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Therapeutic Role of *Curcuma longa* L. on Pulmonary Disorders: A Review

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Abstract: In India, Turmeric (Curcuma longa L.) is traditionally used as a spice, food preservative, and coloring material. It has been used in Ayurveda for various diseases, including colds, coughs, anorexia, arthritis, biliary disorders, diabetes, ophthalmic care, urinary diseases, wound healing, etc. It supports immune cell activity and the body's natural cellular defense system. For the last few decades, extensive work has been done to establish the biological and pharmacological activities of Curcuma longa L. Curcumin (diferulylmethane), is the main dazzling yellow bioactive component of turmeric (Curcuma longa L.) has been shown to have a wide spectrum of biological actions in therapeutic activities. These include its anti-inflammatory, antioxidant, anti-fibrotic, anti-mutagenic, anti-bacterial, and neuroprotective properties. Curcumin also protects against pulmonary disorders like chronic obstructive pulmonary disease (COPD), asthma, pulmonary fibrosis, cystic fibrosis, acute lung injury, and lung carcinoma by regulating transcription factors nuclear factor kappa B (NF-κB), matrix metalloproteinases (MMPs), intercellular adhesion molecule 1 (ICAM-1) and proinflammatory cytokines, i.e., interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNFα). Turmeric may protect us from COVID-19. Safety evaluation studies indicate that Curcuma longa L. is well tolerated at a very high dose without toxic effects. Thus, Curcuma longa L. has the potential to develop modern medicine for treating various pulmonary disorders. This review summarizes turmeric's (Curcuma longa L.) effectiveness in pulmonary disorders.

Keywords: turmeric (*Curcuma longa* L.); pulmonary disorders; COVID-19.

1. Introduction

Ayurveda is regarded as the oldest healing discipline by many savants. Ayurveda translates to "The Science of Life" in Sanskrit. The "Mother of All Healing," as Ayurveda is frequently referred to, has its roots in India and dates back more than 5,000 years. [1]. Ayurveda is primeval and complex knowledge system including philosophy, science, and medicine applied to daily life. It is based on three fundamental principles or *doshas* (primary elements), i.e., *vata* (air and ether), *pitta* (fire and water), and *kapha* (water and earth), that regulate all cellular processes responsible for a healthy being. *Vata* governs flow and motion, *pitta* is the energy of digestion or metabolism, whereas *kapha* regulates growth and structural modification. When these principles get disturbed by an unfavorable environment or poor diet, the individual starts suffering from some diseases [2]. In India, the history of medicine can be traced to the remote past, with one of the earliest mentions of the medicinal use of plants reported in Rig Veda, a sacred collection of Sanskrit hymns written between 4,500 and 1,600

BC [3]. Since antiquity, Ayurveda is practiced through its eight specialized branches: *Kayachikitsa* (internal medicine), *Salya* (surgery), *Salakya* (ophtalmology), *Kaumarbhritya* (pediatrics), *Aagada* (toxicology), *Bhuta Vidya* (psychology), *Rasayana* (rejuvenation) and *Bajikarana* (or *Vajikarana*, sexology) [4]. Among these disciplines, *Rasayana tantra* regards the treatments to improve longevity and memory, attain a youthful appearance, and maintain cognitive performance and physique strength. In particular, the rejuvenation therapy prescribed by *Rasayana* should begin in adult life or midlife because it could not be effective when started too late, thus pointing out this approach's preventive rather than curative efficacy [4].

Turmeric derives its name from the Latin word "*terra merita*," meaning meritorious earth, which refers to the color of ground turmeric, resembling a mineral pigment. It was in 1753 that the genus *Curcuma* was established by Linnaeus in his *Species Plantarum* [5]. The generic epithet is derived from the Arabic word *karkum,* meaning yellow, referring to the yellow color of the rhizome, and *Curcuma* is the Latinized version [6,7]. *Curcuma* was described early (1678–1693) by Van Rheede in "Hortus Indicus Malabaricus" [8]. He recorded two species of *Curcuma* under the local names "*Kua*" and "*Manjella Kua*," which were later identified as *Curcuma zedoaria* Rosc. and *Curcuma longa* L., respectively [9]. The genus *Curcuma* consists of about 110 species distributed chiefly in South and Southeast Asia. Hooker confirmed 27 species of *Curcuma* in British India (The Flora of British India) [10].

Curcumin, the main dazzling yellow bioactive of turmeric (Curcuma longa L.), has been shown to have a wide spectrum of biochemical actions in therapeutic activities [11]. Curcumin, also known as diferuloylmethane ($C_{21}H_{20}O_6$), is a low molecular mass (368.37 g/mol) polyphenol compound with a melting temperature of approximately 183 °C. The IUPAC name of curcumin is (1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione, where the two aryl rings containing ortho-methoxy phenolic OH^- groups are symmetrically linked to a β-diketone moiety [12]. The occurrence of intramolecular hydrogen atoms transfer at the β -diketone chain of curcumin leads to the existence of keto and enol tautomeric conformations in equilibrium [12]. In addition, these keto-enol tautomers also exist in several *cis* and *trans* forms. Their relative concentrations vary according to temperature, the polarity of solvent, pH, and substitution of the aromatic rings [13-15]. The amount of keto-enol-enolate of the heptadienone moiety in equilibrium plays a crucial role in curcumin's physicochemical properties and antioxidant activities [16]. Curcuminoids complex, found in the rhizome of turmeric (2.5–6%) comprises curcumin (curcumin I), demethoxycurcumin [4-hydroxy-cinna [pmoyl- (4-hydroxy-3 methoxycinnamoyl) methane] (curcumin II), bisdemethoxycurcumin [bis-(4-hydroxy-3-methoxy-cinnamoyl) methane] (curcumin III) and cyclocurcumin [12]. In commercial grades of curcumin, the major curcuminoid complexes present are curcumin I (77%), curcumin II (17%) and curcumin III (3%).

The biological activities of *Curcuma longa* L. have been attributed to the non-volatile curcuminoids and volatile terpenoids. *Curcuma* volatiles was dominated by α-turmerone, curlone, *ar*-turmerone, β-sesquiphellandrene, α-zingiberene, germacrone, terpinolene, *ar*-curcumene, and α-phellandrene and showed four distinct chemical clusters [17]. More than 100 components have been isolated from *Curcuma longa* L. *Curcuma* contains protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%), and moisture (13.1%). The essential oil (5.8%) obtained by steam distillation of rhizomes has a-phellandrene (1%), sabinene (0.6%), crneol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpines (53%) [3]. Curcumin (3-4%) is responsible for the yellow color, and comprises curcumin I (94%), curcumin II (6%), and curcumin III (0.3%) [18]. Demethoxy and bisdemethoxy derivatives of curcumin have also

been isolated [19]. Curcumin was first isolated in 1815 [20], and its chemical structure was determined [21]. *Curcuma longa* L. has other coloring compounds known as curcuminoids in addition to turmerone, which is the root's primary constituent. Natural antioxidants known as curcuminoids, including curcumin demethoxycurcumin, 5'-methoxycurcumin, and dihydrocurcumin, were present in *Curcuma longa* L. [18, 22]. Curcumin (5–6.6%), extraneous material (less than 0.5% by weight), mold (less than 3%), and volatile oils (less than 3.5%) are all present in turmeric in its conventional form, along with moisture (greater than 9%). Sesquiterpenes, d-sabinene, cineol, borneol, zingiberene, and d-α-phellandrene are examples of volatile oils [23]. Sesquiterpenes come in a wide range, with many of them being specialized for a particular species. Examples include bis-acumol, β-bisabolene, bisacurone, α-curcumene, curcumenone, curlone, curcumenol, epiprocurcumenol, isoprocurcumenol, procurcumenol, procurcumadiol, dehydrocurdione, germacrone, β-sesquiphellanderene, termerone, ar-(+)-termerones, α-termerones, β-termerones, zedoaronediol, and zingiberene. Turmeric contains the aroma-producing compounds turmerone, arturmerone, and zingiberene. Additionally, stigmasterol, β-sitosterol, cholesterol, and 2-hydroxymethyl anthraquinone are reported to be present in the rhizomes along with four novel polysaccharides called ukonans [3]. An analysis of the nutritional content of 100 g of turmeric revealed that it contains 390 kcal of energy, 10 g of total fat, 3 g of saturated fat, 0 mg of cholesterol, 69.9 g of total carbohydrates, 3 g of sugar, 8 g of protein, 21 g of dietary fiber, 0.2 g of calcium, 10 mg of sodium, 2500 mg of potassium, 47.5 mg of iron, 0.26 g of phosphorus, 0.9 mg of thiamine, 4.8 mg of niacin, 0.19 mg of riboflavin, and 50 mg of ascorbic acid [24]. Omega-3 fatty acids and 2.5% of α-linolenic acid are also found in turmeric in significant amounts [25].

2. Medicinal Properties of *Curcuma longa* L.

Turmeric is also a well-known remedy used in ancient Indian traditional medicine and cosmetics, serving as a multipurpose herbal remedy for practitioners of Ayurveda, the ancient system of Indian medicine, and the more recent Siddha and Unani, and also practitioners of Chinese medicine [26]. Turmeric has several traditional uses, starting from Ayurveda. Powdered turmeric is taken with boiled milk to cure cough and related respiratory ailments [27]. Turmeric or *Curcuma* has anti-inflammatory, antioxidant, and anti-apoptotic pharmacological properties [28]. The common use of turmeric is as an antiseptic. Johnson & Johnson, the well-known US drug company, makes turmeric bandages for the Indian market [29]. *Curcuma longa* L., a native plant of India, has been used as a remedy for several health disorders for at least 2,500 years [30]. The main components of this ancestral remedy are aromatic-turmerone (21.4%), alpha-santalene (7.2%), and aromatic-curcumin (6.1%) [31, 32]. However, several reports suggest that the most active component of *Curcuma* are curcuminoids and essential oils [33]. Curcuminoids contain curcumin (diferuloylmethane), desmethoxycurcumin, and bisdemethoxycurcumin [33], but curcumin is the most studied component of the *Curcuma* for its pharmacological properties and yellow color [30, 34]. The active ingredient of turmeric is curcumin, i.e., 2–5% [27]. Curcumin is the substance that imparts turmeric most of its therapeutic properties. The rhizome comprises 70% carbohydrates, 7% protein, 4% minerals, a minimum of 4% essential oils, and about 1% resin. It also contains vitamins and other alkaloids. Clinical and laboratory research indicates that diets including turmeric or curcumin stabilize and protect biomolecules in the body at the molecular level, shown in its antioxidant, anti-mutagenic, and anti-carcinogenic action [27]. For its anti-inflammatory and antioxidant properties, *Curcuma* is used to treat an amazing number of

diseases [35, 30, 34]. Turmeric has powerful antioxidant properties, protecting the person taking it regularly against colon and breast cancer. Current research shows that about 98% of all diseases are controlled by a molecule called NF-κB, a powerful protein that promotes abnormal inflammatory responses in the body. Excess of NF-κB can lead to cancer, arthritis, and a wide range of other diseases. Studies show that curcumin subdues NF-κB, thus preventing nearly all diseases afflicting the human body [27]. Its principal drawback is its low bioavailability, about 60–66%. Based on the most recent reports on nano drug delivery, curcumin encased in nanoparticles and made of silk fiber rich in keratin and chitosan has been highly effective against cancer [36]. Turmeric enhances the flavor of food, aids digestion (in particular, that of protein), promotes the absorption of the digested material and regulates body metabolism. It helps regulate intestinal microflora and is recommended to be taken after a course of antibiotics, thereby reducing the risk of gastritis and ulcer formation in the intestines. In diabetics, turmeric lowers blood sugar [37]. Because it contains natural cyclooxygenase inhibitors, it shows good anti-inflammatory action. Turmeric extract, volatile oil from turmeric, and curcuminoids have been found to be quite effective against arthritis because of their anti-inflammatory properties [38]. The anti-inflammatory property is due to the capacity of turmeric to lower histamine levels while possibly increasing the production of natural cortisone by adrenal glands. It also helps both liver and gall bladder function. It has been shown to be helpful in treating arthritis, rheumatoid arthritis, osteoarthritis, injuries, trauma, and stiffness both under normal activity and hyperactivity [39]. It shows that natural cortisone production by adrenal glands is enhanced. Its most important anti-inflammatory mechanism is based on its positive effects on prostaglandins (PGs), a large family of potent lipids produced by the body [40]. It delays induced cataracts in diabetics and reduces hyperlipidemia in obese rats. Recently, several molecular targets have been identified in turmeric for therapeutic/preventive effects [41]. Turmeric is also used to treat asthma, dysmenorrhea, psoriasis, eczema, arthritis, and hepatic and digestive disorders and to prevent and treat cardiovascular diseases [26]. In the *Unani* system of medicine (Indian), turmeric is used to treat liver obstruction, dropsy, jaundice, ulcers, and inflammation. In the Himalayan system of medicine, turmeric is used as a contraceptive and skin tonic to treat swelling, insect stings, wounds, whooping cough, inflammation, internal injuries, pimples, and external injuries [26]. Curcumin has great biological significance. Because of this, a number of investigations have centered on curcumin. According to these investigations, curcumin exhibits anti-inflammatory [33], antioxidant [42], anti-viral [43], anti-microbial [44], anti-carcinogenic [45], and anti-mutagenic properties protecting the body from mutagens such as smoke and other pollutants. Recent investigations suggest that curcuminoids are active in the external treatment of certain cancerous conditions, and this is presumably related to the cytotoxicity of these substances, which has been demonstrated on cell cultures, including tumor cells [46]. Besides these, curcumin has various potentially therapeutic properties such as anti-neoplastic, anti-apoptotic, anti-angiogenic, cytotoxic, immune-modulatory, anti-thrombotic, wound healing, anti-diabetogenic, anti-stressor, and anti-lithogenic actions [33, 11, 27]. Curcumin also protects against pulmonary disorders like chronic obstructive pulmonary disease (COPD), bronchial asthma, pulmonary fibrosis, cystic fibrosis, acute lung injury, and lung carcinoma by regulating transcription factors nuclear factor kappa B (NF-κB), matrix metalloproteinases (MMPs), intercellular adhesion molecule 1 (ICAM-1) and proinflammatory cytokines i.e., interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNFα) [47]. *Curcuma longa* L. has therapeutic effect on COVID-19 patients [48].

3. Pulmonary Disorders

Turmeric is anti-inflammatory and anti-purulent. Thus, it is useful in the case of respiratory system diseases. In a clinical trial, it was reported that the volatile oil of turmeric as an oral drug was found to be very effective in treating bronchial asthma [49]. Oral administration of turmeric powder significantly relieved asthma and cough [49]. Fresh rhizomes proved effective against whooping cough, other coughs, and dyspnea [50]. In catarrh and coryza, inhaling burning turmeric fumes causes copious mucous discharge and gives instant relief [51]. The parched and powdered root is given in bronchitis [52].

3.1. Chronic obstructive pulmonary disease (COPD).

COPD is a pulmonary disorder caused by bronchial obstruction, which is not fully cured by bronchodilator drugs. It is characterized by increased numbers of macrophages, neutrophils, and T lymphocytes in the lungs. Many inflammatory mediators are increased in COPD, including proinflammatory cytokines such as IL-6 and TNF-α. It leads to chronic inflammation and the progressive destruction of the lungs. Oxidative stress caused by cigarette smoke triggered autophagy impairment in COPD. Increased synthesis of proteases (matrix metalloproteases- MMP-8, MMP-9, MMP-12) and inactivation of anti-proteases (α_1 antitrypsin and tissue inhibitors of metalloproteases) imbalance results in COPD. Oxidative stress can lead to the inactivation of anti-proteases or increased mucus formation. It amplifies inflammation by enhancing NF-kB [53]. Recent studies have revealed that curcumin is used for COPD treatment, and it promotes autophagy and inhibits many illnesses related to endoplasmic reticulum stress through NAD-dependent deacetylase sirtuin-1 (SIRT1) activation. *Curcuma longa* L. has demonstrated anti-inflammatory and antioxidant activity. It has been used to treat various pulmonary disorders, including COPD. Curcumin has a protective role in COPD by modulating the T-helper 17 cell (Th17) and Regulatory T cells (Tregs) balance. It also decreases the levels of IL-6, IL-8, and TNF-α [54].

3.2. Bronchial asthma.

It is an inflammatory disease depicted by lung infiltration of airway hyper-responsiveness and hypersecretion of mucus and granulocytes. When exposed to allergens, epithelial cells of the airway produce interleukin-8 (IL-8) and transforming growth factor beta 1 (TGF-β1), which activates neutrophils. Curcumin, a component of *Curcuma longa* L., decreases the levels of IL-8 and TNF-α. It is effective as an add-on therapy [55]. Recent studies have revealed that curcumin has anti-inflammatory properties involved in the peroxisome proliferator-activated receptor-γ (PPARγ)-dependent NF-κB signaling pathway and can inhibit allergy-causing cytokines *in vitro* [56]. Airway inflammation and mucus hypersecretion were blocked by curcumin via the PPARγ-dependent NF-κB signaling pathway in the lungs [57].

3.3. Pulmonary fibrosis.

It is the final stage of many pulmonary inflammatory disorders. It is characterized by inflammatory cell infiltration, accumulation of myofibroblasts, and an increase in collagen content [58]. In chronic conditions, pulmonary fibrosis leads to a decrease in gaseous exchange in alveoli, respiratory failure, and death. In addition, inhalation of organic pollutants/toxicants may cause damage to endothelial and epithelial cells of the lungs. Oral administration of

curcumin has been shown to inhibit pulmonary fibrosis in an animal model [59]. Curcumin enhances the expression of hepatocyte growth factor (HGF) via PPARγ and cAMP-response element binding protein (CREB) signaling pathway. HGF enters the lungs and exerts anti-pulmonary fibrosis effects.

3.4. Cystic fibrosis.

It is an autosomal recessive disorder caused by mutations in the gene encoding cystic fibrosis transmembrane conductance regulator (CFTR). CFTR, a membrane protein, depends on ATP-dependent channels for electrolyte transport across nasal and airway epithelia [60]. The most common mutation, Delta-F508, forms a misfolded CFTR that does not reach the plasma membrane and is degraded. Inflammation may develop due to dysfunction of CFTR protein in the body. The primary function of CFTR protein is to maintain the salt-water balance on many body surfaces, including the lung's surface. The secondary function is as an anti-inflammatory and anti-microbial agent [61]. Curcumin, found in turmeric, opened CFTR channels by a mechanism that required neither a second nucleotide-binding domain (NBD2) nor adenosine triphosphate (ATP) [62]. The CFTR protein moved to the surface of the cells, and nasal epithelia regained its normal function [60].

3.5. Acute lung injury.

It is a pulmonary disorder triggered by bacteria, intestinal ischemia, or sepsis. It is characterized by an inflammatory response leading to alveolar damage, edema, neutrophil accumulation, and hemorrhage. Its most severe form is acute respiratory distress syndrome. Curcumin exhibits anti-inflammatory properties by regulating inflammatory cytokines. Curcumin I was found to inhibit the growth of *Helicobacter pylori* [44]. Infection of epithelial cells by the microbial pathogen *H. pylori* leads to activation of the transcription factor NF-κB, the induction of proinflammatory cytokine genes, and the mitogenic response [11]. A recent study observed that *H. pylori*-induced NF-κB activation and the subsequent release of IL-8 were inhibited by curcumin I [11]. The results demonstrated that curcumin I could inhibit NF-κB DNA-binding and block *H. pylori*-induced mitogenic response. Curcumin has the ability to suppress the production of inflammatory cytokines via the extracellular signal-regulated kinase (ERK) pathway [63].

3.6. Lung carcinoma.

It is also known as lung cancer. It is subdivided into non-small cell lung cancer and small cell lung cancer. Curcumin exhibits anti-tumor and anti-inflammatory activity [64]. Its chemopreventive activity was studied in a transgenic mouse model of lung carcinoma. Curcumin is recognized as an anti-carcinogenic agent because of its properties to induce cell suicide or apoptosis *in vivo* and *in vitro.* The human diet contains several substances capable of inhibiting chemical carcinogenesis. Curcumin, perhaps, is the active principle in turmeric. It is suggested that turmeric used widely as a spice, may mitigate the effects of several dietary carcinogens [25]. Earlier, it was shown that curcumin protects cells against oligonucleosomal DNA fragmentation and induces a novel apoptosis-like pathway in Jurkat cells [65]. Curcumin has the ability to induce cell death in all tested cells that can be classified as apoptosis-like, and only in human leukemia cell line (HL-60) cells can it be recognized as classical apoptosis [66]. When mixed with cells from head and neck cancer-affected patients, curcumin stopped their

proliferation and induced apoptosis in malignant cells [67]. Turmeric is a conducive agent for lymphocytes and inhibitory as well as apoptotic for tumor cells [68]. A turmeric-based diet can delay apoptosis without modulating NF-κB to not sensitize the mesangial cells to the apoptotic stimuli [69]. Curcumin or *Curcuma longa* L. administered to benzo[a]pyrene-induced animal models showed improvement in scavenger enzymes, antioxidant content, oxidative stress markers, inhibits IL-6 production, inflammatory cytokinesTNF-α, and regulate p^{53} tumor suppressor protein [64, 70, 71]. Curcumin can be an effective adjunct in treating tumors because it regulates oncogenes like p53, early growth response 1 (EGR1), cellular myelocytomatosis, B-cell lymphoma-extra large (Bcl-xL) protein; transcription factors like NF-κB, signal transducer and activator of transcription 3 (STAT-3) and activator protein 1 (AP-1); protein kinases like mitogen-activated protein kinase; and enzymes like lipooxygenase and cyclooxygenase [72].

3.7. Coronavirus disease 2019 (COVID-19).

Coronavirus is one of the major pathogens that primarily targets the human respiratory system [73]. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS)-CoV in 2003 and the Middle East respiratory syndrome (MERS)-CoV in 2012, which have been previously characterized as agents that are a great public health threat [73]. A group of individuals with an initial diagnosis of pneumonia with an unidentified etiology was hospitalized in late December 2019 [73]. An animal and seafood wholesale market in Wuhan, Hubei Province, China, was epidemiologically connected to these cases [74, 75]. Early reports predicted the onset of a potential Coronavirus outbreak given the estimate of a reproduction number for the 2019 Novel (New) Coronavirus (COVID-19, named by WHO on Feb 11, 2020), which was deemed to be significantly larger than 1 (ranges from 2.24 to 3.58) [76]. The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days [77]. The onset of COVID-19 symptoms to mortality ranged from 6 to 41 days, with a median of 14 days [78]. The length of time varies with the patient's age and immune system health. Patients over 70 had shorter times than those under 70 [78]. The most prevalent signs and symptoms at the beginning of the COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, hemoptysis, diarrhea, dyspnea, and lymphopenia [78-81]. Clinical features revealed by a chest CT scan presented as pneumonia. However, abnormal features such as RNAaemia, acute respiratory distress syndrome, acute cardiac injury, and incidence of grand-glass opacities led to death [80]. In some cases, multiple peripheral ground-glass opacities were observed in subpleural regions of both lungs [82], which likely induced systemic and localized immune responses that led to increased inflammation. Regrettably, treatment of some cases with interferon inhalation showed no clinical effect and instead appeared to worsen the condition by progressing pulmonary opacities [82]. It is important to note that there are similarities in the symptoms between COVID-19 and earlier betacoronavirus, such as fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans [80]. However, COVID-19 showed some unique clinical features, including targeting the lower airway, as evidenced by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat [83]. Based on results from chest radiographs upon admission, some cases show an infiltrate in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia [84]. Some patients infected with COVID-19 developed gastrointestinal symptoms like diarrhea, and a low percentage of MERS-CoV or SARS-CoV patients experienced similar GI distress. World Health

Organisation (WHO) has classified COVID-19 as a β CoV of group 2B [85]. Ten genome sequences of COVID-19 obtained from a total of nine patients exhibited 99.98% sequence identity [75]. Another study showed there was 99.8–99.9% nucleotide identity in isolates from five patients, and the sequence results revealed the presence of a new beta-CoV strain [79]. The genetic sequence of the COVID- 19 showed more than 80% identity to SARS- CoV, and 50% to MERS-CoV [75, 79], and both SARS-CoV and MERS-CoV originate in bats [86]. Thus, the evidence from the phylogenetic analysis indicates that COVID-19 belongs to the genus betacoronavirus, which includes SARS-CoV, that infects humans, bats, and wild animals [87]. COVID-19 represents the seventh member of the coronavirus family that infects humans and has been classified under the orthocoronavirinae subfamily. COVID-19 forms a clade within the subgenus sarbecovirus [87]. Based on the genetic sequence identity and the phylogenetic reports, COVID-19 is sufficiently different from SARS-CoV, and it can thus be considered a new betacoronavirus that infects humans [73]. COVID-19 most likely developed from bat-origin coronaviruses. Another piece of evidence that supports the COVID-19 is of bat origin is the existence of a high degree of homology of the angiotensin-converting enzyme 2 (ACE2) receptor from a diversity of animal species, thus implicating these animal species as possible intermediate hosts or animal models for COVID-19 infections [88]. Moreover, these viruses have a single intact open reading frame on gene 8, which further indicates bat-origin CoVs. However, the amino acid sequence of the tentative receptor-binding domain resembles that of SARS-CoV, indicating that these viruses might use the same receptor [79]. So, the therapeutic properties of *Curcuma longa* L. might protect us from COVID-19 caused by SARS-CoV2. Several mechanisms by which *Curcuma longa* L. may reduce anosmia induced by COVID-19. Curcumin may also block the synthesis of the COVID-19 spike protein-ACE-2 complex, thus stopping viral entry into the cells. The anti-inflammatory activity of curcumin may reduce nasal mucosal swelling. Curcumin has been shown to bind and mask the active site of SARS-CoV-2 main proteinase (M^{Pro}) used by the virus to synthesize proteins required for viral replication [48, 89-93].

4. Limitation and Future Prospectives of *Curcuma longa* L.

Turmeric has anti-inflammatory, antioxidant, anti-fibrotic, anti-mutagenic, anti-bacterial, and neuroprotective properties. The main drawback of *Curcuma longa* L. as a pharmacological agent is its mediocre bioavailability after oral administration due to low intestinal absorption and rapid hepatic metabolism through glucuronidation (detoxification process) and immediate excretion via bile and feces. Studies in many animal models show that intraperitoneal injection and inhalation have higher bioavailability and effectiveness than oral administration. Future studies directed toward understanding the effect of turmeric on the visual circuit pathway of pulmonary disorders and the protective role of *Curcuma longa* L. might address the possible mode of action of herbal intervention against pulmonary disorders.

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Conflicts of Interest

The authors declare no conflict of interest.

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