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Review Article

KAFUR (*C. CAMPHORA* L.)–AN UPDATED REVIEW OF ITS ETHNOPHARMACOLOGY, PHYTOCHEMISTRY AND PHARMACOLOGY

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ABSTRACT

The objective of present review was to provide comprehensive information on *Cinnamomum camphora* L. on its ethnomedicinal uses, phytochemical, and pharmacological activities and provide insights into potential opportunities for future research. A thorough literature search was done to gather all the available updates on *Kafūr* for its *mizāj* (temperament), medicinal properties, and traditional uses. Classical Unani books and books on ethnomedicine and ethnobotany in English were referred for literature review. The information on phytochemical and pharmacological activities of *C. camphora* was collected from PubMed, Science Direct, Google Scholar, and Research Gate using keywords *C. camphora*, Kafūr, kapur, and camphor. The species name was checked with www. theplantlist. org. The material published in Urdu, Persian, Arabic, and English was included in the review. *C. camphora* is used as an analgesic and antiseptic in Unani and other traditional systems of medicine for a long. It possesses various bioactive compounds viz. terpenoids, flavonoids, glycosides, coumarins, fatty acids, lignans, alkaloids, etc. Out of all these, camphor is one of the volatile compounds which has many pharmacological activities including anti-nociceptive, anti-oxidant, anti-bacterial, anti-microbial, wound healing, and hepatoprotective.

Keywords: Camphor, Kafoor, Kapur, Unani medicine

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INTRODUCTION

Camphor is a natural product of the *Cinnamomum camphora* L. trees and belongs to the Lauraceae family. It is colorless, transparent crystalline, with blocks of strict consistency or pulverulent masses known as the 'flower of camphor' and yields from all parts of a broad, large-diameter camphor tree [1]. It is said that one hundred horsemen may rest in the shade of a single tree [2]. Some say snakes wind themselves around these trees in summer because they are cold [3].

Due to its peculiar fragrant and medicinal properties, the camphor tree is not only a high-quality timber resource, but it also plays an essential role in the fragrance, pharmaceutical, and chemical industries. For the preparation of camphor, small chips from old tree wood are taken and subjected to steam distillation and resulting in semisolid raw camphor oil, after the centrifugation and sublimation process camphor is obtained. Gustaf Komppa (1903) first synthesized (+)-camphoric acid followed by the synthesis of (+) camphor in 1908 [1]. During the Second World War, camphor was prepared synthetically from pinene from American turpentine oil [4, 5]. *Kafūr* is obtained under the trade names of Laurel camphor, Formosa camphor, Alcamfor, and Camphre du Japon [1]. Camphor is a common ingredient in many analgesic ointments for external application, and it also helps with fibromyalgia. Recently, carbon nanotubes (CNT) were successfully synthesized using camphor in a chemical vapor deposition process and are said to be the green biological source with high efficiency due to the carbon ring (pentagonal and hexagonal) contained in it [6]. Various applications of CNT are carriers for drug delivery, genetic engineering, artificial implant, preservative, diagnostic, and catalysts [7].

Camphor tree has six different chemical variants called chemotypes, which are camphor, 1,8-cineole, nerolidol, linalool, borneol, and safrole. The chemical variants seem dependent upon the area of origin of the tree [8]. Camphor has been used in traditional medicine for antiseptic antirheumatic, skin disorders, uterine pain, muscle, and joint sprains, and various inflammation-related conditions such as liniments and balms; also used for expectorant, carminative and anti-aphrodisiac action [9–12]. This review aims to explore the hidden potential of *Kafūr* as mentioned Unani and other traditional systems of medicine with its phytochemical and pharmacological advancement.

Description of *kafūr* in unani literature

Vernaculars

Arabic: *Aakal* [13]; English: Camphor, Borneo camphor, Formosan wood [9]; Hindi: Kaphur, Kapoor; Persian: Kapoor; Kannada: Kapooram; Tamil: Karupporam, Indu [10]; Unani: *Kafūr*

Morphology (*Māhiyat*)

Kafūr is a plant's gum, with a pungent odor, and viscous fluidity. Camphor's odor suppresses the fragrance of most of the scents and hides them. That is why it is famous for this name [14]. This plant was found naturally and cultivated in Japan and the Island of Formosa. The best quality of camphor is found on Borneo Island. Camphor's plant is about 20-25 feet tall in length. This plant is evergreen; its leaves are broad, thick, and shiny green in color. Its wood is white and with a very good scent [5]. Camphor is found in the cavities of wood and stem; chiefly distilled from the root trunk and branches, and is purified by sublimation and condensed into balls, tablets, or sublime powder [15]. There are different types of *Kafūr* like *Rīyāhi, Āzād, Asfarak, Azraq*, and *Qaisūri* [12, 13, 15]. Its *Qaisuri* type is the best of all, which is found in *Qaisur* [17]. The *Qaisuri* type resembles gum, found in layers, looks transparent and clean, extracted from the cavity of the stem. According to Ibn Sina (Avicenna), its wood is reddish-white and light-weighed [12, 13]. It is mentioned in *Annabhoot Chikitsa Sagar,* that among the various types of camphor three are best: *Arthat Kapoor, Chiniya Kapoor, Bheemseni Kapoor*. Veda describes two kinds of camphor; *Pakva,* and *Apakva* under the name of karpura [5].

Parts used (*Hasas-i-Musta'mla*)

Leaves, bark, fruit, the sublime product (camphor), and camphor oil [5, 17].

Temperament (*Mizaj*)

Hot and dry in the third degree [2, 5, 16, 18, 19].

Action and uses (*Af al aur Mawaq-i-istemal*)

It has several pharmacological properties such as *mubarrid* (refrigerant: an agent which reduces the body temperature from normal limits), *mujaffif* (desiccant: an agent which constricts blood vessels and decreases exudation from them and thus helps in healing of wounds) [13]; *musakkin* (sedative: substance which help in neutralizing the heat of humours) [5, 20]; *mufarrīh* (refrigerant: a drug that reduces tachycardia, palpitation of heart), *muqaww-i-qalb wa dimāgh* (an agent that strengthens the heart and brain), *dafi'-i-ta'affun* (antiseptic: an agent which prevents infection by inhibiting the growth of *Ajsam khabitha* or by changing the composition of putrefied matter or by any other mean hinders the putrefaction process), *dafi'-i-tashannuj* (antispasmodic: an agent which decreases the contractibility of muscles by acting through the CNS), *kasir-i-riyāḥ* (carminative: an agent which expels the gases from the gastrointestinal tract), *muḥarrik-i-mi'da* (gastric stimulant), *mukhaddir zaeef* (weak anaesthetic: an agent which causes loss of sensation in the organ) [5, 20]; *qaṭi'-i-bah* (anaphrodisiac: an agent which suppresses the libido) [12, 16]; *qāṭi'-i-dam* (haemostatics: an agent which suppresses the bleeding), *hābis ishāl wa arq* (reduces diarrhoea and sweat), *naf-i-aṭash wa ḥummā* (anti-thirst and antipyretic) [17].

It is used for the *Ḥummā sil wa* diqq (hectic fever) [5, 16], *ḥummā 'ufuniyya* (septic fever), *ishāl safrawi* (bilious diarrhoea), *sozish-i bawl* (burning micturition) [5]; *naksīr* (epistaxis) [5, 12, 20], *awrām ḥārra* (hot inflammation), *ṣudā'ḥārra* (headache due to excessive heat) [2, 5, 12, 16], *qulā'* (stomatitis/thrush) [2, 12, 16] and *ramad hār* (conjunctivitis) [13, 16].

Method of use

- *Kafūr* is *bārid* and *latīf* (easily disintegrated and absorbed by the body in a short time), it is helpful in *amrāz-i-ḥārrah* (hot aliments) of the brain and the whole body [22]. It is very *latīf* and resolves *'ufunat* (infection) and *ḥār māddah* (hot materials) [20]. Locally it relieves the *safrāwi* (bilious) headache and suppresses the excessive heat of *rūḥ-i-dimāghi* (psychic pneuma/life force) that occurs during *hār* (hot) and *hād* (acute) fevers [23].
- Its dropper with *roghan gul* has a striking effect in *usāba,* caused by *sū'-i-mizāj ḥār sāda* of eye and head; and with fresh coriander is beneficial in otalgia [12, 13].
- Using camphor in gargles with tooth powder or rose water relieves dental caries' pain and is beneficial in stomatitis [13, 20].
- Oral administration of 2 *ratti* (364 mg) camphor with ½ *ratti* (91 mg) opium is beneficial for joint pains and helps to relieve dysuria in syphilis [5].
- Smelling camphor and white sandal are beneficial for headaches caused by excessive heat [17].
- Camphor is mixed with various oils and used in backache, joint pain, and pleurisy as a massage [15].
- If sprinkled over the wound cleans up and heals the wound [21]. *Kafūr* in the form of ointment is applied over the wound to stop bleeding and provide relief from the *ḥarārat* (warmth) and *Sozish* (burning) of the wound [5].
- It is used as an air disinfectant during epidemics [5].

Dose (*Miqdār-i-khorāk*)

In Unani literature, the dose of *Kafūr* has been described as 1-2 *ratti* (182 mg to 364 mg) [5, 14, 20]. Camphor powder, up to 0.5 gm a day divided into three or four intakes [24]. In other traditional literature, the dose is described as 0.12 to 0.3 gm [25]. The concentration of 3%-11% has been approved by the FDA for topical use [6].

Adverse effects (*Muzir*)

It is harmful to kidneys and testicles and produces *burūdat* (Coldness); harmful for the persons of cold and weak temperament, stomach and libido [20]; produces headache, kidney and bladder stone [14].

Corrective (*Musleḥ*)

Hot and aromatic drugs like *Amber* (Ambergris), *Mushk* (Musk), *Jundbaidastar* (Castorium); *Roghan Sosan* (*Iris ensata* oil), *Banafsha* (*Viola odorata*), and *Nargis* (*Narcissus tazetta*) [23]. For headache *Neelofer* (*Nymphaea alba*), *Gulqand* (Rose petal jam), *Zafran* (*Crocus sativa*), *Mushk* [5, 13].

Substitute (*Badal*)

Sandal safed (*Santalum album*), *Kahruba* (*Vateria indica*) in the same dose; *Tabasheer* (*Bambusa arundinacea* Willd.) in a double dose [5, 13, 22].

Unani formulations

Kafūr is used as an ingredient in the following compound formulation.

Table 1: *Kafūr* is used as an ingredient in the following compound formulation

Internal use	References	External Use	References
Qurṣ Kafūr, Qurṣ Zaḥīr, Qurṣ Atash, Jawārish Kafūr Ḥabb Qābiz, Ḥabb Nafsuddam Sillī, Ḥabb Pechish, Ḥabb Iksīr Bukhār, Jawhar Kafūr, Jawhar Naushādar, Imsākīn,	[14, 25, 26]	*Arq Ajeeb, Marham Safeda Kafūri, Marham Khārish Jadīd, Marham Hina, Kahl Māmīrān, Barūd Kafūri, Barūd Soẓish Chashm, Sunūn Muqaww-i-Dandan, Pāyorīn, Roghan Benazīr, Zarūr Qula, Ṭila Nishāt angeẓ*	[26]
Qurṣ Sartān Kafūri, Qurṣ Tabāshīr Kafūri, Ḥabb Jawāhar Mūllif, Ḥabb Kafur Marwareedi, Ḥabb Taun Jawaharwali, Halwa Supāripāk, Mufarriḥ Shaikh ar Raīs, Mufarriḥ Yāqūti Moatadil, Sayyal Kafūr	[27]	*Saiyāl Kafūr, Kahl Jawahar, Kahl Kafūr, Kahl Muqawwi Basr, Marham Raal, Marham Kafūri, Zimad khwab aawar,*	[27]

Uses of *Kafūr* (Camphor) in other traditional medicine

Camphor has a long history of herbal use. Camphor and its essential oil have anodyne, antiseptic, stimulant of skin and heart, rubefacient, anti-spasmodic, narcotic, sedative, diaphoretic, expectorant, carminative, anthelmintic, antirheumatic, and tonic properties; it is anti-aphrodisiac in a large dose [9–11]. In uterine pains, 6-8 grain (389-518 mg) pills are administered, and camphor's liniment is rubbed on the abdomen. Pills containing 3-4 grains (194-260 mg) of camphor and an equal quantity of asafoetida administered for asthma, insomnia, and delirium give much relief. In pruritis and eczema of the genitals, the application of camphor ointment is beneficial. Camphor in olive oil or rectified spirit is used externally in rheumatic pains of joints and muscles [10]. In Asia and Europe, camphor is applied to sprains, inflammations, gout, and rheumatic joints and taken internally to calm hysteria, abate convulsions, and epileptic attacks [29]. Externally, it is used in liniments for joint and muscle aches and balms for chilblains, chapped lips, cold sores, and other skin conditions, and as an inhalant for bronchial congestion [11]. In folk and traditional Chinese medicine, it has been employed for a long for the treatment of inflammation-related diseases, including rheumatic arthritis, muscular strains, abdominal pain, rheumatism, cough, and bronchitis [12].

Description of *Kafūr* in scientific literature

Taxonomical classification

Kingdom: Plantae; Division: Magnoliopsida; Order: Laurels; Family: Lauraceae; Genus: Cinnamomum; Species: *C. camphora*

Synonyms

Camphora officinarum Nees; *Laurus camphora* L.; *Persea camphora* (L.) Spreng.; *Camphora hippocratei* Lukman.

Habitat and distribution

The camphor tree is native to China, Japan, Taiwan, Korea, India, Mongolia, Sri Lanka, Vietnam, Formosa, Malaya, and the Southern United States; a large number of these fragrant evergreen trees are grown, particularly in Florid [6]. They are naturally distributed in tropical or subtropical Asian countries and Pacific islands; they are artificially planted for road and garden landscaping purposes or provide wood, essential oils, spices, and medicine [30]. The *C. camphora* grows in full sun or partial shade and is tolerant of drought, but not remarkably tolerant of cold [11].

Botanical description

Usually, the Camphor tree is 12 meter height but attains 35-40 ft. It has a short and aromatic trunk; dark grey or dark brown, rough, fissured bark; Leaves are simple, alternate, ovate to oblong, lanceolate, entire, pinnate, leaf blade 5-12.5 cm long and 2.5-5 cm broad, with 3-5 prominent nerves beginning a little above the base, dark green, evenly colored on both sides, or lighter or glaucous on the underside, fragrant, leathery and long-stalked; Flower in a short axillary cluster, calyx yellowish-white slightly longer than the pedicel, 3 mm long and 5 mm wide; fruits are round-oval, less than 0.5 inches, fleshy, berry, black with a single seed [28, 30].

Physical description

Camphor is a colorless or white colored crystals, granules, or crystalline masses which burn readily with a bright smoky flame; pungent and aromatic taste; fragrant and penetrating odor; boiling point 205-209 °C; melting point 174-179 °C; molecular weight 152.23; specific optical rotation+41° to+43° (synthetic camphor is optically inactive) [31, 32].

Identification

It burns readily with a bright smoky flame and volatilizes slowly at room temperature.

1g sample of camphor in a test tube and add 5 ml of acetone. Shake the mixture well for 3 to 5 min at room temperature and allow the tube to stand for 30 min. The result shows a clear solution with completely dissolved crystals indicates the purity of camphor. If hexamine is present, it will be insoluble in acetone [32].

Phytochemistry

Chemical taxonomy of camphor

Kingdom: Organic compound, Superclass: Lipids and lipid-like molecules, Class: Phenol lipid, Subclass: Monoterpenoids, Molecular framework: Aliphatic homo polycyclic compound [34].

The main bioactive compounds of *Kafūr* (Camphor) with a focus on their isolation and identification are listed in table 2.

Table 2: The main secondary metabolites identified from *C. camphora*

Chemical constituents	PubChem CID	Dosage form/Parts used	Analytical method	References
Monoterpene				
1,8-Cineol (eucalyptol)	2758	E. oil/leaves, fruit, bark	GC-MS	[35]
		E. oil/leaves	GC-MS	[36]
D-Camphor	159055	E. oil/leaves, fruit, bark	GC-MS	[35]
		E. oil/leaves	GC-MS	[37]
Sabinene	18818	E. oil/leaves	GC-MS	[35, 37, 38]
α-pinene	6654	E. oil/leaves	GC-MS	[35, 37, 39]
β-pinene	6654	E. oil/leaves	GC-MS	[38, 39]
Borneol	64685	E. oil/leaves	GC-MS	[40]
Linalool	6549	E. oil/leaves	GC-MS	[35, 37]
Trans linalool oxide	6432254	Methanolic extract/leaves	GC-MS	[41]
Limonene	22311	Methanolic extract/leaves	GC-MS	[41]
D-Limonene	440917	E. oil/leaves	GC-MS	[39]
α-terpinene	7462	E. oil/leaves	GC-MS	[38]
β-terpinene	66841	E. oil/leaves	GC-MS	[39]
γ-terpinene	7461	E. oil/leaves	GC-MS	[38, 39]
terpinen-4-ol	11230	E. oil/leaves	GC-MS	[38]
		E. oil/Bark	GC-MS	[35]
α-terpineol	442501	E. oil/leaves	GC-MS	[38, 39]
		E. oil/Bark	GC-MS	[35]
(+)-α-terpineol	442501	E. oil/leaves	GC-MS	[38]
Terpinolene	11463	E. oil/leaves	GC-MS	[38, 40]
δ-terpineol	---	E. oil/leaves	GC-MS	[38]
p-Menth-1-en-8-ol	17100	E. oil/leaves, fruit	GC-MS	[35]
β-Terpinyl acetate	88693	E. oil/Fruit	GC-MS	[35]
α-phellandrene	7460	Methanolic extract/leaves	GC-MS	[41]
		E. oil/Fruit	GC-MS	[35]
β-phellandrene	11142	E. oil/leaves	GC-MS	[36]
Myrcene	31253	E. oil/leaves	GC-MS	[40]
β-Myrcene	31253	E. oil/leaves	GC-MS	[39]
4-thujanol	101626350	E. oil/leaves	GC-MS	[38]
2-thujene	520384	E. oil/leaves	GC-MS	[35, 37]
Cymene	---	E. oil/leaves	GC-MS	[40]
O-Cymene	10703	E. oil/Fruit	GC-MS	[35]
Cis-sabinine hydrate	---	E. oil/leaves	GC-MS	[38]
Camphene	6616	E. oil/leaves	GC-MS	[35, 37]
Sesquiterpene				
α-cubebine	86609	E. oil/Bark	GC-MS	[35]
β-cadinine	10657	E. oil/Bark	GC-MS	[35]
γ-elemene	6432312	E. oil/leaves	GC-MS	[35]
Humulene	5281520	E. oil/leaves	GC-MS	[38, 40]
E-Nerolidol	---	Methanolic extract/leaves	GC-MS	[41]
Spathulenol	92231	Methanolic extract/leaves	GC-MS	[41]
Proximadiol	165258	Methanolic extract/leaves	GC-MS	[41]

Chemical constituents	PubChem CID	Dosage form/Parts used	Analytical method	References
Caryophyllene	---	E. oil/leaves	GC-MS	[35, 37]
α-Caryophyllene	6508206	E. oil/leaves	GC-MS	[39]
β-Caryophyllene	5281515	E. oil/leaves	GC-MS	[40]
Caryophyllene oxide	1742210	Methanolic extract/leaves	GC-MS	[41]
Germacrene	---	E. oil/leaves	GC-MS	[40]
Bicyclogermacrene	---			
Germacrene B	5281519			
Coumarins				
Scopoletin	5280460	Hydro methanolic extract/Aerial	HPLC	[42]
Coumaran	10329	Methanolic extract/leaves	GC-MS	[41]
6,7-dimethoxycoumarin	8417	Hydro methanolic extract/Aerial	HPLC	[42]
7-hydroxycoumarin	5281426	Benzene extract/Branch wood	GC-MS	[43]
Anthraquinone				
1-hydroxy-3,6-dimethoxy-8-methyl-anthraquinone				
Triterpene				
oleanolic acid	10494	Pet. ether+ethanol/Twigs	CC	[43]
Sterols				
β-sitosterol	222284	Pet. ether+ethanol/Twigs	CC	[44]
		Methanolic extract/Root	CC	[45]
β-Sitosterol Palmitate	9852570	Petroleum ether–acetone/Root	CC	[45]
Daucosterol	5742590	Methanolic extract/Twigs	CC	[44]
		Methanolic extract/Root	CC	[45]
Campesterol	173183	Methanolic extract/Root	CC	[45]
Cerevisterol	10181133	Acetone extract/Branch wood	GC-MS	[43]
Stigmasterol	5280794	Pet. ether+ethyl acetate	CC	[45]
3-O-β-D-[6′-(3′′-Methylbutanoate) glucopyranosyl-β-sitosterol	---	Methanolic extract/Root	CC	[45]
Flavonoids				
Luteolin	5280445	Hydro methanolic/Twigs	CC	[44]
Luteolin-7-O-β-D-glucoside	---	Hydro methanolic/Twigs	CC	[44]
Tricetin-7-methyl ether	---	Hydro methanolic/Twigs	CC	[44]
Quercetin	5280343	Hydro methanolic extract/Aerial	HPLC	[42]
Quercetin-3-O-β-D-glucoside 4',6,7-trimethoxyflavone	---	Hydro methanolic/Twigs	CC	[44]
Dihydrokaempferol	---	Hydro methanolic extract/Aerial	HPLC	[42]
(-)-(2R,3R)-5,7-dimethoxy-3',4'-methylenedioxy-flavan-3-ol	---	Hydro methanolic extract/Aerial	HPLC	[42]
4',6,7-trimethoxyflavone	12377628	Hydro methanolic extract/Aerial	HPLC	[42]
(2S, 3S)-3'-hydroxy-5,7,4'-trimethoxy-flavan-3-ol	---	Hydro methanolic extract/Aerial	HPLC	[42]
Pelargonidin 3-O-glucoside	443648	Ethanolic extract/Seed kernel	HPLC	[46]
Isorhamnetin 3-O-glucoside	5318645	Ethanolic extract/Seed kernel	HPLC	[46]
Fatty acid				
Tricosanoic acid	17085	Hydro methanolic/Twigs	CC	[44]
Methyl linolenate	5319706	Methanolic extract/leaves	GC-MS	[41]
Octadecanol acetate	69968	Methanolic extract/leaves	GC-MS	[41]
3-Methyl-2-pentanone	11262	Methanolic extract/leaves	GC-MS	[41]
Glycosides				
Hydroxytyrosol 1-O-glucoside	13845930	Ethanolic extract/Seed kernel	HPLC	[46]
Verbascoside	354009	Ethanolic extract/Seed kernel	HPLC	[46]
Dihydroferulic acid 4-O-glucuronide	190069	Ethanolic extract/Seed kernel	HPLC	[46]
1-O-Feruloylglucose	13962927	Ethanolic extract/Seed kernel	HPLC	[46]
1-O-Sinapoylglucose	6168296	Ethanolic extract/Seed kernel	HPLC	[46]
Lusitanicoside	442799	Ethanolic extract/Seed kernel	HPLC	[46]
Lignans				
Piperitol	10282	Hydro methanolic extract/Aerial	HPLC	[42]
(+)-episesaminone	10523159	Hydro methanolic extract/Aerial	HPLC	[42]
Fargesin	10926754	Acetone extract/Branch wood	GC-MS	[43]
(-)-Sesamin	382073	Pet. ether+ethyl acetate/Stem bark	CC	[47]
9α-Hydroxysesamin	---	Pet. ether+ethyl acetate/Stem bark	CC	[47]
Obtusilactone A	6442492	Pet. ether+ethyl acetate/Stem bark	CC	[47]
Isomahubanolide	---	Pet. ether+ethyl acetate/Stem bark	CC	[47]
Dimethyl matairesinol	1286	Hydro methanolic/Twigs	CC	[44]
Alkaloids				
Isocoridine	---	Ethanolic extract/Seed kernel	HPLC	[46]
Papaverine	4680	Ethanolic extract/Seed kernel	HPLC	[46]
Bocconoline	181121	Acetone extract/Branch wood	GC-MS	[43]
Protopine	4970	Acetone extract/Branch wood	GC-MS	[43]
Others (Organic compound)				
Hotrienol	5366264	Methanolic extract/leaves	GC-MS	[41]
Isobutyl acetate	8038	Methanolic extract/leaves	GC-MS	[41]
3-Methyl– 2-pentanone	11262	Methanolic extract/leaves	GC-MS	[41]
Mesityl oxide	8858	Methanolic extract/leaves	GC-MS	[41]
3-Heptanone	7802	E. oil/leaves	GC-MS	[38]

Table 3: Pharmacological studies on *C. camphora*

Pharmacological activity	Tested on	Part/Dosage form/Conc.	Model used	Outcome	Reference
Analgesic	---	Borneol, 5, 25, 50 mg/kg	Acetic-acid writhing, Formalin test, Hot plate test	Significantly ($p<0.05$) reduces pain behavior	[50]
	---	0.25, 1 ml/kg	Migraine mouse model	It inhibits the expression of NF-κB and iNOS and thus induces NO production and reduces neurogenic inflammatory response due to the presence of nerolidol and (E)-α atlantone	[51]
Anti-inflammatory	---	Aerial part, Ethanolic extract, 1 µg/ml	NO assay, MTT assay, Luciferase reporter gene assay on lipopolysaccharide-stimulated RAW 264.7 macrophage	By inhibiting NF-kB regulated inflammatory response	[42]
	---	Leaves, Borneol E. oil	Xylene induced ear oedema	IL-Iβ, IL-6, (TNF-α) level reduced	[40]
	SD rat	Seed kernel oil	High-fat diet induced obese rats	Reduced the levels of inflammatory markers (TNF-α, IL-6, and P65)	[52]
Anti-oxidant	---	Leaves, Flavonoids	DPPH free radical scavenging	Significant activity	[53]
Anti-microbial	*E. coli, P. aeruginosa, Salmonella enterica, S. aureus, B. subtilis*	Leaves, Pinoresinol solution, 10 µl	Agar disk diffusion, Broth dilution	MIC and MBC ranges (3.9-31.25 µg/ml and 7.8–62.5 µg/ml), most effective against *P. aeruginosa* and *B. subtilis*	[54]
	E. coli, S aureus, B. subtilis, S. aeruginosa	Nano-particle (Ag-Nps) from callus extract	---	Inhibition zone 19.6±0.8–15.1±0.4 mm, due to attaching of Ag-Nps to bacterial membrane it damages and stops ATP production causes bacterial cell death.	[55]
	Escherichia coli	E. oil, 200 µl	MIC and MBC	Significant bactericidal action	[56]
	S. aureus, E. faecalis, B. subtilis, S. gallinarum, E. coli	Leaves, E. oil	Micro broth dilution method	Significant activity, probably due to increasing apoptosis rate and disrupting cell structure, decreases the activity of TCA-related enzymes disturbing amino metabolism.	[57]
	E. coli, Pseudomonas, B. cerus	Leaves, E. oil, 100-500 µl/ml	Well diffusion method	Significant maximum activity with methanolic and acetone extract	[58]
Anti-fungal	*Aspergillus niger, Candida albicans, Scolorotium*	Leaves extract, 100-500 µl/ml	Well diffusion method	Significant antifungal activity was found at 200 mg with all extracts.	[58]
	Choanephora cucurbitarum	Leaves, (1R)-(+)- and (1S)-(−)-camphor	Diffusion assay, Poison food technique	(1R)-(+)-camphor showed strong activity due to cytoplasm coagulation and hyphal lysis	[59]
Larvicidal	*Anopheles stephensi*	Leaves, E. oil	Probit analysis method	The E. oil showed strong, dose-dependent activities with LC_{95} 0.237% at 12 h, and 0.128% at 24 h	[39]
	A. aegypti, Culex pipiens and *C. quinquefasciatus*	E. oil, 20 µg/ml	---	Exhibited strong activity with LC_{50} 10.0, 46.4, and 15.1	[36]
Algicidal	*Microcystis aeruginosa* and *Chlamydomonas reinhardtii*	Leaves, Methanolic extract	The neutral red staining method	Potent inhibitory effects by inducing photosynthetic pigment degradation and declining PSII efficiency	[41]
Insecticidal	*Coptotermes curvignathus*	E. oil from wood	Repellence test	Increasing concentration increased the mortality ($p<0.001$)	[60]
	Lasioderma serricorne	E. oil from leaves	Fumigant Toxicity Bioassay and contact toxicity	Strong fumigant toxicity with an LC_{50} value of 2.50 mg/l	[37]
	Aphis gossypii	E. oil from leaves, twigs, and seeds	Contact toxicity bioassay by topical application	With LC_{50} values of 245.79, 274.99, and 146.78 mg/l after 48 h respectively	[61]
Insect repellence	*Tribolium castaneum*	Stem bark, Lipophilic extract	Repellence bioassay	Significant anti-insect property	[47]
Anti-allergic	Female BALB/c mice	Ethanolic leave extract	1% 2,4-dinitrochlorobenzene induced atopic dermatitis	Remarkable improvement of symptoms	[62]
	Human myeloma U266 cells (*in vitro)*	Methanol leaves extract/10, 30, 120 µg/ml	Enzyme-Linked Immunosorbent Assay of IgE	Decrease the amount of IgE in culture medium at dose-dependent	[63]
Anti-obesity	Male SD rats	Seed kernel oil	High-fat diets	Body weight and fat deposition are lower significantly.	[64]
Wound healing	Wistar albino rats	Ethanolic extract	Excision wound healing model	Significant increases in wound healing parameters	[65]
Anticonvulsant and Neuroprotective	Wistar albino rats	Methanolic extract of leaves/50, 100 mg/kg	Maximal electroshock seizure and Pentylene tetrazole induced seizure	Significant ($p <0.05$) increased the time of onset and decreased the duration of seizures, increasing the % protection	[66]

Pharmaceutical products

Kafūr is used in various dosage forms viz. ointment, cream, spray, liquid, drops, gel, oil, patch, tincture, jelly, lotion, stick, emulsion liniment, and aerosol; many pharmaceutical products contain camphor as an ingredient are available over the counter drug. A few examples are Air Saloupas Topical Spray (3%), Bayer Muscle and Joint Cream (4%), Campho-Phenique Pain and Itch relief Antiseptic Gel (10.8%), Flexall 454 Ultra Plus Pain-Relieving Rub (4%), Panalgesic Gold Topical Liquid (3.1%), Vicks VapoRub Cream (5.2%) [6, 48]. Camphor-Phenol Oral Rinse (10.8%), Heet Liniment (3.6%), Mentholatum Decongestant Analgesic (9%), Nuevo Cream (4.8%), Sarna Lotion (0.5%) and TheraFlu Vapor Stick (4.8%) [49]; 714X, Padma 28 [6].

Pharmacological studies

The crude extract and purified constituents of *C. camphora* were demonstrated by *in vivo* and *in vitro* experiments for analgesic, anti-inflammatory, antioxidant, antimicrobial, anti-helminthic, antifungal, and insecticidal activities. Studies reported that it reduces body fat deposition, heals wounds, and has neuroprotective properties (table 3).

DISCUSSION

In Unani medicine, there is a vast collection of single drugs, derived from three sources: plant, animal, and mineral. However, plant-origin drugs are most used. Though many pharmacological properties characterize all single drugs, each drug has a distinct or primary activity due to *mizāj* (temperament) or active principle. Following a review of both Unani and conventional literature, it was noted that *Kafūr* possesses a wide spectrum of pharmacological activities, including notable efficacy as an analgesic and antimicrobial (table 3). *Kafūr* is used since ancient times for its antiseptic and antimicrobial activity in epidemics. Its fumigation is advised to decontaminate the surroundings. Its many pharmaceutical products are used worldwide [49]. *Arq Ajeeb* is an essential Unani pharmacopeial formulation in which camphor is combined with menthol and thymol; this formulation has been proven to be particularly useful in the prevention and treatment of Covid-19. When a few drops are used in steam inhalation, it reduces dyspnoea. After local application, *Arq Ajeeb* provides immediate relief from headaches, colds, and coryza, as well as any form of somatic pain.

As mentioned in the Unani literature regarding its mechanism of analgesia that *Kafūr* has *Musakkin* (sedative) and *Mukhaddir* (anesthetic) actions, which diminishes the sensation in the concerned part. It is beneficial in desensitizing the local nerve which carries the impulse of pain [19]. The sensation is mainly composed of *harārat* and *rutubat,* which perceive pain and an unpleasant feeling in pathological conditions. Hence, the contrasting quality of *mukhadderāt*, which is generally cold and dry in temperament, prevents the transmission of *rūḥ nafsāni* (the sensation of pain) to a specific organ. Further, due to the cold temperament of *mukhadderāt*, the nerve fibers become dense, causing a greater reduction in conduction velocity of *rūḥ nafsāni* (neurotransmission for pain) that is why *kafūr* is found very effective in diminishing the sensation of pain [2].

Studies performed with extracts and essential oil of plants containing camphor as one of the significant constituents demonstrated a reduction of inflammatory mediators, such as proinflammatory cytokines (IL-1β, IL-6, and TNF) and prostaglandin E2 in macrophages culture [67]. Borneol (a chemical variant of *C. camphora*) showed significant anti-nociceptive activity in various pain models [50]. Another constituent of *Kafūr* is linalool which has shown to ease pain and might be due to the suppression of proinflammatory cytokines and regulation of NMDA receptor [68] and eugenol, that block calcium from into the cell and thus loss the pain sensation [69]. *C. camphora* essential oils reduced serum and brain tissue nitric oxide and PGE2 levels. Nitric oxide is an important neurotransmitter involved in the nociceptive process, and it contributes to the development of central sensitization [8]. Camphor activates and then desensitizes transient receptor potential vanilloid-1 (TRPV1) [70] but inhibits the TRPA1 channel, expressed in most nociceptive DRG neurons. Camphor-activated TRPV1 currents underwent significant desensitization and tachyphylaxis, which might exhibit analgesic properties together with inhibition of TRPA1 [71].

Apart from analgesic*, Kafūr* has also been reported for many other pharmacological activities might be due to the presence of monoterpenes, phenolic derivatives, flavonoids, lignans, sterols, and terpenoids [34, 37, 39, 40, 43-45, 46]; which are reported to have antinociceptive/analgesic [49, 50], antioxidant [52], antimicrobial [53-57] and wound healing properties [64]. The antibacterial activity was achieved by different mechanisms like partial degradation of the cell membrane, increased membrane permeability, cytoplasm leakage, noticeable distortion, shrinkage of bacterial cells, and membrane protein structural changes [56]. Eucalyptol, (1, 8-cineole) and α-pinene are involved in the larvicidal activity in conjunction with other compounds [39]. Camphor, α-terpineol, and linalool were found to involve in algicidal activity by inducing photosynthetic pigment degradation and declining PSII efficiency [41]. D-camphor, linalool, limonene, etc. from the essential oil of camphor were reported to be repellent and insecticidal [36, 46, 59, 60].

Not just the *Kafūr* or its active ingredients, but also its wood, leaves, seed kernel, and aerial section in the form of extract or oil have been found to have antiseptic and antimicrobial properties. Many pharmaceutical preparations and Unani Pharmacopeial formulations bear witness to their efficacy in treating a variety of ailments.

CONCLUSION

After reviewing the literature and scientific investigations, it can be concluded that *Kafūr* is a drug that has been used effectively in the Unani system of medicine for the treatment of pain and infection for a long time. It has a variety of formulations that are used both internally and externally to treat several ailments. Its mechanism of action is further supported by phytochemical and pharmacological research.

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CONFLICT OF INTERESTS

There is no conflict of interest.

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