


**Review Article**
**THE ROLE OF AIRWAY MUCUS HYPER SECRETION DUE TO KAPHA VITIATION IN TAMAKA SVASA (ASTHMA): PATHOPHYSIOLOGY AND PHARMACOTHERAPEUTIC APPROACH**
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**ABSTRACT**

*Tamakasvasa* (asthma) is a mucous hypersecretory respiratory disease. The inspissated mucus produced by vitiated *Kapha* obstructs the bronchi and other small air passages in the pathological development of the disease. Physiologically *Kapha dosa* provides strength (*Bala*) to the body due to the intrinsic qualities unctuousness (*Snigda*), coldness (*Sita*), heaviness (*Guru*), slowness (*Manda*), smoothness (*Slasna*), softness (*Mrisna*), stability (*Sthira*) etc. Being an organ in the specific site of *Kapha dosha* i.e., thorax (*Uras*), production of mucus in lungs is normal. Etiological factors that irritate respiratory tract stimulate inflammatory process and due to this, mucus is produced in excess. Due to the excessive vitiation of qualities of *Kapha* the mucus turns highly viscous and the normal clearance of mucus by airflow and ciliary function is hampered. Thus gelatinous mucus plugs tend to develop in the airways. The gel-forming MUC genes MUC2, MUC5AC and MUC5B commonly seen in respiratory secretions and stomach, duodenum, gall bladder etc have major role in the formation of airway mucus. Due to the ingestion of unwholesome food stomach (*Amasaya*) where *Kapha* reside, act as the organ of origin of the disease. The main pharmacotherapeutic objective in the management of *Tamakasvasa* is reduction of airway obstruction and airflow limitation by enhancing mucus clearance. This can be achieved by altering the rheological properties of bronchial mucus and inhibition of mucus hyper secretion and airway hyper responsiveness by procedure based therapies and pharmacological methods of *Sleshmavilayana*, *Srotomardavakarana* and rationale use of taste specific drug therapy (*Rasapravicarana chikitsa*).

**KEYWORDS:** Airway mucus hyper secretion, *Tamaka svasa*, Asthma, *Rasapravicarana chikitsa*.

**INTRODUCTION**

Airway diseases appear a major group of lung disease that affect hundreds of millions of people all over the world. The main risk factors include tobacco smoking, indoor and outdoor air pollution, occupational chemicals and dusts, allergens and vulnerability. All types of airway diseases (*Svasarogas*) are caused by the simultaneous aggravation of *Vata* and *Kapha doshas*.<sup>[1]</sup> Respiratory system (*Pranavaha srothas*) is involved in the manifestation of these group of diseases and hence *Svasaroga* is considered as a dreadful disease.<sup>[2,3]</sup> Apart from the other four *Svasarogas* - *Kshudra*, *Chinna*, *Maha* and *Urdha*, *Tamaka svasa* (asthma) is caused predominantly due to the abundance of *Kapha dosha*.<sup>[4,5]</sup> Asthma is an exaggerated bronchoconstrictor response to stimuli that have little or no effect in normal subjects. The tracheobronchial tree shows increased responsiveness to both immunological and non-immunological stimuli. In pathological development of asthma, lesion is seen in the bronchi and other small air passages due to obstruction with inspissated mucus. Bronchial obstruction leads to bronchial muscle spasm, mucosal oedema and thick secretions. Asthma is clinically characterized by paroxysms of dyspnea, expiratory wheeze and productive cough. The disease is episodic in nature, with exacerbations and remissions.

**PHYSIOLOGY OF KAPHA DOSHA**

*Doshas* -*Vata*, *Pitta* and *Kapha* are the bio regulatory principles in the body and it is with these

*Doshas* body (*Sareera*) survive. When they are balanced (*Samya*) with their normal functions, it is conducive to the preservation of health (*Arogata*). Disease (*Roga*) is nothing but the derangement (*Vaisamyam*) of their regular functions.<sup>[6]</sup> The non vitiated *Doshas* perform the functions situating in the lower, middle and upper part and preserve the body.<sup>[7]</sup> Wholesome (*Hita*) food (*Ahara*) and customary practices (*Vihara*) are the factors that maintain the balancing of *Doshas*.

The specific site of *Kapha dosha* in the body is thorax (*Uras*). Other sites include throat (*Kantha*), head (*Sira*), lung (*Kloma*), joints (*Parva*), stomach (*Amasaya*), plasma (*Rasadhatu*), adipose tissue (*Medodhatu*), nostrils (*Krana*) and tongue (*Jihva*).<sup>[8]</sup> The important organ where *Kapha* reside is stomach (*Amasaya*). Stomach is that organ in the alimentary tract which receives all types of food materials for digestive process. Due to the fluid nature (*Udaka guna*) of *Kapha* in stomach, the food substances become moistened (*Praklinna*), split apart (*Bhinna sankhata*) and digest well (*Sukhajara*). Subsequently sweet, slimy and moisten food, produces sweet and cold *Kapha* in the stomach. Situating in the stomach, *Kapha* nourishes other sites of *Kapha dosha* by its own potency (*Svasakti*) and fluidity (*Udaka karma*).<sup>[9]</sup>

By quality *Kapha dosha* is unctuous (*Snigda*), cold (*Sita*), heavy (*Guru*), slow (*Manda*), smooth (*Slasna*), soft (*Mrisna*) and stable (*Sthira*) in nature.<sup>[10]</sup> It is also white (*Sveta*) in colour, slimy (*Pichila*), and sweet (*Madhura*)

taste in non inflamed (*Avidagtha*) stage and saline (*Lavana*) in inflamed (*Vidagda*) stage.<sup>[11]</sup> Like other *Doshas*, *Kapha* also spreads all over the body to execute its normal functions. Due to the act of fluidity *Kapha* binds the joints (*Sandhi samslesanam*), provide unctuousness (*Snehanam*), heals (*Ropanam*) the injury, fills (*Pooranam*) the organs, and strengthens (*Balam*) and stabilizes (*Sthairyam*) the body.<sup>[12]</sup>

#### **PATHOPHYSIOLOGY OF VITIATED KAPHA DOSA**

Various factors are responsible for the vitiation of *Doshas*. This includes endogenous (*Nija*) and exogenous (*Agantuja*) causes.<sup>[13]</sup> Vitiation due to food and habits are endogenous causes because they have direct association with the *Doshas* in the body to manifest disease. Exogenous factors comprise various environmental factors like seasonal variation, pollution, etc and they have specific mechanism in the manifestation of disease. In order to produce disease the exogenous factors also have to link with the *Doshas*. Irrespective of the causes, whether they are directly associated or not, disease manifest only with the vitiation of bio regulatory principles or *Doshas*.<sup>[14]</sup> According to the diversity of causes *Doshas* vitiating in different ways and get lodged in specific sites or organs in the body.<sup>[15]</sup> Thus different types of diseases manifest by vitiating the body elements (*Dhatus*), their channels (*Srothas*), and excreta (*Mala*) and excretory routes (*Malayanas*).<sup>[16]</sup>

The intrinsic property of *Kapha* is to provide strength (*Bala*) to the body. When it becomes abnormal, *Kapha* turns to be a waste product (*Mala*) and leads to diseased conditions.<sup>[17]</sup> The abnormal *Kapha* produces signs and symptoms like coldness (*Saityam*), itching (*Kantu*), stability (*Sthairyam*), thickness (*Ulsedam*), heaviness (*Gouravam*), unctuousness (*Sneham*), numbness (*Supti*), moistness (*Kledam*), swelling (*Updeham*), obstruction (*Bandham*), sweetness (*Maduryam*) and chronic occurrence (*Chirakaritvam*) of disease.<sup>[18]</sup> Inflammation (*Upachaya*), hindrance (*Vistambha*) and whitish (*Souklyam*) colour may also see due to vitiating *Kapha*.<sup>[19]</sup> Lethargy (*Avasadam*) and laziness (*Tandra*) are also associated with the increase in *Kapha*.<sup>[20]</sup> Manifestations include anemia (*Svaityam*), dislodgment of joints (*Sladhangatvam*), dyspnoea (*Svasam*), cough (*Kasam*) and deep sleep (*Atinidra*).<sup>[21]</sup> Anointing (*Upalepam*), immobility (*Sthaimityam*), oedema (*Sopham*), indigestion (*Apakti*) and salinity (*Lavanarasa*) are the other important *Lakshanas* in *Kapha* diseases.<sup>[22]</sup>

#### **RESPIRATORY MUCUS SECRETION**

The production of mucus in airways by *Kapha dosha* in the lungs is normal. Mucus is secreted from the mucosal epithelium and the connective tissue layer under the epithelium in the lung tissue. In the surface epithelium mucus is produced by the cells called goblet cells. In the connective tissue mucus is produced by sub mucosal glands. Airway mucus is a heterogeneous adhesive, viscoelastic gel composed of water, secreted polypeptides, lipids, glycoproteins (or mucins) and carbohydrates. It contains exogenous bacterial products, endogenous antibacterial secretions, cell-derived mediators and proteins, plasma-derived mediators and proteins and cell

debris such as deoxyribonucleic acid (DNA).<sup>[23]</sup> Respiratory mucus present as a bilayer of an upper mucous sheet ("gel-phase") and a lower, more watery periciliary layer with low viscosity ("sol-phase"). A thin layer of surfactant lies between the sol and gel phases. Much of the mucus portion is produced by sub mucous glands and periciliary fluid by epithelial cells. The function of periciliary layer is "lubrication" of the beating cilia. Surfactant helps the easy spread of mucus over the epithelial surface.

Respiratory tract secretion is an inherent part of the defense system that protects the airways against invading pathogens and environmental toxins.<sup>[24]</sup> Mucociliary clearance of trapped dust particles and foreign matter in the respiratory tract is the important function of mucus. The particles trapped in the sticky mucus layer are moved by the tips of beating cilia and are removed from the airways through the throat; where it is swallowed for gastrointestinal degradation. Mucus also contains antibacterial substance immunoglobulins - lactoferrin, which chelates iron necessary for the growth of some bacteria, and an antibacterial enzyme lysozyme. The high water content act as a humidifier of inspired air and prevent excessive fluid loss from the airway surface.<sup>[23,25]</sup>

#### **AIRWAY MUCUS HYPER SECRETION IN TAMAKASVASA (ASTHMA)**

When respiratory tract is exposed to irritants, *Vata dosa* aggravates and leads to increase of *Kapha* in the lungs. Simultaneously the situation stimulates inflammatory process and due to the activation of inflammatory response, mucus is produced in excess. Inflammation of the mucosa is responsible for mucus hyper production than any other causes in diseases of respiratory system<sup>[26]</sup>. The increased mucus due to inflammation may trigger cough reflex and is cleared as sputum from the respiratory tract. So *Kapha* vitiation in the lungs leads to an important sign - expectoration and spitting of sputum (*Sleshmaudgiranam*), in this disease<sup>[27,28]</sup>. Generally sputum contains expectorated mucus mixed with inflammatory cells, cellular debris, DNA and microorganisms.

High viscosity is the peculiar character of mucus in asthma. The important qualities of *Kapha* such as unctuousness (*Snigda*), sliminess (*Pichila*), heaviness (*guru*), slowness (*Manda*), and stability (*Sthira*) contribute to the high viscous character of mucus. Due to the high viscous nature the mucus resist to flow and get obstructed in the airways. Normal clearance of mucus by airflow and ciliary function may also be hampered by high viscosity. Subsequently airways tend to develop gelatinous mucus plugs.<sup>[29]</sup> Mucus plug formation is due to stabilization of noncovalent interactions between extremely large mucins assembled from conventional-size subunits.<sup>[30]</sup> This suggests that the abnormal secondary structure due to defect in assembly of the mucin molecules leads to increase in viscosity of the mucus plugs. Increased airway plasma proteins (such as serum albumin) exudation also contributes to the plug formation. Structural modifications such as goblet cell hyperplasia (GCH) and hypertrophy of submucosal glands associated with increased mucin production is also seen in asthma.

It is explained that mucins produced in goblet cells and sub mucous glands have major role in the formation of airway mucus. Out of twenty human MUC genes so far identified, only nine, namely, MUC1, MUC2, MUC4, MUC5AC, MUC5B, MUC7, MUC8, MUC11, and MUC13, are expressed in the human respiratory tract.<sup>[31]</sup> Of these, MUC2, MUC5AC and MUC5B are the gel-forming mucins found in respiratory secretions. Among these the principal gel-forming mucins identified in both normal and pathological secretions are MUC5AC and MUC5B glycoproteins. In addition to lungs these MUC genes are distributed in stomach, duodenum, gall bladder, conjunctiva, middle ear, sublingual gland, laryngeal sub mucosal glands, esophageal glands and nasopharynx.<sup>[23]</sup> As described earlier most of these body parts are the sites of *Kapha dosha* and stomach (*Amasaya*), the important organ where *Kapha* reside has a major role in the manifestation of the disease.<sup>[32]</sup>

The process of airway hyper secretion involves the distinct changes in phenotype of mucus-producing tissues and over expression of protein products of MUC genes. Two important characters are seen associated with the mucus hypersecretory phenotype in asthma. They are elevated mucin production that increases the quantity of intracellular mucin in airway secretory cells and elevated mucin exocytosis that increases the thickness and viscosity of the mucus gel.<sup>[33]</sup> The expression of MUC genes is regulated by inflammatory mediators and associated neurohormonal factors. In asthma, inflammation is mediated by allergen-specific helper T-cell type 2 (Th2) cytokines, including interleukin (IL) IL-9 and IL-13. IL-9 may act predominantly via calcium-activated chloride channels (CLCA) and IL-13 through the activation of signal transducer and activator of transcription 6 (STAT6) and FOXA2 channels. Other inflammatory mediators include IL-1 beta, tumor necrosis factor-alpha (TNF-alpha) and cyclooxygenase (COX)-2. TNF-alpha act via NF-kappa B, and IL-1 beta via COX-2 channels. Epidermal growth factor receptor (EGF-R) signaling and FOXA2 also emerge as intracellular pathways for asthma.<sup>[34]</sup> These mediators not only induce mucin secretion but also up-regulate MUC gene expression with resultant increase in mucin synthesis and associated goblet cell hyperplasia.

#### PHARMACOTHERAPEUTIC APPROACH IN MUCOUS HYPER SECRETION

Increased volume of mucus is an important feature in *Tamakasvasa*, especially during the attacks. Usually the pathology of mucus hyper secretion is undervalued in the management of *Tamakasvasa*. Food substances ingested now a days with sweet taste (*Madhura rasa*), and unctuous (*Snigdha*), heavy (*Guru*), slimy (*Picchila*) and cold (*Sita*) qualities are the major cause of *Kapha* vitiation that leads to increased mucus sputum. The accumulation of mucus in the airway tree contributes to chronic airway inflammation, airway obstruction, airway hyper responsiveness and asthma exacerbation. The relationship with airway obstruction and physical properties of the sputum has been demonstrated in many studies.<sup>[35]</sup> There will be a greater decrease in the ventilator capacity when the sputum is thick. The

morbidity and mortality of the disease is associated with the mucus plugs in the airways.<sup>[36]</sup>

There are two objectives in the management of mucus hypersecretion in *tamkasvasa*, namely short-term relief of symptoms and long-term benefit. It is primarily the vitiated *kapha* as phlegm gets lodged in the airways (*srotas*) that put the patient in serious sufferings. Hence, reduction of airway obstruction and airflow limitation by enhancing mucus clearance is the primary objective for short-term relief of symptoms. This involves altering the rheological properties of bronchial mucus and thereby promotes expectoration. Adhesivity and cohesivity ("stickiness" and "stringiness") produced by tenacity is the major cause of adhesion of the mucus to the epithelium in airways. Mucociliary clearance can be increased by decreasing the tenacity and changing the viscoelasticity of mucus. Next step entails inhibition of mucus hyper secretion and airway hyper responsiveness to reduce the amount of luminal mucus in the airways. The long-term benefit embraces pharmacotherapeutic approach for reversal of the hypersecretory phenotype and reducing the number of goblet cells and the size of the sub mucosal glands.<sup>[37]</sup>

Management of mucus hyper secretion can be done by procedure based therapies and pharmacological methods. Liquefaction (*Sleshmavilayana*) is the therapeutic procedure suitable for the clearance of thick phlegm lodged in the *Srotas*. Along with the liquefaction, softening of channels (*Srotomardavakarana*) is also needed to facilitate the free movement of liquefied phlegm. In order to avoid hindrance to mucociliary clearance employ measures to pacify the vitiated *Vata dosha* as well.<sup>[38]</sup> Person who is afflicted with copious sputum and has sufficient strength (*Sareerabala*) purification (*Sodhana*) therapies *Vamana* along with *Virechana* or *Vamana* and *Virechana* are necessary. If the patient is weak, treatment at the outset with unctuous fomentation therapy after applying suitable oil mixed with salt on chest, flanks and back is beneficial. These methods are significantly effective both in removing phlegm from small distal bronchioles to large central bronchi and in promoting their final removal from the lungs.

Pharmacological methods check the production of phlegm in the airways due to vitiation of *Kapha dosa*. Administration of drugs having taste (*rasa*) with acrid (*Katu*), *Tikta* (*bitter*) and astringent (*Kashaya*) consecutively, according to taste specific therapy (*Rasapravicarana chikitsa*) pacify the diseases caused by vitiated *Kapha*. The properties (*Guna*) of these *Rasas* help to modify the properties of bronchial mucus and reduce or inhibit mucus hyper secretion and airway hyper responsiveness. *Katu rasa* acts on the viscid and thick *Kapha* and desiccates hyper secretions due to ununctuous (*Rooksha*), skinny (*Laghu*) hot (*Ushna*) and cleansing (*Vaisadya*) properties. The *Tikta rasa* administered thereafter, reduces the sweetness produced in mouth and dries up the increased *Kapha* as a whole due to ununctuous (*Rooksha*) and skinny (*Laghu*) properties. Subsequent use of *Kashaya rasa*, inhibits the over production of *Kapha* and reduces the unctuous nature due to the action of ununctuous (*Rooksha*) property.<sup>[39]</sup> The rationale use of

food considering the taste approach (*Rasapravicarana*) helpful in maintaining the normalcy of *Dosas*, especially *Kapha dosa* and the fine customary practices accomplish long-term benefits in *Tamkasvasa*.

#### CONCLUSION

Mucus hypersecretion due to *Kapha* aggravation play an important role in the manifestation of *Tamakasvasa*. The effective management of increased mucus in *Tamakasvasa* is possible only by the clearance of phlegm from the air passages and inhibition of over production of mucus in the lungs. This can be achieved by the administration of procedure based cleansing therapies, taste specific drug therapy; use of wholesome food (*Ahara*) and by adopting healthy practices (*Vihara*)

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