>Arade Baqla</i> (<i>Vicia faba</i> flour), each 12 gm, <i>Aashe Jao</i> (Barley water) and <i>Luabe Hulba</i> (<i>Trigonella foenum-graecum</i> mucilage).	All drugs are mixed in <i>Aashe Jao</i> and <i>Luabe Hulba</i> and applied locally.	37
<i>Harq</i> (Burn)	Barley flour and water.	Barley flour is mixed with water to make a paste to be applied locally at the affected site.	38
<i>Salq</i> (Scald)	Barley ash and egg yolk.	Ash of Barley is mixed with egg yolk and applied to the affected part.	39
<i>Hummae muzmin</i> (Chronic fever)	Barley bread	Hot fresh barley bread is broken into pieces and put in a pot filled with water. Then, this pot is buried in the soil for one week. After one week, the pot is removed and the clean water is used in a dose of 24-60 ml with an equal quantity of <i>Arq Gaozaban</i> (<i>Borago officinalis</i> distillate).	19
<i>Daad</i> (Ringworm)	<i>Raughan Jao</i> (<i>Hordeum vulgare</i> oil) and <i>Raughan Gandum</i> (<i>Triticum aestivum</i> oil).	Applied locally to the affected part.	31
<i>Ziabetus</i> (Diabetes mellitus)	Barley water	Barley is boiled in water to make a thick liquid preparation which is consumed orally.	39

Temperament: Different scholars proposed different temperaments of barley. It is cold and dry in first-degree, cold in first and dry in second-degree, cold in second and dry in first-degree, and cold and moist in first-degree.^{19,20,21,22,23,24,26,27,28,40}

Taste: Barley has a vapid mucilaginous taste.^{25,26,27}

Dose: The dose of barley grains is 25-50 gm.¹⁵

Adverse effects: According to Unani physicians, barley is harmful to persons of cold temperament and colitis patients. It produces tenesmus and flatulence, weakens the stomach and intestine, and makes the body feeble on prolonged use. It is harmful to the urinary bladder.^{19,20,21,22,23,25,27,29,33,40}

Correctives

In order to minimize the adverse effects of a drug, another drug in the form of a corrective agent is either admixed or used concomitantly with the first drug. Therefore, *Mastagi* (*Pistacia lentiscus*) and sugar can be used as correctives for the weakness of the stomach and intestine. To avoid the adverse effects of barley on the body and urinary bladder, *raughaniyat* (oils), *ghee* (clarified butter), *makhan* (butter) and *anisoon* (*Pimpinella anisum*) are used.^{19,20,25}

Substitute

Unani scholars have suggested two substitutes for barley namely *Jowar* (*Sorghum vulgare*) and *Moong* (*Vigna radiata*).^{19,20}

Nutritional Composition of Barley Grain

Carbohydrates and Dietary fibers

Carbohydrates account for the majority of the composition of barley grains, generally about 78%–83% of total dry weight.⁴¹ The total dietary fiber content of whole grain barley ranges from 11 to 34%, soluble dietary fiber from 3 to 20% and insoluble dietary fiber from 8-14%.^{42,43} Carbohydrates are primarily categorized into low molecular weight carbohydrates, non-structural polysaccharides and cell wall polysaccharides. Non-structural polysaccharides include starch, whereas cell wall polysaccharides encompass cellulose, β -glucan and arabinoxylans (AXs).⁴¹

β -Glucan, nutritionally classified as a dietary fiber is the most abundant polysaccharide in the cell wall of barley grain.^{44,45} It is primarily distributed in the endospermic cell wall, while a small amount is found in the aleurone layer. Chemically, β -Glucan is a linear unbranched chain consisting of β -D-glucopyranose monomers linked by β -1,3- and β -1,4-glycosidic bonds.^{43,46} The total β -glucan content of barley grains ranges from 2.5% to 11.3%, but typically, it falls between 4 and 7%, although it is reported to be as high as 13–17% for some barley cultivars.⁴⁷ β -glucan exhibits positive health-promoting effects regarding chronic non-communicable diseases, such as diabetes, hypercholesterolemia, obesity, cardiovascular diseases, and cancer. In addition, β -glucan showed antioxidant, anti-inflammatory,

antitumor, immunomodulatory, and prebiotic properties.⁴⁶

Arabinoxylan, another polysaccharide present in the cell wall of barley grain, has potential health benefits including antioxidant activity, prebiotic effects, immunomodulatory properties, and anti-diabetic and cardioprotective effects.⁴⁸

Proteins

Protein content in barley grains can range from 10 to 20% and is accumulated mainly in the endosperm.⁴⁷ According to the solubility, barley proteins are divided into four groups including albumins (water-soluble), globulins (soluble in dilute saline), prolamins (soluble in alcohol/water mixtures), and glutelins (soluble only in dilute acid or alkali).⁴⁹ The second classification is according to their biological functions, distinguished as seed storage proteins and non-storage proteins.⁴⁵ Storage proteins are found mainly in the endosperm, while non-storage proteins are distributed in aleurone and embryo.⁴¹ Hordein, which belongs to the prolamins group, is the major storage protein in barley which accounts for 30 to 50% of the total protein while Glutelin is the second most abundant barley storage protein (35–45%).⁵⁰ In addition, barley has also been reported to constitute a variety of essential amino acids, including histidine, threonine, valine, lysine, leucine, isoleucine, phenylalanine, threonine and methionine.⁹

Lipids

The lipid concentration in barley grains is about 2%–3%, with the endosperm bearing the highest level.⁴⁷ Triacylglycerol is the principal nonpolar lipid in barley, with small amounts of steryl esters, diacylglycerol, monoacylglycerol, and free fatty acids, while phospholipid is the major polar lipid.⁵¹ The primary fatty acids in barley kernel comprise linoleic acid, palmitic acid, oleic acid and linolenic acid.⁴³

Vitamins

Whole grains are generally high in vitamins, particularly some of the B-complex vitamins (such as thiamine, riboflavin, niacin, pyridoxine, biotin, and folates).⁴⁵ Barley is found to comprise vitamins B and E in the majority.^{41,43} Vitamin E, also referred to as tocopherols, is thought to be beneficial to human health in decreasing the risk of various maladies. In addition to having antioxidant properties, tocopherols modulate the immune system, reduce the risk for cardiovascular diseases and stroke⁴⁷, and can suppress cancer by its molecular mechanisms of cellular proliferation, apoptosis, angiogenesis, metastasis, and inflammation.⁵²

Minerals

Barley is considered a good source of macro-elements (K, Mg, Ca, Na, P, S) and trace elements (Fe, Mn, Cu, Zn, I).⁹ with quantitative variations due to several factors including variety and environmental conditions.⁴⁹ The total mineral content of barley grain can vary from 1.5 to 2.5% and is largely concentrated in the outer layers of the grain.^{41,49}

Phytochemistry of Barley Grain

Table 2: Phytochemical Constituents of Barley Grain

Phytochemicals	Key compounds	Pharmacological activities	Ref
Phenolic acids	• Ferulic acid • p-coumaric acid • o-coumaric acid • p-hydroxybenzoic acid • Vanillic acid • 2,4-dihydroxybenzoic acid • Sinapic acid • Syringic acid • Chlorogenic acid • Caffeic acid	• Antioxidant activity • Antiproliferative activity • Anti-adipogenic activity • Hepatoprotective activity • Hypoglycemic activity	53,54, 55,56, 57,58, 59,60
Flavonoids	Flavanols, Flavonols, and Proanthocyanidins: • Catechin • Quercetin • Prodelphinidin B3 • Prodelphinidin C2 • Procyanidin B3 • Procyanidin C2 Anthocyanins: • Cyanidin 3-glucoside • Delphinidin 3-glycoside • Delphinidin 3-rutinoside • Pelargonidin 3-glycoside • Peonidin 3-glycoside • Malvidin 3-glycoside • Petunidin 3-glucoside	• Antioxidant activity • Antiproliferative activity • Neuroprotective effect • Anticancer activity • Anti-inflammatory activity	55,61, 62,63
Lignans	• Pinoresinol • Medioresinol • Syringaresinol • Lariciresinol • Secoisolariciresinol • Matairesinol • Hydroxymatairesinol • 7- hydroxymatairesinol • Lariciresinol-sesquiligann	• Antioxidant activity • Anti-inflammatory activity • Anticancer activity • Antibacterial activity • Cardiovascular disease risk reduction • Lipid-lowering effect	53,64, 65,66

Phytosterols	• Sitosterol • Campesterol • δ5-avenasterol • Stigmasterol • Brassicasterol • Stigmastanol • δ7-avenasterol • Sitostanol • Campestanol • Stigmastadienol	• Cholesterol-lowering effect • Anticancer activity • Antioxidant activity • Anti-inflammatory activity • Antiatherogenic activity • Anti-obesity activity • Antidiabetic activity	53,67, 68,69, 70,71
Folates	• 5-methyltetrahydrofolate (5-HCO-H₄folate) • 5,10-methylenetetrahydrofolate (5-CH₃ H₄folate) • 5, 10- methenyl- tetrahydrofolate (5, 10-CH⁺- H₄folate) • 10- formylfolic acid (10-HCO-PGA)	• Beneficial in several chronic diseases including cancer, cardiovascular diseases, neurological conditions, and metabolic-related outcomes as well as several birth outcomes	53,72
Tocols	• α-tocotrienol • α-tocopherol • γ-tocotrienol • γ-tocopherol • β-tocotrienol • β-tocopherol • δ-tocopherol • δ-tocotrienol	• Antioxidant activity • Anti-inflammatory activity • Immuno-modulatory activity • Cholesterol lowering effect • Reduces the risk of cancer and cardiovascular diseases • Antithrombotic activity • Reduces platelet aggregation	53,73, 74,75, 76,77, 78

Pharmacological and Clinical Studies

Antidiabetic activity

Pharmacological studies

In an *in vivo study* on type 2 diabetes rat models, the consumption of insoluble and soluble fibers isolated from barley significantly reduced fasting blood glucose levels, improved insulin sensitivity, ameliorated liver function, regulated serum lipids, and had a hypoglycaemic effect.⁷⁹ Hydroalcoholic extract of barley seed regulated blood glucose levels in streptozotocin-induced diabetic rats.⁸⁰ Intake of barley seed aqueous extract had protective effects on the pancreas in streptozotocin-induced diabetic rats.⁸¹ Intake of hydroalcoholic extract and aqueous fraction of *Hordeum vulgare* exhibited strong antioxidant potential and ameliorative effects on streptozotocin-induced diabetic nephropathy in Sprague-Dawley rat models.⁸² In a study, the consumption of a diet containing barley regulated blood glucose, lipid profile, and adipose tissue hormones in type 2 diabetic rats.⁸³ The prethanol extract of naked waxy barley showed potential antidiabetic activity in mice with type 2 diabetes by suppressing fasting blood glucose levels and modulating hepatic glycogen

accumulation and glucose metabolism via the PI3K/Akt/GSK3 β pathway.⁸⁴

Clinical researches

Several clinical trials have shown the therapeutic effects of barley in hyperglycemia which is primarily attributed to the effect of soluble fiber, β -glucan. Ames *et al.*, conducted a double-blind, randomized, and controlled clinical trial to confirm the beneficial effect of barley β -glucan on improving insulin response. Twelve healthy adults were given different amounts of barley β -glucan enriched meals (low: 4.5 g, medium: 7.8 g, and high: 11.6 g). There was a lower glucose and insulin response after high β -glucan consumption than the low- β -glucan treatment.⁸⁵ The impact of different β -glucan concentrations on postprandial glycaemic response was investigated by Chillo *et al.* The glycaemic response of nine healthy subjects who consumed spaghetti meals enriched with different amounts of barley β -glucan (0%, 2%, 4%, 6%, 8%, and 10%) was evaluated. Blood glucose measurements taken 120 minutes after consuming different β -glucan enriched spaghetti diets, revealed a reduction in glycaemic index with increasing β -glucan concentration.⁸⁶ In a recent clinical trial, the intake of barley mixed rice lowered the postprandial

glucose concentrations in treatment-naïve and metformin-treated T2DM patients. Moreover, the Mean amplitude of glycaemic excursions (MAGEs) lowered in patients who consumed barley-mixed rice.⁸⁷ In an important RCT, bread prepared by replacing wheat flour with either 50% high-amylose or 75% hullless barley flour reduced postprandial glucose levels compared to 100% wheat bread signifying a positive effect on glucose regulation in T2D subjects.⁸⁸ Azam *et al.*, investigated the impact of barley on postprandial blood glucose response in 20 diabetic subjects. Subjects were divided into two groups, with ten serving as the control group while the other ten comprised the experimental group which received barley porridge made from 100 g of barley for four weeks. Each subject's blood glucose level was determined at both fasting and after ninety minutes of barley diet consumption. Results showed a significant decrease in blood sugar levels after barley intake.⁸⁹

Antiobesity activity

Pharmacological studies

Administration of hullless barley polyphenol (HBP) extract inhibited the obesity-related enzymes, adipocyte differentiation, and intracellular lipid accumulation *in vitro*.⁹⁰ Aly AA *et al.*, investigated the effect of high levels of whole barley (60% and 80%) supplemented bread against high-fat diet-induced obesity in rats. At the end of 12 weeks of the experimental period, all treated groups with whole barley bread showed a reduction in the mean value of body weight gain. Moreover, the mean value of liver, kidney and heart relative weight was decreased in response to the administration of whole barley breads when compared to other obese groups. All treated groups with barley bread caused a significant reduction in serum glucose, cholesterol, triglycerides, and low-density lipoprotein-cholesterol (LDL) levels compared with the control bread.⁹¹ Mio K *et al.*, evaluated the effects of β -glucan rich barley flour on lipid metabolism in the ileum, liver, and adipose tissues of male mice fed a high-fat diet. Liver weight and the weights of retroperitoneal and mesenteric fat were significantly reduced in the barley flour-treated group compared with the control group ($p < 0.05$). Accumulation of cholesterol and triglyceride in the liver as well as the serum total cholesterol and low-density lipoprotein-cholesterol concentrations were decreased significantly in the treatment group compared with the control group.⁹²

Clinical researches

An important clinical trial investigated the effect of high- β -glucan barley (4.4 g β -glucan per day) in reducing visceral fat obesity in 100 Japanese subjects. The intake of high- β -glucan barley led to significant and safe decrement in visceral fat area, body weight, BMI, and waist circumference in the subjects.⁹³ In a single-blind study, the antiobesity effect of extracts of fermented barley with *Lactiplantibacillus plantarum*dy-1 (LFBE) was demonstrated in humans probably via its interactions with the gut microbiota. LFBE intervention resulted in the reduction of body fat percentage, visceral fat area, and serum lipid levels.⁹⁴ Rajesh K *et al.*,

investigated the impact of barley and oat flour on body weight and a variety of parameter characteristics of the metabolic syndrome in 48 overweight (defined as BMI>23/m²) individuals. The study participants were randomly assigned to receive either barley flour (150 mg/day) or oat flour (150 mg/day) in *chapatti* form once a day for 2 months. At the end of the trial, considerable improvement in Body weight, BMI, BMR, Visceral fat, Body fat, Lipid profile and Skin fold thickness was recorded in both barley and oat flour groups, however, the barley flour group was more effective than oat flour group.⁹⁵

Hypocholesterolemic activity

Pharmacological studies

In a study conducted by Tong LT *et al.*, the hypocholesterolemic effects of hullless barley β -glucan (HBG) were investigated in hamsters who were given a hypercholesterolemic diet. Administration of dietary HBG led to a decrease in plasma LDL cholesterol levels by enhancing the excretion of lipids in feces and modulating the HMG-CoA reductase and CYP7A1 activities in hypercholesterolemic hamsters.⁹⁶ In another study, administration of 5% and 10% barley bran to the hypercholesterolemic rats for 8 weeks improved the level of lipids, lactate dehydrogenase, liver enzymes, and creatine kinase-MB. Furthermore, abnormal histology of heart, liver, and kidney tissues nearly restored the normal state in barley bran-treated rats.⁹⁷ The hypocholesterolemic effect of whole-grain highland hullless barley (WHLB) was studied in rats fed a high-fat diet by Xia X *et al.*, Intake of high-dose WHLB significantly decreased the indices of liver and abdominal fat as well as declined levels of Total cholesterol and LDL-cholesterol in the plasma and the liver.⁹⁸

Clinical researches

An important RCT was devised to study the effect of high β -Glucan barley on serum cholesterol levels and visceral fat area in forty-four hypercholesterolemic Japanese men with a body mass index of more than 22 kg/m². The placebo group was given rice and the test group received a mixture of rice and pearl barley with a high β -glucan content (7.0 g β -glucan/day) for 12 weeks. Results showed that consumption of pearl barley significantly decreased the serum concentrations of total cholesterol and low-density lipoprotein-cholesterol. Significant differences were also recorded between the test and placebo groups for the visceral fat, BMI, and waist circumference at the end of the trial.⁹⁹ In a clinical trial, a diet containing barley significantly lowered lipids in mildly hypercholesterolemic men and women.¹⁰⁰

Cardioprotective activity

Pharmacological studies

In a study, the long-term dietary intake of pasta enriched with barley beta-glucan demonstrated a cardioprotective effect against post-ischemic reperfusion injury in adult male mice. Consumption of barley beta-glucan showed a 109% survival rate after cardiac ischemia (30 min)/reperfusion (60 min) injury,

reduced left ventricular anion superoxide production and infarct size, and increased capillary and arteriolar density and vascular endothelial growth factor (VEGF) expression in the hearts of mice.¹⁰¹ Whole grain highland barley supplementation demonstrated alleviation of atherosclerotic plaque formation via modulating the NLRP3 inflammasome pathway and the synthesis of anti-inflammatory metabolites by the gut microbiota.¹⁰²

Clinical researches

A meta-analysis of 28 randomized controlled trials revealed that higher consumption of barley β -glucans is associated with lower systolic and diastolic blood pressure. Diets rich in β -glucans reduced systolic blood pressure by 2.9 mmHg and diastolic blood pressure by 1.5 mmHg. Another large meta-analysis of 126 studies demonstrated the effect of β -glucan intake of 3 g/day on measures of blood cholesterol levels. A significant reduction in Total Cholesterol, Low-Density Lipoprotein, and Triglycerides was found following consumption of oat and barley β -glucans.¹⁰³ In an RCT, intake of barley β -glucan-based diet improved cardiovascular disease risk factors including body mass index, waist circumference, blood pressure, and triglyceride levels in mildly hypercholesterolemic individuals.¹⁰⁴

Bowel health improvement

Pharmacological studies

Intake of barley beta-glucan in two hundred male Sprague-Dawley rats for 6 weeks showed positive effects on improving intestinal functions and gut health.¹⁰⁵ Chen M *et al.*, studied the effect of β -Glucan extracted from highland barley (HBBG) against dextran sulfate sodium-induced ulcerative colitis (UC) in the C57BL/6J Mice model. Following the administration of the HBBG diet, there were reductions in the disease activity index score, histopathological damage, and the concentration of colonic myeloperoxidase, along with an enhancement in colonic atrophy, all of which indicated alleviation of UC. Also, HBBG modulated the structure of the intestinal flora and preserved the balance of proinflammatory and anti-inflammatory cytokines.¹⁰⁶ In an *in vivo* study, the administration of a barley-based probiotic food mixture for 7 days was useful in controlling *E. coli*-induced diarrhea in mice.¹⁰⁷

Clinical researches

In an RCT, eighteen patients with mild to moderate active Ulcerative Colitis were evaluated by Kanauchi O *et al.*, to investigate the efficacy of germinated barley foodstuff (GBF) for the treatment of UC. Following four weeks of treatment, a significant decline in clinical activity index scores and mucosal inflammation was recorded in the GBF-treated group when compared with the control group. Additionally, GBF administration increased fecal concentrations of *Bifidobacterium* and *Eubacterium limosum* which are known to prolong the remission of UC.¹⁰⁸ In another trial, Faghfoori Z *et al.*, studied the effect of germinated barley foodstuff (GBF) administration on serum C-reactive protein (CRP) levels and clinical signs in patients with Ulcerative Colitis. The study concluded that GBF intake along with routine

medication could help to reduce inflammation, prolong remission, and improve clinical signs in UC patients.¹⁰⁹

Skincare

Pharmacological studies

In an *in vivo* study, intake of fermented barley and soybean mixture in hairless mouse model showed synergistic protective effects that prevent UVB-induced skin dehydration, oxidative stress, matrix degradation, and collagen synthesis.¹¹⁰ Fermented Barley Extract suppressed the development of Atopic Dermatitis-like skin lesions in mice, probably by modulating the cytokine production involved in chronic inflammation, such as IFN- γ or IL-17.¹¹¹ Hordenine as an active compound from germinated barley (*Hordeum vulgare* L.) showed inhibition of melanogenesis in human epidermal melanocytes by suppressing cAMP production, which is involved in the expression of melanogenesis-related proteins and proposed that hordenine could act as an effective inhibitor of hyperpigmentation.¹¹² Water-soluble extracts from barley, malt and germinated barley in Melan-a cells demonstrated antimelanogenic activity most probably through suppression of tyrosinase and tyrosinase-related protein 2 expression.¹¹³

Clinical researches

A randomized, placebo-controlled trial was conducted by Lee S *et al.*, to evaluate the effect of a fermented barley and soybean dietary supplement (BS) on skin hydration in healthy volunteers. Subjects were given a placebo (n=33) or BS (3g/100 ml/day) enriched drink (n=32), orally for 8 weeks. A significant improvement in hydration was observed on the faces of participants after 4 and 8 weeks, and on the forearm after 4 weeks in the BS group when compared to the control group.¹¹⁴

Other studies

Anticancer activity

In an *in vivo* study, germinated barley foodstuff treatment demonstrated anti-tumor activity against colonic carcinogenesis in rat models. GBF treatment significantly augmented the caecal butyrate content and production of slc5a8, which is a tumor suppressor gene, whereas reduced the number of aberrant crypt foci (ACF) and β -catenin formations in the colonic mucosa.¹¹⁵ In an *in vitro* study, phenolics extracted from hullless barley showed strong antiproliferative activity against HepG2 human liver cancer cells.¹¹⁶ In an *in vivo* study, aqueous extract of fermented barley induced apoptosis in the transplantation tumor model of human HT-29 Cells in nude mice.¹¹⁷

Anti-inflammatory activity

In an *in vitro* and *in vivo* study, methanol extract of the aerial parts of barley (*Hordeum vulgare*) demonstrated anti-inflammatory activity by causing a significant reduction in serum TNF- α , IL-6 and IL-1 β concentrations. Phenolic compounds were identified as the main constituents responsible for the activity.¹¹⁸ Intake of the wholegrain barley diet for 25 days in the animal model demonstrated anti-inflammatory activity

against high-fat diet-induced inflammation possibly due to the formation of short-chain fatty acid and changes in microbiota composition.¹¹⁹ Rats supplemented with fermented barley extract for 10 days demonstrated a reduction in plasma interleukin (IL)-1, IL-6, and tumor necrosis factor in response to lipopolysaccharide-induced inflammatory liver injury.¹²⁰

Wound healing activity

In an *in vivo* study, barley β -glucan accelerated the wound-healing process in mouse skin by promoting the migration and proliferation of human dermis fibroblasts.¹²¹ In another animal study, the healing activity of visceral fat and barley seed ash (*Hordeum Vulgare* L.) was compared with silver sulfadiazine on burn wounds in male Wistar rats. The preparation significantly decreased inflammation, accelerated wound healing and wound contraction and promoted epithelization in treated rats.¹²² The application of roasted barley in sesame oil mixture promoted wound healing and tissue debridement in animal models of burn.¹²³

Effect against COVID-19

A randomized controlled trial was conducted to assess the clinical efficacy of a barley-based remedy (a decoction of Barley, Jujube and Cordia) plus conventional medicine in comparison to the conventional therapy in 70 patients with COVID-19. From the second day of intervention, the oxygen saturation level was significantly improved in the barley-based remedy group in comparison to the control group ($P < 0.05$). From the third day of treatment, the herbal remedy significantly reduced fatigue ($P < 0.05$). The average respiratory rate and temperature in both groups were in the normal range.¹²⁴ Tavakoli A *et al.*, conducted a single-blind, add-on therapy, randomized controlled clinical trial to assess barley water (250 ml/day) effectiveness in controlling the clinical outcomes of hospitalized COVID-19 patients with moderate severity. According to the results, the intervention group's length of hospital stay was found to be 4.5 days less than that of the control group. Also, there was a significant decrease in the intervention group's body temperature, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and creatinine when compared to the control group.¹²⁵

Conclusion

Barley (*Hordeum vulgare* Linn.) is a cereal grain that has been utilized for centuries for its nutritional value and medicinal properties. The use of barley as a functional food has gained remarkable attention in recent times due to advancements in consumer awareness of healthy and natural foods and a better understanding of the chemical makeup of grain and its impact on human health. The present review article attempted to explore barley (*Hordeum vulgare* Linn.) in Unani literature with recent scientific studies. Based on the information retrieved above, it can be concluded that Unani physicians recommended several tested barley formulations based on their observations and experiences, that have been effectively utilized to cure a

variety of illnesses. Recent studies have revealed anti-inflammatory, antioxidant, and wound-healing properties of barley that are aligned with its traditional uses in the treatment of wounds, swelling, burns, pain, fever, etc. Several other therapeutic effects including anti-obesity and antidiabetic are validated by experimental pharmacological and clinical studies, as described in this article, and are attributed to specific bioactive compounds including β -glucan, flavonoids, folate, lignans, phenolic acid, phytosterols, and tocopherols. Ultimately, these findings further encourage more intense scientific research to ascertain the efficacy of barley in the prevention and treatment of numerous disorders. Also, this review may thus be helpful for the research community as well as common people to avail the benefits of this drug.

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Conflict of Interest

None declared

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