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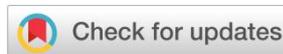
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Review Article

Khaksi (*Sisymbrium irio* L.): An updated review of its ethnopharmacology, phytochemistry and pharmacology

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Abstract

Sisymbrium irio L. (Khaksi) is an annual or biennial winter herb belonging to the Brassicaceae or Cruciferae family. It has been used as a medicine since antiquity. Today, it is used as a Unani and folk medicine in various regions of the world for its antipyretic, anti-choleric, aphrodisiac, expectorant and appetizer properties. The various parts of the plant possess many phytochemicals such as flavonoids, alkaloids, tannins, saponins, glycosides, beta-sitosterol, oils, etc., which are known to exhibit several pharmacological actions like antioxidative, antimicrobial, antipyretic, anticancer, and hepatoprotective activities. The literature is taken from Unani classical books and online databases like PubMed, Google Scholar, Science Direct, with the keywords khaksi, *Sisymbrium irio*, phytochemicals, and their pharmacological actions.

Keywords: Khaksi; London Rocket; Pyrexia; *Sisymbrium irio*; Unani medicine

Introduction

The Unani system of medicine is one of the oldest traditional medicinal systems that have been used for centuries to prevent and treat a wide range of diseases. Unani system of medicine addresses homeostasis of the body, which depends on the balance of the four humors (akhlat) and temperament (mizaj) which are balanced by six essential factors¹. Unani medicine promotes health and treats ailments using a variety of approaches such as regimental therapy, diet therapy, and pharmacotherapy. This system relies mainly on plant-origin drugs, then animal and mineral-origin drugs^{2,3}. Numerous clinical studies have demonstrated the effectiveness of Unani medicines with little or no adverse effects. Many herbal medications have recently undergone standardization, quality assurance, toxicity profiling, and formulations listed in the Unani Pharmacopeia of India have been validated².

Sisymbrium irio L. (*S. irio*), belonging to the family Brassicaceae or Cruciferae is an important medicinal plant used in Unani system of medicine. *S. irio* is often known as Khaksi, Khubah, Khub kalan, London rocket/Rocket mustard, and is found in different parts of the world⁴. *S. irio* is native to southern Europe, North Africa and temperate Asia but has been carried by migrants to North America, Australasia and South Africa. The tap-rooted herbaceous plant reproduces entirely by seed⁵. It grows near roadways, fences, and ditches^{6,7}.

It is used as febrifuge, expectorant, anti-asthmatic, aphrodisiac, cardio-tonic, diuretic, laxative, lubricant, hepato-protective, rubefacient⁸⁻¹⁰ anti-rheumatic, anti-inflammatory, and also used for dietary purposes; as it is rich in nutrients and protein¹¹. *S. irio* contains numerous bioactive compounds, including alkaloids, tannins, saponins, flavonoids, glycosides, phenolics, glucosinolates, carbohydrates, fatty acids, amino acids, proteins, and steroids^{4,12-14}. These compounds possess various pharmacological actions such as antipyretic,

analgesic, antioxidant¹⁵, antibacterial, antifungal, anti-inflammatory, anticancer, hepatoprotective, and bronchoprotective properties^{16,17}. This review explore the potential of Khaksi as mentioned in Unani literature with its phytochemical and pharmacological scientific advancement.

Material and Methods

Khaksi was searched in classical Unani literature for its temperament (mizaj), medicinal properties, and therapeutic applications. Urdu translations of classical textbooks such as *Muheet Azam* of Hakeem Mohammad Azam Khan, *Khazainul Advia* of Najmul Ghani,

Makhzanul Mufaradat and *Bayaz e Kabir* of Hakeem Mohammed Kabiruddin, *Qarabadeen e Majeedi*, National Formulation of Unani Medicine, and others were conferred. Published publications from PubMed, Science Direct, and Google Scholar and Research Gate were used to gather all available information about its phytochemicals and pharmacological research. The proper Unani terminologies were described using Standard Unani Medical Terminology, which was published by the Central Council for Research in Unani Medicine in collaboration with the World Health Organization.

Description of Khaksi in Unani Literature

Table 1: Alternative name in different languages

Language/ Region	Common name
Arabic	Khubba ¹⁸⁻²⁰ , Bazarulkhamkham ^{17,19}
Ayurvedic	Khaaksi ⁹
Chinese	Shuisuanjie ¹⁷
English	London Rocket ^{9,18} , Rocket mustard ¹⁷ , Hedge-mustard ¹⁸ , Desert rocket ¹⁷
Hindi	Asalio ¹⁷ , Khubkalaan ¹⁸
Japenese	Hosoegarashi ¹⁷
Korean	Git-teol-jang-dae ²¹
Marathi	Ranteekhee ¹⁸
Persian	Shibbawa Khakchi ¹⁸ , khubkalas ¹⁸ , Shaftarak ¹⁷ , Tukhm e shehwa ¹⁹
Punjabi	Janglisarson ^{17,18} , Maktrusa ^{17,18}
Rajasthani	Parjan ¹⁷
Spanish	Matacandil ¹⁷
Sindh	Junglisurson ¹⁷
Urdu	Khaksi ¹⁸ , Khubkalan ⁹

Morphology (Māhiyat): Khaksi is an annual or biennial, highly variable, stiffly erect, 20 - 60 cm tall, tap-rooted herb. Stems 2-10 mm thick, leaves stalked, pinnatifid or partite, lower leaves are broader than the upper leaves, lobes not auricled, tooth distant, terminal large, rarely hastate. The Flowers are yellow, minute, pedicle slender. Pods narrow, erect, 3-5 cm long, subtorulose, glabrous, valves 3 nerved, pedicles curved ascending, and stigma sessile. Seeds are small, pitted, present in series, reddish brown / orangish-brown, mucilaginous with a warty surface; odor pungent like mustard oil and taste like bitter mustard oil^{7,17,21}. The beans of the herb resemble mustard beans but are much smaller and filled with seeds that resemble poppy seeds (Tukhm-i-khashkhash)^{19,20,23}. They are Self-pollinated, and disseminated through seeds⁷.

Parts used (Hasas-i-Musta'mla): Leaves and seeds²⁴

Temperament (Mizāj): Unani system of medicine places a strong emphasis on drug temperament as a fundamental notion for understanding drug activity. The relationship between a person's temperament and a drug's temperament provides a foundation for the effective use of drugs, forecasting its effects, and determining potency. Unani physicians categorize medications into four categories (hot, cold, wet, and dry) based on their impact on a moderate human body²⁵. The temperament of Khaksi is hot and wet in the second degree^{18,20,23}; hot in second degree and wet in first degree²⁶.

Action and uses (Af'āl wa Mawāq-e-istemāl)

Table 2: Action and uses of Khaksi in Unani medicine

Action (Af'āl)	Uses (Mawāq-e-istemāl)
<i>Dāfi-i-hummā</i> (Antipyretic) ^{9,18-20,27} and <i>Mu'arriq</i> (Diaphoretic) ¹⁸	Fever, measles, smallpox, <i>Diq-ul-atfāl</i> (T.B. in children)
<i>Munaffith-i-balgham</i> (Expectorant) ^{18,23,27,28}	Chronic cough, asthma, pulmonary infections, <i>Diq-ul-atfāl</i>
<i>Munaffith akhlat-i-sadr</i> ¹⁸	Infections of throat and chest, hoarseness of voice
<i>Mushtahi</i> (Appetizer) ¹⁹ and <i>Muqawwi-i-mi'da</i> (Stomachic) ¹⁹	Appetizer, helps in digestion, stomach tonic, gastric ulcer
<i>Musakkin-i-alam</i> (Analgesic) and <i>Muḥallil-i-awrām</i> (anti-inflammatory) ¹⁷	Rheumatism, arthritis, inflammation, clean wounds
<i>Mufattiḥ sudda</i> (Deobstruent) ¹⁹	Vascular and airway disorder, atherosclerosis, asthma
<i>Muqaww-i-bāh</i> (aphrodisiac) ^{19,20,26,29,30}	Powder is used in <i>ḡuf al-bāh</i> (sexual debility), <i>sur'a al-inzāl</i> (premature ejaculation), <i>jarayān</i> (semorrhoea) and <i>kathra al-ihtilām</i> (nocturnal emission)
<i>Musammin-i-badan</i> ^{21,30,31}	Increases the weight when taken with milk
<i>Mudirr-i-bawl</i> (Diuretic) ^{17,30}	Decoction is used in the retention of urine, dysuria, and urinary tract infection
<i>Naf-i-haiḍa</i> ^{18-20,23,30}	Effective in cholera and decreases vomiting when taken as decoction with rose water (arq-i-gulab)
<i>Amrād-i-jild</i> (Skin disorders) ¹⁷	acne, boil/furuncle, urticaria
<i>Amrād-i-niswan</i> ³⁰	Used in amenorrhoea and dysmenorrhoea. Also used as vaginal pessary in some vaginal and uterine infections

Dose (Miqdār-i-khorāk): The dose of khaksi is 5-7g or 9 g.^{18,23,30}

Adverse effects (Muzir): As per Unani concept hot temperament (*garam mizaj*) individuals may show headache when used higher to therapeutic dose^{26,30}.

Correctives (Musleh): Katira (*Sterculia urens*)^{26,30}, Gulab (*Rosa damascena* Mill.)³⁰

Substitute (Badal): Toodri (*Cheiranthus cheiri* L.)^{26,30}

Compound formulation:

Table 3: Famous Unani compound formulations of Khaksi, uses and doses

Name of compound formulation & their forms	Therapeutic use	Dose
Sharbat-i-Khaksi (syrup form) ^{18,23,31,32}	<i>Judri</i> (smallpox), <i>Hasba</i> (measles) <i>Moti jhara</i> (enteric fever), <i>Naubati hummiyat</i> (intermittent fever)	25 ml
Dawa-e-Diqq-ul-Atfal (powder form) ^{33,34}	Humma-e- Diqq-ul-Atfal (Juvenile tuberculosis)	1 g

Description of Khaksi in the Scientific Literature

Taxonomical classification: Domain: Eukaryota; Kingdom: Plantae; Phylum: Spermatophyta; Subphylum: Angiospermae; Class: Dicotyledonae; Order: Capparidales; Family: Brassicaceae; Genus: *Sisymbrium*; Species: *irio*¹⁷

Phytochemistry

Various important secondary metabolites viz. alkaloids, flavonoids, glycosides, phenols, terpenes, tannins, steroids, and others like amino acid, proteins, carbohydrates and minerals are found in the seed of khaksi^{35,36,37}. Abdul Haleem et. al. (2017) has performed the standardization and safety profile of seeds of khaksi. Important bioactive compounds from different parts of *S. irio* have mentioned in the table 4.

Table 4: Important bioactive compounds identified in various part of Khaksi

Chemical constituents	Parts used/ Dosage form	Ref
Flavonoid, isorhamnetin	Seeds	9
Fatty acid: linolenic acid, linoleic acid, oleic acids, erucic acid, cis-11-Eicosanoic acid, palmitic acid, stearic acids and minerals viz. calcium, iron, sodium, zinc, potassium, strontium, titanium, chromium, manganese, copper, boron, aluminium, silicon, barium, phosphorus,	Seeds	9,38,39
Phenol; Oleic acid, Docosanoic acid, Tetradecanoic acid, Pentadecanoic acid, Hexadecanoic acid, 9-Octadecenoic acid (Z)-, Benzene-1,2-dicarboxylic acid; 4-(Dimethoxymethyl)-1,2-dimethylbenzene; 2,4-bis(1,1-dimethylethyl); 2-propenyl ester, 2-hydroxy-1,3-propanediyl ester, palmitoyl chloride, 2-hydroxy-1-(hydroxymethyl)ethyl ester, methyl ester, docosyl ester, 2,3-dihydroxypropyl ester; 7-(Bromomethyl)-7-pentadecene, Cholesta-3,5-diene; 2-Cyclohexen-1-one, 3,5,5-trimethyl-2-(2-propenyl); Palmitoyl chloride	Seeds / Ethanolic	40
Vitamin C, beta-carotene and minerals	Leaves	9
Apigenin (apigenin-7-O-glucoside), apigenin, isoquercetin, isorhoifolin, trans-p-coumaric acid, trans-ferulic acid, galocatechin, luteolin, nicotiflorin, naringenin, glucobrassicin, glucoputranjivin	Leaves / Ethanolic	41
Cyclopentanol, Decane, Dodecane, Tetradecane, Hexadecane, Eicosane, Hexadecanoic acid, methyl ester, 1,2-Benzenedicarboxylic acid, Orotic acid, Hexadecanoic acid, 1,2-Benzenedicarboxylic acid, 10-Octadecenoic acid, methyl ester, Phytol, Colfosceril palmitate, Campesterol, β -sitosterol, tert-butyl dimethylsilyl ester, Di-n-octyl phthalate, bis(2-ethylhexyl) ester, diundecyl ester,	Leaves/ Methanolic	42
Phenols: chlorogenic acid, ferulic acid, kaempferol, coumaric acid, protocatechuic acid, vanillic acid	Leaves / Methanolic	43
Beta-sitosterol, quercetin, isorhamnetin and 3 beta-D-glucoside ⁸	Aerial	9
Flavonoids: apigenin, kaempferol-3-O -xyloside-7-galactoside, kaempferol, apigenin-7-galactoside, apigenin-7-O-gluco(6",1") rhamnoside-5-methoxide, apigenin-7-O- β -D-glucoside, apigenin-7-O-gluco(6",1") rhamnoside, luteolin-7-O-glucoside, apigenin-7-O-gluco(6",1") rhamnoside, apigenin-7-di-glucoside, apigenin-7-O-(6" acetyl) glucoside, apigenin-7-O- β -D-galactoside	Aerial	12,44
Ascorbic acid, vanillin, benzoic acid, catechol, salicylic acid, quercetin	Ethanolic	45
Sitosteryl-6'-O-undecanoate- β -D-glucoside, (Z)-8, 11, 12-trihydroxyoctadec-9-enoic acid, 1,2-dipalmitoyl- 3-O- α -6" sulfoquinovosyl glycerol, naringenin-4'-O- glucopyranoside, -adenosine, crotonoylcosmosiin, tetracosanoic acid, apigenin, β -sitosterol, ursolic acid, -sitosterol-D-glucoside, indole-3-carboxaldehyde and indole-3-carboxylic acid	Aerial	13
Quercetin, dioctyladipate, Isorhamnetin, N-(n-propyl) acetamide, Isopropyl isothiocyanate, Isobutyl isothiocyanate, n-butyl isothiocyanate, Indole-3carboxaldehyde, Indole-3-carboxylic acid, 3-Methyl indole, Apigenin, 2E-Hexenal, Dimethyl sulphone, beta-Terpinyl acetate, p-Anisaldehyde, Indole, p-Vinylguaiaicol, 1,1,6-Trimethyl-1,2,3,4tetrahydronaphthalene, o-Benzyl-L-serine, Isovanillin, Methoxyeugenol, 2-(2-Methylpropylidene)-1H-indene-1,3(2H)-Dione	Aerial	13,14,46
Nicotine (alkaloid)	Aerial / maceration in HCl	47
Fatty acids - (7Z,10Z,13Z)-hexadecatrienoic acid (roughanic acid), 9Z,12Z,15Z)-octadecatrienoic acid (α -linolenic acid), 8,11,12-trihydroxy-9Z-octadecanoic acid Indole alkaloids- 1H-indole-3-acetonitrile, 1-methoxyindole 3-acetonitrile, 1-methoxy-1H-indole-3-carboxamide, α -amino-3-indole propanamide (L-tryptophanamide)	Aerial / Ethanolic	48

Pharmacological actions

Pharmacological activities	Parts used/ Dosage forms	Model used	Outcome	Ref
Antibacterial and Antifungal	Roots / Methanolic	In-vitro	Effective against Gram positive bacteria (<i>Bacillus subtilis</i> , <i>B. pumilus</i> and <i>S. aureus</i>), and Gram-negative bacteria (<i>P. vulgaris</i> , <i>P. aeruginosa</i> and <i>E. coli</i>) and yeast (<i>Candida albicans</i>)	49
	Leaves / n-hexane	Agar well diffusion and Tube dilution method	Inhibit the growth of <i>K. pneumonia</i> and <i>S. epidermidis</i>	50
	Seeds / n-hexane	-do-	Inhibition against <i>P. aeruginosa</i> and <i>S. epidermidis</i>	
	Leaves / Ethyl acetate	-do-	Inhibit <i>K. pneumonia</i> , <i>E. coli</i> and <i>P. aeruginosa</i>	
	Seeds/ Ethyl acetate	-do-	Inhibit <i>K. pneumonia</i> , <i>S. epidermidis</i> and <i>S. aureus</i>	
	Leaves and roots/ Methanolic, n-butanol and chloroform	---	Potent anti-fungal constituents for the management of <i>Macrophomina phaseolina</i> , a soil borne plant pathogen	6
	Leaves / Silver nanoparticles	strain ATCC <i>E. coli</i> -25922 by agar well diffusion method	showed a dose-dependent response and effectively inhibited the intrinsic MDR pathogens <i>A. baumannii</i> and <i>P. aeruginosa</i> ⁴⁵	51
	Seeds / Aqueous (Si-AgNPs)	---	Si-AgNPs at 80µg/ml demonstrated a marked reduction in mycelial growth and spore germination of potent fungal phytopathogens that includes <i>Alternaria alternata</i> , <i>A. brassicae</i> , <i>Fusarium solani</i> , <i>F. oxysporum</i> , and <i>Trichoderma harzianum</i>	7
	Seeds/ Maceration in different solvents like methanol, chloroform, acetone, etc.	Agar-well diffusion method	The ethanolic extract was found to be active against <i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> strains as compared to other solvent extracts	40
	Aerial/ Successive extraction	Agar well diffusion and Disc diffusion methods	Growth of <i>E. aerogenes</i> , <i>A. baumannii</i> , <i>K. pneumoniae</i> was inhibited	44
Aerial / ethyl acetate fraction	Mice	The bacteriuria decreased and disappeared from urine after 6 days against <i>E. faecalis</i> , <i>Citrobacter freundii</i> and <i>A. baumannii</i> .	44	
Aerial/ Crude Aqueous	Disc diffusion methods	Shows potent inhibition against six MDRB isolates viz. <i>P. aeruginosa</i> , <i>A. baumannii</i> , <i>E. cloacae</i> , <i>E. faecium</i> , <i>K. pneumoniae</i> , <i>S. aureus</i> and <i>Candida albicans</i> .	52	
Antipyretic	Seeds / Ethanol	Albino Rats	Antipyretic effect starts within 1 hour and last for 5 hours. (peak at 3 hour)	15
	Decoction and aqueous	Wistar albino rat	Shows mild activity after 3 rd and 4 th hr of drug administration	53
	Aqueous	Yeast-induced pyrexia	A highly significant effect was observed in animals in pre-treated and post-treated	54

		model in rats	aqueous group	
Anti-inflammatory	Decoction	Rat	Hind paw oedema reduced by 27.7% at higher dose	53
	Aqueous	Rat	Hind paw oedema reduced by 23.3% at higher dose	
	Seeds / Ethanol	Cotton Pellet induced Granuloma Pouch in Wistar rat	Showed significant ($p < 0.001$) anti-inflammatory effects at a dose of 100-200mg/kg	16
Analgesic	Seeds / Ethanol	Albino rat	Showed marked analgesic effect	15
	Seeds/ Decoction and aqueous	Rat	It shows mild to moderate analgesic effect	53
Antioxidant	Aerial parts / successive extraction	DPPH free radical scavenging assay	The highest antioxidant property was found in total alcohol, butanol, ethyl acetate	12
	Leaves, stem/ ethyl acetate, butanol, chloroform	DPPH free radical scavenging assay	showed marked scavenging activities ranging from IC ₅₀ : 74.2 to 89.6 µg/ml,	35
Anti-ulcerogenic	Aerial / Ethanol	Acetic acid-induced colitis on male Wistar rat	The result shows potent dose-dependent anti-ulcerative colitis activity in prophylactic and curative models at doses (125mg, 250 and 500 mg/kg)	55
	Aerial / Ethanol	Ethanol induced gastric ulcer model in Wister rat and Swiss albino mice	At the high dose (500 mg/kg) S. irio was as effective as lansoprazole (30 mg/kg) in reducing all parameters of peptic ulcer by decreasing serum gastrin level	56
Cytotoxic	Aerial / n-hexane, n-butanol, ethyl acetate fractions	Human cancer cell lines HCT-116, HepG2, and MCF-7 / Crystal Violet Staining method	The n-hexane extract was found to have potent cytotoxic effects	57
	Seeds / Aqueous (Si-AgNPs)	The MTT assay on HeLa (human cervical cancer cell line)	At higher concentration the number of viable cells decreased, with an IC ₅₀ value of 22.06 ± 0.86 µg/ml, which demonstrated good activity against cancer cells	7
	Whole plant (ZnO NPs) / Methanol, hexane, ethyl acetate, chloroform	Normal-Baby hamster kidney cell line (BHK) Malignant-hepatocellular Ca cell line (HepG2)	The methanol fraction showed the highest activity of 90%, followed by hexane - 86.72%, ethyl acetate - 85%, and chloroform 84% against BHK and HepG2 cell lines	37
	Aerial / Aqueous	VERO cell line from kidney of an African green monkey	Dose dependent effect was observed	52
Antiproliferative	Leaves / Hydroalcoholic	HT-29 Cancer Cells	after 48 and 72 h of treatment, the MTT assay shows concentration- and time-dependent inhibitory effects on HT-29 cell	41
Bronchoprotective	Seed / Ethanol	Aerosol-Induced Bronchospasm in Guinea-pig	The result shows protection from the bronchospasm stimulated by histamine aerosol at the dose of 100-200mg/kg	16
	Seed / Aqueous-	Isolated rabbit trachea	exhibited nonspecific relaxant effect on carbachol (1µM)-and high concentration	58

Bronchodilator	methanolic	strip	K ⁺ (80 mM)-induced tracheal contractions suggesting the coexistence of Ca ²⁺ antagonistic and/or antimuscarinic properties	
Hepatoprotective	Aerial / methanol and ethyl acetate	CCL ₄ induced liver damage in Albino rat	The extracts show significant hepatoprotective activity due to decrease in concentration of bilirubin, ALP, SGPT, and SGOT	59
Hypoglycaemic	Leaves / Lipophilic and hydrophilic fraction	α-amylase inhibition assay using α-amylase porcine pancreatic enzyme	The lipophilic fraction shows higher porcine pancreatic α-amylase inhibitory effect in comparison with Acarbose, while the hydrophilic fraction of this plant has less α-amylase inhibitory effect	60
Vasodilator/ Antihypertension	Seed / 70% aqueous-methanolic	Isolated rabbit aorta	relaxed the phenylephrine (1 μM) and high concentration K ⁺ (80 mM)-induced aortic contraction (0.01-3 mg/mL), suggesting blockade of Ca ²⁺ channel	58
Scientific studies of Khaksi as ingredient in compound formulation				
Antipyretic	Polyherbal formulation/ Khaksi Seeds as ingredient	Yeast-induced pyrexia model in rats at dose of 150 and 300 mg/kg bw	high dose (300 mg/kg bw) showed a substantial (p<0.001) decrease in rectal temperature 60 minutes after treatment	61
Analgesic	Polyherbal formulation/ Khaksi Seeds as ingredient	acetic acid-induced writhing test in mice	A reduction of writhes by 36.71% and 68.71% respectively at doses of 300 and 600 mg/kg bw	61
Antibacterial	Sharbat Khaksi	<i>Salmonella typhi</i> isolates	77% isolates were sensitive to sharbat khaksi and showed bacteriostatic action	62

Acute toxicity study

The seeds of Khaksi were tested for Acute toxicity in Wistar rat and Swiss mice at different doses level following OECD guideline-423. The result showed that seeds have safe upto the doses of 1000mg/kg, but at dose of 2000 mg/kg few percentages of mortality was recorded in both strains⁶³.

Conclusion

After reviewing the literature and scientific studies, it can be concluded that Khaksi is a drug that has been used in Unani system of medicine for the treatment of pyrexia in epidemic conditions since a long time, that is supported by advanced phytochemicals and pharmacological research. The flavonoids found in Khaksi, particularly apigetrin has drawn attention due to its potential to target cancer cell of multiple organs selectively, it may be a good candidate for further exploration in various ailments.

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