AN EXTENSIVE ANALYSIS OF BUNIUM PERSICUM: AN IMPORTANT SPICE FOR MEDICINE

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Abstract
Bunium persicum (Boiss), or B. Fedtsch, or Black cumin, is a medicinal spice with significant economic value and is frequently utilized in many food systems as a preservative and taste enhancer. It was used additionally within conventional Indian, Iranian, and Unani medical systems. Belonging to the Apiaceae family, it has a wide range of phytochemicals, primarily cuminaldehyde, α-terpinene-7-al, γ-terpinene-7-al, γ-terpinene, ρ-cymene, β-Pinene, and so on. These phytochemicals have been shown to have several established medicinal benefits, such as antioxidant, antimicrobial, lipid/glucose lowering, and anti-carcinogenic properties. Because this plant is overused and only grows in a few places in the wild, conservation of it—both in vitro and in situ—is a top priority.

Furthermore, little study has been done to identify and characterize this valuable plant's molecular makeup or to generate prospective high-yielding cultivars or variants. This review offers insight into the phytochemistry, financial significance, nourishment, and medicinal properties. Employs morphological ones such as biochemical processes., and cellular properties of Bunium persicum, along with the work being done towards preserving it and moving ahead, to draw potential stakeholders' focus to the enormous potential and endless characteristics of black cumin.

1.Introduction:

Black cumin, or Bunium persicum (Boiss) B. Fedtsch, is a significant spice that grows wild in the Central Asian region's arid temperate areas, which include Afghanistan, Kazakhstan, India, Egypt, Pakistan, and Iran [1,2]. In the northwestern Himalayan area of India, Bunium persicum is a significant spice plant with therapeutic properties that grow uncontrolled. A plant from the Apiaceae family, Bunium persicum (Boiss) B. Fedtsch is referred to by a variety of names, including kala jeera, siah zeera, and shahi zeera in Jammu & Kashmir; kali zeeri in specific patches in Himachal Pradesh; and zireh kuhi in some regions of Iran. This crop has an excellent value, with prices ranging between Rs. 1200 and Rs. 2800 per kilogram in India [3,4].

The number of individuals who consume this significant spice crop in India's Jammu & Kashmir, Uttarakhand, and Himachal Pradesh areas has drastically declined due to excessive use [5]. Because of its unique qualities and characteristics, the Indian state of Himachal Pradesh has designated it as a Geographical Indication (GI) with the GI number 432 [6]. In its native environments, this species can only be propagated by seed, which takes approximately four months to germinate and allows for crop harvesting after three years. This plant's lengthy life cycle significantly hinders its commercial production [7,8].

Farmers are not interested in cultivating it because of its sluggish development and lengthy crop retention. These elements have led to an alarming depletion rate of this commercially and

medicinally significant spice crop in its native habitats. As a result, the plant is currently listed as endangered [9]. Effective agronomic techniques, management approaches, and conservation techniques, including tissue cultivation (for mass multiplication and preservation) and cryogenic preservation, must be developed to preserve this essential plant species. The species, sometimes mistaken for Nigella sativa and Carum carvi, has been the subject of much phytochemistry research. Fruit and seed extracts taken from the plant have been demonstrated to have a range of valuable characteristics, including antibacterial, antiseptic, anti-inflammatory, and anti-diabetic effects [10,11].

It may find application as an organic preservative and antioxidant in specific food systems. Additionally, it has come into use in cutting-edge culinary applications such as creating biologically active coatings or films extending food items' nutritional value [12]. Even though a small number of authors have previously examined the health benefits of B. persicum, the goal of this review is to give policymakers thorough, current information on the morphological, biochemical, and molecular features of B. persicum as well as phytochemistry, which is novel nourishment, and therapeutic uses for consumers, the dietary supplement, and pharmaceutical sectors [13,14].

1. Botanical characterization

Bunium persicum (Boiss) B. Fedtsch (2N=2X=14) belongs to the Umbelliferae or Apiaceae family. There are around 423 genera in this family, most of which are herbs, trees, shrubs, and aromatic substances [15]. Bunium contains approximately 166 species, primarily found in Central Asia, the Caucasus, and Europe. These species include B. bulbocastenum L., B. caroides (Boiss) Hausskn ex Bornm, B. chaerophyllocides (Regel & Schmalh) Drude, B. cylendricum (Boiss & Hohen) Drude, B. elegans (Fenzl) Freyn, B. flerulaceum Sm., B. kopetdagense Geld, B. persicum (Boiss) B. Fedtsch, etc [16].

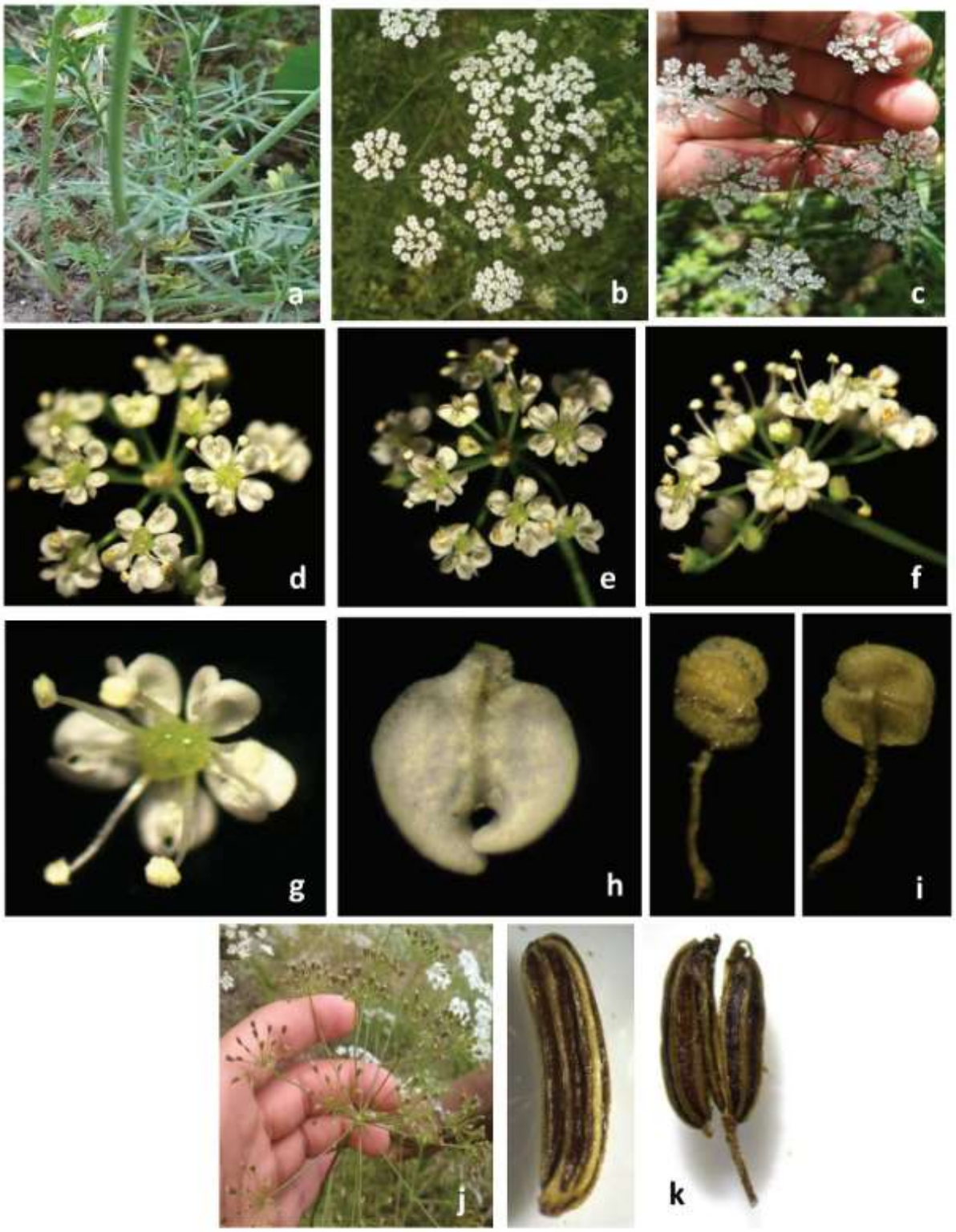

Fig 1: a) stem and leaves, b) umbels carrying flowers, c) enlarged picture of inflorescence, d) flower, h) petal, i) stamen, j) fruit-bearing umbels, k) fruit are the morphological aspects of Bunium persicum. [17,18]

The herbaceous perennial geophyte Bunium persicum grows to 40–80 cm. Subterranean tubers are usually used for cultivation, while seeds are used infrequently. It might have one or many stems that extend from the center. The internodal area of the hollow stems houses secretory

channels for oils and resins. The leaves are filiform, coarsely divided, and widely pinnate (2-4) [19,20]. It has an umbel inflorescence, typical of the Apiaceae family, and consists of 8–20 convex or flat-topped flower clusters that emerge from a single apex. The pedicle of the hermaphrodite flowers is twice or three times longer than the length of the bloom. Petals are bifid and free [21,22].

Five stamens alternate with petals; the zygomorphic flowers have five white, pink, or purple petals. The epigynous disc gives birth to the stamens—dorsifixed, introrse, and bilobed anthers [23]. The inferior ovary has two styles joined at the bottom, making the gynoecium bicarpelate. Because the blooms are protandrous, insects aid in cross-pollination [24]. The fruit is a schizocarp comprising two mericarps with a sickle form joined by a slender central stalk (carophore). The fruits, sometimes but incorrectly referred to as seeds, are 4-5 mm long, 0.8–1 mm in diameter, and brown to dark brown in hue. The 1,000 seed weight falls in the 1–2 g range. Five longitudinal crests (costae) and furrows (valleculae) are typically present in each mericarp, with oil ducts (vittae) situated underneath the furrows [25,26].

2. Customary applications

In Iranian customary medicine, B. persicum seeds are widely recognized because of their antidiarrheal, anti-asthma, anti-convulsive, anthelmintic, anti-dyspnea, and anti-nociceptive qualities [27]. They have also historically been used to treat digestive and urinary diseases. An ethnopharmacological survey with ten villages and eight nomadic tribes in Iran's Khabr National Park found that the traditional uses of B. persicum fruit preparation included treating menstruation aches, spasms, flatulence, and infections [28,29].

Bunium is helpful for allergies and has been used widely in Unani treatment for rheumatism, asthma, bronchitis, cough, and other inflammatory illnesses. According to research based on data from elderly individuals in various Malakand, Pakistan, areas where the Unani medical system is more common, bell peppers are used for medicinal purposes as lactagogues, carminatives, stomachics, and antiseptics. Indian traditional medicine uses the plant's leaves to treat stomach discomfort and the heads of flowers as a carminative [30]. A fruit decoction diluted with water treats fever, TB, joint discomfort, headaches, stomachaches, and colds [31].

3. Phytochemistry

Terpenes (monoterpene, oxygenated monoterpenes, sesquiterpene, oxygenated sesquiterpenes), terpenoids, esters, campesterol, stigmasterol, alkaloids, fatty acids, resins, tannins, thymoquinone, saponins, phenolics, and flavonoids are among the many phytochemicals found in black cumin seeds. Cuminaldehyde, gamma-terpinene-7-al, alpha-terpinene-7-al, γ-terpinene, α-pinene, β-pinene, myrcene, α-terpinene, α-cymene, ρcymene, limonene, α-terpinolene, β-sinensal, β-selinene, Germacrene-B, and Dillapiole are among its constituents that are present. The fragrance of cuminaldehyde adds to the pleasing aroma of oils and is a component of fragrances as well as other pharmaceuticals. The substances that lower the spice's aroma include γ-terpinene, ρ-cymene, and β-pinene. In B. persicum, ρ-cymene and cuminaldehyde have potent antifungal properties [32,33].

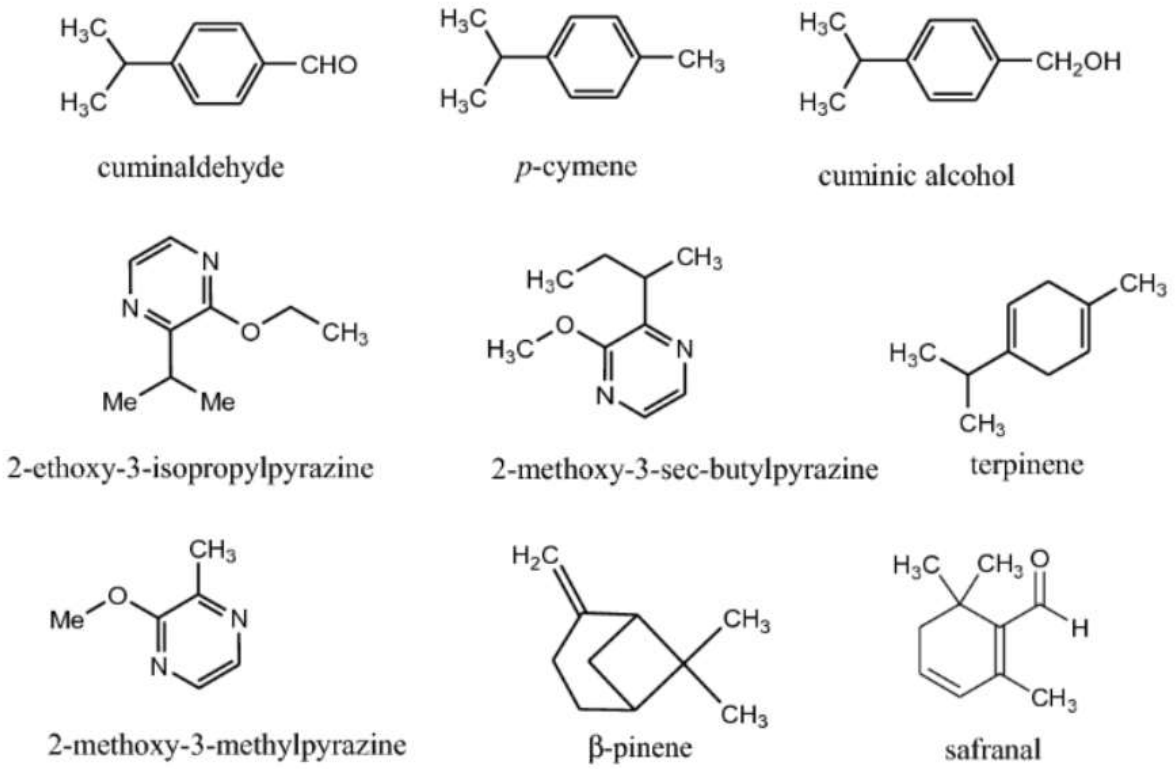

Fig 2: Representation of major Phyto-constituents [34]

4. Components of essential oils chemically

Cuminaldehyde, ρ-mentha-1,3-dien-7-al (αterpinen-7-al), p-mentha-1,4-dien-7-al (γ-terpinene-7-al), γ-terpinene, β-pinene, and ρ-cymene are the main ingredients of B. persicum essential oil [35]. Ripe Bunium seeds may have a 2-9% monoterpene aldehyde-rich crucial oil content. The untamed or not quite ripe Poor-quality spices are produced from bunium seeds, which include terpene hydrocarbons such as γ-terpinene, ρ-cymene, β-pinene, and limonene [36]. Extraction of the essential oil from Bunium seeds is best achieved by hydro-distillation for 3–4 hours using Clevenger-type equipment, then drying on anhydrous sodium sulphite (Fig. 2). Pourmortazavi et al. conducted research whereby they compared the hydro-distillation extraction of essential oil with the supercritical fluid extraction (SFE) technique [37,38].

The results of the GC-MS analysis demonstrated that the oil extracted using the SFE technique and the hydro-distilled oil had distinct compositions. The hydro-distilled oil also had more significant amounts of γ-terpinene and cuminaldehyde, supporting the widespread usage of hydro-distillation extraction [39]. The most popular method for separating different components of extracted essential oil is GC-MS utilizing an HP-5 MS fused silica capillary column (30 m × 0.25 mm i.d. with 0.32 mm film thickness). Chemicals have been identified by comparing the acquired retention indices and mass spectra with those found in the information available, the National Institute of Standards and Technology (NIST) library, and/or the retention coefficients of actual samples on the GC [40].

Most phytochemical investigations on seed essential oil have been carried out in Iran, with a few papers on samples from India and one investigation that used samples from Pakistan and Tajikistan following [41]. The claimed essential oil concentration varied between a minimum of 0.8% and a highest of 9.1%, with both samples being Iranian. The predominant constituent of essential oil in the majority of the samples was γ-terpinene (9.77–46.1%), with cuminaldehyde (5.96–37.1%) and γ-terpinen-7-al (2.6–22.3%) following closely behind (Table

1). The concentrations of ρ-cymene (5.25–20.1%), β-pinene (0.24–14.9%), and limonene (0.16–10.6%) were also significant [42,43].
Geographical, altitude, soil, temperature, and other environmental variables, as well as distinct types of species (inherited variability), are responsible for these variations in essential oil quantity and structure [44]. According to a study by Sharopov et al., at least seven distinct chemotypes were identified by cluster analysis based on the chemical makeup of various Bunium samples: i) Rich in α-terpinen-7-al; ii) high content of γ-terpinene with limonene, p-cymene, and cuminaldehyde; further divided in to two sub-clusters: one with plentiful γ-terpinen-7-al and the other with less; iii) abundant in p-cymene; iv) predominant in cuminaldehyde, γ-terpinene, and γ-terpinen-7-al; v) wealthy in α-pinene; vi) wealthy in γ-terpinen-7-al; and vii) abundant in β-pinene and cuminaldehyde. More research is necessary to confirm these variations and identify a superior genotype that may be utilised as a priceless genetic material for breeding [45].

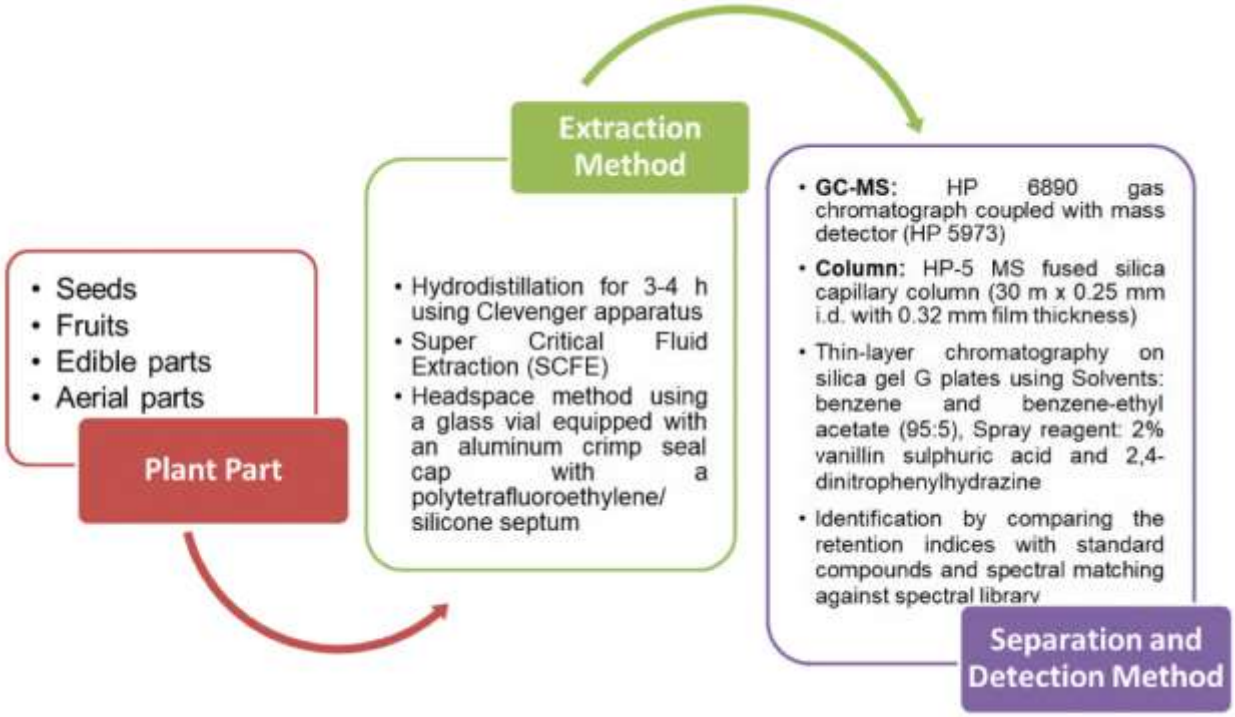

Fig 3: In most phytochemical investigations on Bunium persicum, plant sections, essential oil, the extraction process, segregation, and identification methods are employed. [46,47]
Additionally, studies were carried out to compare the essential oil content of wild and farmed samples to evaluate the impact of environmental variables. In a particular submission a complaint, Thappa et al. discovered that while wild collected seeds had less aldehydes and more γ-terpinene (25.6–42.9%) and ρ-cymene (24.0–27.8%) than plants that were grown, the oil obtained from cultivated sources was more effective compared to that from wild sources of information. Cultivated plants also contained more cuminaldehyde (27.3–34.1%), α-terpinen-7-al, and γ-terpinen-7-al (29.6-36.6%) [48,49]. Compared to producing mature seed specimens (5.5%), wild seed samples had a greater essential oil concentration (7–10.2%). In a related study, Azizi et al. used the GC and GC/MS techniques to evaluate fruit oils of B. persicum cultivated in four (CY1) and five (CY2) year cultivars grown at an altitude of 1000 m as well as wild type (WT) populations growing at an altitude of 2850 m [50]. Compared to the CY1 (6.2% v/w) and CY2 (5.1% v/w), the WT's essential oil content (9.1% v/w) was more remarkable. γ-terpinene (WT: 44.2%, CY1: 40.8%, CY2: 36.8%), cuminaldehyde (WT: 16.9,

CY1: 14.1 and CY2: 11.8%), and γ-terpene-7-al (WT: 16.9, CY1: 10.6, CY2: 18.7%) were the principal compounds reported [51,52].

5. Pharmacological Potential

The seeds and their fruits of black cumin are an excellent resource of fiber for the body and contain a variety of phytochemicals with anti-flatulent, carminative, and antioxidant qualities [53]. B. persicum seed oil helps manage gastrointestinal problems, such as diarrhea and can reduce the early stages of inflammatory processes [54]. The anticonvulsant qualities of Bunium seeds are attributed to monoterpenic chemicals found in their essential oils, which effectively regulate severe seizures in the body. The anti-ulcerative and anti-diarrheal attributes of this plant's primary oil were investigated by Jalilzadeh et al. It was discovered that B. persicum and Rhus coriaria, an ancient Persian remedy known as Persumac, worked well together to alleviate nausea and vomiting from resistant chemotherapy [55,56]. According to Sharififar et al., B. persicum has anti-spasmodic, carminative, anti-obesity, and lactogage effects. They also investigated the plant's antioxidant activity and therapeutic qualities [57].

5.1. Antidiabetic and hypolipidemic properties

By inhibiting glycoside hydrolase activity, B. persicum extracts were shown to have hypoglycemic, antiobesity, and antidiabetic properties. Further research by Seri et al. found that the hydroalcoholic extract of B. persicum included a substantial amount of polyphenolic chemicals, significantly reducing albumin glycation, the thiol group oxidation, and aggregation. Animals treated with an aqueous extract of B. persicum have demonstrated notable hypolipidemic effects [58,59]. When B. persicum aqueous extract was administered, high-density lipoprotein concentrations increased while total cholesterol, triglycerides, and lipoproteins with a low density were markedly decreased. In hyperlipidaemic mice, the aqueous extract has been more successful in improving their cholesterol levels than exercise. Its administration resulted in an improvement in cardiovascular capacity in addition to prolonged physical activity [60].

5.2. Antimicrobial qualities

When various extracts and BPEO were tested against various bacterial strains, the results indicated that gram-positive bacteria are more susceptible to essential oil's inhibitory effects than gram-negative bacteria. Lipophilic phenolic chemicals in cells, including cuminaldehyde, γ-terpinene, and ρ-cymene, cause the cell's membrane instability and are responsible for the action [61]. The chemical reactions of essential oil components with polysaccharides, fatty acids, and phospholipids enhance the permeability of the bacteria membranes; the absence of ions and cellular material causes cell death.

By denaturing cytoplasmic proteins, deactivating cellular enzymes, interfering with the proton pump, causing membrane coagulation, and causing the cell's contents inside to burst, essential oils can kill bacteria [62].

Bunium persicum essential oil has been shown to have inhibitory effects on a number of pathogens transmitted through it, including Salmonella enteritidis, Bacillus cereus, Bacillus subtilis, Escherichia coli O157:H7, Klebsiella pneumonia, Listeria monocytogenes, Proteus vulgaris, Pseudomonas aeruginosa and Staphylococcus aureus, among others. Aqueous and hydroalcoholic bunium preparations were additionally demonstrated to exhibit growth-inhibiting properties against Acinetobacter baumannii. Against various food spoilage, infectious, and phytopathogenic fungal organisms, such as Aspergillus species, Saccharomyces cerevisiae, Candida albicans, Penicillium chrysogenum, Alternaria mali, Botrytis cinerea, Colletotrichum lindemuthianum, Fusarium oxysporum, and Verticillium dahliae, BPEO has demonstrated noteworthy antifungal characteristics [63,64].

The antifungal effects of ρ-cymene and cuminaldehyde, two of BPEO's main constituents, were most effective against several phytopathogenic fungi. Aspergillus flavus, aflatoxin B1 secretion, and fifteen other common food-borne molds were all suppressed by BPEO when they were kept in storage masticatories [65].

5.3. Anti-Covid

A method in accordance with blocking curcumin's ability to replicate SARS-CoV and inhibiting 3CL protease in Vero E6 cells has been published by Wen et al. In these Vero E6 cells, they also discovered an inhibitory effect against the cytopathogenic impact of SARS-CoV. It's additionally essential to note how well curcumin works against other viruses, including the hepatitis C virus, herpes simplex virus, influenza A virus, enterovirus 71, and human papillomavirus. Curcumin could, therefore, be an excellent antiviral option. A 2008 study by Poylin et al. suggested that curcumin's capacity to suppress NF-κB could prevent muscle proteolysis by sepsis. After testing on mice, Huang et al. reported in 2015 that oral administration of curcumin might function as an anti-fatigue and anti-stress agent [66,67].

In the same year, Nicol et al. showed that supplementing with curcumin might lessen discomfort in healthy individuals experiencing "Delayed Onset Muscle Soreness." 2016 saw the publication by Franceschi et al. of a unique curcumin phospholipid system of transportation called Meriva®. It has been discovered that maintaining muscular mass can prevent the onset of sarcopenia in healthy people. This promising finding might help researchers better understand how well curcumin works to treat COVID-19-related myalgia and tiredness. Furthermore, curcumin's antinociceptive, anti-inflammatory, and antipyretic qualities are noteworthy, as reported by Eke-Okoro et al. in 2018 and Haider et al. in 2013. It has been demonstrated that curcumin can reduce circulating TNF-α and IL-6, two significant mediators of inflammatory disorders [68,69].

2019 saw the discovery by Lin et al. that curcumin has the potential to be transformed into carbon quantum dots, which would enhance its antiviral properties in vivo and in vitro, especially against enterovirus 71. Łoczechin et al. published the effectiveness of carbon quantum dots against the human coronavirus (HCoV) in the same year. The investigators claimed that the process functioned by blocking HCoV-229's entrance receptor [70]. E. In 2019, Morris et al. suggested curcumin as a potential treatment for myalgic encephalomyelitis and chronic fatigue syndrome (ME/CFS). Human vaginal mucosal epithelial cells have been demonstrated to be protected by curcumin's anti-inflammatory effects. Additionally, it prevents the multiplication of HIV-1 and HSV-2 by preventing the activation of proinflammatory chemokines, including RANTES and IL-8 [71].

The sudden development of widespread lung inflammation is a hallmark of respiratory failure known as acute respiratory distress syndrome, or ARDS. This syndrome is associated with elevated permeability, pulmonary edema, severe arterial hypoxemia, and poor carbon dioxide excretion. The primary inflammatory mediators in ADRS include cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukins (IL-1β, IL-6, IL-8, and IL-10), chemokines (including variables such as macrophage inhibitory factor (MIF) and macrophage chemoattractant protein), and free radicals [72].

Research on animals has demonstrated that curcumin lowers TNF-α, IL-1β, IL-6, IL-8, and IL-10, all connected to lung conditions such as asthma, ARDS, COPD, and pulmonary fibrosis. Lung fibrosis is caused by collagen deposition and the proliferation of fibroblasts. Curcumin has been demonstrated to inhibit fibroblast proliferation effectively and has been able to lower inflammation and the advancement of fibrosis in animal specimens of lung damage generated by bleomycin [73].

Curcumin's bronchodilator and antiapoptotic properties are also significant. Asthma and respiratory tract infections are acute and chronic inflammatory diseases for which bradykinin is essential. Curcumin, an inhibitor of activated protein-1 (AP-1), prevents human airway smooth muscle cells induced by bradykinin from expressing IL-6. Curcumin is probably going to be helpful in a combination regimen with ACE inhibitors (angiotensin-converting enzyme inhibitors and AT1 antagonists (angiotensin II receptor antagonists) to help COVID-19 patients conquer fibrosis [74].

6.4. Antiparasitic properties

B. persicum essential oil and preparations have demonstrated antiparasitic activity. A viable approach for treating the flagellated protozoan infection Trichomonas vaginalis, which causes STDs, is BPEO nano-liposomes. In the investigation, liposomal vesicles composed of phosphatidylcholine and cholesterol in a 70:30 ratio were loaded with BPEO (51.64 ± 1.24% loading rate) [75]. After 12 and 24 hours, the IC50 value of BPEO-loaded liposomes versus T. vaginalis (105) cultivated in a TYI-S-33 environment was determined to be 45.19 µg/mL and 14.41 µg/ml. It has demonstrated antitoxoplasmosis solid properties as well as strong scolicidal efficacy without causing any appreciable harm [76].

6.5. Food Applications

Common culinary applications: B. persicum's subterranean tuberous roots, essentially taproot, can be eaten raw or cooked as a vegetable. The most valuable component of this plant is its seeds, which are frequently used as flavorings and spices. The seeds resemble cumin seeds but are much smaller, have a dark brown hue, and have a strong scent [77]. The flavor of B. persicum seeds is bitter, stringent in nature, and pine-like. Seeds are utilized in cuisine and drink to add taste because of their powerful, less earthy scent. Because of its scent, it has applications in bread, rice, dairy products, cheese, confections, and cosmetics. Numerous investigations have been conducted on its functioning and medicinal properties [78].

Food preservation: Because bunium persicum seed possesses strong antioxidant and antibacterial qualities, they are frequently employed in food to stop chemical and microbiological deterioration and illnesses caused by food. In addition to its use as a natural flavoring, essential oils from seeds have health benefits. It may be utilized as a form of preservation to prevent microbiological contamination in meals, including fish, masticatories, edible oils, Gouda cheese, Iranian white cheese, and more. It may be employed as a natural antioxidant in order to improve the longevity and oxidative durability of oils, either by itself or in conjunction with different either synthetic or natural antioxidants, according to research comparisons on the impact of BPEO on upkeep and antioxidant equilibrium of many different kinds of edible oils, such as olive, linseed, and soybean oil [79].

Bioactive film and the coatings: BPEO may also be employed as an active component in biodegradable film/nano-emulsion compositions to extend the shelf life of different foods and food items because of its vigorous antioxidant activity and inhibitory impact on various viruses. Biodegradable maize starch films have revealed the antioxidant properties of BPEO. To make the film, a 3% corn solution of starch with 1.8% glycerol was prepared and gelatinized for 10 minutes at 90°C while being continuously stirred. Different BPEO quantities (1, 2.5, 5, 10, 15, and 20 mg/ml) were incorporated, and the Ultra-turra homogenized the mixture for two minutes at 2000 rpm. Teflon Petri plates were used to cast the films and left to dry. Optimum TPC (20 mg gallic acid/g film) and antioxidant capacity were noted at BPEO levels greater than 20 mg/m. The starch film's total phenolic composition climbed as BPEO concentrations rose [80]. Product packaging with BPEO-containing polylactic acid (PLA) sheets may help extend the product's longevity and security. Solvent casting is one method of making PLA films. This procedure created 1% w/v polylactic acid solution in chloroform with constant stirring at room temperature for eight hours. Mentha piperita (MPEO) and B. persicum essential oils (0.5%) and 1%, as well as 1% of nano-cellulose particles, were added and mixed for 20 minutes [81]. After two minutes of homogenization at 12,000 rpm, the resulting mixture was cast onto glass Petri plates and dried. While the nanoparticles of cellulose exhibited no antibacterial action, BPEO was shown to be far more effective than MPEO in this investigation at suppressing bacteria, particularly gram-positive (Staphylococcus aureus ATCC 65138, Bacillus cereus ATCC 11778) [82].

Since the encapsulating B. persicum essential oil (BPEO) suppressed the growth of fungi and the generation of mycotoxin, it may be used as a natural preservative for botanical masticatories that have been preserved. The BPEO-loaded chitosan nano-emulsion (CS-NP-BPEO) is

prepared in this work [83]. The technique of dynamic light scattering (DLS) was used to examine the zeta potential of BPEO-loaded nanoparticles, and X-ray diffraction (XRD) and scanning electron microscopy (SEM) were used to analyze the morphology and structure of the particles. According to SEM examination, the formed nanoparticles varied in diameter from 80 to 300 nm, with a mean size of the particles of 291.7 nm and a Xeta potential of +291.7 nm based on DLS examination [84].

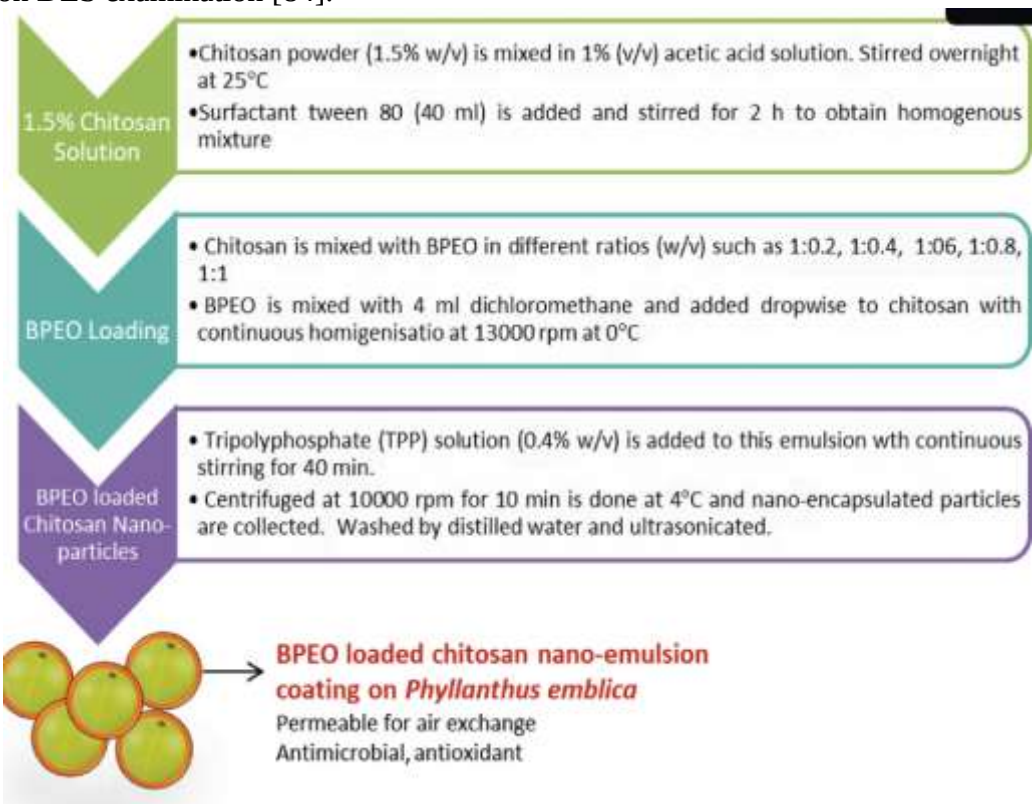

Fig 4: Development of a chitosan nano-emulsion coating coated with Bunium persicum essential oil (BPEO) [87]

The formulation with a CS: BPEO ratio of 1:1 had the highest loading capacity (3.04 ± 0.16%) among BPEO-loaded chitosan (CS) nanoparticles. In contrast, the formulation with a CS: BPEO ratio of 1:0.2 had the highest encapsulation effectiveness. The highest levels of CS-NP-BPEO's antifungal (83.64%) and anti-aflatoxigenic (76.56%) properties were noted at a concentration of 0.8 µL nano-emulsion/mL of medium [85]. When added to vacuum-packed rainbow trout fillets, chitosan combined with a 1% BPEO nano-emulsion coating has the potential to inhibit the growth of E. Coli O157:H7 drastically.[58] A solution containing two percent (w/v) chitosan (LMW 1.03 × 105 and 91% deacetylation grade) was made by combining 1% (v/v) acetic acid at 40°C for ten minutes [86].

This translucent solution was given a plasticizer (0.75% ml/g glycerol) and agitated for half an hour before adding 1% BPEO and 0.2 g of Tween 80 emulsifier. Rainbow trout fillets were then submerged in a nano-emulsion that had been prepared and vacuum-packed [88].

Safety and effectiveness of BPEO storage: In Phyllanthus emblica, BPEO showed a robust protective effect against aflatoxin B1 (AFB1) contamination for a full year of preservation. AFB1 concentrations in control inoculated and uninoculated samples were 46.33 and 40.19 µg/Kg, respectively, while no AFB1 was detected in BPEO-fumigated specimens. Lethal Dose50 (LD50) of BPEO was determined to be 14584.54 µg/Kg body weights in toxicity experiments conducted on mice [89]. Similarly, no mortality was seen in another investigation on mice up to a BPEO dosage of 4 g/kg. Because of its lengthy historical use and relatively high LD50 value, BPEO is a safe, nutritious food ingredient and preservation with potent antioxidant and antibacterial properties [90].

6. Phylogeny and genetics

Not much is known about the cytomorphology and genetics of B. persicum. The development of understanding in cytogenetics, genomics, the genetic variation of Bunium populations in general, and specialized markers is necessary for effective administration, eventual domestication, and selection for improved germplasm. It has been revealed that black cumin, which possesses 14 chromosomes and the karyotype formula of 1-2 M + 2-3 Sm = 3-5 St, is diploid. Similarly, the number of haploid (meiotic) and diploid (mitotic) chromosomes in different ecotypes found in the valley of Kashmir, India, showed that the ecotypes present are diploid, with 2 n = 14 chromosomes, and haploid, with n = 7. It confirms that only B. persicum, not Carum carvi or Bunium bulbosanum, are prevalent at the highest elevations of multiculturalism [91].

Employing fluorescent in situ hybridization (FISH), the physical locations of 5S rDNA and 18S-5.8S-26S (45S) ribosomal RNA (rDNA) on metaphase chromosomes were determined in different research [92]. The investigation verified that the 18S-5.8S26S rRNA gene was found in two locations in the telomeric domain of chromosomes 1 and 2, along with seven separate sets of homologous chromosomes (1 to 7). Similarly, the 5S rRNA gene is located in sub-telomeric regions of chromosomes 5 and 7. There haven't been many molecular studies on Bunium persicum that use random amplified polymorphic DNA (RAPD) markers to evaluate the genetic diversity of particular samples [93].

Using 26 RAPD primers, the genetic linkages of 20 wild black cumin populations that were obtained from Iran (15), India (2), Afghanistan (2), and Europe (1) were examined. The population's overall shared genetic makeup varied from 0.95 to 0.37. In the subsequent subsection, Iranian and non-Iranian people formed distinct clusters, while the European community grouped apart from the remaining populations. Pezhmanmehr et al. examined the genetic diversity of 20 Iranian communities of Bunium persicum using RAPD and amplified fragment length polymorphism (AFLP) indicators. Compared to AFLP primers, which give 75% of polymorphic bands, RAPD primers produce 86%. The comparable scores for RAPD and AFLP markers varied between 0.4 to 0.82 and 0.39 to 0.96 [94,95].

The geographical spread was not correlated with the relative genetic distances, and many populations aggregated into distinct groupings, indicating a high degree of genetic variation and different genetic backgrounds. DNA barcode psbA-trnH was shown to be the most effective in authenticating black cumin, according to a separate molecular investigation that used cumin-specific markers and DNA bar codes for identifying adulteration in B. persicum [96]. Since pricey B. persicum is frequently combined with other spices that resemble inferior spices, such as Cuminum cyminum, the investigation is helpful in the authenticity of the food. Furthermore, the species is sometimes mistaken for the visually similar Carum carvi and the similarly named Nigella sativa (black cumin); as a result, molecular techniques have shown promise in the precise differentiation of several species.

7. B. persicum propagation and preservation

Typically, B. persicum is grown using tubers; however, seeds are occasionally used. The main issues with B. persicum propagation are the impact of seasonal changes and the plant's lengthy juvenile stage. The in vivo culture of B. persicum has not been successful because of seed dormancy and an absence of hypocotyl development following cotyledon emergence. Effective seed germination in Bunium requires cold stratification for around eight weeks at 4–5°C, regardless of the presence of growth hormones, according to a few experiments conducted on breaking dormancy of seeds. A new propagation method has also been attempted using tissue culture techniques; however, the results are primarily homogeneous and have poor response rates [97].

Although the replies it received from the various explants utilized for B. persicum micropropagation differed, they all produced callusing and somatic embryogenesis, and there isn't a single successful study describing B. persicum direct reproduction. Majeed attempted B.

persicum in vitro conservation. The investigation obtained callus induction from leaf and stem explants on MS media combined with 4 mg l−1 Kin + 2 mg l−1 2,4-D. Additionally, shoots were generated by adding 0.25 mg l−1 TDZ and 0.05 mg l−1 IBA to the MS medium, which was then rooted on. Plantlets were conserved at a low temperature of 9°C, and the MS medium enriched with 3% sucrose and sorbitol each and 0.5 mg^{-1} Kin showed the best microshoot viability [98].

To support the vegetative growth of B. persicum, attempts were also undertaken to induce microtuber in vitro. Grewal commented on the induction of microtubers using MS media with varying concentrations of sucrose and kinetin. Although the tuber size remained just a third of a fully formed medium-sized tuber, one-half MS media may cause higher conversion of somatic embryos (55%), becoming more extensive and more lengthy tubing shoots throughout development. Mardani et al. effectively discovered an arrangement of MS + 5 mM Jasmonic acid and incubation at 15°C for microtuber development using seed explants of B. persicum [99].

While there are numerous investigations on the cultivation of tissues, there hasn't been much progress made in creating micropropagation techniques for this species that have any real field utility. As of yet, there is no practical method for shortening the B. persicum propagation cycle. In addition, the plant's extreme niche specificity poses a significant barrier to this priceless species' domestication.

8. Challenges

The pharmacokinetic characteristics of N. sativa's constituent parts must be established to identify them as potential drug candidates. It is crucial to consider the highest safe dosage while maintaining the efficacy of particular medicinal applications. It is accurate to say that N. sativa can be used in food and medication for brief periods without causing harm. There isn't enough research to establish if a bigger dosage is safe in different health scenarios [100]. No prescribed amount of N. sativa has been met, with a few exceptions. For instance, 2 g of powder samples for 12 weeks is sufficient for most respiratory illnesses. Furthermore, 500 mg of black cumin oil can be administered twice daily for four weeks, according to the Fallah Huseini et al. paper [101].

Therefore, it is suggested that before utilizing N. sativa for therapy, people speak with their doctors. Medications and N. sativa may interact when administered together, influencing the pharmaceutical effects and intestinal accessibility. Even in vitro studies have shown that N. sativa extract may hinder or interfere with some drugs' metabolization ability. It is accomplished by blocking cDNA production on substrates metabolized by cytochrome P-450 3A4, 2C9, 3A5, and 3A7 [102].

Conversely, curcumin is frequently used to treat various illnesses, particularly cancer. Nevertheless, a number of factors, including low water solubility, quick metabolism, low bioavailability, systemic elimination, minimal penetration, shortened stability, and low targeted efficiency, have restricted its usefulness. Although curcumin-containing nanoparticles have been developed to treat cancer, more excellent studies are required to prove their clinical usefulness because of the possibility of side effects, including interactions with other medications and toxicity characteristics of the nanoparticles [103].

9. Future Direction

Considering its many medicinal benefits to serve as anti-diabetic, immune-modulatory, antibacterial, liver-protective, kidney-protective, anti-inflammatory in nature, anti-allergic, gastroprotective, and anticancer agent, Nigella sativa is a notable element in Ayurveda medicine. Thymoquinone was the most prevalent and significant therapeutic component in the N. sativa seed oil extract [104,105].

A medicinal compound that is helpful in both the prevention and therapy of cancer is thymoquinone. Minimal dosages of thymoquinone can be given as lipophilic biogels or nanoparticles. Because these nanomaterial-encapsulated thymoquinone nanoparticles are

significantly smaller than cells and harmless, scientists are optimistic that they may be able to create derivatives with better pharmacokinetic qualities to facilitate subsequent medication development. They exhibit enhanced biodegradability and the ability to control the release of medicinal compounds. Consequently, many polymeric nanoparticles may be employed for this kind of drug encapsulating; nonetheless, PLGA (poly-lactide-co-glycolide) nanoparticles are among the most frequently utilized formulations. Because N. sativa contains thiamine, riboflavin, and niacin in addition to soluble dietary fibers, carbohydrates, protein, and fat, in addition to ions like Fe2+ and Zn2+, it is also very advantageous for many biological functions [106].

Synthesized thymoquinone-PLGA nanoparticles have demonstrated more effectiveness than free thymoquinone. It is also possible to combine thymoquinone with other well-known chemotherapy medicines. Targeting certain cancer therapies is a primary emphasis of modern anticancer medication. Thus, specific molecular targets for thymoquinone should be investigated. In the short term, thymoquinone's molecular means function needs to be better understood to create operational analogues with less adverse reactions and an additional appropriate drug delivery system, which will ultimately enhance cancer treatment. It will require broad research in the laboratory.

Contrarily, curcumin is a gift from the environment that has demonstrated strong tumor-suppressor action in pre-clinical and clinical research. It stops apoptosis in normal cells by lowering ROS levels. By inhibiting carcinogenic pathways, curcumin delays the spread of cancer. Additionally, it can prevent inflammation by suppressing NF-κB, restoring normal organ function. Curcumin's α,β-unsaturated component in its chemical architecture makes it a more potent acceptor of electrons once it interacts with proteins' thiol activity. The metabolic metabolites of curcumin are not the same as those resulting from its breakdown.

The efficacy of curcumin has been investigated in a range of inflammatory-based mental conditions, such as autism, depression, and schizophrenia. Curcumin's appreciation as an announcing alternative healthcare option is increased by its antioxidant, anticarcinogenic, and anti-inflammatory properties as well as its capacity to inhibit the development of bacteria, adhesion, invasion, compliance, and toxin generation on wounds, particularly Staphylococcus aureus, Escherichia coli, Streptococcus sp., and Pseudomonas aeruginosa.

Once more, because nanomedicine may package nanoformulations and precisely distribute them throughout specific tissue areas, it has lately become a viable therapeutic alternative. Moreover, nanomedicines are an excellent option for both the treatment and the avoidance of various biological disorders because of their high specificity and minimal cytotoxicity.

To deal with concerns about curcumin's inability to dissolve in water, poor stability, fast metabolism, and low bioavailability, investigators have looked into novel drug delivery methods like cyclodextrin, micelles, nanogels, and lipid-based and nanoparticles made of polymers. Few doubt these methods will pave new paths for the drug manufacturing industry.

Given the worldwide pandemic, combining turmeric and cumin can provide a preventative measure and potential therapy for viral and bacterial diseases. Also, creating curcumin conjugates with metal and metal oxide nanoparticles has much potential as a medication delivery method in nanomedicines. Quantum dots made from carbon-based curcumin can also be essential in medicine.

10. Conclusion

Bunium persicum is a valuable seed spice and plant for medicinal purposes. Its flavor and many benefits make it a common ingredient in people's diets. Additionally, the indigenous populace eats the tuberculous roots as a vegetable. High concentrations of essential oils with cholesterol and glucose-lowering, antibacterial, anti-inflammatory, and antioxidant properties may be found in its seeds. The culinary and pharmaceutical sectors may use this plant to produce functional foods and nutraceuticals and improve food goods' nutritional value and shelf life. Since the species' natural habitats are endangered, efforts should be made to save it from

extinction by conserving its priceless genetics, creating effective propagation techniques, screening for superior material, and breeding for it.

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