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REVIEW ARTICLE

Traditional Medicine — A Gold Mine in the Treatment of Asthma

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Abstract

Asthma is one of the chronic respiratory disorder whose incidence and intensity is rising day by day. Globally, this devastating disease affects almost 300 million people. Since ancient times, various plants had already been identified as traditionally and utilized by medical practices for managing asthma in many countries. This goal of the article is to investigate and consolidate information on the ethnomedical applications, phytochemistry, and preparation techniques of frequently used medicinal herbs to treat asthma. With soaring efficiency, the search for new, high-value molecules continue, and there are still many medications with side effects that need to be identified. Phenolics, sterols, and terpenoids, which are a key class of phytoconstituents against asthma are only a few examples of the active compounds against asthma that may be found in medicinal plants. It is advised that further research is required to identify adverse effects, effectiveness, and safety, as well as other factors of anti-asthmatic herbs and standardize herbal treatments.

Keywords: Asthma, Anti-asthma, Bronchoconstriction, Herbal Plants, Phytomedicine

1. Introduction

A prevalent chronic respiratory disorder called asthma is characterized by a variety of airflow restrictions brought on by the constriction of the airways, the hardening of the airway walls, and the excessive production of mucus[1]. Chronic airway inflammation brought on by plasma leakage and entry of inflamed cells such neutrophils, eosinophils, macrophages, lymphocytes, and mast cells causes respiratory tract constriction. One significant physiological aspect of asthma is airway hyperresponsiveness (AHR). AHR is a heightened reaction of the airways to unspecific stimuli, which in healthy individuals would have little or no impact. Asthma is frequently described as a reversible airway constriction; it has the potential to progress to an irreversible decrease in lung function. Remodelling of the airways includes diseases such as cartilage integrity, excessive subepithelial collagen deposition, goblet cell hyperplasia, and diminished airway smooth muscle hyperplasia, epithelial, or enhanced vascularity, which is another cause of persistent airflow restriction. The term "asthma" currently refers to a broad group of clinical manifestations (phenotypes) and unique pathophysiology causes (endotypes)[2]. The most prevalent type of asthma is allergic asthma, which has a Th2-mediated background, early symptoms, and sensitivity to an antigen[3,4]. The immune response type 2 is made up of Th2 cells, group 2 (ILC2) innate lymphoid cells, a minor proportion of IL-4-producing NK cells and NK-T cells, IgE-producing mast cells, B cells, eosinophils, basophils, their primary cytokines[5]. Alarmins (TSLP, IL-25, and IL-33) are secreted by epithelial cells, and type 2 cytokines Interleukin-4, IL-5, IL-9, and IL-13, mostly produced by immune cells type 2, combine to form a complex network. A fraction of individuals with non-Th2 inflammation has non-allergic or intrinsic asthma[2,6]. A non-type 2 reaction is most likely caused by an aberrant innate immune reaction that includes activation of the IL-17-mediated pathway and intrinsic neutrophil abnormalities. The cellular and molecular causes of asthma remain poorly understood while being well-defined (Figure 1).

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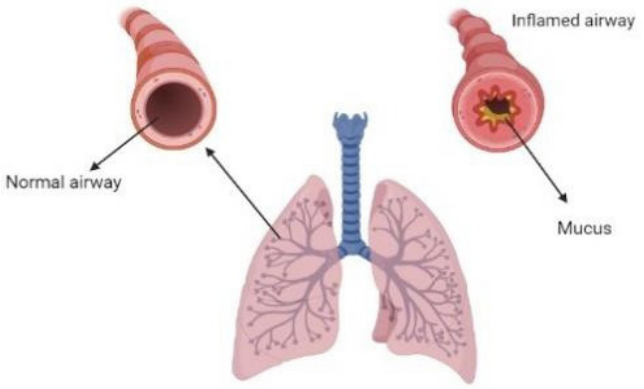

Figure 1. If you suffer from asthma, the inside walls of your lung airways may swell and itch. Your airway linings could also secrete way too much mucus. Then comes an asthma attack. During an asthma attack, you could cough and wheeze because your constricted airways make breathing more challenging.

2. Therapy

Despite avoidance attempts, asthma symptoms typically worsen; medication is frequently required. The aim of treatment is control of asthma, with symptomatic relief, maintenance of the regular level of activity, reduction of worsening, and protection against lung capacity loss, as well as avoidance of fatalities, hospitalizations, and ER visits. The treatment type is decided upon by the severity of the symptoms, the findings of the physical assessment, and, in a few cases, the forced expiratory volume in the peak expiratory flow rates and the first second of expiration (FEV1)[7].

3. Medications

3.1 β2 Adrenergic Agonists

The Short-Acting 2 Adrenergic Agonists (SABA), called bronchodilators, are used to treat difficulties that occur while taking daily regulator drugs or during an exacerbation. It is advisable to take more daily regulator medicine if these medications are required for more than two nights per week or two days per month. The drug in this class that is used the most frequently is albuterol. After using it for five minutes, the bronchodilator effects reach their peak after 1 hour, and they can last up to six hours. A least of 2 puffs every four hours is advised. Individuals should be advised to take more inhaled corticosteroids, start taking oral corticosteroids, and/or call their healthcare provider for guidance if a higher dose of 2 adrenergic agonists is necessary; occasionally, an examination at the emergency department is required. Palpitations, tachycardia, tremors, and perhaps hypokalemia (due to intracellular K+ movement) are common side effects of β2 adrenergic agonists. Overuse of SABAs has been linked to fatal asthma cases. The deaths are most likely the result of underlying asthma not receiving proper care. Therefore, doctors should carefully watch how much SABA they prescribe to each patient. SABAs are useful for preventing exercise-induced asthma in additionto treating its acute symptoms[7,8].

3.2 ICS Inhaled Corticosteroid

The first line of defence against persistent asthma is Inhaled Corticosteroids (ICS). They decrease inflammation and enhance lung health, quality of life, and asthma symptom scores. Additionally, they minimize the need for hospital stays, urgent care visits, and oral steroids. A frequent adverse effect of ICS involves voice changes and oral candidiasis (hoarseness). Gargling, mouth washing, and using an inhaler correctly can all help to reduce the likelihood of getting thrush. It is believed that Systemic side effects of ICS depend on dosage (2 days/week). When used by approved dosages, ICS is not thought to raise the risk of glaucoma, cataracts, or bone density reduction. According to studies, higher-dose Inhaled corticosteroids can have therapeutic impacts on the hypothalamic-pituitary-adrenal axis in sensitive subjects, especially when administered more than the label's suggested dosage. Use the smallest amount of ICS that still manages the patient's respiratory function and asthma symptoms.

3.3 β1 Adrenergic Agonist

For around 12 hours, beta-2 adrenergic agonists cause bronchodilation. Individuals with mild-to-severe chronic asthma benefit from increased lung function and asthma management when a LABA is combined with ICS. LABA therapy might make it possible to deliver ICS at a lower dose[8]. Beta 2 adrenergic agonists must be used in conjunction with Inhaled corticosteroid (ICS), not alone[9].

3.4 Oral Corticosteroids

Asthma treatments are most effective with oral corticosteroids because of their strong anti- inflammatory properties[10]. Oral corticosteroids are taken long-term

and in large doses produce some negative side effects, such are the inhibition of the hypothalamic-pituitary-adrenal axis, gain weight, hyperglycemia, and cataracts. As a result, it is advised to use them for short periods during acute asthmatic exacerbations, as well as a diagnostic-therapeutic trial may be conducted to treat cough, alleviate dyspnea, or clear airway obstruction in people who have a moderate-to-severe persistent illness that is not treated with other drugs. Systemic corticosteroids may save the lives of many patients, so using them in the right circumstances shouldn't be restricted out of concern about side effects. When taken every other day, a patient who needs long-term steroid medication may experience fewer side effects (such as hypertension, diabetes mellitus, or life-threatening infections). Prednisone is often administered to adult patients with asthma flare-ups at a dose of 0.5 to 1 mg/kg daily for five days; the dosage for a child is 1-2 mg/kg daily. Observed practice Patterns can change despite the recommended dose levels[10].

3.5 Leukotriene Receptor Inhibitor

Bronchoconstriction and Inflammation occur in asthma, including aspirin-intolerant asthma, and are attributed to leukotrienes. Leukotriene D4 (LTD4) effects are blocked by leukotriene receptor antagonists, which are licensed to treat asthma, urticaria, and allergic rhinitis (Hay Fever). Leukotriene receptor inhibitors are not the optimal treatment in moderate chronic asthma since they are less effective than ICS, according to a comprehensive review of the literature[11]. They are also less effective than LABAs when used with ICS for mild to severe chronic asthma. Depending on the medicine, response to zafirlukast or montelukast can take anywhere from days to four weeks to manifest. Zileuton is a 5-lipoxygenase oral leukotriene synthesis inhibitor that reduces leukotriene production by 26% to 86%. It is vital to measure baseline and ongoing liver function tests since transaminase elevations can be reversed.

3.6 Immunotherapy

Some sufferers of allergic asthma need to have subcutaneous immunotherapy, often called allergen-specific or allergy shots immunotherapy. Immunotherapy can help some patients with mild to severe atopic asthma by easing their symptoms and lowering their medication intake. Immunotherapy for hay fever patients may also have a lower chance of developing asthma[12,13].

3.7 Bronchial Thermoplasty

To reduce the bulk of the smooth muscles lining the airways, the procedure known as bronchial thermoplasty uses the heat of the airway while, bronchoscopy uses targeted radiofrequency pulses. An increase in asthma attacks has been linked to bronchial thermoplasty in the first three months of treatment, then the following decline in attacks, without having a positive impact on lung health. Some individuals with badly managed asthma who are receiving treatment with high to moderate doses of ICS-LABA may want to consider it. In comparison to control individuals, the long-term impacts, such as on lung function, are not yet known[14]. Bronchial tissue is heated with radiofrequency throughout 3 sessions (the first was directed toward the right lower lobe, the second toward the left lower lobe, and the third toward both upper lobes) (Figure 2).

Figure 2. Asthma involves cells and mediators, which have a variety of impacts on the airways.

4. Methodology

The evidence used for this review study was gathered from articles included in databases including Scientific Information Database, Scopus, PubMed, and Google Scholar. Further research was conducted on the relevant article on medicinal herbs with anti-asthmatic properties.

5. Therapeutic Plants Have Anti-Asthmatic Effects

5.1 *Allium cepa* Linn (Liliaceae)

A bulbous perennial or biennial plant called *Allium cepa (A. cepa)* belongs to the family Liliaceae and the genus Allium, which includes over 3700 species and 250 genera. The origin of *Allium cepa* is evidently in

central Asia, maybe in Iran as well as Pakistan. But now it's accessible everywhere, including in Europe, North America, and Africa. Onion has tiny, typically purple or white blooms. This plant has a superficial root system and a very short, flattened stem at the base that gets bigger as it grows. Onion leaves are cylindrical, long, linear, and hollow. The leaf bases thicken and develop into a bulb when the plant reaches a certain stage of growth[15]. The phytoconstituents present in *Allium cepa* are mainly quercetin, saponin, and anthocyanin (Figure 3). The flavonoid categories found in onions are flavanones flavonols, catechins, anthocyanidins, and flavanonols. Kaempferol and luteolin are two more flavonoids found in onions[16]. Onion contains sulfur compounds and an alliinase enzyme which is responsible for the lacrimatory effect[17]. The plant has traditionally been used to treat many diseases, such as asthma, inflammatory ailments, diarrhoea, ulceration sores, scars, wounds, keloids, and discomfort and swelling after bee or wasp stings. Additionally, research has indicated that onions have many pharmacological effects, such as lowering blood triglycerides, thromboxanes, and cholesterol levels, which are factors that help in the progression of cardiovascular disease; inhibiting platelet-mediated thrombosis as well as platelet aggregation, which results in heart attacks and strokes; and acting as neuroprotective, anti-convulsant, anti-hypertensive, anti-depressant, hepatoprotective, hypoglycemic, anti-bacterial, anti-fungal, anti-asthmatic, anti-oxidant, anti-inflammation, anti-carcinogenic[18], vasodilator, and anti- allergenic activities[19]. *Allium cepa* aqueous extract decreased neutrophil, eosinophil, and lymphocyte counts as well as lung inflammation. According to a different study, the methanol extract of *Allium cepa* reduced the activity of eosinophil peroxidase and inflammatory cytokines like IL-5 and IL-13. As well the extract relaxes tracheal smooth muscle. In contrast, it has been established that onions have been shown to lower vascular permeability, which leads to a reduction in the amount of protein exudation in bronchoalveolar lavage fluid[20]. Flavonoids (like quercetin) have anti-asthmatic properties by lowering inflammatory indicators, including NF-κB, leukotrienes, PGD2, and granulocyte-macrophage colony- stimulating factor (GM-CSF), also suppression of T helper (Th) 2 cytokine synthesis like IL-4 and IL-13[21]. Along with kaempferol, thiosulfinates, quercetin, and cepaenes reduce bronchoconstriction by blocking the cyclooxygenase and lipoxygenase enzymes[22].

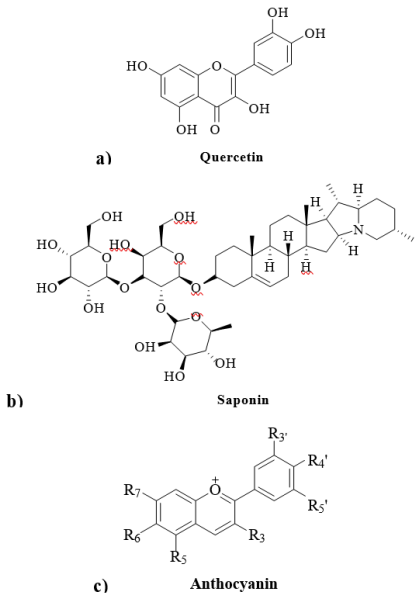

Figure 3. **(a)**. Quercetin, **(b)**. Saponin, **(c)**. Anthocyanin.

5.2 *Allium sativum* L

Garlic, also known as *Allium sativum* L., is an essential spice that belongs to the Alliaceae family and has wide use for various illnesses and physiological abnormalities. The Celtic word "all", which means pungent, may have been the source of the name garlic. Garlic originated in Asia, travelled to the Mediterranean region and China, and then moved to Central Europe, Mexico, and North Africa[23]. *Allium sativum* L. has some bioactive substances with many health benefits, such as saponins, organic sulfides, phenolic compounds, and polysaccharides[24]. The Phytochemicals including sulfur-containing compounds includes such as ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H) -1,3-dithiin) (Figure 4), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS))[25]. *Allium sativum* has different biological properties such as antibacterial, antifungal, antiviral, antiprotozoal, anticancer, immunomodulatory, anti-inflammatory, antidiabetic, antioxidant, anti-obesity, antihypertensive, hypolipidemic, and cardiovascular protective activities, as proven by severalrecent studies[24,25]. In the experiment, the anti-inflammatory properties of various garlic fraction extracts against allergic asthma were produced by Dermatophagoides pteronyssinus (Der p) *in vitro* and *in vivo*. The histological finding indicates that the water extract may improve lung mucus hypersecretion, goblet cell hyperplasia, and inflammatory cell infiltration. The water extract reduced IgG1 as well as IgE, decrease inflammatory cells as measured in

bronchoalveolar lavage Fluid (BALF), and improved IgG2a in serum. In addition, the water fraction extracts raised the levels of IFN- γ and IL-12, which are both Th1 cytokines, in BALF while decreasing the levels of IL-13, -4, and -5, which are all Th2 cytokines, and also inhibiting the expression of IL-1, IL-6, and TNF-α. Additionally, PI3K/Akt/NF-B-κB signalling pathways in A549 cells were suppressed by the water fraction. This result suggests that Der p- induced allergic asthma can be successfully treated with *Allium sativum* water fraction extracts that have a clear anti-inflammatory activity[26].

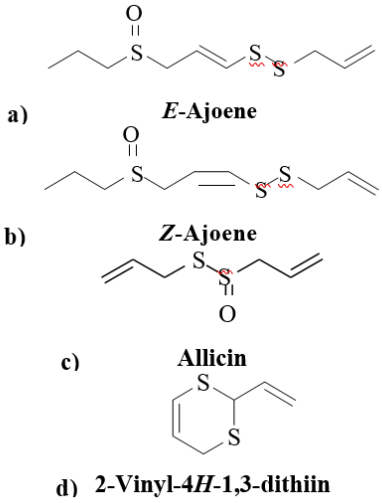

Figure 4. **(a).** E- Ajoene, **(b).** Z-Ajoene, **(c).** Allicin, **(d).** 2-vinyl-(4H) -1,3-dithiin.

5.3 *Carica papaya*

Carica papaya Linn is a belongs to Caricaceae family and known as a papaya. The plant wasbrought to India in the sixteenth century and is indigenous to tropical America. The plant can reach a height of 20 meters and can be recognized by its unbranched, weak stem that produces copious white latex and is crowded by a terminal cluster of huge, long-stalked leaves[27]. Usually, leaves have been used for the treatment of different illnesses, like in the treatment of malaria, dengue, immunomodulatory, jaundice, and antiviral activity. The phytoconstituents present in *Carica papaya* include alkaloids (pseudocarpaine, carpaine, dehydrocarpaine I and II), flavonoids (myricetin and kaempferol) (Figure 5), cyanogenetic compounds like benzyl glucosinolate, phenolic compounds like ferulic acid, caffeic acid, chlorogenic acid present in leaves. Fruit and leaf of the *Carica papaya* contain carotenoids, generally anthraquinones glycoside, lycopene, β-carotene as compared to matured leaves[27]. The pharmacological effectsthat have been documented include analgesic effects, anti-thrombocytopenic effects, anti-plasmodial effects, antifertility, antitumor, immune-modulatory effects, anti-diabetic effects, antimicrobial effects, anthelmintic effects, wound healing, anti-inflammatory, hepatoprotective, abortifacient, recently its antitumor and antihypertensive properties have also been confirmed[28]. In the experiment, *Carica papaya* leaf extracts significant reduction of lung infiltration of inflammatory cells, alveolar thickening, and goblet cell hyperplasia after treatment with extract and reduces the expression of IL-4, IL-5, TNF-α, NF-κB, iNOS, and eotaxin in a mice model of ovalbumin (OVA) induced allergic asthma, hence extract possesses anti-inflammatory effect[29].

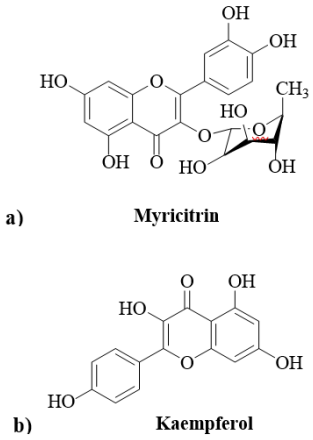

Figure 5. **(a).** Myricitrin, **(b).** Kaempferol.

5.4 *Calotropis gigantea*

Calotropis gigantea, often well-known as the madar or crown flower in Hindi, is a member ofthe Asclepiadaceae family and a milky shrub that spreads up to 1-3 cm high and is widespread throughout India[30]. It produces waxy clusters of either lavender or white blooms. Every single flower has five sharp petals, a tiny "crown" that rises from the middle, and stamens. They have milky stems and oval-shaped light green leaves on the shrub. Numerous phytochemicals have been found by *C. gigantea* in various plant sections, according to reports[31]. There have been extractions of triterpenoids, alkaloids, saponins, flavonoids, steroids, fatty acids, alcohol, glycosides, esters of calotropeols, and proteases from a variety of plant parts. Cardiac glycosides have been extracted and investigated from the latex and leaves of *C. gigantean*[32]. Two epidioxysterols, 9,11-dehydroergosterol peroxide, and

ergosterol peroxide (Figure 6), were also isolated from the flowers of *Calotropis gigantea*[33]. Hepatoprotective effects of stems, antimicrobial, cytotoxic, and analgesic effects of flowers, antioxidant and anti-diarrheal effects of leaves, antipyretic, cytotoxic, wound-healing, and insecticidal effects of roots, procoagulant and purgative effects of the latex. In reality, due to their medicinal qualities, all plant components are significant and are used to cure diseases including cancer, hysteria, leprosy, gout, fever, epilepsy, and warts in addition to other conditions[34]. In the experiment, *C. gigantea* had impressive action against rat asthma, which was caused by ova albumin (OVA). It was observed that multiple enzymes, activity on various body cells, and histological abnormalitieswere occurring. At 200 and 400 mg/kg, *C. gigantean* observed a notable decrease in lymphocytes, neutrophils, eosinophils, and total leukocytes in bronchoalveolar lavage fluid. Due to their anti-lipoxygenase, antioxidant, and anti-inflammatory capabilities, these data suggested that the plant could be employed as a medicinal medication for treating asthma[35].

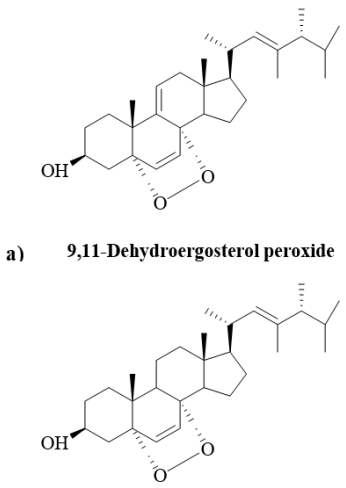

Figure 6. **(a)**. 9,11-Dehydroergosterol peroxide, **(b)**. Ergosterol peroxide.

5.5 *Cymbopogon citratus*

Cymbopogon citratus (DC.), a fragrance member of the Poaceae family, is frequently known as Indian lemongrass, lemongrass, or Madagascar lemongrass[36]. *C. citratus* is an evergreen plant with needle-like, tiny, long leaves. The strap-like leaves are about 1.3 – 2.5 cm in width and 0.9 cm long with drooping tips and shiny bluish-green coloration with an aroma (citrus) when grounded due to the presence of citral and high content of aldehyde geranial and neral. This plant can grow as wide as 1.2 meters and as long as 2 meters overall. Most plants grow without a stem directly from the ground. Their width ranges from 5 to 15 mm, while their length exceeds 1 m. There is no flowering on the species that have been discovered so far[37]. The phytochemical compounds such as anthocyanin, phytosterols, organic acid, amino acids, phenolic compounds, fatty acids, volatile components, flavonoids, fumesol, isovaleranic aldehyde, valeric esters, linalool, p-coumaric acid, methyl heptenone, isopulegol, furfurol, (Figure 7)[38]. *Cymbopogon citratus* have different pharmacological properties anti-bacterial, anti-inflammatory, antinociceptive, anti-fungal, anti-obesity, and antihypertensive[39]. The research was conducted using a murine model of allergy disorder caused by a typical allergen.This study has shown that *Cymbopogon citratus* reduced the infiltration of total leukocytes, particularly eosinophils, mucus production, and NF-κB expression in the lung tissue of Bt- sensitized animals. Treatment with the extract also reduced the production of eosinophil peroxidase and suppressed levels of IgE, IgG1, and IL-4. This result shows that *Cymbopogon citratus* extract modulates allergic asthma[40].

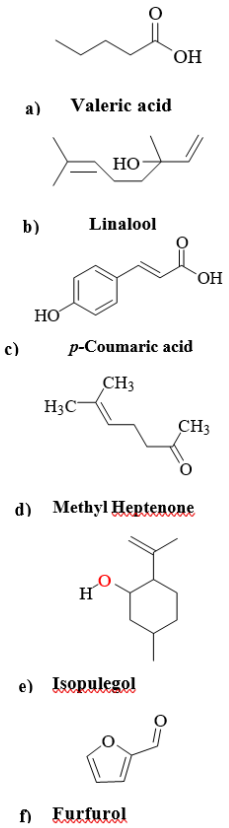

Figure 7. **(a)**. Valeric acid, **(b)**. Linalool, **(c)**. p-coumaric acid, **(d)**. Methyl Heptenone, **(e)**. Isopulegol, **(f)**. Furfurol.

5.6 *Datura stramonium* Linn

Datura stramonium (Jimson weed) is commonly known as Datura, which belongs to the Solanaceae family. *Datura stramonium* is dense and smooth that is capable of height growth 6feet in rich soil. Spreading, bushy, upright, smooth, pale yellowish-green stems that repeatedlybranch out create a forked shape. The leaves, which are normally light green, 4 to 6 inches in length, oblong to triangular-oval shapes, irregular base, and have curved and rough-toothed edges, are extremely clearly formed with strong, branching veins. The backside is paler and slightly wrinkled when dry. The outermost layers are often smooth and dark greyish-green. Flowers with axillary buds, upright, white, and with fragrant (particularly at night). The typical flower measures 3 inches[41]. The phytochemicals found in Datura include alkaloids, phenolic compounds, tannins, cardiac glycosides, and flavonoids (Figure 8). In addition,

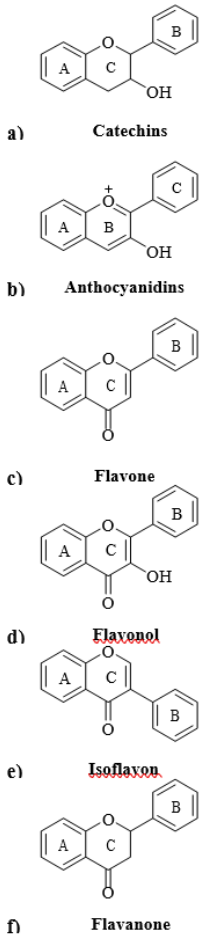

Figure 8. Flavonoids structure. **(a)**. Catechins, **(b)**. Anthocyanidins, **(c)**. Flavone, **(d)**. Flavonol, **(e)**. Isoflavon, **(f)**. Flavanone.

many amino acids such as alanine, phenylalanine, glutamate, and tyrosine have also been isolated from the seeds. Datura species are particularly rich in tropane alkaloids such as hyoscyamine and scopolamine[42]. According to *et al*[43]. *Datura stramonium* includes several alkaloids, such as scopolamine and atropine, which have bronchodilating and anticholinergic effects. Bypreventing muscarinic receptors, specifically the M receptor, on submucosal gland cells and airway smooth muscle, scopolamine and atropine increase bronchial smooth muscle and decrease asthmatic attacks. In asthma patients with only minor airway obstruction, *Datura stramonium* is a powerful bronchodilator[44]. But if a pregnant woman takes *D. stramonium* to treat her asthma, it will generate a constant production of acetylcholine and desensitize nicotinic receptors, which could potentially harm the fetus permanently[45].

5.7 *Euphorbia hirta*

Euphorbia hirta belongs to the Euphorbiaceae family, and the genus of plants is Euphorbia. It is an annual plant that is reddish or purplish, hairy and has a narrow stem and several branches that extend upward from the base. The opposing leaves are elliptic-oblong, acute or subacute, dark green above, pale below, 1 to 2 cm long, purple-blotched in the center, and toothed at the margin. The fruits are yellow capsules with three-celled hairs that are 1-2 mm in diameter[46]. Numerous bioactive substances, including polyphenols, anti-oxidants, gallic acid, ascorbic acids, (Figure 9), myricitrin, terpenoids, anthocyanins, flavonoids, and volatile oils, are present in *Euphorbia hirta*[47]. Bioactive components of the plant were shown to have various pharmacological effects, involving antibacterial, anti-diabetic, anti-oxidant, anti-diarrheal, anti-inflammatory, sedative, analgesic, anti-asthmatic, anti-tumour, larvicidal, diuretic, anti-spasmodic, and anti-cancer effects[48]. In the experiment using a histamine aerosol test model, the bronchodilator effect of an alcoholic extract of *Euphorbia hirta* Linn was assessed at various doses (50, 100, and 200mg/kg p.o.). Animals pre-treated with *E. hirta* indicated a dose-dependent bronchodilator effect. The extract of *E. hirta* was revealed to be more effective in reducing histamine-induced bronchoconstriction, and it considerably inhibited histamine-induced bronchospasm in a dose-dependent way; this suggests that it may have an H1 blocking effect[49].

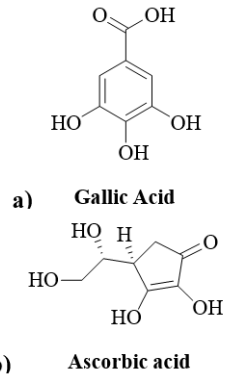

Figure 9. **(a)**. Gallic Acid, **(b)**. Ascorbic Acid.

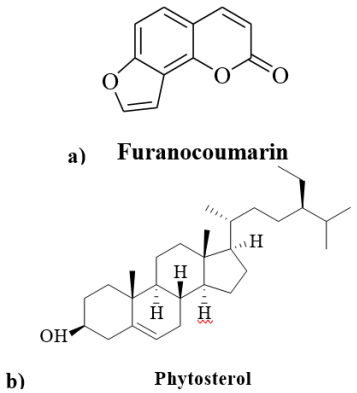

Figure 10. **(a)**. Gallic Acid, **(b)**. Ascorbic Acid.

5.8 *Ficus religiosa*

Ficus religiosa L. is the most popular species of the *ficus* genus, which belongs to Moraceae, the mulberry or fig family. They know as the bodhi or peepal tree and have more than 150 different names. The sub-Himalayan region, Bengal, and central India are its native lands. Through cultivation, it has been distributed widely throughout the world. The *F. religiosa* tree grows up as an epiphyte before strangling its host with its deep, spreading roots to become an independent tree. It is found in regions up to above 1500 meters sea level with a yearly rainfall of 50 to 500 cm during the monsoon season and can withstand a wide range of temperatures (below 0°C and beyond 40°C). The phytoconstituent's investigation on *Ficus religiosa*, furanocoumarins, phytosterols (Figure 10), hydrocarbons, amino acids, phenolic components, volatile components, and aliphatic alcohols are extracted from various plant parts. Phenolic components [tannins and flavonoids] and amino acids are present in almost all the parts of *F. religiosa*[50]. The *Ficus religiosa* exhibit a wide spectrum of activities such as anticancer, antioxidant, anti-diabetic, antimicrobial, anticonvulsant, anthelmintic, antiulcer, antiasthmatic, and anti-amnesic[51]. In the experiment perform *in vivo* model, pre-treatment with aminophylline could significantly delay the onset of histamine-induced pre-convulsive dyspnea, compared with vehicle control. Administration of an aqueous extract of *F. religiosa* leaves also produced a significant effect on latency to develop histamine and acetylcholine-induced pre-convulsive dyspnea. In the mast cell stabilizing model, an aqueous extract of *F. religiosa* leaves could significantly increase the number of intact cells[52].

5.9 *Moringa oleifera*

Moringa oleifera Lam. belongs to the Moringa genus and Moringaceae family. It's a 2.5–10 m tall shrub and small deciduous tree. It is grown throughout Asia and Africa's tropics and subtropics[53]. It has spreading, fragile branches, feathery foliage of tripinnate leaves, and whitish-gray bark. Flowers are fragrant, bisexual, and yellowish-white flowers are hairy stalks in spreading or drooping axillary panicles 10 - 25 cm long. Fruits are tri-lobed capsules and are referred to as pods. It is pendulous, brown triangular in shape[54]. The entire plant has antibacterial properties and is also used to treat rheumatism, poisonous bites, and ascites, and to improve heart function[55]. Strong hypotensive, diuretic, and spasmolytic properties are present in the leaves, which have also been found to be beneficial in treating scurvy, anaphylaxis[53], helminthiasis, and inflammation[56]. The plant's roots have been employed as diuretics, anthelmintics, carminatives, and treatments for chronic rheumatism, epilepsy, and intermittent fever. The plant's seeds are utilized as antipyretics, anti-inflammatory and purgative medications. The ethanolic extract's efficacy has been demonstrated that seeds possess antiarthritic, anti-asthmatic, and anti-anaphylactic actions in rats. In adolescents with upper respiratory infections and skin conditions, treatment with the plant is also said to provide positive therapeutic results. One of the plant's alkaloids, known as moringin, is said to relax bronchioles and is thought to be effective in treating asthma[57]. Phytochemical components of the plant *Moringa oleifera* Lam include methionine, quercetin, cysteine, D-glucose, kaempferitin, ascorbic acid, D-mannose, kaempferol, benzyl isothiocyanate, isoquercetin (Figure 11) and protein. In managing asthma, *Moringa oleifera* has been

very beneficial. Mahajan, *et al*. investigated the efficacy of n-butanol extracts of the seeds of *M. oleifera* (MONB) versus ovalbumin-induced bronchitis in guinea pigs. They concluded that MONB's antiasthmatic effects resulted from the modification of Th1/Th2 cytokine imbalances[58]. The effectiveness of *Moringa oleifera* seed kernel in bronchial asthma patients was examined. For three weeks, individuals of either sex who had moderate asthma received treatment with 3 g of finely dry seed kernels powdered. A spirometer was used to measure the clinical efficacy both before and after the treatment. Most patients showed an increase in hemoglobin (Hb) values and a reduction in the Erythrocyte Sedimentation Rate (ESR). Improvement was also observed in symptom scores and severity of asthmatic attacks. After three weeks of treatment in asthmatic subjects, the drug produced significant improvement in forced vital capacity, forced expiratory volume in one second, and peak expiratory flow rate[59].

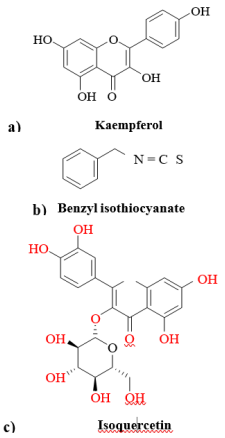

Figure 11. **(a)**. Kaempferol, **(b)**. Benzyl Isothiocyanate, **(c)**. Isoquerctin.

5.10 *Nigella sativa*

The annual plant *Nigella sativa* Linn., often called black cumin or black seed and goes to the Ranunculaceae family, has historically been utilized in the Asian subcontinent, Arab countries, and European countries for both edible and medical uses[60]. *N. sativa* is an annual flowering plant that grows up to 20-90 cm tall, with finely divided leaves, the leaf segments narrowly linear to threadlike. The flowers are delicate, usually coloured in white, yellow, pink, pale blue,or pale purple, with 5-10 petals. The fruit is a large and inflated capsule composed of 3-7 unitedfollicles, each containing numerous seeds[61]. The presence of many active medicinal components, including thymol, thymoquinone, limonene (Figure 12), t-anethole benzene, carvacrol, longifolene, 4-terpineol, alpha-pinene, and p-cymene has been shown in research on the *N. sativa* seeds[62]. Several phytochemical research has shown that the seeds of plants contain two types of alkaloids, including pyrazole alkaloids, which include nigellidine and nigellicine, and isoquinoline alkaloids, including nigellimine-N-oxide[63]. Unsaturated fatty acids like linoleic, palmitic, and oleic acids are abundant in *N. sativa* seeds[64]. Its seeds include vitamins, several essential minerals like calcium, phosphorus, iron, and other compounds as well as flavonoids, saponins, cardiac glycosides, and indazole-type alkaloids. Biological activities of *N. sativa* possess a wide spectrum of activities viz. as diuretic, antihypertensive, antidiabetic, anticancer and immunomodulatory, analgesic, antimicrobial, anthelmintics, analgesics and anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective and antioxidant properties[61]. In the management of asthma, NS, as well as its components are crucial. Due to its several targets, including anti-inflammatory, immunomodulatory, and antihistaminic properties. The conclusion of the significant research comparing the inhibitory activity of the main NS constituent's curcumin and thymoquinone, one of the bioactive ingredients in turmeric, on the biological modification linked to asthma showed that thymoquinone (TQ) is much more effective at suppressing the inflammatory alteration related to asthma[65]. According to the findings of a separate investigation, TQ lowersallergic or atopic airway inflammation by reducing the generation of cytokines (Th2) T helper2and eosinophil infiltration[66]. In a mouse model of allergic asthma, the effect of TQ on the airway or bronchitis inflammation was investigated vide Table 1.

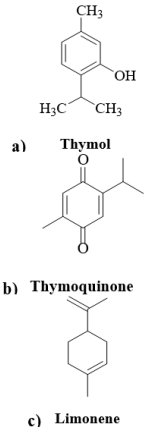

Figure 12. **(a)**. Thymol, **(b)**. Thymoquinone, **(c)**. Limonene.

Table 1. Ethnobotanical medicinal plants used in the management of asthma

S/N	Names of plants	Standard name	Specific names	Utilised part(s)	Traditional method	Administration route	Ref
1	***Allium cepa L***	Onion	Key shinkurt	Bulb	One teaspoon is consumed every morning by squeezing the bulb.	Oral	79
2	***Allium sativum L***	Garlic	Nech shinkurt	Bulb	A solvent is used for dissolving	Oral	79
3	***Carica papaya L***	Pawpaw	Papaya	Leaf	Inhaled fumes from burned leaves.	Oral	79
4	***Calotropis Gigantea***	Arka	Giant milkweed	flower	Flowers are collected, dried in a sunshade, and made into fine powder.1-2 pinches of this is mixed with little rock salt powder and used for chewing or else this combination can be taken along with warm water.	Oral	80
5	***Cymbopogon citratus***	Lemongras s	Tegesar	Leaf	Two cups of water are mixed with two teaspoons of dried lemongrass, a half teaspoon of ginger, a small piece of cinnamon stick, and a half teaspoon of cloves. For five minutes after bringing, it to a boil, simmer it. When you have asthma, strain the mixture, add some honey, and a small bit of Lemon juice should be consumed once every day.	Oral	79
6	***Datura stramonium L***	Dhatoora	jimsonweed	seeds and leaves	Seeds and leaves combined when consumed orally as smoke or decoction	Oral	81
7	***Euphorbia hirta***	Asthma Weed	Hairy spurge	Flower	Extraction is taken orally	Oral	79
8	***Ficus religiosa***	Peepal	Peepal	Bark, Fruit, Roots	Fruit powder to cure asthma, take 4-6 g daily. cough remedy made from bark Fruit juice and consumed orally for respiratory conditions including asthma. Root decoction together with a little salt,	Oral	82
9	***Moringa oleifera***	Drumstick, Moringa	Moringa	Leaves	Decoction	Oral	79
10	***Nigella sativa***	Kalonji	Black cumin	Seed	Seeds mixed with garlic, rutachalepensis, and honey, then left in a jar with a tight lid for a few days before being consumed every morning.	Oral	79

6. Some Important Bioactive Compounds

6.1 Quercetin

Quercetin is a vital bioflavonoid that researchers have broadly studied over the past 40 years. The phenolic structure of flavonoids, which are extensively distributed in nature, can be seen in the root, bark, grains, wine, fruits, stems, bulbs, and tea. The plant *Allium cepa* L. is the most typical source of quercetin[67]. It is a member of the flavanol group of flavonoids and aids in theproduction of numerous other flavonoids, including those found in citrus flavonoids like rutin, naringenin, hesperidin, and tangeritin[68]. According to several studies, quercetin prevents the release of pro-inflammatory mediators (IL-6, TNF-α, IL-8, and IL-1β) and histamine from mast cells triggered with IgE, this is because of suppression of (p38 MAPK) p38 mitogen-activated protein kinase and NF-kB. As a result, quercetin can influence both the early and late phases of asthma. Moreover, isoquercitrin, which is quercetin bound to glucose, reduced IL-5 levels in the BALF more effectively than quercetin aglycone. Quercetin has also demonstrated the potential to reduce airway hyperresponsiveness, bronchial hyperactivity, and mucus production[69].

6.2 Kaempferol

It is a yellow substance that is primarily present in foods with a plant origin and traditional medicines plants. The chemical name of kaempferol is 3,5,7-trihydroxy-2-(4-hydroxyphenyl)- 4H-(benzopyran-4-one) and has a low molecular weight (MW: 286.2 g/mol). Kaempferol can be found in many plants, such as Aloe vera, *Bryophyllum pinnatum* L., etc., and its absorption occurs in the small intestine. Although studies have shown that facilitated diffusion or active transport can also be used to absorb kaempferol, passive diffusion is favoured by the lipophilicity of kaempferol[70]. In allergic asthmatic mice or airway epithelial cells, kaempferol inhibits inflammation, eosinophil infiltration, and fibrotic remodelling[71]. Tyrosine kinase/signal transducers and activators of transcription (Tyk-STAT) signalling were disrupted in airway epithelial cells and asthmatic mice by this compound, which significantly reduced airway inflammation[72].

6.3 Alkaloids

The alkaloids have historically been used to treat asthma in various ways like smoke from burned Atropa belladonna in different countries. Alkaloids such as vasicine, vasicinolone, deoxyvasicinone (Figure 13), l-vasicinone, vasicinal, and moringin, showed bronchodilatory effects, trigonelline improved airway congestion, dergamine, and piperine serve as a respiratory stimulant and potential role in the managing of asthma[73].

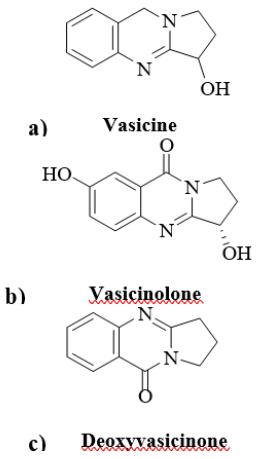

Figure 13. **(a).** Vasicine, **(b).** Vasicinolone, **(c).** Deoxyvasicinone.

6.4 Carotenoids

Total vitamin A consists of provitamin A and vitamin A (retinol), known as carotenoids, the most significant beta-carotene (Figure 14). Carotenoids are pigments that are present in microbes and plants[74]. Based on their pharmacology and structural makeup, dietary carotenoids are believed to provide beneficial anti-asthmatic action in the body for health management[75]. The study led by Hazlewood, *et al.,* demonstrated how a mouse model of (AAD) allergic airway disease with lycopene supplementation decreased allergic inflammation. Further, Th2-type cytokines Interleukins IL-4 and IL-5 that were produced in response to ovalbumin were also decreased by lycopene administration. These results suggested that by lowering the activity of Th2 cytokines, lycopene supplement decreased allergic inflammation in the blood vessels andlungs. To prevent asthma, lycopene supplementation may be used[76].

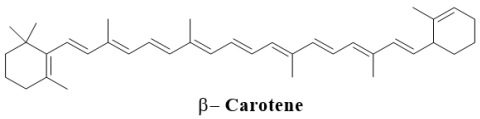

Figure 14. β-Carotene.

6.5 Curcumin

Curcumin, a main active ingredient of turmeric, polyphenolic phytochemical having anti- inflammatory, anti-amyloid, antibacterial, anticancer, antiallergic, and antioxidative activities[77] (Figure 15). Curcumin was used as a traditional treatment for atherosclerosis, urinary tract infections, insect bites, blood purification, indigestion, rheumatoid arthritis, and liver disease (especially jaundice)[77]. Curcumin reduced nasal airflow resistance by reducing congestion, sneezing, and rhinorrhea. Nasal administration of curcumin prevented bronchitis and maintained structural integrity in mice models of allergic asthma. In ovalbumin (OVA)-treated Balb/c mice, the different doses of curcumin significantly control airway obstruction and inflammation, mostly by modifying cytokine levels (IFN-γ, TNF-α, IL-4, and IL-5) and sPLA2 activity, and subsequently preventing PGD2 release and COX-2 expression. Furthermore, In rats with asthma, curcumin reduced the activation of p38 MAPK (mitogen-activated protein kinase), ERK 42/44, and JNK54/56[78].

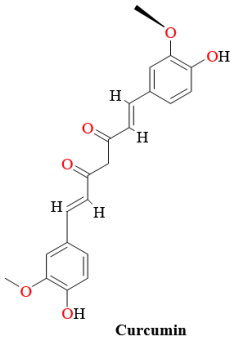

Figure 15. Curcumin.

7. Conclusion

Asthma is a common issue. Different biosynthetic medications are utilized to cure the acute signs of asthma, but their long-term safety has not been established. As a result, efforts to locate traditional medicine that can be utilized to manage asthma have once again been made. Due to their bioactive characteristics, medicinal herbs have been a key resource of natural medicine for humans, saving their lives from a variety of illnesses. Many of the currently available medicines are most likely based on medicinal plants. Most contemporary medications have their roots in conventional herbal therapy. In tribal cultures, more than 100 plant species were employed to treat respiratory conditions, particularly asthma, using decoctions, juices, and dry powders. The hazardous effects, side effects, and negative effects of medicinal herbs are not defined in many journals or theses. In this review, ethnobotanical knowledge of medicinal plants is gathered, however, additional study is needed to estimate the safety, effectiveness, and value of plants used to treat asthma. Furthermore to these to determine if medicinal plants are safe to use, there has recently been a need for literature and methodical research into assessments of heavy metals, the presence of aflatoxins, etc., as well as quantitative analyses of phytochemistry.

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9. References

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