A Comprehensive Review on Applicability and Bioactivity of *Rogan-I-Kunjad* (Sesamum indicum L-Oil): Unani Prospective

Saima Naseem[1] Asif Ahmad Khan[1] Qamar Uddin[1] Arzeena Jabeen[1] Kamal Ahmad[1] Mohd Asad[1]

[1] Department of Medicine, National Research Institute of Unani Medicine for Skin Disorders, Erragudda, Hyderabad, Telangana, India

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Address for correspondence Asif Ahmad Khan, MD, Department of Medicine, National Research Institute of Unani Medicine for Skin Disorders, A.G Colony Road, Opposite ESI Hospital, Erragudda, Hyderabad 500038, Telangana, India (e-mail: asifahmadkhan77@gmail.com).

Abstract

Sesame oil has a long history of usage as a food and medicine. It is the most used oil as a medicine or as a base oil for preparations of many compound drugs in the Unani system of medicine. It has a wide range of biological activities as mentioned in Unani classical text; this review highlights its pharmacological activities and their possible mode of action. Searched many Unani classical literature online and offline and simultaneously did parallel search on databases like PubMed, and Science Direct, and extraction of data related to sesame oil, sesame seeds with its pharmacological activities, mode of action, then interpretation and summarization of all related data. Sesame oil possesses many biological activities like anti-inflammatory, antihyperlipidemic, antiatherosclerotic, hepatoprotective, antiasthmatic, analgesic, emollient, antipruritic, and wound healing effects, which were scientifically demonstrated as mentioned in Unani literature. Sesame oil has a hopeful effect on modulating diseases with no significant toxic effect; so, there is a need to identify its safety and efficacy on human subjects to develop a new potential drug.

Keywords
- pharmacology
- *Rogan-I-Kunjad*
- sesame oil
- Sesamum indicum L.
- Unani medicine

Introduction

Rogan-I-Kunjad (sesame oil) is obtained from the seeds of Sesamum indicum L., a herbaceous annual plant in the family of the Pedaliaceae, and is grown for its palatable seeds, oil, and therapeutic uses.[1] Sesame seeds are said to be the earliest oil seeds used by humans. Their farming practices were more than 5000 years old. Sesame comes in various varieties, with the earliest wild species being found in Africa and India. It is widely used as food, medicine, and in ceremonial or spiritual rites. The entire seeds are commonly utilized in cuisines throughout Asia and the Middle East. In North America and Europe, it is used as a flavoring and garnish for a variety of meals, including bread.[2] Sesame oil is regarded as a nutrient-dense food since it is stable, rich in medicinal benefits, and has a high nutritional quality, giving it an edge over other vegetable oils.[3] Nowadays with increasing awareness of the importance and long-term benefits of traditional or herbal medicines, the global traditional medicine industry has started growing rapidly, resulting in a rise in demand and use of herbal products. In 2020, the global market for herbal medicine was estimated to be around US$ 185 billion. The industry is estimated to expand at a Compound Annual Growth Rate (CAGR) of around 11% to around US$ 430 billion by 2028.[4] This has contributed to an increased demand

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for sesame seeds, as they are considered nutritious and have various health benefits. However, it is important to note that the status of sesame seeds in the Indian market is that India is one of the largest producers of sesame seeds in the world and will produce 0.75 million metric tons of sesame seeds in FY (Financial Year) 2023.[5] India exported 328.46 tons of sesame seeds worth 3012.31 in 2015 to 2016.[6] Sesame oil exports from India totaled 798.58 thousand tons in April 2023 FY, down from 880.51 thousand tons in the corresponding period of April 2022 FY.[7]

Sesame oil, seeds, roots, and leaves are utilized for a variety of therapeutic purposes. African and Asian nations use sesame more frequently as a traditional medicine.[8] Sesame seeds and their oil have great importance in the Indian System of Medicine, especially in the Unani system of medicine dealing with a wide range of illnesses like inflammation, asthma, dry cough, constipation, dysuria, wounds, neurodegenerative disorders, musculoskeletal pain and stiffness, alopecia, and thrombosis.[9,10]

The purpose of the current review is to summarize and keep updated the information that is currently accessible on the morphology, ethnobotanical, phytochemical, and most significantly, pharmacological utilization of *Rogan-I-Kunjad* (*Sesamum indicum* L. oil), along with their possible mode of action based on scientific parameters. The main goal of this review is to perform a critical analysis of the Unani medical literature about the nutritional and therapeutic benefits of *Rogan-I-Kunjad*, which will be supported by data from reliable sources. Such observations may help researchers to gain insight to develop novel therapeutic approaches for a wide array of diseases with minimal toxicity, promoting the overall health and well-being of society.

Methodology

In this review article, the data are generated by COPE guidelines. The source of data is Avicenna's "Al-Qanun-fil-Tibb" (The Canon of Medicine), Al-Jami-li-Mufradat-Al-Adwiya-wal-Aghziya, Muhit-I Azam, Khazain-ul-Advia, etc. The source was searched for equivalent (Urdu, Persian, Arabic) words for "*Rogan-I-Kunjad*," "*Tukham-I-Kunjad*," "simsim," and "Til. A parallel search in databases like PubMed and Science Direct was done by using keywords with appropriate Boolean operators ("AND" and "OR") "Sesamum indicum," "Sesame oil," "phytochemical," "pharmacology" "Medicinal use," "preclinical study," and other relevant terms. Title, abstract, and keywords were used for screening the literature for potential articles. The full text of these articles was then used to extract relevant data. The duration of data was from the past 10 years (►**Table 1**). The author visited the library of the National Research Institute of Unani Medicine for skin disorders to find out relevant data from unpublished Unani literature and the botanical name of the plant was confirmed from an authentic website namely The plant list.

Observation

Taxonomy of *Kunjad* (*Sesamum indicum* L.)

Kingdom: Plantae—(plant), Subkingdom: *Tracheobionta*(vascular plants), Superdivision: *Spermatophyta*—(seed plants), division: *Magnoliophyta*—(flowering plants), Class: *Magnoliopsida*—(dicotyledons), Subclass: *Asteridae,* Order: *Scrophulariales,* Family: *Pedaliaceae*—Sesame, Genus: *Sesamum*, Species: *S. indicum* L.[11]

Habitat and Distribution of *Kunjad* (*Sesamum indicum* L.)

The suitable soil for satisfactory production of sesame is on soils with a pH range of 5.4 to 6.7 but is seriously affected by pH below this critical range. These, however, do not tolerate heavily salted or waterlogged soils well. Ninety to one-hundred twenty frost-free days are required for commercial sesame production. Over 23°C (73°F) warm conditions are favorable for growth and yields.[12] It is cultivated all over the world and in India it is widely distributed in Assam, Bihar, Gujarat, Uttar Pradesh, Madhya Pradesh, and Rajasthan.[13]

Morphology of Seeds of *Sesamum indicum* L

Macroscopic

The seeds are compressed, ovoid, pear-shaped pointed at one end and broader at the other end, approximately 3 to 4 mm long, 2 mm broad, 1 mm thick; an indistinct longitudinal ridge running through the center of one of the sides represents the position of the raphe, other ridges run around each side near the edge, and the hilum lies at the pointed end.[14] The color of sesame seeds is of three types that are white, black, and Red/brownish red.[9,15] It has an oily taste without any characteristics or smell.

Microscopic

The diagrammatic transverse section (TS) of the seed is oval with four elevated arrow ridges, one at each end of its long axis, and a faint raphe ridge on one side. Underneath the testa, a narrow, hefty cotyledon is positioned in the center, taking up most of the section. The longitudinal section of the seed has an oval shape that narrows at one end, and the embryo is straight, with two big piano-convex cotyledons and a little cylindrical radicle pointing in the direction of the hilar end.[14]

A detailed TS of the seed reveals the outer epidermis of the testa, which is made up of compact, palisade-like cells with sinuous walls that are radially extended. At the periphery of each cell is a cluster crystal of calcium oxalate that is encased in a thick spherical membrane. The cell under the ridges is devoid of such crystals; beneath this layer is a short band of tegmen and a collapsed parenchyma. The endosperm is a narrow, parenchymatous layer that varies in thickness, being 2 to 3 in rows at the margins and 4 to 5 on the sides. The embryo's cotyledons exhibit one layer of palisade cells next to the inner epidermis, with isodiametric cells making up the majority of the ground tissue. There were aleurone grains and oil globules inside the embryo and endosperm cells.[14]

Characteristics of *Rogan-I-Kunjad* (*Sesamum indicum* L.)

As per the Unani classical text, sesame oil of the Indian verity is pale yellow to golden in color, while some of its verities are also dark yellowish in color. The oil which is extracted from

Table 1 Keys terms used for search in this review

Database	Keyword used	No of articles
PubMed	Sesamum indicum, sesamum indicum AND phytochemistry, sesame oil, animal study on sesame	471
Science Direct	Sesamum indicum and transcriptional regulation, pharmacological action	608

Gair Mukasher (with covering) and *Gair Birya Kunjad* (without roasted) is known as *Dahn-ul-Heel* and its color is dark brownish, having a different flavor with mucilaginous, more stickiness, and the oil that is derived from *Gair Mukasher* (with covering), and *Birya Kunjad* (roasted seeds) is light pale yellow in color with less stickiness.[9,11] According to a study, the amount of lignans, tocopherols, and sterols in the oil produced from roasted sesame seeds was much lower than that of unroasted sesame seeds. The extracted oil's oxidative stability, and antiradical activity were all increased by roasting. In seeds oil roasted at high temperatures, a modest increase in Trans Fatty Acids (TFA) as well as triglyceride and diglyceride dimers was noted. For obtaining highly nutritious grade oil within the allowable range, 210 °C was the ideal roasting temperature. Utilizing this roasted sesame oil seed in plant-based diets may result in improved nutritional quality due to the great antioxidative efficacy of roasted seed oil.[8,16] Refined sesame seeds have more oxidative stability than unrefined sesame seeds oil due to more saturated fatty acids (SFA) and less Mono Unsaturated Fatty Acid (MUFA) and Polyunsaturate Fatty Acid (PUFA). The TOTOX value of refined sesame oil was significantly lower than unrefined. Oil processing was introduced as an effective way to reduce heavy metals.[17] The temperament of the sesame oil is *Har* (hot) and *Ratab* (moist) in second grade and it is liquid at standard room temperature (37 °C).[9,10,18,19] As mentioned in classical Unani literature called "Muhit-i-Azam" by renowned Unani philosopher "Hakim Azam Khan," the oil derived from the white luster surface seeds of sesame is the best form of sesame oil.[9] Much research has been done on its genotypic verities with their significant characteristics. The comparison of the quality of oil derived from different types of sesame seeds showed that oil from white-colored seeds is the best in terms of its oil-yielding capacity, protein, PUFA, and MUFA. This indicates that light-colored seeds that are white and tan are superior in their quality and good for consumption as well as medicinal use[20] (►**Table 2**). Its life span is 2 years for its best use because it is prone to decomposing its phytochemicals and starting to oxidize and become rancid.[21]

Composition of *Rogan-I-Kunjad* (*Sesamum indicum* L.)

Sesame seed oil is rich in polyunsaturated fatty acids that is (43.62%) monounsaturated fatty acids (41.53%) and only (14.85%) SFA natural antioxidants, lignans like sesamin 0.07–0.61%, sesamolin 0.2–0.48%, sesaminol, sesamol, pinoresinol), (►**Fig. 1**) sterols (16–40%), and tocopherol derivatives (10–12%) claiming that oils with this quality are suitable for consumption.[1,8,22] The sesame oil extracted from white and black varieties of seeds contains 14.90% and 14.70% carbohydrates, respectively.[23] Its seeds are a rich source of protein (18–40%).[24] These bioactive components improve sesame oil's stability and shelf life, as well as provide several health advantages (►**Table 3**).

Uses of *Rogan-I-Kunjad* as per Unani System of Medicine

According to the Unani system of medicine, this oil has a hot and dry temperament, which is very much favorable for the person of *Sawdāwī-al-Mizāj* (Malencolic temperament—A type of temperament caused by the predominance of Sawda' (black bile) in the body, which is cold and dry; individuals with this type of temperament have thin built with prominent veins, blackish skin—Standard Unani Medical Terminology [SUMT]-UMI-0161, WHO International Standard Terminology on Unani Medicine [IUMT]-3.1.176).[9] This oil is widely used as a medicine in the Unani system of medicine for the management of many diseases like *Iltihāb* (inflammation—(SUMT)-UMI-2358), *Surfa Yabsiyya* (dry cough—[SUMT]-UMA-0311, National Unani Morbidity Code [NUMC]-D-7.6, International Classification of Diseases [ICD-10]-R.05), *Dīq-un-nafas* (asthma[SUMT]-UMA-0247, [NUMC]-D-4, [ICD-10]-J-45), *Sudda* (obstruction—[SUMT]-UNI-0484), *Waja' al-Mafāṣil* (arthritis [NUMC]-L-4), *Ḥudār* [rheumatism [NUMC]-L-3), *Dā' al-Tha'laboratory* (alopecia areata [NUMC]-J-16), *Ṣudā'* (cephalgia/headache [NUMC]-A-36), *Shūṣa* (pleurodynia [NUMC]-D-11), *Ramad Sawdāwī* (melancholic conjunctivitis [NUMC]-B-1.4), *Qīḥ al-Ṣadr* (Empyema thoracis [NUMC]-D-26), *Qishr al-Ra's* (seborrheic dermatitis [NUMC]-J-15) *Saraṭan* (carcinoma [NUMC]-M-17] as well as all types of *Qurūh* (ulcer—[SUMT]-UMA-

Table 2 Characteristics features of *Rogan-I-Kunjad* from different types of sesame seeds

Sr. no	Coat color of seeds	Oil yielding capacity	Protein%	MUFA	PUFA	SFA	Ref
1	White	51.80%	20.00%	37.61%	46.03%	5.48%	20
2	Black	34.33%	14.87%	37.91%	44.34%	4.48%	
3	Red/ brownish red	42.48%	18.02%	37.41%	46.66%	4.53%	

Abbreviations: MUFA, Mono Unsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; SFA, saturated fatty acids.

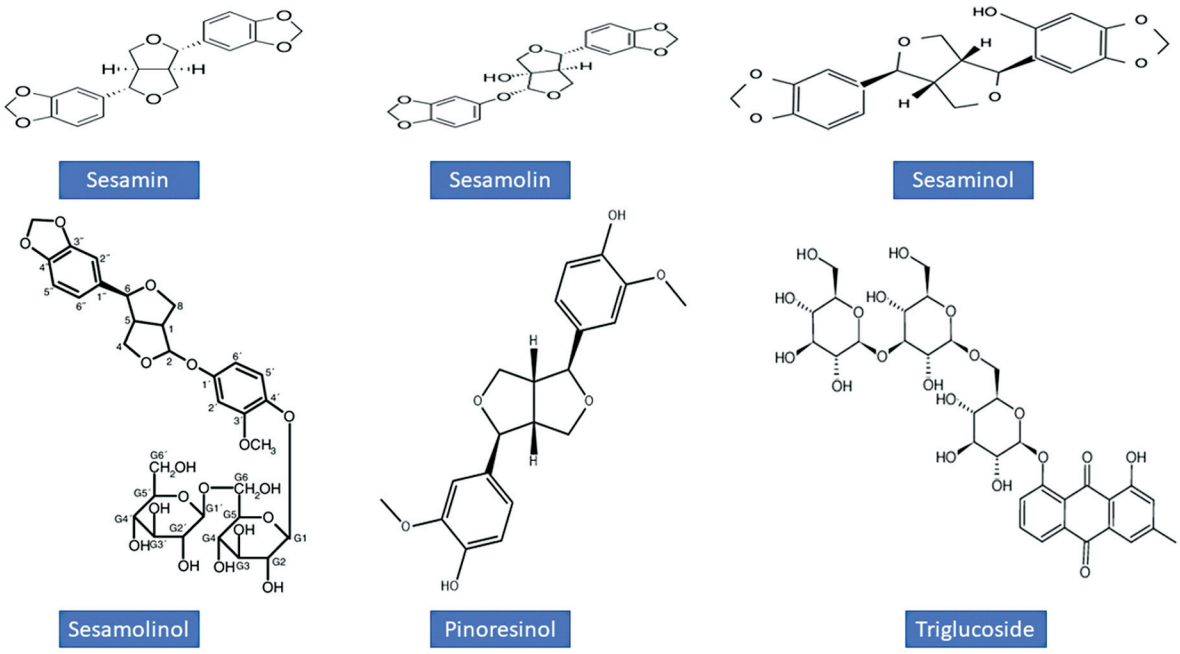

Fig. 1 Lignans of *Rogan-I-Kunjad* (sesame oil).

0200) as its properties are described in Unani medicine as a *Muliyyan* (laxative), *Muḥallil* (resolvent—[SUMT]-UMI-1910), *Mufattiḥ* (obstruent—[SUMT]-UMI-1942), *Mufattiḥ-i-urūq* (vasodilator—[SUMT]-UMI-0753), *Muḥallil-i-waram* (anti-inflammatory), *Mundamil-i-qurūh* (cicatrizing), *Mualid-e-mani* (spermatogenic[SUMT]-UMI-1937),[24–26] *Hikka* (pruritis—[SUMT]-UMI-1162, [NUMC]-J-57, [ICD-10]-L29-L29.9).[6,7,16,19,25–29]

Rogan-I-Kunjad compound compositions have long been employed in Unani medicine. Here, some of the compound compositions that are most frequently utilized were discussed. In case of alopecia areata, seborrheic dermatitis, or dandruff, a mixture of *Rogan-I-Kunjad* and *Barg-I Murad* (leaf of Myrtus communis L.) is applied over the scalp. *Rogan-I-Kunjad* with *Aspaghol* (*Plantago ovata*) is used as a liniment in xerosis, burn, and ulcer. *Rogan-I-Kunjad* in the form of *Qairooti* (Cerate or salve) is used for cosmetic purposes. Eye ointment made up of *Rogan-I-Kunjad* with egg white is intended to treat conjunctivitis and other inflammatory condition of the eye. Preparation in the form of ear drop made up of *Rogan-I-Kunjad* with *Filfil safaid* (*Piper nigrum* L.) and *Mastagi* (*Pistacia lentiscus* L.) is used for otalgia and ear obstruction. *Rogan-I-Kunjad* with Munaqqa (*Vitis vinifera* L.) is used in *Ḥikka* (pruritus) and a solution of *Rogan-I-Kunjad* with *Rogan-I gul* (rose oil) in *Ṣudā'* (headache) is used as an oral administration.[9,18] Some of the marketed compound formulations of *Rogan-I-Kunjad* are mentioned in ►**Table 4**.

Phytochemicals in *Rogan-I-Kunjad* (*Sesamum indicum* L.)

There have been various types of phytochemicals isolated from seeds, seed oil, and other parts of the sesame plant, including polyphenols (whole plant), Phytate 5.18%, oxalic acid 2.2%, tannins 5.26mg/100 g, sterols (seeds), phenols (seeds), naphthoquinones (roots), anthraquinones (roots), triterpenes (seeds), cerebroside (flower), fatty acids (seeds), vitamins (seeds), essential amino acids (seeds, leaf, stems, flower), carbohydrates (seeds), and other organic compounds.[2] (►**Table 3**) However, higher amounts of sesamin (2.45 mg/g seed) and sesamolin (1.10 mg/g seed) were observed for Indian sesame species when compared with 65 sesame seeds harvested in Texas, United States (1.63 mg/g seed for sesamin and 1.01 mg/g seed for sesamolin).[30]

Pharmacological Activities of *Rogan-I-Kunjad* (*Sesamum indicum* L.)

Antinociceptive Effect

In the Unani system, sesame oil has *Muskin-I Alam* (analgesic) and *Muhalil-I warm* (anti-inflammatory) properties and is used for the treatment of pain.[9,10] In an animal model of pain induced by acetic acid and formalin-induced writhing response, tail immersion, and hot plate latency test. It was shown that sesame oil caused significant reduction in abdominal writhes and sesamin inhibited biphasic paw licking response as compared with morphine. In the hot plate, latency time was increased after 60-minute administration of the drug[31] (►**Fig. 2**).

Inflammation and Sesame Oil

Sesame oil showed a potential anti-inflammatory effect on carrageenan-induced inflammatory animal models. Sesame oil reduced paw edema after 3 hours of drug administration. In model of pleurisy induced using intrapleural carrageenan, sesame oil inhibits accumulation of exudate as compared

Table 3 Constituents of *Rogan-I-Kunjad*

Sr.no	Bioactive compounds	Name of components	Organ studied	Quantity	References
1	Fatty acids	SFA Palmitic acid (16:0) Margaric acid (17:0) Stearic acid (18:0) Arachidic acid (20:0) Behenic acid (22:0) Lignoceric acid (24:0)	Seeds Seeds Seeds Seeds Seeds Seeds	14.20 g/100 g 8.9 g/100 g 4.8 g/100 g	63
		MUFA Palmitoleic acid (16:1) Oleic acid (18:1) Gadoleic acid (20:1)	Seeds Seeds Seeds	39.70 g/100 g 0.2 g/100 g 39.3 g/100 g 0.2 g/100 g	63,64
		PUFA Linoleic acid (18:2) Linolenic acid (18:3)	Seeds Seeds	41.7 g/100 g 41.3 g/100 g 0.3 g/100 g	63,64
2	Lignans	Sesamin Sesamolin Sesaminol Sesamolinol Triglucoside Pinoresinol	Aerial part, seeds Seeds Seeds Seeds Seeds	6.20 mg g^{-1} 2.45 mg g^{-1} 0.01 mg g^{-1} 58 mg/100 g	65,66
3	Tocopherol derivatives	ϒ Tocopherol	Seeds	0.68 mg g^{-1}	63,67
4	Phytosterols	B Sitosterol Campesterol stigmasterol Δ^5 avenasterol Sitostanol Campestanol	Aerial part, Flower Flower Areal part Seeds Seeds Seeds	2.63 mg g^{-1} 1.35 mg g^{-1} 0.47 mg g^{-1} 0.82 mg g^{-1} 0.04 mg g^{-1} 0.02 mg g^{-1}	68,69
5	Carbohydrates	D-glucose D-galactose D-fructose Sucrose Raffinose Stachyose Planteose Sesamose Pentasaccharides Hexasaccharides	Seeds Seeds Seeds Seeds Seeds Seeds Seeds Seeds Seeds Seeds	3.24% 0.06% 2.63% 0.17% 0.24% 0.23% 0.59% 0.38% 0.16% 0.08%	70
6	Protein	Albumin Globulin Prolamin Glutelin	Seeds Seeds Seeds Seeds	8.6% 67.3% 1.4% 6.9%	71
7	Phenolic acid	Ferulic, Vanillic Cinnamic p-coumaric 4-hydroxybenzoic Protocatechuic acid Gallic acid			72,73

with indomethacin.[31] Another study on ($LDLR^{-/-}$) female mice showed a significant reduction in proinflammatory cytokines like monocytes chemoattractant protein-1, normal T-cells expressed and secreted, interleukin-1α (IL-1α), IL-6, and chemokines ligand 16 and upregulation of anti-inflammatory gene IL-13, IL-1β, and macrophage inflammatory protein-3β and 3α.[32] An in-vitro study was conducted on RAW 264.7 cells, which showed an inhibitory effect on tumor necrosis factor-α (TNF-α), TNF-1, TNF-2, IL-6, monocyte chemoattractant protein-1, vascular cell adhesion protein-1, and granulocytes-macrophage colony-stimulating factor by application of aqueous extract of sesame oil.[33] In an animal model wherein acute inflammation was induced by monosodium urate monohydrate crystals, the study showed sesame oil significantly reduced inflammation after 6 hours of administration, and significantly decreased total cell count, TNF-α, IL-1β, IL-6, and mast cells in tissue pouch and skin tissue[34] (►**Fig. 2**).

Table 4 Compound formulation of *Rogan-I-Kunjad*

Sl. no	Drug name	Action	Therapeutic use	Therapeutic doses/ route of drug administration	References
1	Raughan-E-Gul	Anti-inflammatory, refrigerant, laxative/ softener	Acute arthritis Headache Constipation	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
2	Raughan-E-Kaddu Shireen	Hypnotic agent	Insomnia Meningitis Melancholia	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
3	Raughan-E-Kahu	Hypnotic agent Sedative	Insomnia Epilepsy Melancholia	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
4	Raughan-E-Luboob-E-Saba	Hypnotic agent	Insomnia	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
5	Raughan-E-Luboob-E-Saba Barid	Hypnotic agent Sedative	Insomnia, headache	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
6	Raughan-E-Turb	Analgesic	Otalgia	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
7	Raughan-E-Babuna Sada	Anti-inflammatory, Analgesic	Arthritis, pneumonia	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
8	Raughan-E-Banafsha	Sedative Hypnotic agent	Headache Insomnia Ankylosing arthritis	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
9	Raughan-E-Amla	Muqawwi-e-Shar (drug which enhance hair growth) Musawwid-e-Shar (drug which enhance hair color)	Alopecia Gray hair	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
10	Raughan-E-Amla Sada	Muqawwi-e-Shar, Musawwid-e-Shar	Alopecia Gray hair	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
11	Raughan-E-Chahar Barg	Anti-inflammatory, Analgesic	Arthralgia Arthritis	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
12	Raughan-E-Haft Barg	Nervine tonic Analgesic	Paralysis Facial palsy Arthritis Flaccid palsy	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
13	Raughan-E-Qust	Nervine tonic	Paralysis	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
14	Raughan-E-Surkh	Anti-inflammatory	Arthritis Gout	Quantum Satis (Q.S)/ Local Application (L.A)	[74]
15	Raughan-E-Hina	Anti-inflammatory, analgesic	Arthralgia ulcers	Quantum Satis (Q.S)/ Local Application (L.A)	[75]
16	Raughan-E-Bars	Blood purifier rubefacient, sedative	Vitiligo, pityriasis alba	Quantum Satis (Q.S)/ Local Application (L.A)	[75]
17	Raughan-E-Dhatura	Nerve stimulant, Nervine tonic	Paralysis Facial palsy Arthritis Flaccid palsy	Quantum Satis (Q.S)/ Local Application (L.A)	[75]
18	Raughan Beer Bahooti	Aphrodisiac	Erectile dysfunction	Quantum Satis (Q.S)/ Local Application (L.A)	[76]
19	Raughan-E-Benazeer	Brain tonic	Cerebrasthenia baldness Asthenopia/Amblyopia	Quantum Satis (Q.S)/ Local Application (L.A)	[77]
20	Raughan-E-Muqawwi-E-Asab	Nerve stimulant, nervine tonic Analgesic anti-inflammatory	Neuralgia Paralysis Facial paralysis Polyarthritis Myalgia	Quantum Satis (Q.S)/ Local Application (L.A)	[77]
21	Marham-E-Dakhliyun	Anti-inflammatory	Uterine ulcer Vaginitis	Quantum Satis (Q.S)/ Local Application (L.A)	[76]

Table 4 (*Continued*)

Sl. no	Drug name	Action	Therapeutic use	Therapeutic doses/ route of drug administration	References
22	Marham-E-Kafoor	Antiseptic	Ulcer	Quantum Satis (Q.S)/ Local Application (L.A)	76
23	Marham-E-Saeeda Chob Neemwala	Anti-inflammatory	Piles	Quantum Satis (Q.S)/ Local Application (L.A)	76
24	Tila Aroosak	Nerve stimulant, Nervine tonic	Erectile dysfunction	Quantum Satis (Q.S)/ Local Application (L.A)	76
25	Tila Benazeer	Aphrodisiac	Erectile dysfunction	Quantum Satis (Q.S)/ Local Application (L.A)	77
26	Zimad Muqawwi	Aphrodisiac	Erectile dysfunction	Quantum Satis (Q.S)/ Local Application (L.A)	77

Pulmonary Diseases and Sesame Oil

In a study on an animal model of allergic asthma, ovalbumin (10 mg intraperitoneal) induced pulmonary edema and inflammation in female BALB/c mice, sesame oil showed a significant reduction in lung weight (wet-to-dry) as a result of improvement in pulmonary edema and significant decreases in proinflammatory cytokines (IL)-1β and IL-6, as well as total cell count and neutrophils; biomarkers like nitric oxide, inducible nitric oxide synthase, and immunoglobulin E (IgE) were also downregulated. This showed that sesame oil has the potential in treating allergic asthma.[35] Another preclinical study on an allergic asthma model treated with lignan of sesame oil called sesamin showed a significant decrease in cytokines of T-helper cell-2 (IL-4, IL-5, IL-13) and increase in interferon-gamma, and inhibited the production of IgE as well as decreased NF-κB P65 level by blocking the phosphorylation of IκB-α and P38 MAPK pathways[36] (►**Fig. 2**).

Cardiovascular Diseases and Sesame Oil

Sesame oil (5%) significantly reduced total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), apo A, serum glutamate pyruvate transaminase (SGPT), and serum glutamic oxaloacetic transaminase (SGOT) in comparison to the hypercholesteremic diet (1% cholesterol) in the rat model.[37]

A randomized, triple-blind, crossover clinical study was conducted to demonstrate the effect of sesame oil on the APOA-1 gene in adults with and without type 2 diabetes mellitus. The result showed no significant differences in TC, triglycerides, LDL-C, HDL-C, apo A, apo B, or lipoprotein (a); however, significant differences were observed in LDL:

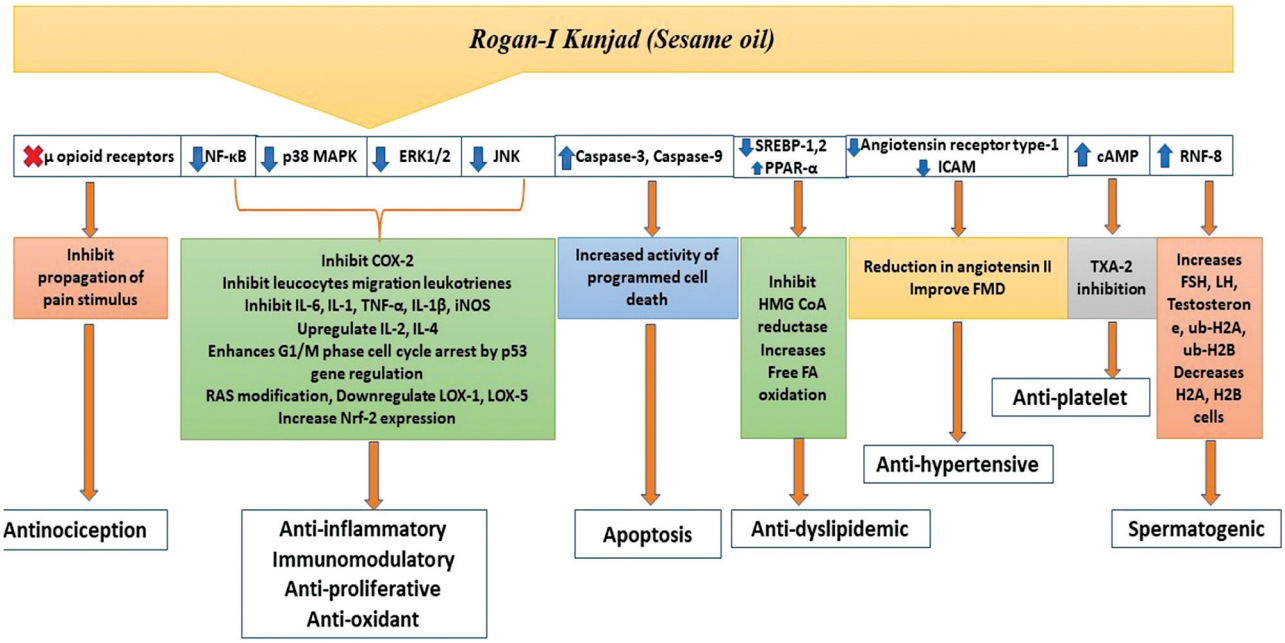

Fig. 2 Pharmacological target for *Rogan-I-Kunjad* (sesame oil).

HDL and TC:HDL ratios, blood pressure, as well as cardiovascular risk scores.[38] A study was conducted on a hypertensive animal model induced with cardiac hypertrophy using an injection of deoxycorticosterone and 1% sodium chloride. Sesame oil showed significant reduction in the size of cardiomyocytes, cardiac renin, angiotensin-converting enzyme, and angiotensin- II, and downregulated the expression of angiotensin receptor type-1, p38 MAPK, and JNK.[39] In a two-phase clinical trial, the first phase (acute phase) involved 30 hypertensive participants who consumed 35 g of sesame oil and were given corn or olive oil as a comparison. After 15 minutes, the objective parameters were observed, and the second phase (chronic phase) involved 60 days of treatment before the participants were evaluated. The study showed significant improvement in flow-mediated dilatation, and a significant decrease in intracellular adhesion molecule was observed after 60 days of treatment.[40] An antithrombotic activity was examined in animals by inducing thrombus using He–Ne laser; the sesame seeds significantly inhibited thrombosis in mice[41,42] (►**Fig. 2**).

Hepatic Diseases and Sesame Oil

In a study on C57BL/6J mice, a steatohepatitis animal model, sesame oil showed a significant reduction in hepatic fatty acid and cholesterol synthesis by downregulating both sterol element binding proteins (SREBPs)—SREBP-1 responsible for the synthesis of FAS enzyme and SREBP-2 responsible for synthesis of 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase)—and increased fatty acid oxidation by upregulating Peroxisome Proliferator Activated Receptor Alpha (PPAR-α) expression responsible for synthesis of CTP-1. Endoplasmic reticulum (ER), stress and apoptosis maskers like glucose-regulated protein-78, protein kinase like endoplasmic reticulum kinase, phosphorylated eukaryotic initiation factor-2α, and X-box-binding protein-1 were significantly reduced; these markers showed there was significant improvement in ER stress, and apoptosis biomarkers like BAX, caspase-3, caspase-9, and C/EBP homologous proteins were also reduced.[43] On an animal model another study on nutritional fibrosing steatohepatitis was conducted, and it was found that there was a significant decrease in the degree of steatosis, activity of matrix metalloproteinase-2, 9 (MMP-2, 9), α-SMA expression, fibrotic collagen, SGPT, SGOT, and upregulated PPAR-ɣ expression.[44,45] (►**Fig. 2**).

Carcinoma and Sesame Oil

A preclinical study was conducted on C57BL/J6 mice, in which the mice survived that received whole-body ɣ-radiation with sesame oil compared with the control group due to the ability of sesame oil to diminish MN frequency in nucleated bone marrow cells and eliminate apoptotic cells. This study also demonstrated significant improvement in B-cell (CD 19) and T-cell (CD 4 and CD 8), decrease in TBARS, and significant enhancement in splenocytes proliferation in pretreated sesame oil mice.[46] An in-vitro study was conducted on human head and neck squamous cell carcinoma, that is, HSC-3 (tongue cell line), FaDu (pharynx cell line), and Ca9–22 (Gingiva cell line) to understand the anticancer and anti-metastatic effect of sesamin. This study showed there was a marked reduction in cell mortality, invasion, and migration in all cell lines at 40 μM of sesamin. There was downregulation of MMP-2 expression in HSC-3 and FaDu by 23 and 19%, respectively, and also downregulation of P-p38 and pJNK1/2 expressions leading to inhibition of MAPK pathway. It indicates that sesamin inhibits the synchronized movement of the tumor cell population.[47] In an in vitro study on colon cell lines, Human Colorectal Adenocarcinoma Cell Line (HT-29) and Human Colon Cancer Cell Line (HCT-111) demonstrated that ethanolic extract of *Sesamum indicum* L (ESL) significantly enhanced the radical scavenging activity and decreased cell growth in HT-29 and HCT-116 cells, respectively. The same study revealed a 3.2-fold increased population in sub-G1, G1/M by 2.3–6.6 population and reduction in G0/G1 and S phase of cell cycle as compared with control, which indicates that ESL significantly arrests cell cycle at G2/M.[48] An in vitro study was conducted on a lung adenoma cancer cell line to demonstrate the anticancer effect of sesame oil which showed that there was marked decrease in cell viability and enhancement in apoptotic activity by upregulation of Bax, PARP, TRAIL-R1, and TRAIL-R2 and downregulation of Bcl-2 expression.[49] An in vivo study was conducted to demonstrate the anticarcinogenic effect of sesame oil on serous papillary ovarian carcinoma. The result of this study indicated that there was a significant reduction in the size of the tumor, as well as downregulation of many metabolic enzymes responsible for cellular metabolism and growth and singling pathways like hypoxia inducible factor-1, ER pathways, and proteoglycans.[50] Another study on adult UChB, an experimental model of ovarian cancer, showed the anticancer effect of melatonin, while the result showed there were significant increases in plasma melatonin and downregulation of Her-2, p38 MARK, and p-AKT expression[51] (►**Fig. 2**).

Male Sexual Health and Sesame Oil

An animal study was conducted on streptozotocin-induced diabetic rats to demonstrate the effect of sesame on testicular structure and male reproductive parameters. Sesame oil showed a significant improvement in histopathological changes and prevented testicular atrophy as compared with diabetic control; also, there were significant increases in male reproductive parameters, i.e., follicular stimulating hormone, testosterone, and luteinizing hormone, and decreases in serum glucose level in sesame-treated group as compared with control group.[52] Male Sprague Dawley rats were used in an animal study to show the impact of melatonin on epididymis and sperm characteristics after exposure to fructose and bisphenol A. This study showed marked improvement in epididymis morphology, enhancement of sperm motility, and reduction in apoptotic sperm cells in the 20 mg/kg melatonin-treated group as compared with the fructose and bisphenol A group.[53] Another animal study was conducted on cyclophosphamide-induced spermatogenic dysfunction in which sesamin showed significant increases in the weight of testis, sperm concentration and motility,

Johnsen's score, RNF8 expression, ub-H2A, and ub-H2B, and reverse morphological damage of sperm as well as testicular tissue derangement, significantly lowering the H2A and H2B[54] (►**Fig. 2**).

Arthritis and Sesame Oil

In an animal model of osteoarthritis, sesame oil significantly reduced muscular oxidative stress by decreasing LPO and ROS, and increased GSH level, GPx, and Nrf-2 expression after 7 days of administration.[55] A randomized, double-blind, clinical trial on knee arthritis was conducted to find out the effect of topical application of sesame oil, in which the result showed significant improvement in participants' walking speed, knee flexion angle, VAS, and WOMAC, after 4 weeks of intervention; this result suggested that sesame oil has a significant effect on OA.[56] The effect of sesame seed extracts on Freund's complete adjuvant-induced rheumatoid arthritis model showed that sesame oil markedly reduced paw volume, body temperature, IL-6, TNF-α, and ESR, and significantly upsurges spontaneous activity, body weight, hemoglobin, and RBC[57] (►**Fig. 2**).

Discussion

Rogan-I-Kunjad (sesame oil) is derived from seeds of *kunjad* (*Sesamum indicum* L.) widely used as edible oil as well as a medicine in many traditional systems of medicine; for example, in the Unani system of medicine *Rogan-I-Kunjad* is a well-known drug for the treatment of various *Sawdāwī-Amrāz* (melancholic diseases) diseases like asthma, arthritis, rheumatic arthritis, xerosis, pruritus, ulcer, obstructive pathology, headache, and carcinoma.[58] Additionally, *Rogan-I-Kunjad* has hot and moist temperament, owing to anti-inflammatory, analgesic, laxative, emollient, obstruent, resolvent, diuretic, and vasodilator properties of this drug. According to Unani philosophy of temperament, it has been well documented that the drugs having hot and moist temperament are used in the management of *Sawdāwī-Amrāz* (melancholic diseases).[59,60] Sesame oil is a versatile oil, so it is important to look at the current pharmacological research on it to learn about its traditional uses as well as its possible mechanism of action. In this review, we discovered that the various ethnomedical uses of sesame oil, including their anti-inflammatory, anticholesterol, antifungal, antibacterial, antidiabetic, antiulcer, wound healing, and anti-infertility properties, have been confirmed by contemporary pharmacological investigations using a variety of in-vitro and in-vivo techniques.

The findings reported in all the studies suggest a promising effect of *Rogan-I-Kunjad* (sesame oil) targeting antinociceptive and anti-inflammatory effects by inhibiting prostaglandin synthesis, especially PGE_2 and $PGF_{\alpha 2}$ synthesis from arachidonic acid by downregulation of the cyclooxygenase 2 (COX-2) enzyme. It acts as a COX-2 inhibitor, blocking μ-opioid receptors. It also inhibits the migration of inflammatory cells like leucocytes and leukotrienes synthesis.[61] Sesame oil, which contains active compounds such as sesamin, sesamol, melatonin, and pedaliin, acts as an anticancer agent by suppressing the phosphorylated JNK, p38 MAPKs, NF-κB, and ERK1/2 signaling pathways, thereby reducing abnormal cell proliferation and proinflammatory cytokines such as IL-6, IL-1, and TNF-α, and increasing the activity of the immune cell cytokine IL-2.[33,62] Pedaliin also arrested the cell cycle at G2/M phase and induced apoptosis by regulating caspase-3 and caspase-9.[48] Sesamin and episesamin have potent anti-dyslipidemic effects by blocking SREBP-1, SREBP-2, and HMG-CoA reductase and activating PPAR-α.[38] Sesame oil reduces oxidative damage and inhibits MAPK activation to modify cardiac RAS to alleviate LVH.[39] Through a rise in cyclic nucleotides (i.e., cAMP) and inhibition of MAPK phosphorylation, sesamol has significant antiplatelet action.[42] The limitation of this review article is that the studies included in this manuscript are of particular time duration and set field. As far as strength is concerned the manuscript included some of the clinical studies, preclinical studies, toxicological studies, in vivo, in vitro, in silico studies, and phytoconstituents. The main goal of this review article is to perform a critical analysis of the Unani medical literature about the nutritional and therapeutic benefits and their mechanism of action of chemical constituents found in *Rogan-I-Kunjad*.

Conclusion

Rogan-I-Kunjad is a medication that has been used since antiquity to cure and prevent a variety of ailments. However, it has been shown that the mechanism of action of *Rogan-I-Kunjad* showed its phytopharmacology. The in vitro, in vivo, and in silico models have sufficiently validated its phytopharmacology. The traditional literature showed the significance of *Rogan-I-Kunjad*. But there are still certain gaps that need to be filled. To begin with, *Rogan-I-Kunjad's* traditional pharmacological actions demand additional new pharmacological interpretations to clarify its fundamental mechanism; however, just a few recent researches have been conducted so far. Second, it has frequently been mixed with other Unani medicine, so drug interactions should be studied more thoroughly by traditional therapy. However, some of the clinical studies were conducted on cardiometabolic marker modulation, diabetes mellitus, hypertension, etc., but there is a need to conduct more clinical as well as toxicological studies to generalize stronger evidence. It is important to document the complete pharmacological profiling of *Rogan-I-Kunjad* for its future prospective.

Conflict of Interest
None.

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