ORIGINAL ARTICLE

Exploring siddha medicine: The efficacy of polyherbal combinations (*Āṭātōṭai Kuṭinīr*) in managing bronchial asthma through anti-inflammatory mechanisms

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Abstract

Introduction: Bronchial asthma (BA) is a chronic respiratory condition characterized by hyperresponsiveness, inflammation, and mucus secretion, affecting approximately 262 million people worldwide. Traditional medicine, including Siddha medicine, offers a holistic approach to managing asthma, with polyherbal formulation like *Āṭātōṭai Kuṭinīr* (AK) being used for centuries. **Objective:** This review aims to summarize the preclinical and clinical evidence supporting the therapeutic potential of AK in the management of BA, with a focus on antiasthmatic, bronchodilator, anti-inflammatory, and antioxidant properties. **Materials and Methods:** A comprehensive review of traditional Siddha literature, preclinical and clinical trials was conducted to gather information on the phytochemical composition, pharmacological effects, and therapeutic uses of AK. **Results:** AK comprising *Adhatoda vasica*, *Solanum xanthocarpum*, and *Tinospora cordifolia*, exhibits a range of pharmacological effects, including anti-inflammatory, bronchodilator, antiasthmatic, and antioxidant activities. Preclinical studies have demonstrated the efficacy of these herbs in alleviating asthma symptoms, reducing eosinophilia count, stabilizing mast cells, and decreasing capillary permeability. Clinical trials have shown that AK is effective in improving lung function, promoting viral clearance, and modulating immune responses in COVID- 19 patients. **Conclusion:** The polyherbal formulation AK ingredients offer a promising therapeutic approach to managing BA, with its anti-inflammatory effects providing a holistic solution for respiratory health. Further research is needed to fully elucidate the mechanisms of action and optimal dosing regimens for AK in the management of BA.

Key words: Asthma, *Āṭātōṭai kuṭinīr*, *Cīntil, Iraippu*, siddha medicine

INTRODUCTION

Bronchial asthma (BA) is a chronic respiratory condition marked by airway hyperresponsiveness, inflammation, and mucus secretion.[1] Common symptoms include coughing, shortness of breath, and wheezing. Chest X-rays may reveal hyperinflation of the alveoli. From 2020 to 2023, the World Health Organization estimates that approximately 262 million people worldwide are affected by BA, resulting in around 455,000 deaths each year.[2] Respiratory diseases, including BA, significantly contribute to morbidity and mortality in South Asian countries. Among these, India has the highest prevalence of asthma at 6.3%.[3] The primary objective of asthma treatment and management is to attain effective control of symptoms and to mitigate the risk of future complications, including acute exacerbations. A cross-sectional study involving patients with mild asthma across eight countries indicated that 25% of these individuals exhibited uncontrolled asthma. In addition, a systematic review highlighted that patient with mild asthma experienced an average of 2.9 exacerbations annually. Moreover, it was

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reported that up to 42% of these patients made unscheduled visits to their healthcare providers due to asthma-related concerns.[4] The management of BA encompasses the use of long-acting beta-2 agonists, corticosteroids, and the avoidance of triggering factors. Inhalation therapy is extensively utilized for the management of BA as well as for conditions such as status asthmaticus. It is important to note that inhaled corticosteroids may lead to adverse effects in patients with BA, including suppression of the hypothalamic-pituitary-adrenal axis and the development of osteoporosis. Furthermore, the long-term administration of corticosteroids is associated with various side effects, including an increased risk of infections, diabetes, hypertension, and psychological disturbances.[5]

Asthma is a condition resulting from a complex interplay of genetic and environmental factors. Numerous triggers can exacerbate asthma symptoms, including allergens, air pollution, respiratory irritants, cold air, tobacco smoke, and physical exertion. The pathophysiology of asthma is characterized by inflammation and constriction of the airways, which compromises airflow and leads to significant breathing difficulties. Given the intricate interactions among genetic, physiological, and environmental components, it is essential to implement individualized treatment strategies tailored to the specific needs of each patient. Patient education serves a critical role in empowering individuals to identify and manage their specific asthma triggers. Regular monitoring, accompanied by the establishment of action plans, facilitates effective symptom tracking and allows for timely adjustments to treatment protocols. The pharmacological management of asthma typically includes bronchodilators and anti-inflammatory agents, such as inhaled corticosteroids, which aim to mitigate airway inflammation and enhance lung function. Despite the widespread use of contemporary pharmaceuticals, substantial evidence continues to support the efficacy of traditional medicine in the treatment of asthma on a global scale. Traditional medicine encompasses the medical knowledge and practices that have developed over generations before the emergence of modern scientific medicine. In general, this form of medicine involves the utilization of plant-based and herbal ingredients, which are often administered to patients as concoctions or powdered mixtures. The therapeutic potential of many of these ingredients has been validated through empirical observations and has been transmitted across generations. In many countries throughout Asia and Africa, as much as 80% of the population relies on traditional medicine as their primary source of healthcare. Traditional medicine has a rich history in the treatment of asthma and has been utilized across various cultures for centuries.[6]

The Siddha system of medicine represents an ancient medical tradition primarily practiced in southern India. Historical records indicate that the therapeutic applications of Siddha medicine have been in existence since before 4000 BCE. This system posits that the human body consists of "96 *Tattuvaṅkaḷ*" (fundamental principles), which encompass physical, physiological, psychological, and intellectual dimensions. The principal components of Siddha medical formulations comprise various herbs, minerals, and animal products. The classical literature of Siddha medicine elucidates a comprehensive classification of diseases based on their pathophysiological characteristics. Numerous traditional Siddha formulations are employed for the treatment of diverse ailments, including viral fevers, arthritis, skin disorders, and diabetes, particularly within southern India. The Siddha system of medicine plays a significant role in safeguarding individuals from diseases, including COVID-19, by offering treatments that enhance and protect the immune system. In the contemporary era, these immune-boosting therapies are particularly relevant in promoting health and resilience against infectious diseases.[7] In the Siddha system of medicine, *Kuṭinīr* represents a specific type of decoction. This aqueous extract is traditionally prepared using a 1:4 ratio of medicinal ingredients to water. However, Siddha texts also prescribe alternative ratios, such as 1:8 or 1:16, for certain preparations. The process may occasionally involve the addition of milk. Various extraction techniques are documented, including boiling and percolation methods. It is recommended to consume the preparation within 3 h of its preparation.[8] *Āṭātōṭai Kuṭinīr* (AK), a classical Siddha formulation described in Siddha literature *Guṇapāṭam mūlikai vakuppu* (Siddha Materia Medica Medicinal plants division), is indicated for the treatment of *Aiya Irumal* (severe cough with expectoration), *Kōl̲zai Kattu* (phlegm in throat and trachea), and *Aiya curam* (fever due to vitiated *Aiyam* humor- related to COVID-19).[9] Furthermore, AK is utilized in the management of BA and its associated conditions in clinical practice. This comprehensive review seeks to highlight the therapeutic potential of AK in the context of BA. The analysis encompasses scientific validation, including an examination of phytochemical components and pharmacological effects, while also incorporating perspectives from Siddha medicine.

MATERIALS AND METHODS

The literature review spanned 3 months from October 2024 to December 2024. Siddha literature and medicinal properties (including taste, potency, bioavailability, and medicinal uses) of the ingredients were extracted from traditional Siddha texts. The correlation between Siddha disease terminologies and their English counterparts was established using the World Health Organisation International Standard Terminologies on Siddha Medicine publication. The Foundation for Revitalization of Local Health Traditions - ENVIS website served as the source for scientific and vernacular nomenclature (in Tamil, Hindi, and Sanskrit), as well as information on habit, distribution, family, and utilized plant parts. Phytochemical compositions and pharmacological activities of each medicinal component were compiled from published

Siddha literature, bibliographic references, abstracts, and full-text articles from PubMed, Scopus, Web of Science, and other indexed journals and books. The search employed keywords such as BA, anti-asthmatic, bronchodilator, anti-inflammatory, *Iraippu noi*, and S*wasakasam*, among others. Data compilation, processing, and statistical analysis were performed using basic statistical methods in Microsoft Excel 2010.

Ingredients and Standard Operating Procedure of AK

Table 1 represents the ingredients of the AK. Figure 1 shows images of the ingredients used in the AK. All ingredients are to be pulverized into a coarse powder. Five grams of coarsely powdered AK should be combined with 240 mL of standard water and subsequently boiled until the total volume is reduced to one-fourth, resulting in 60 mL. The resulting decoction must then be filtered. This preparation is intended for oral administration in the morning and evening, preferably sweetened with honey.

RESULTS

In AK formulations, two ingredients have a bitter taste, while the other has a pungent taste. All ingredients associated with digestive bioavailability exhibit a pungent flavor. According to Siddha literature, all three ingredients are primarily linked to respiratory illnesses, as shown in Tables 2 and 3. The pharmacological actions of all ingredients in BA include Bronchodilatory, antiallergic, anti-asthmatic, anti-inflammatory, immuno-stimulant, and antioxidant properties. In addition, the phytoconstituents of each ingredient demonstrate potent pharmacological effects in BA, as illustrated in Table 4.

Table 1: *Āṭātōṭai Kuṭinīr* ingredients and parts used

S. No.	Name of the ingredient	Botanical name	Parts used
1	*Āṭātōṭai*	*Justicia adhatoda L*	Dried root
2	*Kaṇṭaṅkattiri*	*Solanum virginianum L.*	Dried root
3	*Cīntil*	*Tinospora cordifolia* (willd.) HOOK.F. and THOMS.	Dried stem

DISCUSSION

BA is a chronic inflammatory disorder in which mast cells, eosinophils, and T-lymphocytes play pivotal roles. These cellular components contribute significantly to airflow obstruction and airway hyper-responsiveness through their bronchodilator, anti-inflammatory, and antihistaminic properties. In the field of allergic respiratory diseases, various indigenous drugs have been effectively tested and used as conservative therapies for asthma. The focus of asthma treatment has evolved from merely relieving symptoms to achieving comprehensive disease control, which also ensures the overall well-being of the patient.[22] Polyherbal combinations are particularly noted for being well-accepted, safe, and effective in managing asthma.[23] Siddha medicine, a traditional and holistic healthcare system from India, addresses both the preventive and curative aspects of many illnesses. In Siddha medicine, BA is associated with the concept of *Iraippu*, which encompasses several treatment modalities. AK formulation contains three unique herbal ingredients that have been used for respiratory diseases for many years in Siddha medicine. All three ingredients have bronchodilator, anti-inflammatory, antihistaminic, and anti-asthmatic properties.

Preclinical Studies

Anti-asthmatic activity

An antiasthmatic and antiallergic agent functions by preventing the release of histamine and the production of additional mediators, such as leukotrienes, which are associated with anaphylaxis. This mechanism occurs through the inhibition of degranulation following exposure to antigens, thereby providing essential protection against allergic responses.[24] Pyrrolo-quinazoline compounds, such as vasicine and vasicinone, have demonstrated potential antiasthmatic activity. Certain studies suggest that the alkaloids vasicinol and vasicine can significantly inhibit allergic reactions induced by ovalbumin.[25] In addition, vasicinone has proven effective as an anti-allergen in studies conducted on mice, guinea pigs, and rats.[26] Compound 73/602 (AA), a structural analog of vasicinone, also exhibits strong antiallergic activity in these animal models.[27]

The ethanol extract of *Solanum virginianum* has antiasthmatic effects, stabilizes mast cells, and decreases

Table 2: Scientific and selected vernacular names, families of the medicinal ingredients[10]

S. No.	Name of the ingredient/ vernacular name	Sanskrit name	Hindi name	Family	Habit
1	*Āṭātōṭai*	*Vasha, Panchamukhi*	*Arusha, Vasaka*	Acanthaceae	Shrub
2	*Kaṇṭaṅkattiri*	*Kantakarika, Chudra*	*Kataikhuadda, Satyanasi*	Solanaceae	Herb
3	*Cīntil*	*Guduchi, Amritavalli*	*Adharvela, Amrta*	Menispermaceae	Climber

Table 3: Morphology, organoleptic characters, and therapeutical uses of the herbal ingredients[9]

Name of the ingredient	Taste	Potency	Digestive bio-transferring state	Therapeutical uses as per siddha medicine
Āṭātōṭai (Justicia adhatoda L)	*Kaippu* (bitter)	hot	*Kārppu*	*Curam* (fever), *Irumal* (cough), *Iḷaippu* (tuberculosis), *Iraippu* (bronchial asthma), *muppiṇi* (delirium), *Vānti* (vomiting), *kuruti aẕal nōy* (hypertension)
Kaṇṭaṅkattiri (*Solanum virginianum L.*)	*Kārppu* (pungent)	hot	*Kārppu*	*Kācam* (cough), *Iraippu* (bronchial asthma), *Iḷaippu* (tuberculosis), *Irumal* (cough), *Pīṉicam* (sinusitis)
Cīntil (*Tinospora cordifolia* [*willd.*] *HOOK.F. and THOMS.*)	*Kaippu* (bitter)	hot	*Kārppu*	*Curam* (fever), *Irumal* (cough), *Iraippu* (bronchial asthma), *Ceriyāmai* (indigestion), *Matumekam* (diabetes), *kuruti aẕal nōy* (hypertension).

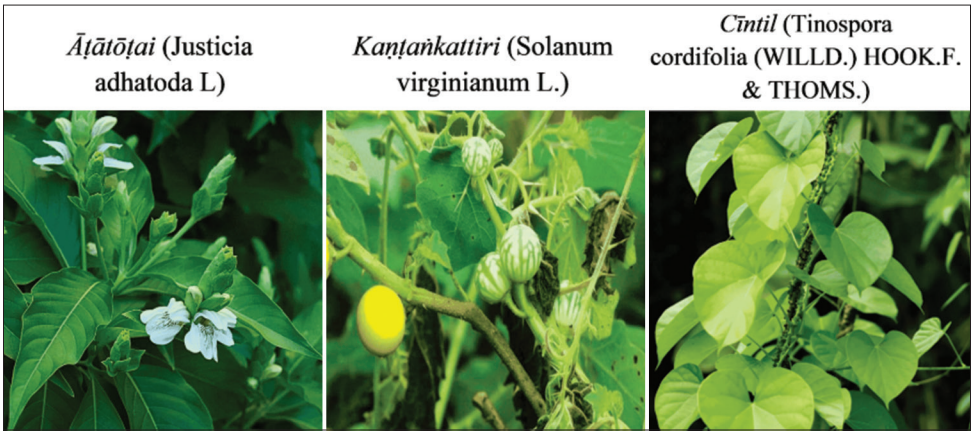

Figure 1: *Āṭātōṭai Kuṭinīr* ingredients

capillary permeability; thus, it may play a significant role in treating asthma and allergic disorders.[28] The therapeutic effects of the entire plant have been assessed by Gautam *et al*. (2008), highlighting its properties in alleviating asthma symptoms, as well as its antihistaminic and antiallergic capabilities. The study showed that the ethanolic extract from *Solanum xanthocarpum* flowers effectively blocks histamine reactions that cause constriction in goat tracheal tissue. This means that the extract has antihistamine properties by acting on H1 receptors. In addition, when given at doses of 50 and 100 mg/kg, the extract reduced eosinophilia caused by milk, and the results were statistically significant.[29]

The extract of *Tinospora cordifolia* (TC) leaves exhibits anti-asthmatic activity in rats subjected to acetylcholine and citric acid-induced asthma.[30] The aqueous extract of TC stem has shown significant efficacy against mast cell-mediated allergic reactions. It effectively inhibits cutaneous anaphylaxis triggered by histamine in rat models and blocks histamine-induced contractions in the guinea pig ileum. In addition, this extract reduces tumor necrosis factor-alpha (TNF-α) secretion in immunoglobulin E -stimulated rat mast cells and lowers calcium levels inside activated mast cells. These results suggest that TC could be a useful treatment for both acute and chronic allergic disorders.[31]

Bronchodilator activity

Both *in vivo* and *in vitro* investigations have demonstrated that vasicine and vasicinone exhibit significant bronchodilatory activity.[32] The bronchodilating effects of the ethanolic extract of *Adhatoda vasica* (AV) were assessed through experiments involving histamine aerosol and acetylcholine-induced bronchoconstriction in guinea pigs. The findings indicated that the bronchodilatory effects of AV are comparable to those of ketotifen.[33] Vasicinone has shown promising bronchodilator activities[34] and vasicine showed bronchodilatory activity both *in vitro* and *in vivo* studies.[35]

S. xanthocarpum has been identified to possess bronchodilator activity attributed to the presence of solasodine. The results indicate that this compound exerts a bronchodilator effect, likely functioning as a histamine antagonist and potentially inhibiting the H1 receptors located on bronchial smooth muscle.[36] The ethanolic extract of *S. xanthocarpum* Schrad and Wendl exhibits a bronchodilator effect, effectively reduces bronchial mucosal edema, and diminishes secretions within the airway lumen.[37]

The bronchodilator effects of an aqueous extract from the TC stem were evaluated in several experiments: its impact on bronchospasm induced by histamine in guinea pigs, capillary permeability in mice, and mast cell disruption in rats. The results showed that the extract significantly decreased

Table 4: Phytochemicals compositions and pharmacological actions of the ingredients

Name of the ingredient	Pharmacological activity	Pharmacological actions in BA	Phytochemicals	Pharmacological actions of phytochemicals
Āṭāṭōṭai (*Justicia adhatoda L*)	Bronchodilatory, Antiallergic, Antiviral, anti-asthmatic, Anti-tubercular, Anti-inflammatory, Immuno-stimulant, Wound-healing, Antimicrobial, Abortifacient, Hepatoprotective, Antitussive, ACE inhibitory, Analgesic, Anti-typhoid, Anticancer, Anti pyorrhoeal activity[11]	Bronchodilatory, Antiallergic, anti-asthmatic, Anti-inflammatory, Immuno-stimulant, Antiviral	Alkaloids: Vasicine, Vasicol, Vasicinone, Vasicinol, Adhatodine, Adhatonine, Deoxyvasicine, 9-acetamido-3,4-di-hydropyrido-(3,4-b)- indole, Deoxyvasicinone. Flavonoids: Kaempferol, Astragalin, Apigenin, Luteolin, Rhamnosylvitexin, Violanthin, Anthocyanin. Phenolic acids: 3,4-dihydroxy benzoic acid, p-coumaric acid, 4-hydroxybenzoic acid, Syringic acid. Steroids: Sitosterol, Daucosterol, Epitaraxerol Terpenoids: Neoandrographolide, β-carotene. Glycosides: β-sitosterol-d-glucoside, β-glucoside-galactose, Sitosterol-β-d-glucoside. Organic acids: Adhatodic acid, Stictic acid[12]	Vasicine and vasicinone have bronchodilatory activity and antioxidant properties. Bromhexine, a derivative of vasicine, has demonstrated mucus-liquefying and expectorant effects. Vasicine also exhibits antimicrobial and anti-allergic activities. Kaempferol possesses a wide range of beneficial effects, including antioxidant, anti-microbial, anti-carcinogenic, anti-inflammatory, analgesic, antibacterial, anthelmintic, and antiallergic properties. Additionally, apigenin, luteolin, and syringic acid also exhibit antioxidant, anti-microbial, cardioprotective, anti-inflammatory, and anticancer properties. Furthermore, p-coumaric acid, 4-hydroxybenzoic acid and 3,4-dihydroxybenzoic acid are known for their antioxidant activity. Notably, 3,4-dihydroxybenzoic acid has additional properties, including anti-inflammatory, antiproliferative, anti-microbial, and anti-angiogenic effects. Both sitosterol and β-sitosterol demonstrate anti-inflammatory, antimicrobial, anti-atherosclerotic, and cardioprotective effects. Daucosterol has more potential pharmacological properties, such as anti-inflammatory, antidiabetic, antioxidant, neuroprotective and anti-cancer effects. Lastly, β-carotene is recognized for its antioxidant, anti-inflammatory, anti-microbial, hepatoprotective, antidiabetic, and anti-carcinogenic effects. β-sitosterol-d-glucoside also offers analgesic, cardiotonic, anti-inflammatory, anti-microbial, antiviral, and anti-carcinogenic properties. Adhatodic acid has antioxidant properties.[12]
Kaṇṭaṅkattiri (*Solanum virginianum L.*)	Anti-asthmatic, anti-inflammatory, hepatoprotective, cardio-protective, bronchodilator, antidiabetic,[13] Analgesic, Anti-inflammatory, Antidiabetic, Antiulcer, Wound healing, Diuretic, Anti-hyperlipidaemic activity,[14] anti-tubercular activity[15]	Anti-asthmatic, anti-inflammatory, bronchodilator	Alkaloids: α- Solamargine, Tomatidenl, Carpesterol, Solanine, Solasurine, Salanidine, Solasodine Flavonoids: Apigenin Phenolic acids: Coumarin, Caffeic acid, Methyl caffeate, Scopoletin, lupeol Steroids: β-sitosterol, stigmasterol , Campesterol, Cycloartanol, Norcarpesterol, Sitosterol Glycosides: Solanacarpine, Galactose β-sitosterol[16] Volatile oils: Solavetivone, palmitic acid, linoleic acid (8.2%)[17]	Solasodine has antipyretic effects. Lupeol, apigenin, and solamargine have anticancer properties. Solamargine also has antifungal properties. Apigenin possesses antiallergic and antiasthmatic activities. Stigmasterol and carpesterol exhibit anti-inflammatory activities.[16]

(*Contd...*)

Table 4: *(Continued)*

Name of the ingredient	Pharmacological activity	Pharmacological actions in BA	Phytochemicals	Pharmacological actions of phytochemicals
Cīntil (Tinospora cordifolia [Willd.] HOOK.F. and THOMS.)	antipyretic, anti-allergic, antispasmodic, anti-leprotic, immuno-modulatory, anti-inflammatory, hepato-protective, anti-arthritic, anti-stress, antimalarial, anti-diabetic, antioxidant activities[18]	antispasmodic, immuno-modulatory, anti-inflammatory, antioxidant, anti-allergic	Alkaloids: Tinosporine, Choline, Magnoflorine, Jatrorrhizine, Berberine, 1,2-Substituted pyrrolidine, tembeterine, palmatine.-Terpenoids: Tinosporide, Tinosporaside, Furanolactone Furanolactone, diterpene, ecdysterone makisterone, furanoid diterpene, and several glucosides isolated as poly acetate, disaccharides phenylpropene cordifolioside A, B and C, cordifoliside D and E, Tinocordioside, tinocordifolioside, tinocordifolin, cordioside. Steroids: Giloinsterol, β-Sitosterol, 20a- Hydroxyecdysone. Lignans: 3 (a, 4-dihydroxy-3- methoxybenzyl)-4 -(4-hydroxy-3-methoxybenzyl) Others: Giloin, Heptacosanol, sinapic acid, Tinosporan acetate, Tinosporidine, Octacosanol, Tinosporal acetate, Tinosponone, two phytoecdysones an immunologically active arabinogalactan[19]	Choline, palmatine, tetrahydropalmatine, and magnoflorine have antioxidant properties. Palmatine, jatrorrhizine, and magnoflorine exhibit hypoglycaemic activities. Tinosporin has antiviral properties. Magnoflorine, N-methyl-2-pyrrolidone, cordial, cordioside, cordifolioside, tinocordiside, and syringin possess immunomodulatory properties.[20] Sesquiterpenoids and Tinocordifolin exhibit antiseptic activity, along with choline, berberine, jatrorrhizine, magnoflorine, isocolumbin, tinosporin, palmetine, aporphine alkaloids, and tetrahydropalmatine, which demonstrate anti-cancer, anti-inflammatory, anti-diabetic, anti-viral, and immunomodulatory effects[21]

bronchospasm caused by a 5% histamine aerosol, reduced capillary permeability, and lowered the number of disrupted mast cells.[38]

Anti-inflammatory activity

Phytochemicals from *Justicia adhatoda*, such as vasicinone, vasicine, and vasicine acetate, exhibit anti-inflammatory properties. The anti-inflammatory effects were assessed using carrageenan and Complete Freund's Adjuvant (CFA)-induced paw edema models. Vasicine showed the strongest anti-inflammatory effect, with a 59.51% inhibition at a dose of 20.0 mg/kg, while vasicinone demonstrated a maximum inhibition of 63.94% at 10.0 mg/kg after 4 days of CFA injection.[39] Vasicine is a pyrroloquinazoline alkaloid that can be found in concentrations reaching up to 12% within the alkaloid fraction of AV. This significant presence underscores its potential as a therapeutic agent for the treatment of various inflammation-mediated diseases.[40]

A hydroalcoholic extract of *S. xanthocarpum* has demonstrated significant anti-inflammatory properties.[41] In addition, the potential anti-inflammatory activity of compounds derived from *S. virginianum* was assessed using the RAW264 cell inflammation model, which is induced by lipopolysaccharide.[42]

The study by Niraj *et al*. demonstrated that the extract of TC inhibited the gene expression of inflammatory cytokines, including TNF-α and Interleukin-1 beta, and reduced nitric oxide production in RAW 264.7 cells.[43] Pilip *et al*. conducted a study on the chloroform extract of TC, which demonstrated significant anti-inflammatory properties and a statistically significant decrease in paw edema ($P \leq 0.05$). High-performance liquid chromatography characterization revealed the presence of stigmasterol and β-sitosterol.[44] The extract also showed significant anti-inflammatory effects in the carrageenan-induced inflammation test using an albino mouse model.[45]

Molecular Docking Analysis

The formulation *Aadathodai Kudineer Chooranam* encompasses a range of phytoconstituents, including adhatodine, tinosporide, anisotine, vasicoline, diosgenin, berberine, apigenin, lupeol, and vasicinone. These compounds demonstrate significant binding affinities to target proteins, indicating their potential to inhibit the ACE-2 receptor, thereby disrupting the host-viral interface. Furthermore, they may effectively inhibit the 3CL pro enzyme, which is critical for the production of non-structural proteins (nsp1-nsp16) that are essential for viral replication. Consequently, this formulation may assist in preventing viral survival within the host environment. Additionally, the compounds present in this formulation exhibit high binding affinities toward the C3-like protease and the angiotensin-converting enzyme-2 receptor spike protein associated with COVID-19.[46]

Clinical Studies

Verma *et al*. conducted a randomized open-label three-armed study involving a total of one hundred and fifty COVID-19-positive patients exhibiting mild to asymptomatic, with ages ranging from 19 to 65 years. Among the participants, 136 completed the study and presented negative reverse transcription polymerase chain reaction results. The study participants were randomly assigned to receive herbal treatments orally over a period of 14 days: Group A received AV at a dosage of 500 mg (n = 50), Group B received TC at a dosage of 500 mg (n = 43), and Group C received a combination of AV and TC at 250 mg each (n = 43). All patients across the three treatment groups successfully recovered from COVID-19, and none reported adverse effects associated with the herbal interventions. Importantly, patients in Group C, who received the combination of AV and TC, experienced a more rapid viral clearance in comparison to the other groups. The findings of this study present the first clinical evidence of AV herbal extract functioning as a modifier of hypoxia-inducible factor 1-alpha in COVID-19 patients. Additionally, a reduction in the levels of ferritin, vascular endothelial growth factor, and prothrombin time/international normalized ratio–markers associated with hypoxia, inflammation, and thrombosis–was observed, highlighting the extract's potential utility in later stages of the disease. Conversely, the TC group exhibited significant immunomodulatory effects.[47]

A pilot study looked at how effective and safe a single dose of certain herbs is for people with mild to moderate BA. Researchers measured lung function using a spirometer before and 2 h after participants took 300 mg of powdered whole plants of either *S. xanthocarpum* or *S. trilobatum*. They compared these results with standard bronchodilator drugs, salbutamol (4 mg) and deriphyllin (200 mg). The results showed that treatment with either herb significantly improved lung function in people with asthma.[48]

Preclinical studies have provided substantial evidence that all three ingredients exhibit significant anti-asthmatic, bronchodilator, anti-inflammatory, and antioxidant properties. These findings suggest that the compounds can effectively alleviate asthma symptoms and improve respiratory function. Furthermore, the specific phytoconstituents within these ingredients have been shown to target BA, indicating a potential mechanism of action that warrants further exploration. Clinical research corroborates these preclinical findings, demonstrating that these ingredients are not only effective but also highly beneficial in the management of BA. This suggests that they could play a crucial role in therapeutic strategies aimed at improving patient outcomes in asthma management.

In the context of *Iraippu*, the disruption of the Aiyam humor adversely affects the vali, while the azhal humor serves as a significant etiological factor in the disease's progression. This relationship ultimately results in *Iraippu* and its associated complications.[49]

The diagnosis and treatment methods in the Siddha system of medicine are based on fundamental principles such as Mukkurram (three humors), Cuvai (taste), Vīriyam (potency), Vipākam (post-digestive biotransformation), and Ceykai (drug action), which are crucial for assessing the prognosis of a disease. To balance the elevated Aiyam humor, herbs with bitter (Kaippu), astringent (Tuv ar ppu), and pungent (Kārppu) tastes are emphasized in Siddha literature. Bitter tastes, which comprise Vāyu (air) and Ākāyam (space), increase the Vali humor and decrease both Alal and Aiyam. They purify the body and dry out all secretions. Bitters also help regulate Aiyam due to their pungent Vipākam. Astringent tastes, made primarily of Vāyu (air) and Pirutivi (earth), also increase the Vali humor while decreasing Alal and Aiyam. In addition, they function as blood purifiers. Pungent tastes, composed of Tēyu (fire) and Vāyu (air), increase both Alal and Vali while decreasing Aiyam. They act as appetizers and cardiac tonics and stimulate all secretions in the body.[50]

The ingredients of AK possess a bitter and pungent taste, characterized by a hot potency that transforms into a more pronounced pungency during post-digestive biotransformation. This formulation is effective in mitigating the vitiated aiyam humor and alleviating the clinical manifestations of BA along with its associated complications.

CONCLUSION

The use of polyherbal combinations in Siddha medicine for managing BA through anti-inflammatory mechanisms shows promising results both in preclinical and clinical studies. The polyherbal formulation AK, containing AV, *S. xanthocarpum and* TC exhibits anti-asthmatic, Bronchodilator, and anti-inflammatory properties. These herbs have been shown to inhibit histamine release, reduce eosinophil count, stabilize mast cells, and decrease capillary permeability, all of which are crucial in managing asthma symptoms. Furthermore, the molecular docking analysis of the phytoconstituents in these herbs suggests that they have significant binding affinities to target proteins involved in asthma and may function as potent inhibitors of viral replication and inflammation, which is particularly relevant in the context of COVID-19. Clinical studies have demonstrated the efficacy and safety of these polyherbal combinations in improving lung functions and promoting viral clearance in COVID-19 patients. The combinations of AV and TC were found to be more effective in accelerating recovery and modulating immune responses in COVID-19.

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