RESEARCH PAPER

Phytopharmacological Potential of *Carica papaya* in the Management of Acute Respiratory Distress Syndrome

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Abstract
Background: Carica papaya has been traditionally used in various systems of medicine for its wide range of therapeutic properties. Its bioactive compounds have attracted attention for their potential role in inflammatory and oxidative stress-related conditions, including respiratory disorders such as Acute Respiratory Distress Syndrome (ARDS).
Objective: This review aims to systematically evaluate the phytochemical composition, pharmacological activities, and therapeutic potential of *Carica papaya*, with particular emphasis on its relevance in inflammatory respiratory conditions like ARDS.
Methods:A narrative review of literature was conducted using electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar. Articles related to phytochemistry, pharmacological effects, traditional uses, and experimental studies of *Carica papaya* were selected and analyzed.
Results:*Carica papaya* is rich in bioactive constituents such as flavonoids, phenolic compounds, alkaloids, vitamins, and enzymes like papain and chymopapain. These compounds exhibit significant anti-inflammatory, antioxidant, immunomodulatory, and tissue-protective effects. Evidence from experimental studies suggests that these properties may help attenuate cytokine-mediated inflammation, oxidative lung injury, and immune dysregulation associated with ARDS.
Conclusion: The findings highlight *Carica papaya* as a promising natural agent with potential applications in managing inflammatory and oxidative stress-related respiratory disorders. However, there is a need for well-designed clinical trials to validate its efficacy and safety in ARDS and related conditions.

Keywords: Carica papaya; phytochemistry; anti-inflammatory; antioxidant; ARDS
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Introduction

Acute Respiratory Distress Syndrome is an onset of respiratory failure characterized by hypoxaemia with bilateral lung opacities on chest imaging, not fully explained by cardiac failure or fluid overload. WHO describes Acute Respiratory Distress Syndrome as a condition that develops within one week of a known clinical insult or worsening respiratory symptoms, with bilateral infiltrates on imaging and impaired oxygenation [1]. Globally, ARDS ranges from 1.5 to 75 cases per 100,000 population per year, depending on diagnostic criteria and region. It accounts for about 10% of all ICU admissions and 24% of patients requiring mechanical ventilation [2]. Epidemiological data on Acute Respiratory Distress Syndrome (ARDS) in India remain limited, as most available information is derived from hospital-based studies rather than large population-based surveillance. According to Indian ARDS clinical guidelines, the true national incidence of ARDS is still uncertain due to the lack of comprehensive epidemiological research. However, studies conducted in tertiary care hospitals in India report mortality rates ranging from 33% to 56%. The common underlying causes include pneumonia, sepsis, and tropical infections such as malaria and scrub typhus [3]. Studies from South India suggest that ARDS accounts for approximately 7–8% of pediatric ICU admissions and around 6% of adult autopsy cases in tertiary hospitals, highlighting the burden of ARDS in the region [4].

Acute Respiratory Distress Syndrome (ARDS) develops as a result of either direct injury to the lungs or indirect systemic conditions that damage the alveoli and surrounding capillaries, leading to inflammation, increased permeability, and accumulation of fluid within the alveolar spaces. This process interferes with normal gas exchange and results in severe respiratory distress [2]. The causes of ARDS in adults and children are generally similar, although their frequency may vary between age groups. Direct pulmonary causes include conditions that directly injure lung tissue, such as severe pneumonia caused by bacterial, viral, or fungal infections, aspiration of gastric contents into the lungs, inhalation of smoke, toxic gases, or chemical fumes, pulmonary contusion due to chest trauma, and near-drowning events. Severe viral infections, including influenza and COVID-19, are also important triggers. In children, viral respiratory infections such as Respiratory Syncytial Virus Infection and influenza are particularly common precipitating factors. In addition to direct lung injury, ARDS may arise from indirect systemic

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conditions that initiate widespread inflammatory responses affecting the lungs. These include sepsis, which is the most frequent cause in adults, septic shock, major trauma or multiple injuries, severe burns, acute pancreatitis, massive blood transfusion or transfusion-related acute lung injury, cardiopulmonary bypass surgery, and severe head injury or shock. Such systemic conditions stimulate the release of inflammatory mediators that increase the permeability of the alveolar–capillary membrane, resulting in pulmonary edema and the development of ARDS [5,6].

The overall mortality rate of ARDS is approximately 30–50% among affected patients. A large systematic review and meta-analysis involving 24,158 patients reported a pooled mortality rate of 39.4%. Mortality varies according to severity of ARDS (Berlin definition): Mild ~27% mortality, Moderate ~32% mortality, Severe ~45% mortality [7,8].

Management of Acute Respiratory Distress Syndrome (ARDS) primarily involves supportive care, lung-protective mechanical ventilation. It involves several supportive and advanced therapeutic strategies aimed at improving oxygenation and preventing further lung injury. Higher levels of Positive End-Expiratory Pressure (PEEP) are commonly applied in patients with moderate to severe ARDS to improve oxygenation and prevent alveolar collapse. Most patients require management in an intensive care unit (ICU), requiring neuromuscular blocking, corticosteroids. In cases where severe hypoxemia persists despite optimal mechanical ventilation, venovenous extracorporeal membrane oxygenation (VV-ECMO) may be considered as a rescue therapy [2,9]. Supportive measures such as chest physiotherapy, early mobilization when feasible, and pulmonary rehabilitation are important in preventing complications like muscle weakness and prolonged ventilator dependence. Furthermore, adequate enteral nutritional support plays a crucial role in maintaining metabolic balance, supporting immune function, and aiding recovery in critically ill patients with ARDS [9,10].

Homeopathy is defined as the therapeutic system that uses highly diluted substances which, in larger amounts in healthy individuals, would produce symptoms similar to those of the disease being treated. The key principles are Law of Similars, Minimum Dose, and Individualization [11]. There is no single specific remedy for ARDS in Homeopathy, but several remedies are used to manage symptoms such as severe breathlessness, inflammation of lungs, anxiety, and respiratory failure as complementary therapy along with conventional treatment. ARDS is a life-threatening medical emergency characterized by severe lung inflammation and respiratory failure, requiring ICU management, oxygen therapy, and mechanical ventilation. Homeopathy may be used as a complementary therapy, not as a replacement for conventional critical care treatment [12]. Commonly indicated remedies include Arsenicum album, Antimonium tartaricum, Bryonia alba, Phosphorus, Carbo vegetabilis, and Ipecacuanha, selected based on the totality of symptoms [13].

Carica papaya is used in traditional medicine and homeopathic preparations for its anti-inflammatory, antioxidant, and immunomodulatory properties. These pharmacological actions may provide supportive benefits in inflammatory lung conditions, including Acute Respiratory Distress Syndrome. However, it is considered adjunct or complementary therapy, not a replacement for conventional intensive care [14]. Bioactive compounds present in papaya leaves have been shown in experimental studies to possess notable anti-inflammatory properties. Research indicates that papaya leaf extracts can suppress important inflammatory mediators such as nitric oxide, COX-2 enzymes, and pro-inflammatory cytokines including IL-1β, IL-6, and TNF-α, all of which contribute to inflammatory damage in lung tissues [15]. Animal studies have demonstrated that these extracts can significantly reduce inflammatory responses, suggesting a possible role in managing inflammatory conditions. In addition, papaya leaves are rich in phytochemicals such as polyphenols, flavonoids, and saponins that provide strong antioxidant effects [16]. These compounds help neutralize free radicals and reduce oxidative stress, which is known to play a major role in lung injury associated with ARDS. Experimental findings also suggest that papaya leaf extract may regulate immune responses through pathways involving TLR-7 and TLR-9 while lowering the expression of inflammatory enzymes like COX-2. Such immunomodulatory effects may help control excessive immune reactions, including the cytokine storm observed in severe respiratory infections [15,16].

MATERIALS AND METHODOLOGY

This review article was prepared using a thorough and structured search of the literature, with a focus on the role of Carica papaya in managing acute respiratory conditions, especially Acute Respiratory Distress Syndrome (ARDS), from a homoeopathic perspective.

Table 1: Literature review on relevant research publications on Carica papaya

S.No	Author / Country / Year	Title	Aim	Conclusion	Reference
1	Haider U et al., Pakistan, 2025	Immune modulatory potential of *Carica papaya*	To evaluate anti-inflammatory effect of papaya in lung injury model	Papaya showed significant reduction in inflammatory pathways (NF-κB, MAPK), suggesting	[17]

		against acute lung injury		potential role in ARDS-like conditions	
2	Kumarasinghe HS et al., Korea, 2024	Bioactive constituents of *Carica papaya*	To review pharmacological properties of papaya	Rich in flavonoids, phenolics, and antioxidants with anti-inflammatory and immunomodulatory effects	[18]
3	Akanda MKM et al., Bangladesh, 2025	*Carica papaya* in health and disease	To analyze anti-inflammatory and therapeutic potential	Demonstrates strong anti-inflammatory and antioxidant activities useful in systemic inflammatory diseases	[19]
4	Sharma A et al., India, 2022	*Carica papaya* leaves: antioxidant bioactives	To review medicinal uses of papaya leaves	Widely used in traditional medicine; shows antioxidant and immune-supportive effects	[20]
5	Masooma et al., 2024	Papaya in viral infections	To assess antiviral potential	Papaya exhibits antiviral and immune-enhancing effects; may help in viral-induced lung injury	[21]
6	Srikanth BK et al., India, 2019	Papaya leaf extract in dengue	To evaluate clinical efficacy in thrombocytopenia	Demonstrated safety and efficacy in increasing platelet count	[22]
7	WHO / Global studies	ARDS management guidelines	To standardize ARDS treatment	Emphasizes ventilatory support, corticosteroids, and supportive care	[23]
8	Bellavite P et al., Italy	Homeopathy in respiratory diseases	To evaluate role of homeopathy	Some evidence for symptom relief, but limited high-quality trials in ARDS	[24]
9	Mathie RT et al., UK	Homeopathic treatment review	To assess effectiveness of homeopathy	Individualized homeopathy shows benefit in respiratory conditions, but evidence is low certainty	[25]
10	Fan E et al., USA	ARDS clinical review	To evaluate treatment strategies	ARDS requires evidence-based ICU care; herbal therapies need further validation	[26]
11	Traditional medicine reports (India)	Herbal use in lung disorders	To document plant-based therapies	Papaya and other herbs used for inflammation and immunity boosting	[27]
12	Siddha/Ayurveda sources	Polyherbal formulations for respiratory disease	To explore herbal combinations	Herbs with anti-inflammatory action may support ARDS management adjunctively	[28]

Data Sources and Search Strategy

A wide range of sources was explored, including both classical homoeopathic texts and contemporary scientific databases. Standard homoeopathic Materia Medica and repertories were consulted to understand the drug profile, preparation, and therapeutic uses of Carica papaya. Electronic databases such as PubMed, Scopus, Embase, Elsevier, and the Cochrane Library were systematically searched to identify relevant peer-reviewed studies. The keywords and combinations were used Carica papaya, Homeopathy, Acute respiratory distress syndrome, Respiratory disease, Lung disease, Oxygen saturation, Herbal and complementary medicine in ARDS.

Inclusion and Exclusion Criteria

Inclusion Criteria:

Studies related to Carica papaya in homoeopathy or herbal medicine

Research articles addressing respiratory diseases, especially ARDS

Experimental, clinical, and review studies published in English

Exclusion Criteria:
Irrelevant studies not related to respiratory conditions
Articles lacking scientific or clinical relevance
Duplicate publications
Data Extraction and Analysis
The collected information was critically analyzed and synthesized to identify the potential role and target actions of Carica papaya in managing ARDS and other acute respiratory diseases.

Study Drug Evaluation
The homoeopathic preparation of Carica papaya, including its source, method of potentization, and therapeutic indications, was reviewed. Its target actions on respiratory pathology—such as inflammation, oxidative stress, and immune modulation—were explored based on available literature.

Preparation
Mother Tincture (1/10 strength): 100 g moist magma + 400 ml plant moisture + 635 ml strong alcohol → 1000 ml tincture.
Potencies: 2x prepared with Mother Tincture, water, and alcohol; higher potencies use
dispensing alcohol.
Clinical Indication: Abortion; dyspepsia; hepatomegaly; splenomegaly; uterine disorders;
jaundice. An efficacious remedy helping digestion in very weak patients.
Abdomen: Enlarged liver and spleen with fever, dyspepsia, indigestion and weakness. Pain in
the hepatic region; complications of liver; jaundice, conjunctiva yellow, tongue coated white,
intolerance of milk, even a small quantity causes indigestion and pain in the hepatic region.
Stool: Lienteric in small quantity passed several times a day.
Female: It aids menstrual discharge; helps uterine contraction and induces abortion when
locally applied to the mouth of the uterus.

Table.2 Therapeutic activities of the major phytoconstituent of carica papaya

S.No	Plant Part	Major Phytochemicals	Therapeutical Activity	Reference
1	Leaves	Flavonoids, Alkaloids, Tannins, Saponins	Antioxidant, anti-inflammatory, antimicrobial; reduces oxidative stress and lung inflammation	[14], [29]
2	Fruit (Unripe & Ripe)	Papain, Chymopapain, β-carotene, Lycopene	Digestive, antioxidant, anti-inflammatory; protects lung tissue and reduces inflammatory mediators	[14], [30]
3	Seeds	Benzyl isothiocyanate, Fatty acids	Anthelmintic, antimicrobial; anti-inflammatory and may reduce cytokine activity	[31]
4	Latex	Papain, Chymopapain	Wound healing, digestive; anti-inflammatory effect in lung injury	[14]
5	Roots	Glycosides, Alkaloids	Antimicrobial; possible anti-inflammatory role in respiratory conditions	[32]

Discussion

Homoeopathic Approach in the Management of Acute Respiratory Distress Syndrome

Management of Acute Respiratory Distress Syndrome in homoeopathy is based on the fundamental principle of the "law of similars," as proposed by Samuel Hahnemann, which states that a substance capable of producing symptoms in a healthy individual can be used to treat similar symptoms in disease conditions. Homoeopathy employs highly diluted remedies that are considered potent in stimulating the body's self-healing mechanisms [33]. Furthermore, homoeopathy emphasizes an individualized approach, focusing on the totality of symptoms, including physical, emotional, and mental aspects of the patient [34]. In ARDS, homoeopathic management remains largely supportive, aiming to reduce inflammation, improve respiratory function, and enhance immune response [2,6].

Role of Carica papaya in Homoeopathic Indications (Classical Perspective)

Carica papaya is regarded as a minor clinical remedy in homoeopathy and is commonly used as a supportive medicine in conditions associated with respiratory distress due to infections, general weakness following illness, and digestive or hepatic dysfunction. Its primary sphere of action is on the digestive system, liver, and immune modulation, which may indirectly contribute to respiratory recovery [35].

Phytoconstituents of Carica papaya

Carica papaya contains a wide range of bioactive constituents, including enzymes such as papain and chymopapain; alkaloids like carpaine and pseudocarpaine; flavonoids and phenolic compounds; carotenoids such as beta-cryptoxanthin; and organic acids including gallic acid and ferulic acid. These constituents contribute to its diverse pharmacological properties [14,30].

Relevance of Phytoconstituents in Acute Respiratory Distress

The bioactive components of Carica papaya play a significant role in inflammatory and oxidative pathways relevant to ARDS. Enzymes such as papain and chymopapain exhibit notable anti-inflammatory effects, while alkaloids like carpaine further contribute to the reduction of inflammation. Carotenoids, particularly beta-cryptoxanthin, support respiratory health through antioxidant mechanisms. Additionally, phenolic compounds such as gallic acid and ferulic acid enhance immune response and reduce oxidative stress, which is a key factor in the pathogenesis of ARDS [14,30].

Target Symptomatology Based on Materia Medica

From a homoeopathic materia medica perspective, Carica papaya is indicated in respiratory conditions characterized by asthmatic breathing with sudden, spasmodic cough, cough worsening at night, easy expectoration, and associated chest symptoms such as heaviness, radiating pain, and a sensation of tired lungs. Hoarseness of voice in the evening, along with fever and anxiety, are also noted indications [35].

Therapeutic Implications in ARDS

ARDS is a severe inflammatory condition marked by alveolar damage, cytokine storm, and oxidative stress, with conventional management primarily focusing on supportive care such as oxygen therapy and mechanical ventilation [2,6]. Homoeopathy offers a holistic and individualized approach addressing both respiratory and systemic manifestations. In this context, Carica papaya, although a minor remedy, demonstrates potential supportive benefits due to its combined phytochemical, anti-inflammatory, antioxidant, and immunomodulatory properties. The presence of enzymes such as papain and chymopapain may aid in reducing pulmonary inflammation, while antioxidants like carotenoids and phenolic compounds help mitigate oxidative damage, thereby potentially reducing the severity and complications of ARDS [14,30].

Limitations and Future Scope

Despite these promising properties, the role of Carica papaya in ARDS remains adjunctive. There is limited clinical evidence specifically evaluating its efficacy in ARDS management. Therefore, further well-designed clinical trials are necessary to validate its therapeutic potential and establish its role in evidence-based practice [2,36].

Conclusion

Acute Respiratory Distress Syndrome (ARDS) is a critical inflammatory condition associated with oxidative stress and respiratory failure. Homoeopathic management, based on the law of similars and individualized treatment, provides a supportive approach targeting the overall symptom complex.

Carica papaya, though a minor remedy, exhibits potential relevance in ARDS due to its anti-inflammatory, antioxidant, and immunomodulatory properties attributed to its phytoconstituents such as papain, chymopapain, alkaloids, and phenolic compounds. Its correspondence with symptoms like spasmodic cough, chest discomfort, and respiratory weakness further supports its clinical applicability in selected cases.

However, the current evidence is largely theoretical and based on traditional and pharmacological insights. Further clinical studies are required to validate its efficacy in ARDS. Thus, *Carica papaya* may be considered a supportive adjunct within an individualized homoeopathic treatment framework.

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