

ASL KHALIS (HONEY) A NATURAL REMEDY OF PEPTIC ULCER (QARHE
HAZMIYA) - A COMPREHENSIVE STUDYDr. Swaleha Khan^{*1}, Dr. Mohammad Usama², Dr. Mohammad Danish³, Dr. Mahboob Alam Khan⁴, Dr. Seemab
Alam⁵ and Aaquib Jaweed⁶¹Professor & HOD, Dept. of Ilmu Jarahat (Surgery), Inamdar Unani Medical College and Hospital Kalaburagi.²Assistant Professor, Dept. of Ilaj-bit-Tadbeer, Inamdar Unani Medical College and Hospital Kalaburagi.^{3,5}Assistant Professor, Dept. of Moalajat, Inamdar Unani Medical College and Hospital Kalaburagi.⁴Professor & HOD, Dept. of Moalajat Inamdar Unani Medical College and Hospital Kalaburagi.⁶Assistant Professor, Dept. of Pharmacology, Vastanvi College of Pharmacy, Kunjkhera Kannad, Sambhaji Nagar.***Corresponding Author: Dr. Swaleha Khan**

Professor & HOD, Dept. of Ilmu Jarahat (Surgery), Inamdar Unani medical college and Hospital Kalaburagi.

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ABSTRACT

Peptic ulcer disease remains a common health problem, despite all the progress made in the diagnosis and treatment, both medical and surgical, of this condition. The incidence of gastroduodenal ulcer disease is approximately 1 to 2 per 1000 inhabitants per year. Two thirds of patients with ulcers are male. Ancient eminent physicians of Unani system like Ibne Sina, Razi, Abul Mansoor Qumri and Ibn Hubl Baghdadi have described extensively about GIT ulcers and its causes, clinical features, treatments and its consequences in their treatises. GIT ulcers are described according to the organ affected by ulcer namely Oesophageal Ulcer as *Qarahe Mari*, Stomach Ulcer as *Qarahe Medi* and Duodenal Ulcer as *Qarahe Mevi*. Later on the term "*Qarahe Hazmia*" coined for peptic Ulcer by Unani Scholars. The use of *Asl Khalis* (Honey) in the treatment of external and internal ailments is much older than the history of medicine itself. *Asl Khalis* (Honey) as a natural product has clinched the attention of researchers as a complementary and alternative medicine. According to Unani Medicine, it is used as nutritive agent, as a natural food supplement and therapeutically has antibacterial, anti-inflammatory, detergent, deobstruent, lithotryptic and wound healing properties in skin and Peptic Ulcer.

KEYWORDS: Asl Khalis, Peptic ulcer; Qarahe Hazmia; Unani Medicine.**I. INTRODUCTION & HISTORICAL
BACKGROUND OF PEPTIC ULCER (QARHE-
HAZMIYA)**

Peptic ulcer was well known in antiquity. It is not clear when the medical history of peptic ulcer was first written, possibly with the Egyptians, or with Hippocrates [460 BC, or (Diocles of Carystos 4th century BC)]. One of the earliest descriptions is carved on a pillar of the temple of Aesculapius at Epidaurus (4th century BC) where what might be considered the first surgery for a gastric ulcer was described by Goldstein "A man with an ulcer in his stomach was tied to the doorknocker and incised his stomach. Asklepios opened his stomach, cut out the ulcer, sewed him up again, and loosed his bonds."^[1]

Peptic ulcer is defined as the discontinuation of the inner lining of the gastrointestinal tract. It develops when hydrochloric acid in the digestive fluids and the enzyme

pepsin in the stomach damage the gastrointestinal tract. An ulcer in the stomach is called gastric ulcer which occurs within 15-30 minutes after a meal. A duodenal ulcer occurs 2-3 hours after a meal in the duodenum. Duodenal ulcers are four times more common than gastric ulcers. The gastric and duodenal ulcers together are referred to as peptic ulcers.

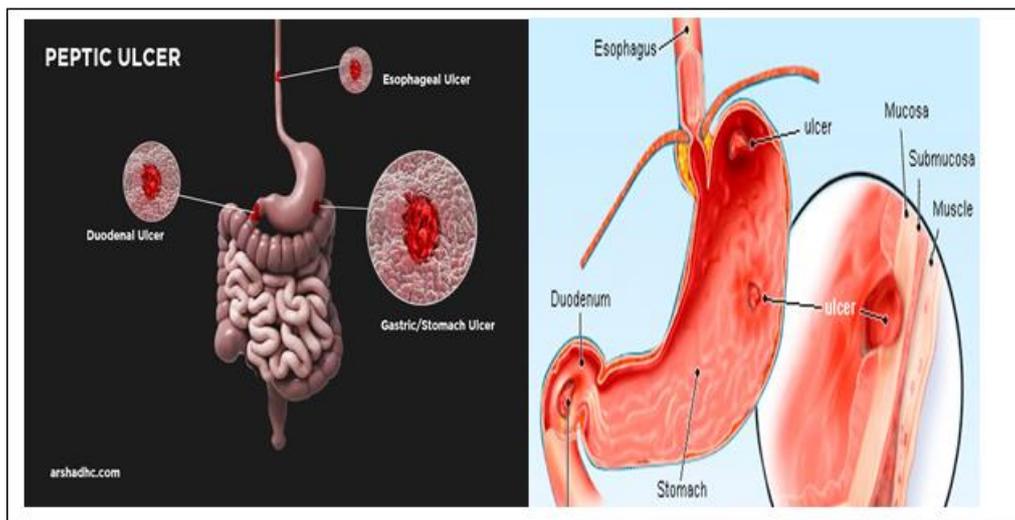


Fig. 01: Anatomy of Stomach in Peptic Ulcer.

Gastric ulceration as such is first mentioned by Celsus, in his *de Medecina* (A.D. 30). Dealing with the rules governing diet for the preservation of health, he wrote, 'but if ulceration attacks the stomach, milk and glutinous food are given, but not to satiety; all acrid and acid things are withheld. It is tempting to believe that this fundamentally sound counsel was based upon actual observation of cases of gastric ulcer occurring in the upper strata of Roman society. Indigestion and heartburn have been described for thousands of years, but it was only in the 16th century that the disease peptic ulcer was established by autopsy. One of the first autopsies - proven pyloric peptic ulcers was studied in 1586 by Donatus of Mantua. Bauhin, in 1679, concluded that inflammation of the stomach led to a gastric ulcer which then ruptured. The first known gastric hemorrhage was reported in 1704. First classification of stomach diseases came in 1793 from Matthew Baillie, with clear descriptions of acute inflammation, ulcer, perforation, pyloric stenosis, and ulcerated cancer. In 1817, patients with perforated gastric ulcer were reported in Dublin by Crampton and patients with perforated duodenal ulcer were reported in London by Travers, who also noted bleeding, stenosis and penetrating gastric ulcers.^[1,2]

Although ulcers have long been known to medical science, ulcer disease only became a popular diagnosis in the late 19th century. This change in frequency of diagnosis can reflect a change in incidence or a change in diagnosis (i.e., the symptoms of ulcer were previously attributed to some other process). Alternatively, the prevalence or virulence of *H. pylori* might have changed such that new disease patterns emerged. There are examples of populations where *H. pylori* are rare, such as ethnic Malays in whom peptic ulcer and gastric cancer were long recognized to be rare. While, it is possible that *H. pylori* was either largely absent from Western countries or became widespread or more virulent in the 18th and 19th centuries. The first definite peptic ulcer in a human was described in the 20th century was from the autopsy of a mummy of a man from the Western Han

dynasty who died in 167 BC. The autopsy showed a clearly visible perforated prepyloric ulcer resulting in acute diffuse peritonitis complicated by disseminated coagulopathy.^[1]

In 1st century AD, Jalinoos mentioned about *quroohe medah*; cause, symptoms and its specific site. Rabban Tabri (770AD) enumerated the cause, symptoms and treatment of *quroohe medah*. Later on eminent scholars of Tibb like Razi (850AD), Ibn Sina (980AD), Majusi (994 AD), Zahravi (1013AD) and Azam Khan (1813AD) also put forward the detail descriptions on GIT ulcer.^[3,7]

II. Unani concept of peptic ulcer (*Qarhe Hazmiya*)

Qarhe Hazmiya is a Unani medical terminology coined and used as synonym for peptic ulcer. *Qarhe Hazmiya* is described under the entities of *Qarhe Mari* (ulcer of oesophagus), *Qarhe Medi* (gastric ulcer) and *Qarhe Mevi* (intestinal ulcer) in different classical text of Unani Medicine along with their management and prevention.^[29,6] The term *Qarha* derived from Arabic word which means an ulcer or injury. Further a breach / break or loss of continuity in muscle or in similar organ is defined as *jarahat* (wound).^[3,10] Further Loss of continuity / break or breach in skin or membrane is known as *kharash* or *sahaj* (erosion). In Unani Medicine an ulcer is defined when there is any type of discontinuity spreading over an organ or especially in a muscular organ associated with pus formation.^[4]

There are four natural types of *medah* (stomach) accordingly, *Haar*, *Barid*, *Yabis* and *Ratab*. Diagnosis of disease is made by comparing the original and altered *mizaj* in Unani system. Original *mizaj* of *medah* is hot and moist as it is a muscular organ.^[11]

A. Characteristics of *haar taba-i medah* (stomach)

- Good digestion of heavy diets such as beef and goose etc.
- Soft and light diet such as young chicken, milk etc. are get spoiled due to over digestion.

- Favorable for heat producing food.
- Digestion overwhelms appetite.

B. Characteristics of *barid taba-i medah* (Stomach)

- Appetite is not impaired.
- Impaired digestion comparing to *Haar taba-i Stomach*
- Light and soft diets will get digested properly.
- Favorable for cold producing foods. Characteristics of *yabis taba-i medah* (stomach):
- Mild thirst quenched by intake of little liquid.
- Additional intake of liquid will easily leads to fullness and borborygmi.
- Favorable for dryness producing foods. Characteristics features of *ratab taba-i medah* (stomach)
- Thirst is reduced with tolerance to oil and fat consumption.
- Additional liquid will not easily produce fullness.
- Hence there is no overflow.
- Favorable for moist producing foods.^[4]

III. Causes of peptic ulcer (*Qarhe Hazmiya*)

Causes of acid peptic disease include

- **Helicobacter pylori:** H.pylori is responsible for around 60%-90% of all gastric and duodenal ulcers.
- **NSAIDs:** Prostaglandins protect the mucus lining of the stomach. Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, diclofenac and naproxen prevent the production of these prostaglandins by blocking cyclo-oxygenase enzyme leading to ulceration and bleeding.
- **Smoking, alcohol and tobacco:** Cigarettes, alcohol and tobacco cause an instant and intense acid production.
- **Blood group O:** People with blood group "O" are reported to have higher risks for the development of stomach ulcers as there is an increased formation of antibodies against the Helicobacter bacteria, which causes an inflammatory reaction and ulceration.
- **Heredity:** Patients suffering from peptic ulcer diseases usually have a family history of the disease, particularly the development of duodenal ulcer which may occur below the age of 20.
- **Steroids/Other medicines:** Drugs like corticosteroids, anticoagulants like warfarin (Coumadin), niacin, some chemotherapy drugs, and spironolactone can aggravate or cause ulcers.
- **Diet:** Low fiber diet, caffeinated drinks and fatty foods are linked to peptic ulcer.
- **Other diseases:** Chronic liver, lung and kidney diseases especially tumors of the acid producing cells all predispose to peptic ulcers. Zollinger-Ellison Syndrome (ZES) is a rare pre-cancerous condition which causes peptic ulcer disease. It is a syndrome disorder wherein tumors in the pancreas and duodenum also known as gastrinomas produce a large amount of gastrin which is a hormone that stimulates gastric acid secretion. Endocrine

disorders such as hyperparathyroidism are also implicated in the development of peptic ulcers.

- **Stress:** Stress and neurological problems can also be associated with the Cushing ulcer and peptic ulcer.

IV. Aetiopathogenesis of peptic ulcer (*Qarhe Hazmiya*)

Disease is not a localized phenomenon, but a disturbance in the equilibrium of *akhlat arba* to be maintained in the state of health. The disturbance is known as *sue mizaj*. The aetiological classification of any disease are of three types

- *Sue mizaj sada* and *maddi* (intemperamental)
- *Sue tarkeeb* (disturbed structure)
- *Tafarruqe ittesal* (loss of continuity).^[12]

The cause of ulcer is loss of continuity (*tafarruqe ittesal*) in general either external / internal. Causes of internal wound/ulcer are; corrosive, caustic, moistening and relaxing humours or humours with drying and cleaving action, gases causing distension or penetrating gases, repletion of humours causing distension.^[4,13] According to classical Unani text, accumulation of abnormal superfluous *akhlat* and the *ghair taba-i barid* and *ratab* (cold and moist) morbid condition alter the functions of the stomach. Further this accumulation of *morbid akhlat* in turn will lead to *sue mizaj*, *sue tarkeeb* and *tafarruqe ittesal* in the *ghisha-e mukhati wa jirme meda and ama* (mucus membrane and muscular wall of stomach and Intestine).^[4,13]

V. Factors responsible for peptic ulcer (*Qarhe Hazmiya*)

- *Khilte haad laze* produced in stomach itself or descends / dribbles from other organ; brain (*khilte balgham*), liver (*bile*), spleen (*black bile*). Excess of bile poured into stomach at the time of severe pain, anxiety, depression and due to delayed emptying of stomach.^[3]
- Ingestion of acids (*turshi*) and spicy (*tez*) like vinegar (*sirka*) and mustered lead to formation of pustules and ulcers of stomach.^[14]
- As a consequence of inflammation (*warme medi*).^[3]

Infiltration (*tashar'rub*) and enduring of the hot and concentrated humour (*haad wa tez khilt*) in stomach muscle wall leads to ulcers and pustules formation. Dribbling of humour over the stomach takes place from other organ. Gastric ulcer in particular is caused by the constantly dribbling of morbid fluid (*nazlavi rutubat*) from the brain (*dimagh*), which is irritant (*laze*) or corrosive in nature.^[13,15]

Ulcer develops due to infiltration of *khilte had* (irritant and corrosive humours) in stomach. These *akhlat* dribbles or descends from the brain in the form of *nazla*. Thick *khilth* are more prone to putrefaction. *Insebabe nazlavi rutubat* (descends or dribbling from brain), *Insebabe safra* (poured from liver e.g. bile), *Insebabe sauda* (poured from spleen- black bile).^[4]

VI. *Alamat wa Nishaniyan* (clinical features) of peptic ulcer (*Qarhe Hazmiya*)

Razi has enumerated two symptoms of gastric ulcer. First symptom is severe pain during ingestion of food and second one is frequent haematemesis and further he described that salty, spicy, sour, hot and cold stuffs are not only causes discomfort but also aggravate the ulcer.^[3]

Stomach ulcers specifically ulcers at the greater curvature (*Qa'ere medah*) will cause shortness of breath (*Tange'e tanaffus*), syncope (*Ghashi*), coldness of extremities, and indigestion, and also cause less production of blood and *rooh*, which leads to the development of above complications.^[14]

Unani physicians have given detailed description of signs and symptoms related to the disease Qarahe Medah. The descriptions of the clinical features are quite similar to the modern gastro-enterologists described in their scientific researches. According to Unani literature a typical patient may present with the following features

1. Shortness of breath (shallow breathing).
2. Fullness of vessels.
3. Syncope.
4. Cold extremities.
5. Bad odours eructation (foul smelling belching).
6. Dry tongue.
7. Vomiting.
8. Excessive perspiration.
9. Weak/ feeble pulse.
10. Severe nausea.
11. Difficulty in swallowing.
12. Feeling of discomfort and aggregation of symptoms on taking spicy food.

VII. *Tashkheeshe Fariqa* (Differential diagnosis) of *Qarhe Mari, Medi wa Mevi*

Ulcers can appear at oesophagus (*mari*), cardiac end (*fam'me medah*), pyloric antrum / greater curvature of

the stomach (*Qa'ere medah*), and intestines (*ama'a*). Differentiating site of the ulcers according to symptoms.

A. *Qarhe Mari* (ulcers of the oesophagus)

Pain will be felt between the shoulders at the back. Pain is felt in the neck while food passes through it and disappears after passing food. To observe and confirm this condition, some mustard added to patient's food.^[3,4,6,10,16]

B. *Qarhe Medi* (ulcers of the stomach)

Pain increases while passing food from the stomach and pain is felt near the navel. When ulcers is in the lower part of the stomach, there will be shallow breathing (*sighre nafas*), dryness of tongue, fullness of vessels, unconsciousness, cold extremities, foul smell belching and excessive vomiting with debris.^[3]

C. *Qarhe Mevi* (ulcers of the intestine)

Pain increases while dribble of food (*inhdare ghiza*) and felt below the navel. Debris from the ulcer will come out with faeces.^[4,9]

VIII. *Usoole Ilaj* (Principles of treatment) of peptic ulcer (*Qarhe Hazmiya*)

1. Removal of causative factors and causes (*Izala-e sabab*)
2. Coction and elimination or excretion of morbid matter (*Nuzj wa isthifragh*)
3. Removal of causes that results in drabbing of morbid matter and pouring into stomach followed by elimination or evacuation.
4. Use of astringent action (*qabizat*) drug to heal fresh ulcer
5. Use of *munaqqi fuzlat* followed by *jazib wa mujaffif rutubaat, jali* followed by *mdammile qurooh and mumbite laham* drugs.
6. Regiminal therapy: *Fasd* - If condition is favorable and not contraindicated, when ulcer (*Qarha*) is fresh and prior to suppuration and specially there is a predominance of blood.^[4,14,15]

IX. Foods to Avoid in peptic ulcer (*Qarhe Hazmiya*)

A. Fried Foods



Fig. 02: Fried Food & Alcohol are prohibited in Peptic Ulcer.

People with stomach ulcers should avoid fried foods like chips, fried chicken, onion rings, fried chicken, doughnuts and onion rings. Food items fried at high temperatures harm the natural layer of protection in the digestive tract and develop stomach ulcers. Fatty foods also take longer to digest, causing bloating and stomach pain. So, you ensure not to have fried foods like potato chips, fries, fried chicken and doughnuts if you have stomach ulcers.

C. Acidic Foods



Fig. 3: Acidic Food and Milk are prohibited in Peptic Ulcer.

It is best to keep acidic foods away from the food list of a stomach ulcer diet. For example, people should avoid eating citrus fruits like oranges, lemons and grapefruits if they have stomach ulcers. Moreover, they must avoid white bread, processed cereals and white rice.

D. Milk

It will be a good idea not to consume milk. Though drinking milk will help in soothing the ulcer pain, it will be temporary. Milk also makes the stomach produce acid and digestive juices in large numbers. This can worsen the condition of stomach ulcers.

X. Treatment of peptic ulcer (*Qarhe Hazmiya*) by *Honey (Asl)*

Asl Khalis (Honey) is a high viscosity product of

B. Alcohol

Consumption of alcohol will inflame and damage the stomach lining. Moreover, it irritates stomach ulcers. Even if you do not have gastric ulcers, excessive drinking of alcohol can lead to its development. If you have stomach ulcers, it is a good idea to avoid any alcohol consumption.

characteristic flavor and aroma, color and texture, produced by honey bees and derived from the nectar of flowers. *Asl Khalis* (Honey) is produced by several honey bees e.g. *Apis mellifera*, *Apis dorasta*, *Apis indica* etc. *Asl Khalis* (Honey) is used as medicine since a long time for a variety of ailments and it forms the basis of many preparations in Unani system of medicine, acting as preservative and nutritive agent. (Vohra & han 1979).^[51] Prophet Mohammad (PBUH) recognized *Asl Khalis* (Honey) for the treatment of diarrhoea and wound healing.^[6]



Fig. 04: Honey- A medicine in Greek 2400 B.C.

Records of bee honey in history are difficult to locate, but it is certain that it is among the first documented evidence discovered. Cave paintings from Spain from 7000 B.C. shows the first records of beekeeping, but bee honey fossils date back about 150 million years! Its “magical” properties and versatility have given honey an important role in history. The earliest evidence of the existence of an apiary was found in the temple of the sun erected in 2400 B.C. near Cairo. The bee is frequently presented in Egyptian hieroglyphs and, being favored by the pharaohs, often symbolizes royalty. The ancient Egyptians used honey as a sweetener, as a gift to their gods, and even as an embalming ingredient. Honey cakes were baked by the Egyptians and used as an offering to reconcile the gods. The Greeks also made honey cakes and offered them to the gods.

The Greeks saw honey not only as an important food, but also as a medicine for healing. Greek recipe books were full of sweets and cakes made of honey. The cheeses were mixed with honey to make cheesecakes, described

by Euripides in the 5th century B.C. as being “best immersed in the rich honey of golden bees.” The Romans also used honey as a gift to the gods and used it widely in cooking. Beekeeping flourished throughout the Roman Empire. With Christianity, the production of honey and beeswax increased greatly, to meet the demand for candles for the church. Honey continued to be of great importance in Europe until the Renaissance, when the arrival of sugar meant the use of bee honey on a smaller scale.

Because bees were considered to have special powers, they were often used as emblems

- Pope Urban VIII used the bee as his emblem.
- The bee was the sign of the king of Egypt during the first dynasty (3,200 BC).
- In the third century BC, the bee was the emblem used on coins in the Greek city of Ephesus.
- The bee was a symbol of the goddess Artemis.
- The bee was the emblem of Eros / Cupid



Fig. 05: Extraction & Collection of Honey in Ancient Greek.

Uses of honey in Unani Medicine are well established since the time of Hippocrates. Ayurveda and Unani system of medicines emphasized topical application of honey as an effective treatment for wounds, burns, **skin ulcers** and recent studies are proving this claim valid. Oenomele is an ancient Greek beverage consisting of honey and unfermented **grape juice**. It is sometimes used as a folk remedy for gout and certain nervous disorders. Hippocrates, the great Greek scientist, prescribed a simple diet, favouring honey given as oxymel (vinegar and honey) for pain, hydromel (water and honey) for thirst, and a mixture of honey, water, and various medicinal substances for acute fevers. Hippocrates also utilized honey to treat baldness, as a contraceptive and for wound healing, laxative action, cough and sore throat, eye diseases, topical antiseptics, prevention, and **treatment of scars**. Avicenna, the great scientist and physician, almost 1000 years ago, had recommended honey as one of the best remedies in the treatment of Respiratory Tract infections. Unani classical literature describes some pharmacological actions of

honey to be anti-inflammatory, pain killer, antiseptic, blood purifier, wounds healer, expectorant, appetizer, nutrient, de-obstruent (a drug which removes obstructions in the body by aiding the opening of ducts), nutrient, lithotriptic, digestive tonic for stomach and an aphrodisiac among numerous other benefits.

XI. Chemical composition of Asl

Natural honey contains about 200 substances, including amino acids, vitamins, minerals and enzymes, but it primarily contains sugar and water. Sugar accounts for 95– 99% of honey dry matter. The principal carbohydrate constituents of honey are fructose (32.56 to 38.2%) and glucose (28.54 to 31.3 %), which represents 85–95% of total sugars that are readily absorbed in the gastrointestinal tract. *Asl Khalis* (Honey) contains trace amounts of several vitamins and minerals. Vitamins e.g. Thiamin, Riboflavin, Niacin, Pantothenic acid, Vitamin B-6, Vitamin B-12, Folate, Vitamin C, Vitamin A, Vitamin D, Vitamin E, Vitamin K and minerals e.g. Calcium, Copper, Iron, Magnesium, Manganese,

Phosphorous, Potassium, Sodium, Zinc are found in *Asl Khalis*. *Asl Khalis* (Honey) also contains tiny amounts of several compounds thought to function as antioxidants, including chrysin, pinobanksin, vitamin C, catalase, and pinoembrin.

XII. Medicinal properties of *Asl Khalis*

For about 4,000 years, *Asl Khalis* has been a popular folk remedy around the world for ailments ranging from diarrhea to inflammation of the eyelids. Ancient Unani physicians described it as an effective treatment for wounds, and modern studies have verified *Asl Khalis* superiority to the standard medical treatments for burns, skin ulcers, and wounds.

The Greek Muslim Scholar used to take an *Asl Khalis* (Honey) drink: a teaspoon of *Asl Khalis* mixed well with a cup of water in the early morning before eating anything. The recent medicine discovers that such drink activates the digestive system to work in a better way. Furthermore, *Asl Khalis* has been shown to be far superior to conventional antibiotics in treating infections and without the negative side effects associated with antibiotic use. It is amazing that the bacteria-killing properties of *Asl Khalis* increases two-fold when diluted with water.^[18]

XIII. Af'aal (Pharmacological actions) of *Asl*

- *Muhallil-e-Waram* (Anti-inflammatory)
- *Musakkin-e-Auja'a* (Pain killer)
- *Mughazzi* (Nutrient)
- *Jali* (Detergent)
- *Mufatteh Sudad* (Deobstruent)
- *Mufattit e Hisa't* (Lithotryptic)
- *Muqawwi e Mida* (Tonic for stomach)
- *Mushtahi* (Appetizer)
- *Muqawwi e Bah* (Aphrodisiac)
- *Daf e Taffun* (Antiseptic)
- *Hadim* (Digestive)
- *Munaffith e Balgham* (Expectorant)
- *Musaffi e Dam* (Blood purifier)
- *Mundamil-e-Qurooh* (Wounds Healer)

XIV. Therapeutic uses of *Asl*

- *Istisqa* (Ascites)
- Oligouria
- *Laqwa* (Bell's palsy)
- *Falij* (Paraplegia)
- *Sual e Balghami* (Productive cough)
- Cataract
- Epiphora
- Otitis media
- *Waja al Uzn* (Earache)
- Qurooh (Wounds)
- Chloasma
- Ring worm
- *Waram e Lauzatain* (Tonsillitis)
- Dog bite
- *Yaraqan* (Jaundice)
- *Azm e Tihal* (Enlargement of spleen)

- *Khushunat e Halaq* (Sore throat)
- *Amraz e Ria* (Chest diseases)
- *Du'fal Bah* (sexual debility)
- *Hisat e Kuliya* (Renal calculi)
- *Deedan e Ama* (Intestinal worms)
- *Amraz e Qalb* (Heart diseases)
- *Juzam* (Leprosy).

XV. Pharmacological studies Antibacterial activity

- *Antibacterial properties* of *Asl Khalis* (Honey) are the result of the low water activity causing osmosis, hydrogen peroxide effect and high acidity (Wahdan, 1998).^[52]
- Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has now been described globally, as a clinically significant pathogen, particularly associated with skin and soft tissue infections. The study demonstrated that, *in vitro*, these natural products had an *antimicrobial activity* against the CA-MRSA organisms tested (Maeda, *et al.* 2008; Temaru, *et al.* 2007).^[30,46]
- Mixture of *Asl Khalis*, olive oil, and beeswax was effective for treatment of diaper dermatitis, psoriasis, eczema, and skin fungal infection. The mixture has *antibacterial properties* (Al-Waili, *et al.* 2006).^[3]
- *Asl Khalis* (Honey) was evaluated for its *antimicrobial* potency both in its crude vicious state and diluted form against *Salmonella typhi*, *Shigella dysenteriae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* and crude *Asl Khalis* showed higher *antibacterial* potency on the test organisms (Omoya, *et al.* 2010).^[36]
- Another study indicated that the *Asl Khalis* in pure form (without dilution), was effective against bacteria: *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* using the disk diffusion technique. However, the disk diffusion method had negative effect on the fungus *Candida albicans* (Ansari & Alexander 2009).^[57]
- It is speculated that the amylase present in *Asl Khalis* hydrolyzed the starch chains to randomly produce dextrin and maltose and that this increased the osmotic effect of the media, which consequently increased the *antibacterial activity* (Boukraa, *et al.* 2008).^[14]
- *Tualang Asl Khalis* has a *bactericidal* as well as bacteriostatic effect. It is useful as a dressing, as it is easier to apply and is less sticky compared to Manuka Honey. However, for *Gram positive bacteria*, *tualang honey* is not as effective as usual care products such as silver-based dressing or medical grade *Asl Khalis* dressing (Nasir, *et al.* 2010).^[35]

XVI. Wound healing activity of *Asl* in Ulcer

- Honey acts mainly as a hyperosmolar medium and prevents bacterial growth. Because of its high viscosity, it forms a physical barrier and the presence of enzyme catalase gives honey an

antioxidant property. Its high-nutrient content improves substrate supply in local environment promoting epithelialization and angiogenesis. These properties of honey make it an ideal and cost-effective dressing for burn patients (Bangroo, *et al.* 2005).^[7]

- Salad dressings incorporating honey provided protection against oxidation to a degree similar to that of EDTA, as determined by peroxide value and p-anisidine value (Rasmussen, *et al.* 2008).^[40]
- A study indicated markedly greater efficacy of Honey compared with alternative dressing treatments for superficial or partial thickness burns (Wijesinghe, *et al.* 2009).^[53] Using a medical-grade honey, eight species of problematic wound pathogens, including those with high levels of innate or acquired antibiotic resistance, were killed by 4.0–14.8% Honey, which is a concentration that can be maintained in the wound environment. The data indicate that honey is an effective topical antimicrobial agent that could help reduce some of the current pressures that are promoting antibiotic resistance (Blair, *et al.* 2009).^[12]
- The study shows that antibacterial properties and additional beneficial effects of medical honey on wound healing should encourage other wound care professionals to use CE-certified Honey dressings with standardized antibacterial activity, as an alternative treatment approach in wounds of different natures (Simon, *et al.* 2009).^[44]
- Honey can be used in diabetic foot ulcers in conjunction with standard wound care principles (Eddy, *et al.* 2008).^[16] The studies support the proposition that there are clinical benefits from using honey in wound care (Robson, *et al.* 2009).^[41]

XVII. Honey in Association with Diabetic Wounds

Although DM is almost harmless if controlled, the state of abnormally high blood glucose levels associated with the disease can lead to some serious complications. Although diabetic wounds are similar to wounds in normal patients, the healing process is different from that of other wounds. The most crucial part of diabetic wounds is that the healing process is notoriously slow. Hypoxia occurs in diabetic wounds, and it is caused by early inflammatory responses and a high load of reactive oxygen species (ROS) induced by hyperglycemia in diabetic patients. The formation of advanced glycation end-products (AGEs) under hyperglycemic conditions and interactions with their receptors (RAGE) are also associated with impaired wound healing among diabetic patients. Several dysregulated cellular functions involved in diabetic wounds (defective T-cell immunity, defects in leukocyte chemotaxis, phagocytosis, bactericidal capacity, dysfunctions in fibroblasts and epidermal cells) were attributed to inadequate bacterial clearance and delayed or impaired repair in individuals with diabetes.

In addition, slow wound recovery generally increases treatment costs. It has been reported that the total direct

costs for healing infected diabetic foot ulcers that do not require amputation are approximately \$17,500, whereas the costs for lower-extremity amputations are between \$30,000 and \$33,500 depending on the level of amputation. Because of these high costs, scientists have been searching for a cheaper, naturally sourced remedy for diabetic wounds that is efficacious. Honey is a potential candidate because it is easily available and natural.

XVIII. Honey as an Antimicrobial and Anti-Inflammatory Agent

Honey is considered one of the older wound dressing biomaterials. Gifted with anti-inflammatory, antioxidant, and antibacterial characteristics, honey is a natural substance that is frequently reported as a traditional medicine and has been increasingly investigated, especially for chronic wound treatment. The current evidence shows that honey's composition and antimicrobial properties depend on the geographic conditions, the surrounding environment of the hive, and the metabolic activity of the bees, as well as the processing and storage conditions, which will confer distinct characteristics and levels of effectiveness on different microbial strains. For instance, manuka honey, a honey derived from the nectar of the *Lepstospermum scoparium* (manuka) plant in New Zealand, is recognized for its high concentrations of methylglyoxal (MGO), which confer to pronounced antibacterial activity. The presence of polyphenols is another important factor that contributes to a honey's color, taste, and antioxidant and antimicrobial characteristics, which depend on its floral sources. Despite the differences related to a honey's geographic and botanical origins, almost all types of honey present bactericidal activity as an intrinsic promising property for drug development.

Honey is effective against more than 60 bacterial species and has been widely used in the treatment of acute and chronic wounds, ulcers, and burns. Interestingly, honey is also able to inhibit bacterial cell wall synthesis, changing the cell shape and inducing lipopolysaccharide outer membrane disintegration. In vitro studies carried out on wound healing have shown the benefits of honey, not only as a general antibacterial medicine but also in the treatment of multidrug-resistant bacteria. Different types of honey, such as buckwheat (*Fagopyrum esculentum*), blueberry (*Vaccinium corymbosum*), and manuka, have shown great effectiveness against *E.coli* and *Bacillus subtilis*, as well as vancomycin-resistant *Enterococcus faecium* and MRSA. The effectiveness of honey against multidrug-resistant bacteria was shown in a recent review and it has gained increasing attention, especially due to the worldwide antibiotic resistance concerns. In this sense, honey was reported as an effective treatment for chronic wound infections not responding to antibiotics.

During the wound healing process, honey has a modulatory role in the inflammatory phase, avoiding a

chronic or severe inflammatory state being reached. Importantly, there is some evidence that honey inhibits the nuclear factor kappa B (NF- κ B) pathway through NF- κ B nuclear translocation attenuation, decreasing the inflammatory mediators, such as cyclooxygenase-2 (COX-2) and TNF- α . Conversely, the activation of macrophages and the stimulation of COX-2, TNF- α and prostaglandins (PGE2) were also observed after treatment with thyme honey, suggesting that honey is an immune-modulator of wound healing. This means that honey provides pro-inflammatory and anti-inflammatory properties that are activated according to the wound characteristics. A reduction in the reactive oxygen

species (ROS) released from infiltrated neutrophils is another major mechanism by which honey can decrease the cells' oxidative stress levels and reduce the inflammatory status. Japanese honey also showed effectiveness in reducing the wound area during the inflammatory phase. During the proliferative phase, honey is also able to stimulate angiogenesis and wound contraction through fibroblast, myofibroblast, and collagen deposition, despite improve the re-epithelialization, possibly due to the high osmotic pressure and presence of hydrogen peroxide. During the remodeling phase, honey also shows benefits in decreasing scarring and improving tissue remodeling.

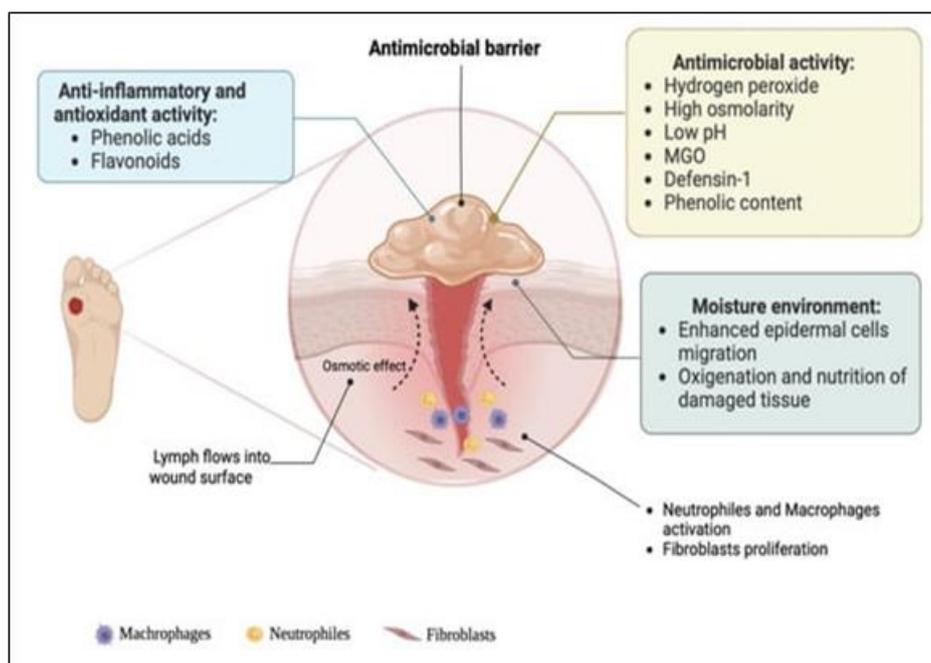


Fig. 06: Honey potential mechanisms of wound healing.

The *in vitro* evidence suggests that honey might initiate healing in recalcitrant wounds by accelerating several mechanisms such as the desquamation of devitalized tissue, the mobilization of macrophages to the wound bed, increasing cellular energy sources, enhancing granulation and epithelization, and preventing infection. Moreover, honey might improve wound healing by preventing the biofilm formation of *S. aureus*, *Streptococcus pyogenes*, and *P. aeruginosa* by impairing bacterial binding at wound sites and on the surfaces of keratinocytes. In mature wound biofilms, manuka and honeydew honey were also able to decrease the viability of *S. aureus*, *Streptococcus agalactiae*, and *P. aeruginosa* within 48 h. This evidence suggests an advantage for honey in chronic wound treatment.

In vivo, honey is widely reported as a safe, cost-effective, and beneficial dressing biomaterial for wound healing. C57BL/6J mice treated with 50 μ L of undiluted indigenous New Zealand rewarewa honey were able to inhibit edema and leukocyte infiltration after four hours of application, supporting honey's anti-inflammatory activity, which targets the neutrophil respiratory burst,

recruitment, and swelling. In humans, treating acute wounds such as burns with honey significantly reduced the healing and infection time due to honey's antimicrobial, cell proliferation, and anti-inflammatory effects. Similarly, chronic wounds, such as venous leg ulcers, treated with honey demonstrated increased rates of healing with lower rates of infection than with hydrogel. In patients with pressure ulcers at stages II and III, five weeks of treatment with gauze dressings embedded with monofloral unprocessed honey decreased the ulcer size when compared to patients treated with ethoxy-diamino-acridine and nitrofurazone dressings, showing honey's effectiveness in wound healing as an advanced treatment.

CONCLUSION

Peptic Ulcer disorder is the major health problem in both developed and developing countries. There are number of modern medicine available for this condition but adverse effects and high cost are the major limitations for the use of these drugs Honey is an alternative medicine that is considered to be a suitable therapy with improved outcomes. It is a cost-effective and safe natural agent

with rapid diabetic wound healing capacity, Peptic ulcer treatment. However, additional successful clinical evidence is required with validated laboratory findings to establish honey as one of the most effective alternative topical medicines for treating diabetic wounds.

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