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PHYTOCHEMISTRY, ETHNO-PHARMACOLOGY, AND PHARMACOGNOSTICAL APPRAISAL OF *IZKHAR (CYMBOPOGON JWARANCUSA* (JONES) SCHULT.) IN UNANI MEDICINE

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ABSTRACT

Cymbopogon jwarancusa (Jones) Schult., commonly known as *Izkhar,* of Poaceae/ Gramineae family is an aromatic perennial grass used therapeutically since ancient times in Unani medicine, mainly in diseases like ascites, hepatitis, gastric and splenic diseases. Literature survey highlighted it activities as potent antioxidant, antimicrobial, diuretic, hypolipidemic, hypoglycaemic and anticancer activities. These activities are attributed to the phytochemical compounds like terpenes (mono and sesquiterpenes), terpenoids, flavonoids, alkaloids, and phenolics compounds. On the contrary, *Cymbopogon jwarancusa* is quite less explored as compared to other species of the *Cymbopogon* genus. This review article intends to incorporate the Unani aspect of *Cymbopogon jwarancusa* (*CJ*), its ethnomedicinal and therapeutic activities, traditional/folklore uses, phytochemistry, and pharmacological studies available in present and previously published research, literatures and manuscript. This compilation may prove to be a novel evidence-based beneficial anthology for researchers and a miracle drug in pharmaceutical industry as it may impose synergistic effect when used with conventional medicines.

Keywords: Unani Medicine, *Izkhar*, *Cymbopogon jwarancusa* (Jones) Schult., Antioxidant, Carminative

1. INTRODUCTION

The Unanisystem of Medicine (USM) is a renownedalternative and complementary system of medicine set up onthe ideology of the Greek physicians Hippocrates (460–377 BC) and Galen (131–199 AD) **[1]**. It was the Hippocrates who liberated Medicine from the realm of superstition and magic, and gave it the status of a science **[2]**. It treats the diseases related to all organs of the human body and deals precisely with many states of diseases and health; offers promotive, protective, remedial, and rehabilitative healthcare **[3, 4]**.

Scientific evidences and researches have shown that conventional medicines are prone to cause further damage to the various bodyorgans. Hence, medicinal plants have become increasingly popular due to their safety, efficacy and cost effectiveness **[5, 7]**. *Cymbopogon*is a genus that constitutes about 45 species under the Poaceae family, native to tropical Asia and India**[8]**.Among them, *Izkhar* (*Cymbopogon jwarancusa* (Jones) Schult.) showed various pharmacological actions as elaborated and discussed in numerous Unanimanuscripts.

Itis commonly known as *Khavi* or *Khawi*in Hindi and *Gurgiyah* in Persian **[9]**. It is an aromatic perennial grass that grows upto 6 feet in height and has densely tufted roots. The leaves are about 2 feet long and 0.2 inch broad. It occurs in Himalayas from Kashmir to Assam ascending up to 10,800 feet and in north western plain reaching down to Bombay **[10]**.

The geographical distribution of *Izkhar* presents its two main varieties, as *Izkhar hindi* (cultivated and procured in India) and *Izkhar makki* (cultivated and procured in Mecca). In this review, we have covered the features of the marketed sample in New Delhi, probably *Izkhar hindi* which was identified as *Cymbopogon jwarancusa* (Jones) Schult. (Syn. *Andropogon jwarancusa* Jones) by NISCAIR, New Delhi (Ref No.- NISCAIR/RHMD/ Consult/2021/3791-92).

The essential oil extracted from it, constitutes majorly monoterpenes and sesquiterpenes**[11]**. Some of itsprominent pharmacological actionare*Muhallile-awraam* (anti-inflammatory), *Muqawwie-meda* (stomachic), *Mufattehe-sudad* (deobstruent), *Mudire-baul* (diuretic), and *Kasire-riyah* (carminative) etc. **[12-15]**. Scientific study showed that *Cymbopogon jwarancusa* (*C. jwarancusa*) possesses antioxidant, anti-allergic, antimicrobial, analgesic, antipyretic, anticancer **[16]**, diuretic **[11]**, hypolipidemic, and hypoglycaemic activities **[17]**. Thus, it is explored and critically reviewed through Unani, Scientific, and other ancient literatures.

2. MATERIALS AND METHODS

The extensive literature survey for maximum informationon *C. jwarancusa* was carried out from Unani texts and medicinal plant books.The search engines such as PubMed, NCBI, Scopus, Google Scholar, Web of Science, Springer, Elsevier, Science Direct, and Academia were explored for theplant's chemical constituents, therapeutic uses and modern pharmacological activities. TheMeSH terms such as *Cymbopogon*, *Cymbopogon jwarancusa* and Unani, *Cymbopogon jwarancusa* and pharmacological activities", "*Cymbopogon jwarancusa* and ethnomedicinal properties", "anti-inflammatory", "antioxidant", "hepato-protective", cytotoxic, "anti-microbial", and other pharmacologicalactivities were browsed.

3. RESULTS

3.1 Description of *Izkhar* in Unani and other ancient literature

Morphology and Regional Distribution

Izkhar is a popular aromatic grass with numerous thin branches that erupt from its root. The root is stout and hidden in mud. Its leaves are thin and short structurally when compared to *sarkanda* (*Saccharum munja* Roxb.). Buds are in abundance, fragrant and white in colour; have strong taste which on chewing produces irritation on tongue. The medicinally recommended part of *Izkhar* of Mecca (*Izkhar makki)* is its root and bud. The highly appreciable plant has strong aroma, abundant flowers, thin branches, hard texture and ruby-colour. The plant has abundant leaves thatare soft on touch and short in height **[15, 18-20]**. Additionally, according to *Razi* (Rhazes 854–935 AD) it should have fragrance like rose when rubbed on palms**[21]**. *Izkhar* from Arab is considered the best in quality while the worst one is from Babylon**[15]**. The *Izkhar* of *Hejaz* (Western Province in Saudi Arabia) is referred as '*Harmi*', and found to be most efficacious after *Izkhar* grown in '*Antali*' (old city of turkey). On the contrary, the *Izkhar* of '*Qafsa*' (in Tunisia) and coastal Africa is considered as worst among all types**[19]**.

Temperament (Mizaj)

Hot 2^0dry 2^0 **[15, 19, 20, 22]**

Note-whenever a thing is said to be hot or cold, whether it is to be used internally or applied externally, it does not mean it is actually hot or cold on touch, but it means that the internal quality/effectiveness is potentially hot or cold **[20, 23]**.

Dose (Miqdaar e Khora'k)

- 5-7 gm **[22]**;
- 1.45- 4.5 gm **[19]**;
- 1.45gm - 3.5gm or 4.5gm **[15]**

Adverse effect (Muzir) and Correctives (Musleh)

Consumption of *Izkhar* in large dose causes headache, and adversely affects warm temperament of stomach and kidney. This

effect on kidney is due to its diuretic activity. The corrective (*musleh*) prescribed to relieve the headache is equivalent quantity of sandal (*Santalum album L.*), rose (*Rosa damascene Herrm.*), and *arqneelofar* (aq. distillate of *Nympheaalba L.*); while intake of rose alone for stomach and kidney On the contrary, Unani scholars recommend honey as a corrective agent for kidney. The corrective agents are used simultaneously or admixed with *Izkhar* to alleviate its harmful effects **[15, 19]**.

Substitutes (Badal)

The substitute of whole plant of *Izkhar* is *sumbulut-teeb* (*Nardostachys jatamansi* (D.Don) DC.) in equivalent quantity and eighth part of *zafraan* (*Crocus sativus* L.) while alternate of bud (*fuqaah*) is c*hiraita* (*Swertia chiraita* Roxb.). In compound formulations, non-availability of *Izkhar* can be adjusted by the admixing of *qust talkh* (*Saussurea lappa* (Decne.) C.B. Clarke) and/or *Rasan* (*Inula racemosa* C.B.Clarke) **[15, 19]**. Likewise, Unani doctrines also recommend *filfilsiyah* (*Piper nigrum* L.) and/or *aaqarqarha* (*Anacyclus pyrethrum* L.) as a replacement to *Izkhar* **[22]**.

Ethnomedicinal Properties

Unani Pharmacological Actions

Unani scholars used it for *Muhallile-awraam* (anti-inflammatory), *Muqawwie-meda* (stomachic)· *Qabiz*(astringent), *Mufattitehisaat* (lithotriptic), *Munzij*(concoctive), *Mulayyin* (laxative), *Mufattehe-sudad* (deobstruent), *Mudire-baul* (diuretic), *Mudire-haiz* (emmenagogue), *Kasire-riyah* (carminative) actions **[15, 19, 20-22]**.

Traditional/Folklore Uses

According to the Ayurvedic concept, *C. jwarancusa* bears cooling, bitter, digestible and alexiteric effects, along with being appetiser, stomachic and astringent. This makes it useful in blood and skin disorders, strangury, fever, leprosy, biliousness, burning sensations, sweat disorder, thirst, vomiting, unconsciousness, cholera, chronic rheumatism and gout. It is used as blood purifier, anti-tussive, stimulant and diaphoretic agent **[9]**. For diuretic purpose, it is suggested to be boiled with wine and taken as syrup in Q.S. (Quantity sufficient). Its flowers serve beneficial effect as haemostatic agent **[24]**.

Formulations

C. jwarancusa is incorporated as one of the major component in semisolid formulation *Majoon Dabeedul Ward*, *DawaulKurkum (Sagh'eerwa Kabeer)*, *NuskhaLuk Maghsool*, *Dawa-e-Luk (Sagh'eerwa Kabeer)* **[25-29]**, and liquid preparation *Sharbat Izkhar* **[29]**.

Unani Research Studies

Unani formulation *Majoon dabeedul ward* has *Izkhar (C. jwarancusa)* as one of its ingredients, and it exhibits hepato-protective effect against the acetaminophen-induced liver damage in the

animal model and restores the liver enzymes demonstrating its antioxidant properties **[30]**. Similarly, *C. jwarancusa* is an ingredient of *Dawa-ul-kurkum* (DUK), which is found efficacious in *sue-mizaj-kabidbarid* (non-alcoholic fatty liver disease). The DUK potentially reduces NAFLD via correction of temperament and evacuation of phlegm (*balgham*), because a number of its ingredients have *musakkhin* (calorific), *munzij* (decoctive), *mufattehsudad* (deobstruent) and *muhallil* (resolvent) properties **[31]**. Also, DUK protects liver by attenuating oxidative stress against D-Galactosamine induced liver injury in rats **[32]**.

Therapeutic Uses

The root (decoction) and flower (powder) are used in ascites, hepatitis, gastritis and spleenitis. Being *mufatteh*(deobstruent), it opens vascular obstruction of liver, uterus, anus and reproductive organs, and evacuates viscous and harmful humours from. Its bud (*fuqaah*) relieves haemoptysis, haemorrhage, and painful conditions of stomach, lungs, liver, kidneys, teeth, gums and joints. It is effective in muscular injury, convulsions, chorea, paralysis, and facialpalsy. The decoction diminishes flatulence, its sitz bath is recommended in endometritis, decoction amalgamated with *sikanjbeen* (*sirka*/acetic acid + *angbeen/*honey) alleviates the peak period of phlegmatic fever. According to *Razi*, local application (L/A) of paste is effective in firm swellings/gastritis, hepatic ailments. Similarly, leave's paste (L/A) works as antidote at the site of insect bite, in vitiligo, hastens beard growth, and essential oil (L/A) reduces itching. *Ibn-Sina* (Avicena-980–1035 AD) suggeted its oral intake relaxes uterine pain, absorbs secretion of gums and strengthens them, and evacuates (*tanqia*) harmful secretions from brain **[15, 18-20]**.

When admixed with *filfilsiyah*(*Piper nigrum*), it increases appetite, and reduces phlegmatic nausea and vomiting, while admixing with *turanjbeen* (*Fraxinus ornus* L.*)* reduces spleenitis. It is beneficial in cholera and related thirst. Extract's eye drop treats ocular pruritis and pterygium (eye web). Its fragrant volatile molecules are effective as cardiac tonic (*muqawwie-qalb*) and enhance hepatic strength. It alleviates mouth ulcers when used as gargle**[15,19,20]**.

Description of *C.jwarancusa*in Scientific Literature

Taxonomy and classification

Cymbopogon jwarancusa lies in the Kingdom: Plantae, Subkingdom, *Tracheobionta* - Vascular plants, Superdivision- *Spermatophyta* - Seed plants, Division: Magnoliophyta, Class: Liliopsida, Subclass- *Commelinidae,* Order: Poales, Family: Poaceae, Genus:

Cymbopogon Spreng, Species: *jwarancusa* **[33]**. The vernacular names have been listed in **Table 1**.

Table 1: Vernacular Names of *C. jwarancusa*

S.No	Language	Name	References
1	Hindi	Lamjak; Bur; Panni; Karankussa; Ibharankussa; Ghatzari	[24]
		Bur; Ghatyari; Ibharankusha; Karankusha; Khavi; Khawi; Khoi, Lamjak; Panni; San; Solara	[9]
2	Sanskrit	Lamajjaka	[24]
		Amrinala; Avadahaka, Avadataka, Dirghamula; Ishthakapathika; Jalashaya; Laghu, Lamajjaka; Laya; Nalada; Sevya; Shighra; Sunala; Sunila	[9]
3	Bengali	Karankusa	[24]
		Gandhavena; Ibhrabkusha; Karankusa	[9]
		Karankusa	[10]
4	Gujrati	Pilo-valo	[24]
		Jalavalo; Khadajala; Pilovalo	[9]
5	Marathi	Pivalavala	[24]
		Izkir; Lavaja; Pivalavala	[9]
6	Arabic	Izkhir	[9]
7	Canarese	Karilavancha	[9]
8	Bombay	Izkhir	[9]
9	North-West Provinces	Bad; Ganguli; Misiyaban; Piriva	[9]
10	Punjab	Bur; Ghatyari; Ibharankusha; Karankusha; Khavi; Khawi; Khoi, Lamjak; Panni; San; Solara	[9]
11	Persian	Gurgiyah	[9]

Critical approach towards common name

The common name of different species of the *Cymbopogon* family is often times surrounded with confusion more than controversy. In "The Wealth of India", *Cymbopogon citrates* has been mentioned by its common name- West Indian lemongrass, *Cymbopogon flexosus*- East Indian lemongrass; *Cymbopogon martini*- Rusa grass; *Cymbopogon nardus*- Citronella grass, *Cymbopogon caesius*- Kachi grass **[10]**.

Macroscopic Description

The plant has tufted stems and short root stock. The leaves envelop stem, become free and open upwards. The leaves are long (25-35 cm in dried form), flat, up to 1cm broad at the base, narrowly linear, gradually tapering above, ending in long capillary tips. It appears glabrous on both the surfaces with parallel veins, but the lower axial surface is a bit scabrous and has raised veins. The scum on removing enveloping leaf sheaths appears more or less terete, smooth, pale yellow in colour, measuring 6-9 cm in length and jointed at below. A spreading tuft of numerous roots is produced below. Roots are unbranched and appear glaborous about 4-11 cm long, quite tough and terete. The plant has a pleasant aroma. The leaves have pleasing slightly pungent taste **[12, 13]**.

Microscopic Description

Root- Root in a transverse section appears to be decorticated showing at places

remnant of parenchymatous cells of the cortex. The outermost visible layer is a uniseriate, thick walled endodermis which is followed by a large compact zone of sclerenchyma (both fibres and sclerieds are present). Xylem and phloem are radially situated. Xylem vessels are very few mostly single in each vascular bundle, the rest mostly consisting of fibres. Phloem region also shows mostly fibres. The pith is comparatively small and consists of rather walled parenchymatous cells **[12, 13]**.

Stem: A cross section of the stem shows a rather thick walled uniseriate epidermis, covered with a smooth thick cuticle. A few layered hypodermis consisting of sclerieds and collenchymatous cells is also present. Following this, there is a continuous band of distinct fibrous layer. Rest of the large ground tissue consists mostly of parenchyma, gradually increasing in size and thinness of walls. Numerous vascular bundles are scattered in this large ground tissue. Vascular bundles are closed, collateral, having distinct bundle sheath of sclerenchyma. The vascular bundle has few vessels and sieve cells, almost no parenchyma and largely surrounded by fibre cells forming a sheath. Protoxylem lacuna is also present **[12, 13]**.

Leaf: A transverse section of the leaf shows slightly concave adaxial surface while abaxial surface has a waxy outline, deeply concave at each parallel vein area. Adaxial side shows a rather thick walled single layered epidermis, which is covered with a thick cuticle. Mesophyll is 4-6 layered consisting of uniform, spongy parenchymatous cells which are mostly colourless. The largest vascular bundle is in the middle while they taper peripherally. Bundle sheath present while vascular bundle is connected to the abaxial epidermis by a girdle of sclerenchyma. The xylem shows few vessels, the rest consisting mostly of fibres. The phloem also shows little sieve cells or parenchyma. The abaxial epidermal cells are frequently papillose and also show prickly hairs. A small zone of two layered sclerenchyma is also present below the adaxial epidermis opposite to each vascular bundle**[12,13]**.

Chemical Constituents

Aerial part of *C. jawarancusa* affords a yellowish coloured essential oil. Its composition is influenced by climatic, seasonal, geographical or genetic differences as studied from different landscapes worldwide, specifically from India **[34]**. The yield of essential oil (aerial part) is reported to be 0.8-1.0% **[35]**. It constitutes majorly of terpenes classified into monoterpenes and sesquiterpenes **[11]**.

Terpene

Terpenes work as thermoprotectant, help in signalling functions in plants, and also have numerous medicinal uses **[36]**. On the basis of number of isoprene units present,

theyare classified as mono-(C10), sesqui-(C15),and di-terpenes (C20)**[37]**.Their diverse chemical structure **(Figure 1)** is produced due to different terpenoid metabolic pathways along with specialized cell types that play a role in their biosynthesis **[38]**. The biological activities include antioxidant, anti-inflammatory, antiaging, antitumor, neuroprotective, immunomodulatory, insecticidal, antiviral, antibacterial, and antimalarial **[36]**. The essential oil of *CJ*chiefly constitutesof terpenes thatincludepiperitone (20-70%), citronellal (30-40%), Δ-carene (20-24%), γ-terpinene (7.5%), β-pinene (3.5%), *p*-cymene (0.6-3.5%), geraniol (0.04–22.5%).

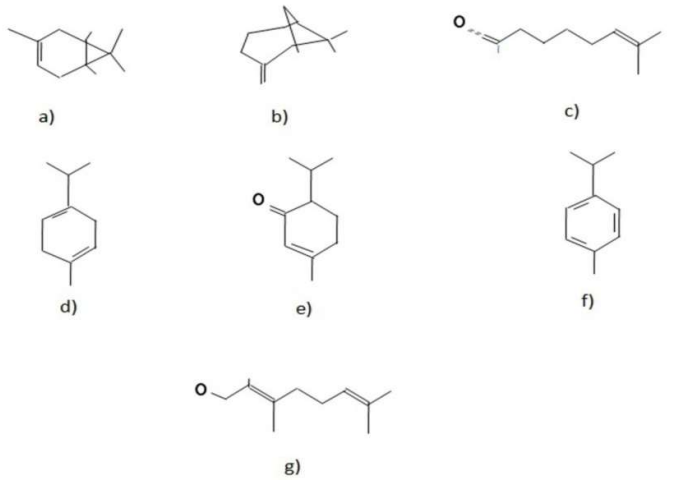

Figure 1: Structure of major terpenes isolated from *Cymbopogonjwarancus*a (Jones) Schult.
a) Δ-carene; b) β-pinene;
c) citronellal; d) γ-terpinene;
e) piperitone; f) *p*- cymene;
g) geraniol

Some constituents are found in traces like alloaromadendrene, *cis*- and γ-allo-ocimene, α-bisabolene, β-bisabolene, borneol, *d*-cadinene, calamine, camphene, camphor,β-caryophyllene, linalool, fenchone, myrcene **[8, 39]**, α-pinene, dipentene, phellandrene, 1,8-cineole, 4-terpineol, α-terpineol, geranyl acetate, β-farnesene, ellemol, eudemol, linalyl acetate, isopulagol, piperitenone **[40]**. Moreover, p-menthenols and monoterpenes were found to be major part of essential oil in winter and summer season, represented by *cis*-p-menth-1-en-3-ol(10.5%–14.2%), *trans*-p-menth-1-en-3-ol(8%–9.2%), δ-2-carene (11.8–15.8%) cis-p-menth-2-en-1-ol (25.3% –31.8%), and *trans*-p-menth-2-en-1-ol (14%–16.6%). Maximum contents of p-menthenols were reported in summers (71%) while minimum in winters (58.8%) **[41]**.

Flavonoids and phenolics

The biological activities as reported of both flavonoids and many other phenolic

components comprise of antioxidants, anti-inflammatory, immune modulatory, cardioprotective, anticancer, antibacterial, and skin protective **[42, 44]**. *Cymbopogon jwarancusa* extract obtained from solvents-Acetonitrile, Ethyl acetate, n-Hexane, Ethanol, Acetone, and Diethyl ether constituted phenolics and flavonoids, though seasonal variation was seen in spring and winter. The highest content of total flavonoid and total phenolics was obtained in ethanolic extract of spring season (40.93±1.12mg quercetin equivalents/g and 31.72±0.08 mg gallic acid equivalents/g, respectively) and acetone extract of winter season (38.32±0.74 mg QE/g and 31.24±0.17 mg GAE/g, respectively); (3.87% w/w) and ethanol extract obtained in winter (4.83%) **[45]**. The extract of *C. jwarancusa (Izkhar)*, which showed positive result for antioxidant and antimicrobial activities, was found to contain phenolics and flavonoids **[46]**. Similar correlation was reported in other medicinal plants as well **[47, 48]**.

Other phytoconstituents

*C. jwarancusa*contains average amount of alkaloids **[49]**. Other species of *Cymbopogon* have been reported to contain alkaloids **[50, 51]**, steroids and fatty alcohol **[52]**, tannins **[53]**, volatile and non-volatile terpenoids **[51, 54]**.

Pharmacological Activities

Antioxidant

Imbalance of pro-oxidants and antioxidants leads to oxidative stress, further giving rise toneurodegenerative disorder, hepatitis,liver cirrhosis, condition of liver due to consumption of alcohol (acute and chronic), elevated level of cholesterol in blood, and chronic kidney disease etc.**[55-58]**. The *in-vitro* radical scavenging capacity of the essential oil of *C. jawarancusa* and its constituents was calculated by the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay.This assay is efficient as relatively short time is required for analysis**[59]**.*CJ* essential oil exhibited a scavenging activity in order of elemol>piperitone> β-caryophyllene> α-pinene, at 10 to 100 µg/ml range of concentrations. All the isolated components independently demonstrated some extent of antioxidant activity over the tested concentration range, and the IC_{50} was found to be 48.9 lg/ml of the essential oil **[60]**. Previous literature survey also revealed that piperitone, α-pinene **[61]** and β-caryophyllene **[62]** possess free radical scavenging activity, using the same method of DPPH assay **[60]**. Kumar *et al.*, (2021) reported antioxidant activity of *C. jwarancusa* by DPPH, FRAP, Nitric oxide assays, and total phenolic content. The total phenolic content was 231.28 + 2.02 mg GAE g−1 while FRAP was found to be 17.08 ± 0.41 mM Fe (II) g−1. The DPPH

and nitric oxide assays showed concentration dependent inhibition potential. As the concentration was increased from 1 to 4mg/ml of essential oil, the % inhibition increased from 21.36% to 49.47% in DPPH assay. Similarly, the increase of essential oil concentration from 1 to 4mg/ml increased scavenging activity of nitric oxide from 55.21% to 81.70%. This may be attributed to the presence of phenolics, terpenoids like p-menthenols with attached hydroxyl group that possess free radical scavenging activity **[41]**.

Anticancer

Cancer creates major health problem, and is one of the main causes of mortality worldwide **[63]**. The adverse effects of of its conventional therapy include nausea, vomiting, inhibition of bone marrow function, and loss of hair (alopecia).With time, around 200 novel compounds have been approved, out of which major portions are natural products, and belong to various groups of secondary metabolites such as alkaloids, flavonoids, terpenes, tannins, lignans, vitamins, glycosides, saponins, and oils etc. **[64-67]**.*C. jwarancusa*oil and its constituents were evaluated by Sulforhodamine - B assayfor *in vitro* cytotoxicity study on human cancer cell lines HEP-2(liver), IGR-OV-1 (ovary), THP-1 (leukaemia) and A-549 (lung). All the cell lines were subjected to increasing order of concentration of oil ranging from 5-100µg/ml for 48hr. At the concentration of 100µg/ml, the percentage of dead cells was found to be 95% in THP-1 (leukaemia) and A-549 (lung), 79% in HEP-2 (liver) and 75% in IGR-OV-1 (ovary). The oil and its major constituents produced a concentration dependent inhibitory effect on the cell lines tested in above mentioned range of dilutions. Also, the IC_{50} values (µg/ml) were 6.5 for THP-1, 6.3 for A-549, 7.2 for HEP-2, and 34.4 for IGR-OV-1. The individual isolated compounds showed less cytotoxic activity when compared to essential oil as a whole which indicates a possibility of synergistic effect among the components of essential oil. The abundant key constituents of essential oil that are piperitone, α-pinene and β-caryophyllene exhibited similar cytotoxicities when evaluated against anticancer agents such as paclitaxel and mitomycin-C on the aforementioned cell lines **[60]**.

Alpha-pinene has been reported to exhibit *in vitro* cytotoxicity to HepG2 (human hepatocellur carcinoma cells) **[68]** and β-elemene, a sesquiterpene has been reported to be cytotoxic and antitumoral agent **[69]**. Piperitone showed cytotoxic activity againstvarious human cancer cell lines such as ANC3A (Uterine), and Hela (Cervical) **[70]**. Betacaryophyllene has been reported to be cytotoxic to MCF-7(human breast), MDA-MB-468(breast) and UACC-257 (human melanoma) cancer cell lines **[71]**.

Antimicrobial

Studies have revealed that medicinal plants with alkaloids, flavonoids, phenolics, coumarins, terpenoids, lectin, polyacetylenes and polypeptides overcome the impact of multidrug-resistant microbes**[72,73]**.

C. jwarancusa oil markedly restrained the growth of various species of *Proteus mirabilis, Klebsiella pneumonia, Shigella flexneria, Citrobacter, Salmonella enteric* sertyphi at the dose of 105 CFU/ml. Geraniol, the most active compound, completely inhibited the growth of the bacteria than fungi and ß– Pinene, Linalool, and α–terpeniol showed an inhibitory activity against some bacteria and fungi. The aqueous extract showed less effect against *Aspergillusflavus*(03.72 ± 0.19 mm) at concentration of 100 ppm while ethanolic extract was established to be quite efficient against *Fusarium oxyporium* sp–*lini* (85.31 ± 0.25 mm) and *Staphylococcus aureus* (94.37 ± 0.28 mm) at 500 ppm while. This shows the ethanol extract can be used as food preservative and as a remedy and against dental diseases **[46]**.

Also, disc diffusion and micro dilution broth assay displayed the anti-microbial activity of *C. jwarancusa* essential oil on microorganisms (bacteria) like *Mycobacterium smegmatis*, methicillin resistant *Staphylococcus aureus, Staphylococcus epidermis* and *Streptococcus mutans*, and fungi *Candida kefyr, Candida albicans, Candida tropicalis*and *Candida krusei.* The net zone inhibition of essential oil, MBC (Minimum bactericidal concentration) and MIC (Minimum inhibitory concentration) against tested strains of bacteria ranged from 2 to 9 mm, 0.47–15.13 mg/mL, and 0.11–7.56 mg/mL, respectively. Similarly, zone of inhibition, MBF (Minimum fungicidal concentration) and MIC of essential oil against fungal strains ranged from 9-31mm, 0.47-5.67mg/ml, and 0.05-3.78mg/ml respectively. This pattern of result justifies a previous study on *Cymbopogondistans*(Nees ex Steud.) W.Watsoncontaining high level of oxygenated monoterpenoid p-menthenols that possessed antimicrobial activity individually or synergistically with other volatile constituents likepiperitone, geraniol andcitral **[41]**.

Flukicidal

*Paramphistomumcervi*and *Fasciola gigantic* and are two main trematode parasites amongst the helminth in the ruminant's liver **[74]**. Flukes produce intense damage to hepatic parenchyma; cause eosinophilia, edema hypo-albuminemia, haemorrhage and anaemia in ruminants **[75]**. The study on methanolic extract of *C. jwarancusa* exhibits its flukicidal effect against buffalo's liver and bile ducts flukes *(Fasciolagigantica, and*

Paramphistomum cervi) as it inhibits their motility, paralyses them leading to their death **[76]**. This potentialof *C. jwarancusa* can be due to aromatic terpenes and alkaloids.Kayani*et al.* (2007), established aromatic alkaloids as effective anthelmintic compounds as they act on CNS (central nervous system) and also intercalate with DNA of fluke eventually leading to paralysis, followed by flukes' death. Terpenes disintegrate tegumental membrane because of their lipophilic compounds that probably results in upsetting the normal physiological as well as biochemical processes of the body **[49]**.

Anti-diabetic and Anti-hyperlipidemic

Diabetes and hyperlipidemia are two of the main factors that may cause cardiovascular diseases in the long run. Plants based drugs serve as new therapeutic agents to treat such illnesses by their antioxidant, hypoglycemic and hypolipidemic activities **[77]**.

Khan *et al.* (2018b) demonstrated that the ethanolic extract of *C. jwarancusa* reduces body weight, lipid parameters and blood glucose levels **[17]**. This effect may be attributed due to presence of active phytochemicals e.g. isoprenoids and terpenoids. Isoprenoids like geraniol, limonene and linalool in *C. jwarancusa* extract have demonstrated to inactivate HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase) and hence may be responsible for antihyperlipidemic effect **[78]**. Terpenoids possess cardio protectiveeffect since they inhibit the production of free radicals**[79]**. Essential oil of *C. jwarancusa* contains higher percentages of sesquiterpenes and monoterpenes **[60]**, which are reported to possess anti-diabetic and anti-hyperlipidemic activities **[80]**. Terpenes play a significant role in the management of Type 2 diabetes by modulating peroxisome proliferator-activated receptor gamma (PPAR-γ) **[81]**.

Diuretic

Diuretic agents that increase excretion of water are likely to be used in oedematous conditions such as nephritis, congestive heart failure, premenstrual tension, toxaemia of pregnancy, and hypertension **[82]**. They alter the excretion of electrolytes and water by acting onrenal tubules. Various classes of diuretics include carbonic anhydrase inhibitors, thiazide, potassium sparing and osmotic diuretics **[83]**. Khan *et al.* (2018a) reported in their study that *C. jwarancusa* extract has dose-dependent diuretic response. At the dose of 500mg/kg, a considerable increase in urine output was noted at its single and multiple doses (9.51 ± 1.3 ml and 34 ± 3.14 ml respectively) as compared to control group. The value of diuretic index after single dose of furosemide and multiple doses (150, 300 and 500 mg/kg) of *C. jwarancusa*

extract were 2.42, 1, 1.36 and 1.48 respectively, whereas multiple doses of furosemide and multiple doses (150, 300 and 500 mg/kg) of *C. jwarancusa* extract showed values of diuretic index as 1.68, 1.22, 1.35 and 1.52 respectively. Also, Lipschitz values of *C. jwarancusa* extract at 150, 300 and 500 mg/kg were noted to be 41%, 56% and 61% respectively, after single dose and 72%, 80% and 90% respectively, after multiple doses, as compared to furosemide. This activity may be due to higher composition of terpenoids which prevents the actions of aldosterone by binding to A1 receptor thus causing dieresis **[11]**.

DISCUSSION & CONCLUSION

The people globally rely on herbal medicines including Unani medicine as part of their primary health care needs. This surge leads to widespread research on more and more plants to establish their possible medicinal value. *Izkhar* (*Cymbopogon jwarancusa* (Jones) Schult.) is one such multipotent drug. It possesses versatile beneficial properties mainly *muhallil, muqawwi* and *mufatteh sudad* due to which it is considered a classical drug for liver ailments. The research studies highlighted its activities as antioxidant, anti-allergic, antimicrobial, analgesic, antipyretic, hypolipidemic, hypoglycemic, anticancer, diuretic, hypolipidemic, and hypoglycaemic. It is highly recommended in *warme-kabidbarid* (hepatitis), *warme-meda* (gastritis), w*arme-tihal* (spleenitis), *istisqa* (ascites), and *sudae-kabid (hepatic obstruction)*. Despite low toxicity of *C. jwarancusa*, it should be taken with precaution, within the safety limit.

The chemical constituents liketerpenes (monoterpenes and sesquiterpenes like piperitone, p-menthenol, citral, citronellal, geraniol), flavonoids, alkaloids, phenolics, saponins etc. and trace elements like calcium, iron, manganese, sodium, zinc, cadmium, phosphorus etc. synergistically enhance its medicinal value.

However, it should be explored (preclinical and clinical trials) in other diseases like *falij* (paralysis), *laqwa* (facial palsy), *tashannuj* (convulsion), e*htabase-baul*(retention of urine), *ehtabase-tams* (amenorrhea), *wajaulmafasil* (arthritis) as per Unani literatures to authenticate its efficacy and safety, as limited research work is available at present. It is further suggested that instead of using plant materials in the crude form, they may be formulated into elegant finished product or active constituents can be isolated to affect the target area in the body. It may be combined with other conventional therapy to reduce the side effects of the conventional drugs, improve the patients' quality of life (QOL), and also can be used in preventive cures.

Declaration of competing interest

The authors declare there is no conflict of interest in this review article.

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