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Perspective Article



Curcumin and Tulsi For Pulmonary Disorders In Pandemic Century

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Abstract: Asthma, a chronic respiratory disorder, is witnessing an increasing global incidence, necessitating exploration of alternative treatments beyond conventional therapies. This study reviews the therapeutic potential of natural products, namely curcumin and tulsi, in managing asthma, juxtaposed against the backdrop of conventional pharmaceuticals. Adverse effects and limitations of current medications such as short-acting agonists, inhaled corticosteroids, and monoclonal antibodies are highlighted. Moreover, embryonic risks associated with these drugs further underscore the need for safer alternatives. Experimental findings suggest the efficacy of curcumin in reducing airway obstruction and inflammation, backed by its safety profile. Tulsi (holy basil), a mainstay in Ayurvedic treatment, also demonstrates promising effects in alleviating asthma symptoms. Future research will expand on this foundation to provide a holistic, natural treatment approach to asthma management.

Keywords: medicinal plant; herbal drug; respiratory disorders; adverse effect; complementary medicine

1. Introduction

Asthma is a chronic respiratory disorder characterized by inflammation and obstruction of the airways, leading to periods of wheezing, chest tightness, shortness of breath, and coughing. A global health concern, the incidence of asthma is on the rise, particularly in the context of increasing environmental pollutants and lifestyle changes^[1,2]. Conventional therapeutic approaches, such as short-acting agonists and inhaled

corticosteroids, have been the mainstay of asthma management. However, adverse effects, limited effectiveness in severe cases, and high cost of certain drugs necessitate exploration of alternative treatments. This has led researchers to investigate the potential of natural products, such as curcumin and tulsi, in the management of pulmonary disorders. This short communication presents a review of the existing scientific literature on the role of curcumin and tulsi in the management of asthma.

Wheezing, dyspnea, and cough are the primary signs and symptoms of asthma, a clinical syndrome that can affect any part of the lower respiratory system. These symptoms and spirometry evidence of reversible airway obstruction are required for an asthma diagnosis. It is helpful to identify allergen sensitivities with clinical significance. Asthma medications can be categorized as controllers or relievers.

Regardless of the aetiology, short-acting agonists inhibit bronchoconstriction. Inhaled corticosteroids are an exceedingly successful controller medication in the vast majority of asthma patients. A controller therapy is a daily medication that reduces the frequency of baseline symptoms as well as exacerbations that need the use of short-acting agonists. Exacerbations, as well as the frequency and intensity of asthma symptoms and quality of life, have been reported to be reduced by inhaled corticosteroids like beclometasone, budesonide, ciclesonide, fluocinolide, fluticasone, and mometasone. When taken with inhaled corticosteroids, long-acting agonists such as salmeterol and formoterol are beneficial for managing symptoms or exacerbations. For example, montelukast is a leukotriene antagonist that has been demonstrated to be beneficial in the treatment of asthma, either alone or in conjunction with other controller medications. This is especially true for people suffering from severe allergy illness or experiencing exercise-related symptoms. Tiotropium and aclidinium are two long-acting muscarinic antagonists that produce bronchodilation but are only slightly effective as supplementary to inhaled corticosteroids or long-acting agonists.

Based on data from several randomised controlled trials, the National Heart, Lung, and Blood Institute's commissioned national asthma and education prevention programme guidelines currently recommend omalizumab, a monoclonal antibody directed against IgE, for the treatment of severe therapy-refractory asthma in atopy patients (RCTs). It minimises the amount of severe asthma exacerbations in both adults and children. However, its applicability is limited due to its expensive cost.

The results of a pharmacovigilance study of antiasthmatic drugs in bronchial asthma patients in a tertiary care facility emphasise the necessity of ADR monitoring, especially in frequently utilized antiasthmatics and delivery systems. When compared to other asthmatics, salbutamol was related with a greater percentage of adverse medication events, such as palpitations, tremors, and a bitter taste. Eleven out of fifty asthmatic patients reported 13 ADRs. The most common adverse effects were induced by salbutamol (57.1%), salmeterol (50%) beclomethasone (30%), and tiotropium (25%). Naranjo scale implies that, 7.69% of ADRs have been both certain and unsure, 30.76% were probable, and 53.85 percent were likely. The vast majority of adverse responses (84.6%) were minor, with symptoms including nausea, gastrointestinal discomfort, dry mouth, a bitter taste, headache, and cough. According to the Hartwig and Seigel scale, 15.4% of ADRs (such as tremors and palpitations) were assessed as moderate, indicating that patients tolerated them well^[3].

Meanwhile, according to the study "Anti-asthma Drugs Formoterol and Budesonide (Symbicort) Induce Orofacial Clefts, Gastroschisis, and Heart Septum Defects in an In Vivo Model," Developmental abnormalities and embryonic mortality were triggered by a single intra-amniotic injection of budesonide or formoterol, or their combo within the patented medication Symbicort. Budesonide emerged as the extremely toxic, causing teratogenic as well as fatal consequences even at 0.003 g doses. Formoterol was really the less toxic, its symptoms only obvious until a greater dose was given (0.3 mg). Between these levels, Symbicort, a combination of budesonide as well as formoterol, displayed embryo-damaging, teratogenic, and fatal effects. Exposure to all three drugs resulted in gastroschisis and orofacial clefts in the embryos. Defects in the heart's septum were discovered after being exposed to formoterol. Women who took bronchial asthma medication while pregnant were found to have these congenital anomalies in their children. The current experimental findings support clinical and epidemiological studies that show pregnant women taking anti-asthmatic medications are at risk of having children with birth defects^[4].

2. Curcumin and Tulsi Potentiality in Pulmonary Diseases

Curcumin capsules aid in reducing airway obstruction, as evidenced by a significant increase in mean FEV1 values, according to the results of an evaluation of curcumin's efficacy as an addition therapy for patients with bronchial asthma. Despite the lack of apparent clinical efficacy, there was a significant improvement in haematological parameters and no clinically significant adverse events, indicating that curcumin capsules have a reliable safety profile. As a result, it can be concluded that curcumin can be used as an additional treatment for bronchial asthma in a safe and effective manner^[5,6].

The study's findings showed that curcumin longa protected sensitised animals from lung inflammation, oxidative stress, and immunological markers. At the measured doses, curcumin longa's anti-inflammatory as well as antioxidant properties were comparable to or greater compared to those of dexamethasone. However, its immunomodulatory activity was so much more localized, inevitably results in an enhanced Th1/Th2 equilibrium. Curcumin longa has the potential to treat asthma, according to these findings^[7].

Curcumin was found to significantly inhibit ovalbumin (OVA) and interleukin-4 (IL-4)-induced airway inflammation and mucus hypersecretion not only for lung but also BEAS-2B cells in the study Curcumin Attenuates Asthmatic Airway Inflammation and Mucus Hypersecretion Involving a PPAR-Dependent NF-B Signaling Pathway In Vivo and In Vitro, suggesting that curcumin may be considered an effective treatment of asthma^[8] (Figure 1).



Figure 1. Mechanism of action of Curcumin

Tulsi, which means "holy basil" in English and "tulsi" in Hindi, is a highly treasured fragrant herb native to the Indian subcontinent and is utilised in Ayurvedic treatment after almost 3000 years. Tulsi is known as a "Elixir of Life" in the Ayurvedic system due to its therapeutic powers. It has been demonstrated to address a variety of common health problems. Tulsi leaf extracts have been indicated to cure pyrexia, rheumatism, and bronchitis, according to the Indian Materia Medica. Other claimed medicinal applications comprise of epilepsy, asthma or dyspnea, hiccups, cough, skin as well as haematological illnesses, parasite infections, neuralgia, headache, wounds, inflammation, and even oral problems. Another study on asthmatics discovered that taking 500 mg of dried tulsi leaves thrice times per day enhanced the total amount of air exhaled after maximal inhalation and alleviated asthmatic manifestation in only three days (Figure 2).



Figure 2. Mechanism of action of Curcumin

An investigation into the antihistaminic and antianaphylactic properties of HK-07, a polyherbal formulation consisting primarily extracts of *Curcuma longa, Zingiber officinale, Piper longum, Emblica officinalis, Terminalia belerica, Ocimum sanctum, Adhatoda vasica,* and *Cyperus rotundus*, was conducted. Demethoxycurcumin, bisdemethoxycurcumin, and curcumin, the primary bioactive component, are all found in the dry rhizome of *Curcuma longa*. There are numerous traditional uses for natural curcuminoids or turmeric in folk medicine. Some of these applications are based on turmeric's antioxidant, anti-inflammatory, and antiallergic qualities, which were validated by a number of scientific investigations. Curcumin was proven to become as powerful inhibitor of the nuclear transcription factor (NF)-kB, that has been associated to a number of disorders including asthma as well as allergies. Ocimum sanctum was proven to prevent from histamine, pollen-induced bronchospasm in guinea pigs as well as antigen-induced histamine production via sensitised mast cells, in addition to its well-known anti-inflammatory as well as antioxidant capabilities.

3. Future Perspective

As the sphere of asthma treatment evolves, the potential of natural remedies like curcumin and tulsi in addressing pulmonary conditions becomes more relevant. This integrative approach, merging modern pharmacology with traditional medicine, is a promising avenue that could redefine asthma management. It is expected that future research will unravel further mechanisms underlying these natural compounds, refining their therapeutic potential and understanding their interactions with conventional drugs^[9]. Moreover, there is the potential for developing combination therapies leveraging these natural products alongside conventional medicines to enhance efficacy and minimize side-effects. Concurrently, robust clinical trials and pharmacovigilance should be prioritized to ensure the safety and effectiveness of these alternative treatments. While we are only

beginning to unveil the potential of natural products, it is hoped that their integration will pave the way for personalized, safer, and more cost-effective asthma treatment regimens.

4. Conclusion

Asthma is a chronic disease that significantly impacts the quality of life of millions of individuals worldwide. Despite the availability of various treatment options, the burden of asthma continues to be high, mainly due to adverse effects and the high cost associated with some treatments. As such, the exploration of alternative therapies, specifically plant-derived compounds, has gained momentum. The reported benefits of curcumin and tulsi in managing asthma symptoms, coupled with their good safety profiles, offer promising avenues for future research and development in the area of asthma management. Although preliminary findings are encouraging, it is crucial to conduct more comprehensive clinical trials to determine the efficacy and safety of these natural compounds in asthma patients. Furthermore, mechanistic studies are required to understand their exact mode of action. Overall, curcumin and tulsi represent promising alternative therapies for asthma management, which may help reduce the disease burden and improve patients' quality of life.

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References

- 1. McCracken, JL, Veeranki, SP, Ameredes, BT, *et al.* Diagnosis and management of asthma in adults: A review. JAMA, 2017; 318(3): 279–290.
- Papi, A, Brightling, C, Pedersen, SE, et al. Asthma. Lancet (London, England), 2018; 391(10122): 783– 800.
- 3. Bhosale, U, Jaiswal, S, Yegnanarayan, R, *et al.* A pharmacovigilance study of antiasthmatic agents in patients of bronchial asthma at a tertiary care hospital. J Clin Exp Res, 2013; 1(2): 26.
- 4. Peterka, M, Heringova, LH, Sukop, A, *et al.*. Anti-asthma drugs Formoterol and Budesonide (Symbicort) induce orofacial clefts, gastroschisis and heart septum defects in an in vivo model. In Vivo, 2021; 35(3): 1451–1460.
- 5. A.Abidi, Gupta, S, Agarwal, M, *et al.* Evaluation of efficacy of curcumin as an add-on therapy in patients of bronchial asthma. J Clin Diagnostic Res, 2014; 8(8): HC19–HC24.
- 6. Reddy, V. R., Babu, A. K., *et al.* A clinical study on therapeutic management and impact of patient counseling on asthma patients. , Int J Res Pharm Sci, 2011; 2(1): 8–11.
- 7. Boskabady, MH, Amin, F, Shakeri, F. The effect of *Curcuma longa* on inflammatory mediators and immunological, oxidant, and antioxidant biomarkers in asthmatic rats. Evidence-Based Complementary Altern Med, 2021.

- 8. Zhu, T, Chen, Z, Chen, G, *et al.* Curcumin attenuates asthmatic airway inflammation and mucus hypersecretion involving a PPARγ-dependent NF-κB signaling pathway in vivo and in vitro. Mediators Inflamm, 2019.
- 9. Wang, Y., Chen, S., Du, K., *et al.* Traditional herbal medicine: Therapeutic potential in rheumatoid arthritis. J Ethnopharmacol, 2021; 279: 114368.



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