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Review Article

## Unravelling the Medicinal Secrets of Khashkhaash (*Papaver somniferum* L.) Seeds: A Powerful Blend of Unani Wisdom and Modern Science

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### Abstract

*Papaver somniferum*, a member of the Papaveraceae family, is also referred to as Khashkhash. It is among the traditional plants that have been used for medicinal purposes for a very long time. The health advantages of the poppy seeds (*Papaver somniferum* L.) are widely recognized. Proteins, oil content, dietary fiber, antioxidants, tocopherols, and other micronutrients are among its many nutrients. It is also being investigated because of its *in vitro* bioactive potential to treat a number of illnesses, including cancer, pain, and hypertension. With particular relation to Unani medicine, we have reviewed habitat, pharmacological activities, and phytochemicals in this paper.

**Keywords:** *Papaver somniferum*, Khashkhash, Unani medicine, pharmacological activities.

### INTRODUCTION (Ta'rif):

Tukhm Khashkhaash seeds are derived from *Papaver somniferum*, a plant in the Papaveraceae family. The history of this medicine revealed that it was known to the Greeks as early as the beginning of the third century B.C. The Greeks connected opium to a number of gods, such as Thanatos (Death), Nyx (Night), Morpheus (Dreams), and Hypnos (Sleep). Growing to a height of 60 to 120 cm, it is an upright annual plant. Turkey, Asia Minor, Persia, India, China, and Southeast Europe are the main places where it is grown. *Papaver somniferum* var. *album*, a poppy with white flowers and white seeds, is typically grown in India<sup>1</sup>. Alkaloids, flavonoids, phenolic compounds, and polyunsaturated fatty acids are among the important bioactive chemicals found in seeds that can be employed as dietary ingredients in a variety of ways. Because of its high amount of polyunsaturated fatty acids, poppy seed oil is regarded as a high-quality oil<sup>2</sup>. Poppy seed medicinal applications have been explored, including some features of their use in the context of Unani medicine. According to Unani literature, it has the

most significant therapeutic benefits, as evidenced by contemporary literature and scientific investigations. It has a variety of uses, including sedative, stimulant, analgesic, narcotic, and nutritional. Additionally, it helps with biliary colic, headaches, coughing, sleeplessness, and cardiac asthma<sup>3</sup>. In this paper we have provide a review on habitat, pharmacological actions, phytochemical with special reference to Unani Medicine.

### BOTANICAL DESCRIPTION (Mahiyat):

**Plant:** erect annual herb with a height of 1 to 1.5 meters. Stalk: hairy, soft, and green. Root: mild and subtle. Long and wide leaves with serrated edges are placed alternately. Flowers might be red, black, or white. Fruit is tiny, has distinct cells, and ruptures on its own. spherical, longitudinally grooved capsule.

**Seeds:** There are many dried seeds that are round to reniform or kidney shaped, white to slate gray in color, and 1.0 to 1.25 mm long. There are polygonal reticulations all over the surface. The micropyle and hilum are located in the notch next to the smaller end<sup>1,4</sup>.



**Figure 1: Khashkhaash Safaid (Plant and Seeds).**

#### **PARTS USED (Ajza-e-Musta'mila):**

Seeds, Capsule and inspissated juice<sup>5,6</sup>.

#### **VERNACULAR NAME (Mutradifat):**

**Arabic:** Bazr-ul-Khashkhash, Abul Nom, **Persian:** Tukhm-e-Anarkewa, **English:** Bale-wort, Caranation Poppy, Joan Silver pin, **Hindi:** Kashkash, Posta, **Sanskrit:** Khasa, Khakasa, **Urdu:** Khashkhaash<sup>6,7</sup>.

#### **SCIENTIFIC CLASSIFICATION<sup>8-10</sup>:**

Kingdom	Plantae
Subkingdom	Viridiplantae
Infra Kingdom	Streptophyta
Super Division	Embryophyta
Division	Tracheophyta
Subdivision	Supermatophyta
Class	Magnoliopsida
Super order	Ranunculanae
Order	Ranunculales
Family	Papaveraceae
Subfamily	Papaveroideae
Genus	Papaver L
Species	Somniferum L.
Bionomial name	Papaver Somniferum L.

#### **TEMPERAMENT (Mizaj):**

Cold in the second degree and moist in the first degree<sup>5,11</sup>.

**DOSE (Miqdar-e-Khurak):** 7 – 17.5 gm<sup>5,11</sup>.

#### **PHARMACOLOGICAL PROPERTIES (Afa'al wa Khawas):**

It possesses *Mukhaddir* (Anaesthetic), *Qabiz* (astringent), *Munawwim* (Sedative/ Hypnotics), *Muqawwi-e-Bah* (Aphrodisiac), *Muqawwi-i-Dimagh* (Brain tonic), *Mulattif* (Demulcent), *Mughazzi* (Nutritive), *Habis* (Retentive), *Musakkin-i-Alam* (Antianalgesic)<sup>5,6,12</sup>.

#### **THERAPEUTIC USES (Istematat):**

It is used in the management of *Ishaal* (Diarrhea) and the treatment of *Zaheer* (Dysentery), *Nazla* (Catarrh/influenza), *Sual* (Cough), *Zeeq-un-Nafs*

(Asthma), *Sahar* (Insomnia), *Su'al Yabis* (Dry cough), *Sailan-ur-Raham* (Leucorrhea), *Ishaal Safrawi* (Bilious diarrhea), *Hurqa al-Masana* (Burning in bladder). If used locally as *Zimad* it is helpful in relieving headaches (*Suda*). Giving enema with its decoction is helpful in managing *Zoosantariya*. When used along with *Ma'al-Asal* it has got *Mullayin* (Laxative) properties. Taking equal quantities of *Maghz-e-Badaam* and *Khashkhaash* has got hematinic properties<sup>5,11,13,14</sup>.

#### **COMPOUND FORMULATIONS:**

*Sharbat-e-Khashkhas*, *Laoq-e-Khashkhash*, *Laoq-e-Nazli*, *Itrifal Muqawwi-e-Dimagh*, *Roghan-e-Kishneez*, *Habb-e-Shaheeqa*, *Khameera-e-Khashkhash*, *Laboo-e-barid*, *Habb-e-Sil*, *Qurs-e-Munawwim Barid*, *Majoon-e-Khadar*<sup>15,16</sup>.

#### **ADVERSE EFFECTS AND CORRECTIVES (Muzir wa Musleh):**

It has been described harmful to lungs. Drugs like *Asal* (Honey), *Mastaghi* (*Pistacia lentiscus*), *Karafs* (*Pimpinella anisum*) has been mentioned as its corrective<sup>5,11</sup>.

#### **SUBSTITUTE (Badal):**

Tukhm-e-Kahu (*Lactuca sativa* Linn)<sup>5</sup>.

#### **CHEMICAL CONSTITUENTS (Kimiya'i Ajza):**

Papaver somniferum seeds contains various active biological compounds. The ethanolic extract of Papaver somniferum recorded the presence of Alkaloid, Cardiac Glycosides, Flavonoid, Phytosterols and Terpenoids whereas the Carbohydrates, Saponins, Tannins were absent in the extract<sup>17</sup>. A globulin, which makes about 55% of the total nitrogen, is the main protein component of the high protein content seeds. Thiamine 420, riboflavin 46, folic acid 30, pantothenic acid 2667, and niacin 1877 mcg/100 g are all present in the seeds. Alpha-tocopherol 40, beta-tocopherol 20 mcg/100 g, and gamma-tocopherol 220 are all present in the seed oil. A fatty oil comprising palmitic, stearic, oleic, linoleic, and linolenic acids is extracted from the seeds (45%). The most common elements found in seeds are potassium and calcium, which are followed by sodium, magnesium,

and phosphorus. With 75.9% of all fatty acids being linoleic acid, it is the most abundant fatty acid. Very trace amounts of morphine, codeine, narcotine, papaverine, and thebaine are found in poppy seeds<sup>1,18</sup>.

### PHARMACOLOGICAL ACTIVITIES:

The plant has been investigated for various biological activities:

#### Analgesic Activity:

Opium has long been used to treat pain and provides the fundamental chemical structure for all opioids. Opium is a narcotic analgesic and central nervous system depressant. Opium affects particular CNS receptors. By integrating painful signals sent by sensitive nerves, the painful signal is blocked<sup>19,20</sup>.

#### Hypnotic Activity:

Opium is the earliest known human hypnotic substance. Its hypnotic and sedative properties are unmatched, and it is commonly used to lower anxiety, promote calmness (sedative effect), and promote sleep (hypnotic effect). Since ancient times, opium has been utilized as a tranquilizer<sup>21</sup>.

#### Antitussive Activity:

One of the most popular and commonly used antitussive medications is narcotic, like codeine, which is used to treat the symptoms of the flu, common cold, hay fever, allergies, and other respiratory conditions including sinusitis and bronchitis. The central nervous system's  $\mu$ -opioid receptor and, to a lesser extent, the  $\kappa$ -opioid receptor are the main mechanisms by which codeine exerts its antitussive effects. These receptors function by blocking the brain stem's cough coordinating area, which throws off the cough reflex arc<sup>22</sup>.

#### Anticancer Activity

Current studies have revealed that alkaloids obtained from *Papaver somniferum* can also be used in cancer treatment and such studies have highlighted the antitumor activity of noscapine through arresting of metaphase and apoptosis induction in dividing cells<sup>23</sup>. Noscapine, a newly developed anti-mitotic drug that interacts with  $\alpha$ -tubulin and possesses anticancer anti-angiogenic effects, is one of the opium alkaloids that exhibit promising outcomes in the treatment of cancer. The interaction between HMGB1 (high mobility group box 1) and RAGE (receptor for advanced glycation end-products) causes glioblastoma (GBM), the deadliest type of primary malignant brain tumor. It has been discovered that papaverine, another anticancer medication, inhibits this interaction<sup>24,25</sup>.

#### Antimicrobial Activity

Papaver somniferum alkaloid extracts demonstrated efficacy against bacterial and fungal infections. The extracts demonstrated stronger inhibitory qualities against gram-positive bacteria than gram-negative bacteria and more against fungal than bacterial pathogens<sup>26</sup>. All investigated fungus species were found to be susceptible to the antibacterial properties of the poppy flower's essential oil. Poppy seed hydroalcoholic,

aqueous, and ethanolic extracts demonstrated efficacy against *Propionibacterium acnes* and *Staphylococcus epidermis*, two bacteria that cause acne<sup>27</sup>.

#### Antiviral Activity:

The antiviral effects of *Papaver* alkaloids when tested against several viruses belonging to various taxonomic groups in-vitro, it showed a great impact on their replication<sup>28</sup>. Certain alkaloids have been shown to have antiviral properties against the replication of poliovirus 1 and human rhinovirus 14. Several influenza virus strains, including respiratory syncytial virus (RSV) infections, human parainfluenza virus 3 (HPIV3), and paramyxoviruses parainfluenza virus 5 (PIV5), are efficiently inhibited by papaverine. Papaverine has a major impact on influenza viral morphology. Moreover, papaverine shown strong antiviral properties against measles, respiratory syncytial virus, cytomegalovirus, and human immunodeficiency virus<sup>20</sup>.

**Muscle Relaxant and Vasodilator Activity:** Opium alkaloid, Papaverine, largely is used for coronary and cerebral vasodilation and find its place as an important antispasmodic drug<sup>29</sup>. It blocks calcium and non-selective phosphodiesterase channels, which impacts the heart muscle and vascular smooth muscles. The pulmonary, systemic peripheral, and coronary arteries are among the bigger blood vessels whose smooth muscle is relaxed<sup>30</sup>. The resulting vasodilation has been potentially attributed to inhibition of cyclic nucleotide phosphodiesterase's, resulting in increased intracellular levels of cyclic AMP and cyclic GMP accompanied by a decrease in  $Ca^{++}$ <sup>20</sup>.

#### Antidiarrheal Activity:

Diarrhea is commonly treated with opiate antidiarrheal medications. By decreasing motility and allowing adequate absorption time, the use of such medications under strict supervision has been shown to be safe and useful in managing a variety of diarrheal disorders. Both  $\delta$  and  $\mu$  opioid agonists prevent mucosal secretion, release acetylcholine in the myenteric plexus, and prevent distention-induced peristaltic contractions via lowering neuronal excitability. Non-propulsive motility patterns increase and muscle tone changes<sup>19,20</sup>.

### CONCLUSION

In addition to *P. somniferum* pharmaceutical relevance, many cultures and nations have long recognized the traditional uses of several *Papaver* species. Because of this, this genus is desirable as a source of pharmacoactive chemicals and extracts (e.g., essential oil, phenolic compounds, and alkaloids). These substances are in charge of the *Papaver* genus's diverse biological properties, which include analgesic, antioxidant, anticancer, and antibacterial effects. However, in order to identify the active compounds or determine whether there is synergism that would make the use of the entire extracts more intriguing, pharmacological research on extracts from these plants should be supported by characterisation studies. Its many ingredients may also contribute to its broad spectrum of nutritional, pharmacological, and therapeutic qualities, according to

certain studies. But there is still a need of more scientific phytochemical, pharmacological, and clinical studies on these seeds.

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