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ETHNOBOTANY, PHARMACOLOGICAL APPLICATION, PHYTOCHEMISTRY AND THERAPEUTIC POTENTIAL OF BLACK PEPPER (*PIPER NIGRUM* L.): AN UPDATED REVIEW

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Review Paper

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ABSTRACT

Background: Black pepper (*Piper nigrum* L.) also known as *Filfil Siyah*, is a significant and commonly used drug in traditional medicine, particularly in the Unani School of medicine. The pharmacological utilization of black pepper, which includes the treatment of respiratory disorders, throat conditions, intermittent fever, and gastrointestinal conditions, is due to the presence of biomolecules such as phenolics, alkaloids, flavonoids, carotenoids, and terpenoids, among others.

Aim and Objective: The objective of the review is to discuss the most recent findings regarding the pharmacognosy, pharmacological use, phytochemistry, and therapeutic potential of black pepper.

Material and Methods: Books and online resources were explored and the source material was compiled from traditional Unani texts like Khazain al-Advia, Makhzan al-Advia, Al-Jami li Mufradat al- Advia wa'l Aghziya, Al Qanoon Fit Tibb, etc. Scientific evidence was searched from databases like PubMed, Scopus, Web of science, Wiley Online Library, Google Scholar, and others.

Results: The potential existence of pharmacologically active biomolecules such alkaloids (piperine), tannins, flavonoids, and carotenoids were discovered through updated phytochemical investigations. Chemicals including sabinene, 3-carene, D-limonene, -pinene, caryophyllene, -phellandrene, -thujene, and -bisabolene are

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all found in the volatile oil composition. The evidence from scientific research also reveals that phytoconstituents have a variety of biological activities, including anti-inflammatory, anticancer, anti-obesity, antidepressant, antidiabetic, antimicrobial, gastroprotective, and insecticidal effects.

Conclusions: The most up-to-date knowledge on black pepper has been reviewed in this study, together with the reports and scientific data that support it. These reports revealed that black pepper has a variety of biological impacts that are helpful in a number of diseases. Future research is therefore required to comprehend the mechanism of bioactive molecules along with the appropriate experimental approach for the welfare of mankind in treating various sorts of ailments.

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INTRODUCTION

Herbal remedies have become popular, due in part to the lower risk of adverse reactions. Thousands of plants have been used traditionally to treat various diseases. Among them, species of the genus *Piper* are important medicinal plants used in various systems of medicine. The *Piper longum* fruit has been used in traditional medicine, including the Ayurvedic system of medicine. Pepper is a short tree that produces fruit and black pepper (*Filfil Siyah*) in particular is sweeter and sharper than white pepper, more pleasant to the palate, and more aromatic since it is ripe[1]. Black pepper, often referred to as the "King of Spices," is one of the most well-known, regularly used, and important spices used worldwide[2]. In addition to being medicinal product used for therapeutic purposes, it also serves as a flavouring agent in culinary preparation, as a preservative, and in perfumery industry.Hot and pungent peppercorns is obtained from black pepper which is the most famous and one of the commonly used spices throughout the world.

SCIENTIFIC CLASSIFICATION[3]

Kingdom: Plantae

Class: Equisetopsida

Sub class: Magnoliidae

Order: Piperales

Family: Piperaceae

Genus: Piper

Species: nigrum

SYNONYMS[4]

Arabic: Filfil Uswud

English: Black pepper, Decorticated pepper, common pepper

French: Poivre

German: Schwartzepfeffer

Hindi: Kalimirch.

Persian: Filfil Siyah

Sanskrit: Maricham, Maricha, Hapusha, Ooshnam, Valliyam

Fig. 1: Botanical description and Vernaculars of Black Pepper (*Piper nigrum* L.).

1.1 Ethnobotany

The genus piper has more than 1000 species but the most recognized species are P.nigrum, P.longum and P.betle. The black pepper plant has been widely cultivated throughout the tropics and is thought to have originated in India and Indonesia. India, Brazil, Indonesia, Malaysia, Vietnam, and Sri Lanka are the main producers of P. Nigrum[5]. In India, it is found in warmer parts from Central Himalayas to Assam, lower hills of West Bengal, Uttar Pradesh, Andhra Pradesh, Western Ghats from Konkan southwards to Trivandrum[6]. Black pepper is a perennial climbing vine that thrives in the shade with supporting trees or poles. The glabrous woody climbers can reach heights of up to 10 metres. The fruiting spikes range in length from 3 to 15 cm. The harvested fruits are sun-dried and have a spherical shape (drupe type), with a diameter of less than 5 mm. The glabrous inflorescence grows opposite the leaves on plagiotropic branches as a pendulous spike. The majority of flowers of the wild variety are dioecious, while flowers of the cultivated type are monoecious. In black pepper, self-pollination predominates, and protogyny is also present. The mature stem of the black pepper plant develops 10–20 primary adventitious roots. Dimorphic branching is used to grow the vines, which have monopodial, orthotropic branches and sympodial, plagiotropic fruiting branches. Each node of the orthotropic shoot has clinging roots that enable the plant to climb over the support trees. The orthotropic shoot grows indeterminately, and its leaf axils form lateral fruiting branches. Simple, alternating leaves have varying length and breadth, and grooved petiole[7]. Leaves rounded ovate to ovate-elliptic or elliptic, 8–17.5 cm long, 3.5–7.5(–11) cm. wide, acuminate at the apex, rounded at the base, with pinnate nerves but all at base in basal 1/4–1/8 of leaf length; petiole 1–1.5(–2.5) cm long. It has stamens 2–3 in number on each side of ovary, stigmas 3–5 in number, sessile. Fruits in particular are drupe red in colour when ripe, drying black in colour when unripe, globose, 3-4 mm in diameter, 5–6 mm long, and 4 mm wide[3].

1.2 Parts Used (Hissae Mustamela)

Dried unripe fruit[8].

Seeds

Leaves

Fruit

Flower

Whole plant

Figure 2: Varied parts of black pepper (*Piper nigrum* L.)

1.1 Temperament (*Mizaj*)

Temperament of *Filfil Siyah* (*Piper nigrum* L.) given by Unani scholars in literature is Hot and Dry [4,9,10].

Black pepper is commonly used as a traditional medicine and food in many countries and has been reported to have anti-oxidant, anti-microbial, anti-fungal, anti-tumor, anti-mutagenic, anti-diabetic, analgesic and anti-inflammatory properties[11]. This study provides detailed recent information about the black pepper, including ethno botany, phyto-chemistry, and pharmacological profile.

2. MATERIAL AND METHODS

This review was accomplished keeping in mind the most recent information regarding black pepper. The information was collected from Unani classical books (Arabic, Persian and Urdu) and electronic search (Pub Med, Science Direct, Wiley online library and Google scholar) during 1999-2023. The Unani terminologies were taken using the Standard Unani Medical Terminology published by the Central Council for Research in Unani Medicine (CCRUM) and the World Health Organization (WHO)[12].

3. RESULTS AND DISCUSSION

3.1 Phytochemistry

The dried black pepper fruit is rich in bioactive phytochemical compounds. The major bioactive compound identified in *P. nigrum* is piperine although other compounds are also present including piperic acid, piperanine, piperettine, piperylin A, piperolein B, pipericine, piperlonguminine, pellitorine, piperamide, piperettine, and (-)-kusunokinin[13]. Black pepper is also rich in minerals (calcium, magnesium, potassium, phosphorus, sodium, iron and zinc), vitamins (Vitamin C, B1, B2 and B3) and nutrients (carbohydrate, protein, and fat). Other reported phytoconstituents are tannin, flavonoids (catechin, quercetin and myricetin), and carotenoids (lutein and β-carotene). The essential oil of black pepper comprised of β-caryophyllene followed by limonene, sabinene, α-pinene,β-pinene, β-bisabolene,δ -3-carene, α-copaene α-cadinol, α-thujene,β-phellandrene, α-humulene, β-Elemene, δ-Elemene , α-Cubebene , α-Guaiene, α-Zingiberene, p-Cymene, bicyclogermacrene, γ-Cadinene, γ-trans-Bisabolene , hedycaryol,germacrene D, 1-napthalenol and β-myrcene; pepper leaves found rich in nerolidol followed by α-pinene and β-caryophyllene7 .

3.2 Pharmacological Actions (Af'aal)

Unani system of medicine has been using *Piper nigrum* L. since antiquity as it possesses diverse pharmacological actions as follows [4,14]-

Table 1: Actions of Black pepper.

Externally	Internally
• *Jali* (Detergent)	• *Mushtahi* (Appetizer)
• *Musakkin-i-Alam* (Analgesic)	• *Kasir-i-Riyah* (Carminative)
	• *Daf-i-Bukhar* (Antipyretic)
• *Jazib-i-Khun* (Absorbent)	• *Hadim* (Digestive)
	• *Muharrik* (Stimulant)
• *Muwallid-i-Luab-i-dahan* (Increased salivation)	• *Muqawwi-i-A'sab* (Nervine tonic)
	• *Muqawwi-i-Mi'da* (Stomachic)
• *Muhallil-i-Auram* (Resolvent)	• *Muqawwi-i-Jigar* (Hepatictonic)
	• *Muqawwi-i-Bah* (Aphrodisiac)
• *Mukharrish-i-Jild* (Irritant)	• *Tiryaq-i-Sumoom* (Antidote)
	• *Tiryaq-i-Mi'da* (Stomach Antidote)
	• *Munaffith-i-Balgham* (Expectorant)
	• *Muhallil* (Resolvent)
	• *Mudirr-i-Bawl* (Diuretics)
	• *Mudirr-i-Hayd* (Emmenogogue)

3.3 Therapeutic Uses (Mawaqe Istemaal) [1, 15, 16]

In general, pepper functions as a warming, diuretic, digestive, dissolving, and cleansing agent. It treats several eye conditions, including pupil darkening. Periodic chills (or fevers) can be treated with it (either applied topically or eaten as a drink), and it also benefits people who have been attacked by poisonous animals. When used as a pessary, it acts as a contraceptive and an abortifacient, preventing conception following sexual activity. It is effective (when taken in syrup or liquid form) for a number of respiratory and chest illnesses including a bad cough. It works well when applied topically with honey to treat tonsillitis. Chewed with adenoid passae as lozenges, it draws mucus out of the head. It promotes appetite, heals wounds, and reduces pain when blended into sauces. It dissolves scrofulous tumours (glandular swellings) when taken with pitch, and it removes vitiligines (a form of leprosy) when taken with nitre (saltpetre). It is also beneficial for spleen disorders when applied topically.

Table 2: Summary of the therapeutic uses of the herb -

●	*Nafakh-i-Shikam* (Abdominal flatulence)
●	*Fasad-i-Hadam/Zof-i-Hadam* (Indigestion),
●	*Kasrat-i-Riyah* (Flatulence)
●	*Bars-o-bahak* (Vitiligo & pityriasis)
●	*Zof-i-Asab (*Weakness ofnerves)
●	*Bawaseer* (Haemorrhoids)
●	*Atshak* (Syphilis)
●	*Hayda* (Cholera)
●	*Shabkori* (Nyctalopia)

●	*Falij* (Paralysis)
●	*Amrad-i- Kabid* (Liver disorders)
●	*Amrad-i- Tihal* (Spleen disorders)
●	*Waja' al-Khasira* (Low Backache)
●	*Waja' al-Mafasil* (Polyarthritis)
●	*Waja' al-Asnan* (Toothache),
●	*Sadr-o-Duwar* (Vertigo and Giddiness),
●	*Humma Da'ira* (Intermittent fevers)

3.4 Therapeutic Doses (Miqdare Khuraak) [4,9,10,17]
As mentioned in various Unani classical textbooks-

- 0.25-1 gm
- 1-2 gm
- 4 -9 masha (4-9 gm)
- 3 ratti-1 masha (375gm-1gm)

3.5 Badal (Substitute)[10]

- *Zanjabeel* (Ginger)
- *Dar-i-filfil* (Long pepper)
- 1 ½ part *filfil safed*

3.6 Adulterants[17]

- The fruits of water knot weed *Polygonum amphibium* L.
- Seeds of *Schinusmolle* L. (Brazil/California-pepper)
- Seeds of *Carica papaya* L.(Papaya)

3.7 Musleh (Correctives)[10,14]

- *A'sl* (Purified honey)
- *Sirka*(Vinegar)
- *Cold Roghiniyaat* (Oils)
- *Ruboob* of acrid fruits
- Ice
- Cold water

3.8 Safety Aspect [17]
The drug used in traditionally prescribed doses may be considered safe.

3.9 Contraindications [10,14]
It is contraindicated in renal disorders and hot temperament individuals.

3.10 Famous Important formulations (Mashhur Murakkabat)[4]

Table 3: Documented preparations consisting of black pepper.

• Habb-e-Azaraqi	• Dawa-ul-Shifa
• Habb-e-Surfa	• Jawarish Kamooni
• Habb-e-Kabid Naushadri	• Jawarish Falafali
• Jawarish Jalinoos	• Habb-i-Tinkar
• Jawarish Bisbasa	• Safoof-i-Bars
• Majoon Falasfa	• Safoof-i-Chutki
• Itrifal Kabir	• Kohl-al-Jawahar
• Anqaroya Kabir	• Majoon Jograj Gogul
• Majoon Fanjnoosh	• Mufarreh Kabir
• Majoon Nisyaan	• Ikseer-i-Gurda
• Tiryaq-i-Meda	

3.11 Recent Evidence Based Pharmacological Activities

Multiple research investigations have been conducted to explain the biological function of black pepper, and it has been found that a number of its secondary metabolites include pharmacological activities like antibacterial, antifungal, antiinflammatory, antioxidative, antipyretic, nephroprotective, hepatoprotective, insecticidal, and fertility promoting effects.

- **Antitrypanosomal, Antimalarial, and Anti-SARS-CoV-2:** The N-Aryl Amide analogues of piperine were investigated for their antitrypanosomal, antimalarial, and anti-SARS-CoV-2 main protease activity. In this study, N-aryl amide piperine analogues were created using a semi-synthesis method that involved first saponifying piperine to produce piperic acid, then esterifying it. In comparison to the previous compounds in this series, the novel 2,5-dimethoxy-substituted phenyl piperamide 5 demonstrated the most powerful biological activities with no cytotoxicity against mammalian cell lines, Vero and Vero E6. Its antimalarial activity against the 3D7 strain of Plasmodium falciparum was 24.55 ± 1.91 M, and its half-maximal inhibitory concentration (IC50) for antitrypanosomal activity against Trypanosoma brucei rhodesiense was 15.46 ± 3.09 M, which were fourfold and fivefold more potent, respectively, than the activities of piperine. Additionally, compound 5 was three times more effective than rutin at inhibiting the activity of 3C-like main protease (3CLPro) towards anti-SARS-CoV-2 activity, with an IC50 of 106.9 ± 1.2 M. The putative binding of 5 in the 3CLpro active site seems to have increased binding interaction and stability, according to docking and molecular dynamic simulation[21].

- **Anti-inflammatory Activity:** Alkaloids from Black Pepper (*Piper nigrum* L.) Exhibit Anti-Inflammatory Activity in Murine Macrophages by Inhibiting Activation of NF-B Pathway. Seven new amide alkaloids, pipernigramides A–G (3, 10, 38, and 41–44), a new piperic ester, pipernigrester A (48), along with 47 known compounds were isolated from the EtOH extract of *P. nigrum*. The inhibitory effects on nitric oxide (NO) of all compounds were then evaluated. Among the tested compounds, three of them (42–44) significantly inhibited inducible nitric oxide synthase (iNOS)-mediated NO (IC_{50} = 4.74 ± 0.18, 4.08 ± 0.19, and 3.71 ± 0.32 μM, respectively), and IL-1β, IL-6, TNF-α, and PGE_2 release in RAW 264.7 cells stimulated by lipopolysaccharide. Moreover, 42–44 suppressed I_kB degradation and further inhibited the cytosol-nucleus translocation of the p65 subunit by targeting IKK-β. In the carrageenan-induced paw edema test, 42–44 demonstrated anti-inflammatory effects as well. These results indicate that all three compounds from *P. nigrum* have the potential anti-inflammatory effects[22]. In another study on piperine, anti-inflammatory activity was established, which inhibits LPS-Induced Inflammatory via the MAPK and NF-B signalling pathways in RAW264.7. HPLC, UPLC-Q-TOF-MS, and 1H NMR were used to characterise and purify piperine, and a reagent test kit, ELISA kits, RT-PCR, and Western blot tests were used to test the anti-inflammatory activity. The findings indicated that piperine (90.65 0.46% purity) at a dose of 10–20 mg/L reduced the formation of NO and ROS, decreased the levels of TNF-α, IL-1, and IL-6 protein and mRNA expression, and increased the levels of IL-10 protein and mRNA transcription. The phosphorylation levels of the ERK, JNK, p38, and p65 proteins might be inhibited by piperine, according to the results of a Western blot[23].

- **Analgesic Activity:** The study was on biology-oriented synthesis (bios) of piperine derivatives and their comparative analgesic and anti-inflammatory activities based on "biology-oriented synthesis approach". Some derivatives of piperine having azomethine, sulfamoyl, propanoyl, acetamoyl and heterocyclic oxadiazole were also synthesized. The structures of synthetic derivatives were confirmed by using different spectroscopic techniques such as ^{1}H-, ^{13}C-NMR, EI-MS, and IR and melting points were also determined for all compounds. Piperine and its all the synthetic derivatives were subjected to comparative in vivo evaluation of analgesic and anti-inflammatory activities at the oral dose of 6 mg/kg/day. Analgesic activity was evaluated by tail immersion, hot plate and acetic acid writhing methods. A number of derivatives showed enhanced antiinflammatory and analgesic activities as compared to piperine and standard drug diclofenac and the study concluded that the newly identified molecules may serve as lead for the future research in connection of potent and safer anti- analgesic drug entity[24].

- **Antifungal activity:** Tube dilution method was adopted to evaluate the antifungal properties of black pepper extract and their biosynthesized gold nanoparticles (AuNPs) against *Alternaria solani*, *Aspergillus niger*, *A. flavus*, and *Candida albicans*. Inoculum from a fungal cultivation was added to each tube and incubated for 7 days and after incubation, tubes containing samples and standard drugs were examined for antifungal properties. Results were expressed in percentages, and all analysis were performed in triplicates and the extract showed moderate antifungal activity as compared with control. The presence of piperine in the skin and seed of the black pepper is responsible for the antimicrobial activity, the research also concluded that the extract of pepper can be used as an antimicrobial agent[25].
- **Anti-tumor Activity:** The piperine analogue exerts in vivo antitumor effect by inducing oxidative, antiangiogenic and immunomodulatory actions. The study was established to synthetize, and to evaluate the toxicity and antitumor action of a new piperine analogue, the butyl 4-(4-nitrobenzoate)-piperinoate (DE-07). Toxicity was evaluated against zebrafish, and in mice (acute and micronucleus assays) and Ehrlich ascites carcinoma model was used in mice. Angiogenesis, Reactive Oxygen Species (ROS) production and cytokines levels were investigated. Results revealed that ninety-six hours exposure to DE-07 did not cause morphological or developmental changes in zebrafish embryos and larvae, with estimated LC_{50} (lethal concentration 50%) higher than 100 μg/mL. Regarding the acute toxicity assay, LD_{50} (lethal dose 50%) was estimated at around 1000 mg/kg, intraperitoneally (i.p.). Moreover, DE-07 (300 mg/kg, i.p.) did not induce increase in the number of micronucleated erythrocytes suggesting no genotoxicity. On Ehrlich tumor model, DE-07 (12.5, 25 or 50 mg/kg, i.p.) induced a significant decrease on cell viability and there was an increase on ROS production and a decrease in peritumoral microvessels density. It is also noted that DE-07 induced an increase of cytokines levels involved in oxidative stress and antiangiogenic effect (IL-1β, TNF-α and IL-4) and no significant clinical toxicological effects were recorded in Ehrlich tumor transplanted animals. These data provide evidence that DE-07 presents low toxicity, and antitumor effect via oxidative and antiangiogenic actions[26].
- **Antioxidant, Hepatoprotective Activity :** In this research, the antioxidant, hepatoprotective and antifungal activities of black pepper (*Piper nigrum* L.) essential oil was documented which proved BPEO's potential as hepatoprotective products and natural food preservatives**.** The essential oil extracted from the black *Piper nigrum* L. (BPEO) was analyzed for antioxidant, hepatoprotective and antifungal activities. BPEO found rich in total phenolics, total flavonoids and proanthocyanidins, and showed good free radicals and lipid peroxidation scavenging capacities. In a CCl4-induced liver injury mice model, the BPEO treated groups showed increases in the catalase (CAT), glutathione (GSH) and total superoxide dismutase (*T*-SOD) activities present in the liver and kidney, and reverses the CCl4-elevated total bilirubin (TBIL), glutamate pyruvate transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (AKP) and malondialdehyde (MDA) level, which were established in further analyses of kidney tissue sections. BPEO showed that it effectively inhibit the growth of *Aspergillus flavus* spoilage fungus in maize and indicated that BPEO disrupt the permeability barrier of the cell membrane and lead to mitochondrial dysfunction in *A. Flavus*[27].
- **Nephroprotective Activity**: The nephroprotective effects of *Piper nigrum* extracts against monosodium glutamate-induced (MSG-induced) renal toxicity in rats of methanol and n-hexane extracts of *Piper nigrum* (MEPN and HEPN, respectively) against MSG-induced renal toxicity in rats was proved . Thirty male Wistar albino rats were used for the nephroprotective study and acute toxicity was evaluated with thirty-two Swiss albino mice. The rats were randomly distributed into 6 experimental groups (n = 5). Group 1 (baseline) was not induced or treated; groups 2–6 were given 2 g/kg body weight of MSG. Additionally, group 2 received normal saline; groups 3–6 were given 250 and 500 mg/kg body weight of MEPN and HEPN, respectively. MSG was administered only for 21 days, after which MSG was concomitantly administered with the extracts for further 28 days. Results revealed that both extracts scavenged 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and reduced ferric ions to ferrous ions in the ferric reducing antioxidant power (FRAP) assay, with MEPN having higher efficacy. The extracts also

ameliorated lipid peroxidation and increased the activities of superoxide dismutase and catalase, as well as the level of reduced glutathione. Furthermore, intervention with MEPN and HEPN provided nephroprotective effects by decreasing urea and creatinine levels and also enhanced the histo-architecture of the kidney. These findings are found critical on abolishing the use of MSG in our food sector and highlighted the health benefits of incorporating *P. nigrum* into our food to avert food and drug toxicity. It was observed that administration of *P. nigrum* methanol and n-hexane seed extracts restored the antioxidant profile, normalized levels of urea and creatinine, and the renal histological architecture and these results exhibit the nephroprotective effects of *P. nigrum* seed extracts against MSG-induced renal toxicity[28].

- **Fertility activity:** The effect of black pepper on infertility induced by ethionamide and para amino salicylic acid was studied on female Sprague-Dawley rats. Ovaries were removed and immersed in Bouins solution for fixation and processed until the embedded in paraffin for histological analysis and chemiluminescence immunoassay of estrogen was performed. In the study it was observed that, black pepper found much effective to compensate the level of estrogen to normal. This study suggests that the antituberculosis drugs in combination with Piper nigrum are effective to cure the disease and to maintain the fertility in rats. The increased level of estrogen may be because of zinc and antioxidant property of Piper nigrum, which may also be responsible for the improvement of histological picture of ovary of Sprague-dawley rats. Additionally, in female gonad study it was observed that the estrogen level was affected due to the administration of ethionamide (ETH), and *Para Aminosalicylic Acid (*PAS). It showed the potential of fertility activity against ETH and PAS by controlling the body weights, ovary weight and estrogen secretion[29].
- **Insecticidal activity:** The study for the insecticidal effect of petroleum ether extract of black pepper and Prunus cerasus seeds against Rhyzopertha dominica was researched. Four concentrations (0.25, 0.5, 1 and 2%) were prepared in acetone and maceration method was used to extract Piper nigrum and Prunus cerasus seeds.The residual film method was used to assess the percentage mortality, while the repellent activity was tested by using the area preference method. The results showed that there was significant difference between petroleum ether extract of pepper and cherry seeds, whereas, the percentage mortality in cherry seeds extract was higher than in pepper and it was found to be 53.33 and 100% within 24 and 48 hours of exposure at 0.25% of cherry seeds extract. In pepper extract, it was found to be 26.66, 36.67 and 56.67% after 24, 48 and 72 hours at 0.25%, respectively, while, the petroleum ether extract of pepper seeds was more repellency than cherry seeds extract. The concentration at 2% of pepper was the strongest repellent effect on R. dominica with mean percentage repellency of 76% followed by 1%,. Finally, it was concluded that cherry and black pepper seeds extracts have insecticidal activity and both could be used as insecticides and has a promising future in plant protection[30].
- **Antipyretic Activity:** The antipyretic activity of piperine, found in black pepper was evaluated with this experimental study. Before the experiment, animals were habituated for two consecutive days on rectal temperature measurement using a thermometer coated with glycerin. In rats, pyrexia was induced by administering freeze-dried Baker's yeast as 20% suspension in 0.9% saline (1 g/kg SC) in the nape of the neck. Baker's yeast was administered 4 h before test drug administration, and the temperature was measured at 0, 3, 4, and 6 h after drug administration and fall in temperature was compared between groups. It was observed that in all the three groups, there was a consistent rise in rectal temperature during the 4-h period time till the test substances were administered ($P = 0.028$ in each of the three groups), and at 0 h, there was no difference between the groups in rectal temperature ($P = 0.961$). It was found that piperine significantly reduced rectal temperature only at 4 h when compared with control, while aspirin reduced only at 3 and 4 h. On the other hand, aspirin reduced rectal temperature significantly than piperine at both 3 and 4 h. With regard to antipyretic effect, piperine significantly reduces fever at 4 h when compared to the controls and concluded that further studies with higher oral doses of piperine may be utilized and compared to aspirin[31].

Table 4: Summarizing the detailed pharmacological activities of Filfil siyah (*Piper nigrum* L.)

Traditional Use	**Modern Use**		
	Cell Based study	**Animal based Study**	**Human Based Study**
Antiseptic,	Antispasmodic,		
Aroma,	Analgesic, Anti-	Increase	Analgesic, Anti Asthmatic,
inflammatory,	Enzymatic Activity,	Anti- Fertility, Bioavailability	Anti-Oxidant, Anti-Toxicant,
Aphrodisiac, Antipyretic,	Increase Lipid Per-	Enhancement,	Anti-Anti-Diabetic, Anti-Hyperlipidemic
Rheumatism,	Diabetes,	Oxidation,	Metastatic, StimulateDiet Induced
Muscular	ache, Diuretic,	Antioxidant,	EnzymaticActivity, Oxidative stress,
Flavor, Dyspepsia, Increase salivary secretion and promote digestion, CNS	Bioavailability Enhancer, Immunomodulatory	Inhibit Mycobacterium Anti-Growth, Antioxidant,	GI Stimulant, Anti-Carcinogenic, LipidMetabolism
Stimulant, Indigestion and flatulence, throat Ache Cold, Blood Purifier, Antibacterial, Religious Kitchen Curry, Cough, Carminative, Insecticide, etc.	Effect, Increase WBC Count And Inhibit Adipogenesis etc.	Hepatoprotective, Increase Digestion By Promoting Bile Secretion, Anti-Amoebic Activity, Anti-Fibrotic Effect, Antibacterial, Anti-Epileptic, Antifungal, Etc.	Acceleration, Ache, Cold, Anti-Inflammatory, Antitumor, Etc.

4. CONCLUSIONS

The current study offers comprehensive data as well as recent knowledge on the importance of black pepper in relation to its ethnobotany, pharmacological usage, phytochemistry, and many therapeutic advantages. The information obtained from the data source for the present assessment made it clear that it contains valuable minerals, vitamins, and secondary metabolites that may contribute to illnesses that are challenging to treat in the modern era.The main alkaloid piperine and essential oils containing useful chemicals like limonene, sabinene, β-caryophyllene, α--pinene, etc can be explored as natural sources for new drug discovery because they have a wide range of therapeutic potential. *Filfil Siyah* (Black pepper) has been used for challenging disorders like neurological illnesses like paralysis, chorea, and numbness, gastrointestinal disorders like gastric ulcers, flatulence, and indigestion, and urological problems like dribbling and burning urine, among others, as a result of its numerous pharmacological benefits that are listed in Unani medicine[32]. It is evident and demonstrated by multiple preclinical, and clinical trials in this review that black pepper has an enormous number of pharmacological effects, including anti-inflammatory, hepatoprotective, antioxidant, anticancer, antibacterial, antifungal, antimicrobial, antihypertensive, antiasthmatic, and insecticidal activities. However, despite traditional claims, insufficient scientific validation for the treatment of neurological disorders, rheumatoid arthritis, asthma, spleen disorder, and puerperal fever, necessitate future research in this direction. Additionally, gaps in the literature became apparent and it was discovered that there is a need for few studies on the shelf life and storage of black pepper essential oil. It has also been noted that preclinical trials are the extent of scientific study, with clinical trials at the next level appearing to be less common in case of black pepper which requires proper attention. It is further suggested that regular consumption of black pepper nutraceuticals and functional foods may be a helpful support for preventative healthcare.

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