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Review Article

### *Tukhm Khashkhaash* (Poppy Seeds): A Unani drug of multitudinous potential

Shahid Shah Chaudhary <sup>1</sup>, Mohd Aslam <sup>2</sup>, Aisha Siddiqui <sup>3\*</sup><sup>1</sup>Assistant Professor, Deptt. of Ilmul Saidla, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi<sup>2</sup> Professor, Deptt. of Ilmul Advia, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi<sup>3</sup>Assistant Professor, Deptt. of Ilmul Advia, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi

#### ABSTRACT

*Tukhm Khashkhaash* is the seeds of *Papaver somniferum* belonging to the family Papaveraceae. The description of Poppy seeds is mentioned in various classical Unani books. Renowned Unani scholar Avicenna had also described poppy seeds in his famous book "The Canon of Medicine". He wrote that *Tukhme Khashkhaash safaid* are the small white seeds obtained from the capsule of white poppy plant. The seeds which are obtained before the incision of capsules for the extraction of opium are considered to be of best quality. They are used since centuries for treating various ailments like diarrhea, dysentery, cough, premature ejaculation, chronic cough, insomnia and skin disorders as well as a nutritive food. Their antibacterial, anti-carcinogenic and hypoglycemic potential have also proved on scientific basis. In this review an effort have been made to collect the disseminated information and summarize the available data of the said drug.

**Keywords:** Khashkhaash, Poppy Seed, Unani

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#### \*Address for Correspondence:

Aisha Siddiqui, Assistant Professor, Deptt. of Ilmul Advia, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi, India

#### INTRODUCTION

*Tukhm Khashkhaash* is the seeds of *Papaver somniferum* belonging to the family Papaveraceae. On tracing the history of this drug it was found that it was known to Greek in the beginning of the third century B.C. The Arabians next became acquainted with it. It is thought that the Persians and Indians became acquainted with opium through the Arabians. The poppy generally cultivated in India is the *P.somniferum* var. album, with white flowers and white seeds, but a red flowered and black seeded variety is found in the Himalayas. The description of Poppy seeds is mentioned in various classical Unani books. Renowned Unani scholar Avicenna had also described poppy seeds in his famous book "The Canon of Medicine". He wrote that *Tukhme Khashkhaash safaid* are the small white seeds obtained from the capsule of white poppy plant. Opium is obtained by incising the unripe seed capsules as milky latex. According to him there are various kinds of poppy seeds, (a) Garden poppy, (b) Wild poppy, (c) black poppy and (d) horned poppy. The latter is

also called *Al-bhahri* having curved seeds. Another kind is spotted poppy which is also called *Hiraqli*. According to him the best and safest kind of poppy is the white poppy.<sup>1</sup>

The whole plant parts of opium poppy are valuable in terms of food, medicine, vegetable and as brew- ages. The seeds of opium poppy are highly nutritious as it contains protein upto 24% and other vital nutrients beneficial for human health. The leaves of the plant are used as vegetable in some places in the world. The seed oil of poppy is also important for health point of view due to having high percentage of linoleic acid (68%) which helps in lowering blood cholesterol level in human body and is also used in the treatment of cardiovascular diseases in human system.<sup>2</sup> Avicenna wrote in his famous book that poppy seeds are somniferous and anesthetic specially the black poppy. It stops catarrh and induces sleep even when used as a suppository. Poppy seeds are useful in hot cough, chest congestion and hemoptysis<sup>3</sup>.



Figure 1

**TAXONOMIC HIERARCHY<sup>4</sup>**

Kingdom	:	Plantae
Subkingdom	:	Viridiplantae
Infrakingdom	:	Streptophyta
Superdivision	:	Embryophyta
Division	:	Tracheophyta
Subdivision	:	Spermatophytina
Class	:	Magnoliopsida
Superorder	:	Ranunculanae
Order	:	Ranunculales
Family	:	Papaveraceae
Genus	:	Papaveraceae
Species	:	Papaver somniferum

**VERNACULAR NAMES<sup>5</sup>**

Arabic	:	Bazr-ul-Khashkhash, Abul Nom <sup>6</sup>
Persian	:	Tukhm-e-Anarkewa
Assamese	:	Pasto Dana
Bengali	:	Pasto Dana
English	:	Bale-wort, Caranation Poppy, Joan Silver pin
Gujarati	:	Aphina, Khushus, Posta
Hindi	:	Kashkash, Posta
Kannada	:	Khasakhasi
Kashmiri	:	Kashkash
Malayalam	:	Kashakasha
Marathi	:	Aphu, Khuskhus, Posta
Oriya	:	Post Dana
Punjabi	:	Khashkhash, khishk
Sanskrit	:	Khasa, Khakasa
Tamil	:	Gasagasala, Kasakasa
Telugu	:	Gasagasala, Kasakasa
Urdu	:	Khashkhaash

**HISSA MUSTAMELA (Part Used)**

Seeds, Capsule and inspissated juice

**MIZAJ (Temperament)**

Cold<sup>2</sup> Dry<sup>1 5</sup>

Cold<sup>2</sup> Moist<sup>1 7</sup>

**MIQDARE KHURAK (Therapeutic Dose)**

7 gm- 35 gm<sup>7</sup>

**MAZARRAT (Adverse Effects)**

For Lungs (In excess)<sup>7</sup>

**MUSLEH (Correctives)**

*Mastagi, Saleekha, Karafs, Shahad<sup>7</sup>*

**BADAL (Substitute)**

*Tukhm-e-Kahu*

**COMPOUNDS<sup>5</sup>**

*Banadiq-ul-Buzoor, Habb-e-Shaheeqa, Habb-e-Sil, Khamira Khashkhaash, Laooq-e-nazli, Laboob-e-Kabir, Laboob-e-Sagheer, Majoon-e-Rah-ul-Momineen, Tiryaaq-e-Nazla, Sufoof-e-Musammin, Roghan Laboob Saba Barid, Roghan-e-Khashkhash*

**HABITAT AND DISTRIBUTION**

Native to Asia; now grown in Uttar Pradesh, Punjab, Rajasthan and Madhya Pradesh.<sup>44</sup> Bihar and Bengal produce what is known as "Patna or Bengal garden opium", Benares and United Provinces of Agra and Oudh produce "Benares opium" and Central and Western India are the sources of what is known as "Malwa opium". Opium is grown in many parts of the World and chiefly in Turkey, Asia Minor, Persia, India, China, Egypt and Southeastern Europe. It is also grown in Nepal, Assam and Burma.<sup>8</sup> For the production of seeds var. album (white seeds) has been cultivated in Dehradun and Tehri Garhwal districts of Uttar Pradesh.<sup>9</sup>

**BOTANICAL DESCRIPTION**

**Plant:** Erect annual herb, about 1 m to 1.5 m tall. Stalk – green, tender, hairy. Root – subtle and medium. Leaves – long and wide, alternately arranged with serrated margins. Flowers – white, red or black in color. Fruit- different cells, small size, and it get ruptures on its own. Capsule – globular, longitudinally grooved.<sup>10</sup>

**Seeds:** Seeds are numerous, dried, white to slate grey in color, about 1.0 to 1.25 mm long, round to reniform or kidney shaped (Figure 1). The surface is covered with polygonal reticulations. Hilum and micropyle are situated in the notch near the smaller end.<sup>11,12</sup>

### Best quality poppy Seeds

The seeds which are obtained before the incision of capsules for the extraction of opium, are considered to be of best quality.<sup>9</sup>

### MEDICINAL ACTIONS (as per Unani Literature)

*Munawwim* (Narcotic),<sup>13,14,15,16,17,18</sup> *Muqawwie Bah* (Aphrodisiac),<sup>16</sup> *Musakkine Alam* (Analgesic),<sup>13</sup> *Qabize Shikam* (Constipative),<sup>14,17</sup> *Musammine Badan* (Adipogenous),<sup>13,14,16,17</sup> *Muqawwie Dimagh* (Brain Tonic),<sup>13,17</sup> *Mukhrije Balgham* (Expectorant),<sup>19</sup> *Murattab* (Humectant),<sup>16</sup> *Mukhaddir* (Anesthetic),<sup>14,17</sup> *Muzaiyade Laban*,<sup>16</sup> *Habis* (Relentive),<sup>16</sup> *Qabiz* (Constipative),<sup>13,16</sup> *Muzaiyade Mani*.<sup>16</sup>

### THERAPEUTIC USES (as per Unani Literature)

*Irqun Nisa* (Sciatica),<sup>16,19</sup> *Ishal* (Diarrhea),<sup>14,18,19</sup> *Khansi* (Cough),<sup>16,17,18,19</sup> *Quwwate bah main ezafa* (Aphrodisiac),<sup>19</sup> *Khushk Khansi* (Dry Cough),<sup>13,14</sup> *Nafasuddam* (Styptic),<sup>16,19</sup> *Chati aur Halaq ki khushunat* (Throat Irritation),<sup>13</sup> *Sozishhe Masana* (Cystitis),<sup>14,17,18</sup> *Seene main Insibab nazla*,<sup>18,19</sup> *Tape Diq* (Tuberculosis),<sup>13,14,17</sup> *Hawas ko sust karta hai*,<sup>13</sup> *Khoon saleh banata hai*,<sup>14,17</sup> *Suda* (Headache),<sup>19</sup> *Sarsaam* (Meningitis),<sup>16</sup> *Quroohe Masana wa Gurda* (Vesicular Ulcer),<sup>16</sup> *Zofe Gurda*.<sup>14,17</sup>

### ETHNOBOTANICAL ACTIONS

Anti-inflammatory,<sup>10</sup> Spasmolytic,<sup>20</sup> Demulcent,<sup>8,20</sup> Cardiotonic,<sup>10</sup> Mild astringent,<sup>8</sup> Emollient,<sup>20</sup> Antitussive,<sup>21</sup> Tonic,<sup>22</sup> Nutritive,<sup>8,20</sup> Antidiarrhoeal,<sup>21</sup> Analgesic,<sup>10,21</sup> Aphrodisiac,<sup>22</sup> Sedative.<sup>10</sup>

### ETHNOBOTANICAL USES

Sciatica,<sup>10</sup> Diarrhoea,<sup>20,21,22,23</sup> Dysentery,<sup>20,22,23</sup> Cough,<sup>8</sup> Premature ejaculation,<sup>10</sup> Chronic cough,<sup>10,21</sup> Internal bleeding disorder,<sup>10</sup> Asthama,<sup>8</sup> Catarrh of Bladder,<sup>20</sup> Dyspnoea,<sup>21</sup> Pertussis,<sup>21</sup> Insomnia,<sup>8,10</sup> Skin care,<sup>23</sup> Obstinate constipation,<sup>20</sup> Scalds.<sup>20</sup>

### OTHER USES OF POPPY SEEDS

#### Poppy Seeds as a Diet

The trainers of ancient Greek and Roman athletes were recommended various nutritious diets to them. They fed the athletes on white bread made of ground meal sprinkled with poppy seeds.<sup>24</sup> Poppy seeds are considered nutritive and are used in breads, curries, sweets and confectionary. Seeds are also used in pharmaceuticals and in production of lecithin.<sup>9</sup>

#### Poppy Seed Oil

Poppy oil is an odorless pale yellow color fixed oil possesses a pleasant almond-like taste. Forty to 60% of the weight of poppy seeds is oil which is extracted by either cold or hot expression. Seeds from the capsules which have not been scarified for opium give higher yield of oil than that scarified.<sup>9</sup>

#### Uses of Poppy Seed Oil:

The plant is commonly grown as a source of edible and industrial oil. It is useful as a salad oil as it is less liable to become rancid than olive oil. The oil is also used to make

margarine and salad dressing, and is employed as cooking oil.

Artists use poppy seed oil as a drying oil, useful in paints and varnishes. It is also a component of some soaps, ointments and emulsions.

### SCIENTIFIC STUDIES

#### a) Phytochemical Studies

The seeds have high protein content, the major component being a globulin which accounts for 55% of the total nitrogen.<sup>9</sup>

The seeds contain Thiamine 420, Riboflavin 46, Folic acid 30, pantothenic acid 2667 and Niacin 1877 mcg/100 g. The seed oil contains gamma-tocopherol 220, alpha-tocopherol 40 and beta-tocopherol 20 mcg/100 g. The seeds yield a fatty oil (45%) containing palmitic, stearic, oleic, linoleic and linolenic acids.<sup>20</sup>

#### Composition of Poppy Seeds:

Potassium and calcium are the predominant elements in the seeds followed by sodium, magnesium and phosphorus. In general, plants have higher contents of potassium than of sodium. The sodium content of poppy seeds is higher than that in most cereals.<sup>25</sup> Seven fatty acids were detected and linoleic acid was the predominant fatty acid, accounting for 75.9% of total fatty acids.<sup>26</sup> Palmitoleic, arachidic and linolenic acids were not reported in most published works. From a nutritional point of view, poppy seed oil is also a good source of essential fatty acids, especially linoleic acid, as compared to the other edible oilseeds. Pantothenic acid in poppy seeds was found in the greatest amount, followed by the vitamins niacin and thiamin.

### OPIATES IN POPPY SEED

Poppy seeds contain very small quantities of morphine, codeine, narcotine, papaverine and thebaine.<sup>27</sup> Following studies also showed that seeds contain narcotic alkaloids in traces.

#### Urine

In two separate trials in year 1984, Giserlher & William measured the urine morphine level after consumption of poppy seeds. They reported level of morphine upto the maximum level of 18µg/ml using RIA, EMIT-ST and GC techniques and even after 60 hr post ingestion positive immunoassay results were found.<sup>28</sup>

In another study poppy seed filling was analyzed for morphine and codeine content. Concentrations in the range 17.4 to 18.6 p.g/g (morphine) and 2.3 to 2.5 g/g (codeine) were found in different lots of the filling, which is widely used in baking. The effect of consumption of poppy seed filling on opiate urinalysis results is discussed. Morphine concentrations as high as 4.5 mg/L are reported, with persistence of concentrations >0.3 mg/L as long as 35 h after consumption.<sup>29</sup>

Opiate urinalysis for morphine and codeine after ingestion of as much as 75gm seed was observed between 2-12 hours and 3-7.5 hours showed the maximum concentration ranged from 291-500 ng/ml and 0-214 ng/ml of morphine and codeine respectively.<sup>30</sup> In another study quantitative analysis of morphine and codeine by GC-MS in human urine was performed after oral intake of cakes containing poppy seeds. Among the nine volunteers most of the participants had urinary concentration higher than 1µg/mL for several



hours and one volunteer showed a maximum concentration of 10.0 µg/mL of urine. Concentration of codeine was observed 0.06 – 0.82 µg/mL in the collected urine samples of volunteers.<sup>31</sup> M. Matyus et al. found that the adults excrete morphine and codeine in their urine above the approved cut-off level for up to 3 days after eating one piece of poppy cake.<sup>32</sup>

Zebelman et al. had analyzed the urine samples of five volunteers before and 2 hr after the consumption of poppy seed cookies. The urine samples were analyzed with the EMIT opiate assay and by GC-MS. Result showed that all the samples collected prior to the consumption of the poppy-seed cookies were negative for opiates, while all the 2-hr post-prandial results were positive for morphine and codeine.<sup>33</sup>

#### Oral Fluid

Analyses of urine for the determination of opioid have been done by various researchers. Oral fluid is a possible alternative to urine for drug testing. Rohrig & Moore in year 2003 analyzed the oral fluid samples of volunteers after ingestion of poppy seeds for the presence of codeine and morphine using GC-MS. Results showed the morphine concentration was greater than the suggested cut off concentration in oral fluid upto 1 hour and 8 hour in urine.<sup>34</sup>

#### Serum

M. Matyus et al. had developed a sensitive method for the determination of free morphine and codeine in blood. This method provides an analytical basis for making a clear distinction between legal (poppy seed ingestion) and illicit use of opiate containing substances.<sup>32</sup>

#### Hair

In an experiment it was demonstrated that consuming high morphine content poppy seeds on a regular basis produce morphine level in hair well below the cutoff level of 2ng/10 mg hair. Morphine concentration in the hair of the subjects who had consumed 50gm of poppy seed (containing 49mg of morphine) weekly for 3 weeks was found ranged from 0.04 to 0.48ng morphine/10mg hair.<sup>35</sup>

#### Chemical composition and oxidative stability of poppy seed oil

Three seeds of Turkish origin, flax, **poppy** and safflower were analyzed for their proximate, fatty acids, tocopherols (tocopherols and tocotrienols) and total phenolic composition, and oxidative stability of their oil. The major fatty acid in the flax oil was α-linolenic acid, comprising 58.3% of total fatty acids, whereas **poppy** and safflower oils were rich in linoleic acid at 74.5% and 70.5% level, respectively. The amount of total tocopherols was 14.6 mg/100 g flax, 11.0 mg/100 g **poppy** and 12.1 mg/100 g safflower seed. Flax and **poppy oil** were rich in γ-tocopherol as 79.4 mg/100 g oil and 30.9 mg/100 g oil, respectively, while α-tocopherol (44.1 g/100 g oil) was dominant in safflower oil. Only α- and γ-tocotrienol were found in the oils. Oxidative stability of oils was measured at 110 °C at the rate of 20 L/h air flow rate, and **poppy oil** (5.56 h) was most stable oil followed by safflower oil (2.87 h) and flax oil (1.57). There were no correlation between oxidative stability and saturation degree of fatty acids and tocol levels of the oils. All of the seeds investigated provide a healthy oil profile and may have potential as a source of specialized oils on a commercial scale.<sup>36</sup>

## (b) PHARMACOLOGICAL ACTIONS

### Antibacterial activity

Antibacterial activity of aqueous infusions and aqueous decoctions of kalonji (*Nigella sativa* L., Ranunculaceae), cumin (*Cuminum cyminum* L., Umbelliferae) and **poppy seed** (*Papaver somniferum* L., Papaveraceae) were investigated against 188 bacterial isolates belonging to 11 different genera of Gram +ve and Gram -ve microorganisms isolated from oral cavity of apparently healthy individuals. Disc diffusion method was performed to test antibacterial activity. The highest antibacterial potential was observed from the aqueous decoction of cumin which inhibited 73% of the tested microorganisms than aqueous decoctions of kalonji (51%) and poppy seed (14.4%). In case of tested aqueous infusions, kalonji and cumin showed inhibitory potential against 17% and 5.9% tested microorganisms, respectively. Besides, all isolates were found resistant to aqueous infusion of poppy seed.<sup>37</sup>

### Anticarcinogenic effects

The anticarcinogenic properties of some commonly consumed spices and leafy vegetables were investigated. The effects of feeding the plant products on the induction of squamous cell carcinomas in the stomachs of Swiss mice by feeding benzo[a]pyrene(B[a]P) and on the induction of hepatomas in Wistar rats by feeding 3'-methyl-4-dimethylaminoazobenzene (3'MeDAB) were investigated. Among the nine plant products tested, cumin seeds (*Cuminum cyminum* Linn) and basil leaves (*Ocimum sanctum* Linn) significantly decreased the incidence of both B[a]P-induced neoplasia and 3'MeDAB-induced hepatomas. **Poppy seeds** (*Papaver somniferum* Linn) significantly inhibited B[a]P-induced neoplasia alone, while the other plant products, asafoetida, turmeric, drumstick leaves, solanum leaves and alternanthera leaves were ineffective. These results suggest that cumin seeds, basil leaves and to a lesser extent poppy seeds, which are all widely used in Indian cooking, may prove to be valuable anticarcinogenic agents.<sup>38</sup>

The seeds were found to increase the activity of carcinogen detoxifying enzyme, glutathione-S-transferase by more than 78% in stomach, liver and esophagus in mice.<sup>20</sup>

### Hypoglycemic Activity

The aqueous extract of seeds showed marked hypoglycemic activity when administered to glucose loaded and alloxan diabetic rats.<sup>20</sup>

### Differentiation between Poppy ingestion & illicit consumption of opium

The free morphine present in the serum rapidly decreases in the case of eating food that contains poppy seed, becoming undetectable after 3 h, whereas in the case of illegal opiate injection, the free level of morphine remains elevated for quite some time. Likewise, the free morphine excreted in urine specimens is in fact undetectable after 3 h in the case of poppy seed ingestion, but in the case of drug abuse, it remains detectable for quite some time.<sup>32</sup>

### Use of Poppy seeds in diagnosis of a disease:

**Poppy Seed Test:** This test involves the oral intake of 50 gm poppy seeds mixed in beverage or yogurt and visual inspection of urine samples during the next 48 hours. Detection of poppy seeds in the urine is interpreted as a positive confirmatory test for enterovesical fistulas.<sup>39</sup>

The diagnosis of Vesico-enteric fistula is puzzling and based on radiography with barium enema, cystoscopy or cystography. However, in up to 50% of patients none of these methods is satisfactory for establishing the diagnosis. Therefore, a simple and low cost diagnostic method involving the oral intake of poppy seed has been used by some researchers. Results showed that the oral intake of poppy seed is a simple method for diagnosing a fistula between the urinary tract and bowel. This method may also support the surgeon decision for an operative procedure when the results of conventional diagnostic tools are not very much clear.<sup>40,41</sup> Another study conducted between year 2000 to 2006 also supports the usefulness of oral intake of poppy seeds in diagnosis of colovesical fistula. In this study researchers found that the poppy seed test is an accurate, convenient and inexpensive diagnostic test as it cost only \$5.37 per study and was positive in 20 of 20 patients (100%). On the other hand chromium nuclear study was positive in 16 of 20 patients (80%) at a cost of \$490.83 per study and Computerized tomography was positive in 14 of 20 patients (70%) at a cost of \$652.92 per study.<sup>42</sup>

In a different series Colovesical Fistula was correctly diagnosed preoperatively in 35 of 37 patients (94.6%) with the poppy seed test.<sup>39</sup> Therefore, they suggest poppy seed test as an ideal initial consideration for evaluating a suspected colovesical fistula.<sup>42</sup>

#### Allergy due to Poppy Seeds

Allergy to poppy seed is a rare phenomenon. So far only few cases have been reported in the literature. About 80% of these patients had an atopic background and other food allergies were present in two thirds of them. Investigators reported clinical and laboratory investigations in a 17 year old patient with a grade III anaphylactic reaction after a single bite of poppy seed cake, they also identified a cross-sensitization between poppy seeds and buckwheat.<sup>43</sup>

In year 1993 Vocks et al did a clinical study on 8 patients, they observed existence of both cross-reacting and unique components having common allergenic structures in hazelnut, rye grain, sesame seeds, kiwi, and poppy seeds.<sup>44</sup> A case of allergy due to inhalation of the poppy seeds was also reported.<sup>45</sup>

#### CONCLUSION

On tracing the history of *Tukhm Kahashkhash* (Poppy seeds) it was found that it was known to Greek in the beginning of the third century B.C. as a nutritive food as well as a drug. Since then it is being used in Unani system of Medicine, to treat various conditions including sciatica, diarrhea, dysentery, cough, premature ejaculation, chronic cough, insomnia and skin disorders. Recent modern pharmacological studies also showed its antibacterial, anti-carcinogenic and hypoglycemic potential. From a nutritional point of view, poppy seed oil is also a good source of essential fatty acids, especially linoleic acid, as compared to the other edible oilseeds. Therefore it is used in various diets. As the seeds also contain narcotic alkaloids in traces, therefore it must be consumed in a prescribed dose only. Some studies also suggest the role of its various constituents for the wide range of its nutritional, pharmacological and therapeutic properties. But there is still a need of more scientific phytochemical, pharmacological, and clinical studies on these seeds.

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