



REVIEW ARTICLE

Integrating Ayurvedic and Modern Perspectives on *Ama* in the Context of Metabolic and Immune Dysfunction- A Review

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Abstract

The concept of *Ama* in Ayurveda is the basis of understanding the disease pathophysiology. *Ama* is defined as a toxic byproduct of improper digestion, formed due to weakened *Agni* (metabolism) and it can occur at any cell of the body. This *Ama* is believed to circulate throughout the body causing *Srotorodha* and as a result the body's physiology is impaired. The derangement to *Agni* may occur either at the *Jatharagni* or *Bhutagni* or *Dhatwagni* level. At *Jatharagni* level, it manifests as diseases pertaining mainly to the *Annavahasrotas*. When *Jatharagni* is not efficient to complete the *Aharapaka*, toxins accumulate in the system, further reducing the *Agni*. This may generate *Ama* which again hinders the *Agni*, which further deteriorates the *Dhatwagni* and *Bhutagni* as well. Reduced *Agni* level or impairment of *Agni* leads to the formation of *Ama*, which is the root cause for manifestation of all diseases. The global prevalence of Metabolic disorders and immune disorders are increasing day by day. These conditions are as a result of low-grade inflammation, oxidative stress and immune dysfunction that can be linked with the concept of *Ama*¹. This review aims to explore the relationship between *Ama* and metabolic as well as immune system disorders, by integrating insights from Ayurvedic perspective and modern scientific findings. Despite its significant importance in Ayurveda, *Ama* lacks a universally accepted biomedical equivalent, restricting its application alongside modern diagnostic methods. This review proposes that *Ama* correlates with chronic low-grade inflammation, formation of ROS and oxidative stress. By understanding the functional relationship between *Ama*, *Agni* and *Srotas*, this study aims to establish a conceptual linking with pathophysiology of metabolic and immune disorders with *Ama*. Methodology involves rigorous review of Ayurvedic *Samhitas* to understand the concept of *Agni*, formation of *Ama*, its pathophysiology of different diseases in Ayurveda and clinical manifestations of *Ama*. Databases will also be reviewed for recent studies related to *Ama*. Modern literature will be analyzed to investigate the potential links between *Ama* and metabolic and immune system disorders. By examining both Ayurvedic and modern biomedical perspectives, the review will propose integrative diagnostic approaches that incorporate Ayurvedic principles of *Ama* with contemporary diagnostic methods. This approach aims to bridge the gap between traditional and modern medical systems, promoting a comprehensive understanding and management of metabolic and immune-related health issues.

Introduction

Ama is a fundamental concept in Ayurveda and is described as a pathological entity arising from impaired digestion and metabolism. *Ama* refers to a substance formed as a result of defective *Paka* (transformation) that plays an important role in the *Samprapti* of a *Vyadhi* (pathogenesis of a disease). The meaning of the word *Ama* is the transforming food that has not yet become *Dhatu* (tissues) or a substance or a group of substances that has failed to become *Dhatu* is termed as *Ama* as it is pathogenic. According to Vagbhata, *Ama* is a substance formed due to the hypo-functioning of *Agni* (weak digestive power)². As a result, the improperly processed *Rasa* (first formed part after digestion) remains in the *Amasaya* (upper part of GIT), where it undergoes fermentation and putrefaction, leading to toxicity and disease development. As per Madhava Nidana, *Ama* represents the initial stage of *Dosha Dushti* or *Dosha-Dushya Sammurchana* (first stage of pathogenesis)³. According to Madhukosha, weak *Jatharagni* (digestive enzyme present in the GIT) leads to incomplete digestion, leaving behind undigested *Ahara Rasa*, which undergoes pathological changes and serves as the root cause of all diseases, referred to as *Ama*⁴. Acharya Vagbhata has also described the concept of *Amavisha*, a state of severe toxicosis resulting from the repeated indulgence in *Viruddhahara* (incompatible diet), *Adhyashana* (overeating), and *Ajirṇashana* (eating before the previous meal is digested)⁵. While the body typically attempts to neutralize and eliminate toxins, in the case of *Amavisha*, a higher-grade toxic state is produced, overwhelming the body's natural detoxification mechanisms and leading to severe pathological consequences. Chakrapani while mentioning *Grahani chikitsa*, mentioned about *Sthularupi* (localized *Ama*) and *Sukshmarupi* (generalized *Ama*). The *Sookshma Ama Rasa*, upon entering circulation, spreads throughout the body but remains unsuitable for either *Bhutagni* or *Dhatwagni Paka*. Since it has not undergone *Bhutagni Paka*, this improperly processed substance (*Sookshma Ama Rasa*) acts as a *Vijaateeya Dravya* (foreign entity) within the body. As a result, it disrupts *Dosha* balance, leading to various diseases. When *Sthula Ama Rasa* accumulates in the *Amasaya*, it primarily manifests as gastrointestinal disturbances. Conversely, if *Sookshma Ama Rasa* persists within the *Shakhas* (peripheral tissues), it contributes to the onset of *Shakhasrita Rogas* (diseases localized in the tissues and extremities)⁶.

Metabolism is the sum of biochemical processes that convert food into energy, regulate cellular function, and maintain homeostasis. Proper metabolic function ensures efficient energy production, nutrient utilization, and waste elimination. However, when metabolism is impaired due to factors such as poor diet, sedentary lifestyle, chronic stress, genetic predisposition, inefficient energy production and

abnormal biochemical reactions may occur, leading to the accumulation of metabolic byproducts. This disruption contributes to oxidative stress, mitochondrial dysfunction, and the overproduction of pro-inflammatory mediators such as tumour necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and C-reactive protein (CRP). These inflammatory markers play a key role in the development of chronic low-grade inflammation, a major underlying factor in metabolic disorders like obesity, type 2 diabetes, and cardiovascular disease. Additionally, improper metabolism can cause gut dysbiosis, leading to increased intestinal permeability, also known as "leaky gut," allowing endotoxins such as lipopolysaccharides (LPS) to enter circulation, further stimulating systemic inflammation. Over time, persistent inflammation disrupts insulin signaling, impairs lipid metabolism, and accelerates the progression of metabolic syndrome, highlighting the critical link between improper metabolism and chronic disease development⁷. This paper aims to explore the relationship between *Ama* and these conditions, integrating Ayurvedic insights with modern scientific findings.

Methodology

The methodology started with a rigorous review of classical Ayurvedic Samhitas to thoroughly understand the foundational concepts of *Agni* and the formation of *Ama*, including their roles in the pathophysiology and clinical manifestations of various diseases. This historical analysis was complemented by a narrative review of relevant contemporary literature from modern databases to gather recent studies that explored *Ama*, particularly its relationship with metabolic and immune system disorders. Modern biomedical literature was then critically analysed to draw correlations between the traditional concept of *Ama* and contemporary findings on inflammation and metabolic dysfunction.

Modern research identifies metabolic disorders (such as obesity, diabetes, and cardiovascular diseases) and immune system dysfunctions (such as autoimmune diseases and chronic inflammatory conditions) as being closely associated with inflammation and oxidative stress⁸.

Correlation of *Ama* with obesity

Obesity is now recognized as a global epidemic and a major risk factor for insulin resistance, type 2 diabetes mellitus, cardiovascular diseases, immune disorders, and non-alcoholic fatty liver disease. Also, obesity has been linked to various types of cancer. Beyond its association with chronic diseases, obesity significantly reduces quality of life, shortens life expectancy, and increases healthcare costs. Obesity is regarded as a consequence of excess calorie intake relative to expenditure, is now recognized as a complex, multifactorial disease with pathophysiological mechanisms that parallel those of the aging

process. Its pathophysiology extends beyond excess energy storage and involves a cascade of metabolic disturbances, including oxidative stress, mitochondrial dysfunction, immune dysregulation, and chronic low-grade inflammation, all of which contribute to the progression of obesity-related complications⁹. White adipose tissue is the fat storing area and it also secretes adipokines and cytokines systematically. Adipokines regulate various physiological signaling cascades while cytokines are involved in resolution of inflammation along with adaptive and reparative angiogenesis. Obesity causes remodelling of white adipose tissue, results in inflamed dysfunctional adipocytes. Inflamed adipocyte releases proinflammatory cytokines both locally and systematically which in turn disturbs the physiology of adipose tissues.

Ayurveda highlights the concept of *Ashtou Ninditiya* (eight unhealthy body constitutions) as described by Acharya Charaka¹⁰. These body types are considered as unwholesome due to their tendency to cause various health issues and *Sthula* (obese constitution) holds significance among them due to its impact on metabolism and overall health. Various etiological factors, including excessive consumption of heavy, unctuous, and sweet foods, a sedentary lifestyle, and excessive daytime sleep, contribute to the impairment of Agni (digestive and metabolic functions), leading to the accumulation of Kapha and the excessive formation of Medas (adipose tissue). In individuals with altered digestive fire, incomplete digestion leads to formation of *Ama*. *Ama* gets lodged in *Srotas* (microcirculation) and thereby impair the further metabolic functions. *Ama* further causes, impaired production of *Rasa Dhatu* and it impacts the *Dhatu Parinama* (formation of tissues). Due to improper metabolism, nutrients fail to be converted into usable energy and leading to excessive fat storage in the body. *Ama* hinders the normal *Dhatu Parinama*, results in excess *Medodhatu* (fat tissue) accumulation and thereby contributing to obesity. In *Sthaulya* (obesity), *Medodhatu* accumulation and the consequent alteration in *Agni* may lead to increased appetite and enhanced digestion of ingested food, resulting in metabolic disturbances that may be associated with increased oxidative stress and the generation of reactive oxygen species (ROS).

Ama and Cancer

Inflammation is the body's natural response to tissue damage caused by physical injury, ischemia, infection, toxin exposure etc. This response triggers cellular changes and immune reactions that promote tissue repair and stimulate cellular proliferation at the site of injury. When inflammatory responses become chronic, they can lead to cell mutation and uncontrolled proliferation, creating an environment that promotes cancer development¹¹. The majority of cancers (90%) stem from somatic

mutations and environmental factors, often linked to chronic inflammation¹². Triggers of chronic inflammation that elevate cancer risk or progression include infections, autoimmune diseases, and inflammatory conditions of unknown origin¹³.

In chronically inflamed cells, excessive secretion of reactive oxygen species (ROS) and reactive nitrogen species (RNS) recruits more activated immune cells, amplifying dysregulated processes and potentially leading to a preneoplastic state. When ROS/RNS levels exceed the body's antioxidant defences, irreversible oxidative damage to nucleic acids, lipids, and proteins can occur, resulting in genetic and epigenetic alterations that disrupt oncogenes and tumour suppressor genes. The close interplay between oxidative stress and chronic inflammation, can drive genetic and epigenetic changes that initiate carcinogenesis¹⁴.

Mandagni (impaired digestive function), particularly *Jatharagnimandya*, is considered the root cause of *Ama* formation and, consequently, of many diseases. *Ama* may originate due to impairment of *Jatharagni* and may subsequently involve disturbances in *Bhutagni* (cellular metabolism) and *Dhatvagni* (tissue metabolism). *Samagni* (healthy digestion) is responsible for *Bala* (strength), *Arogya* (health), *Ayu* (lifespan) and *Prana* so, *Agni* should be protected, as derangement in *Agni* can produce *Apakva Ahara Rasa* (not properly digested) which can be a physiological form of *Ama*. Later, *Ama* becomes pathogenic when it combines with *Doshas*, resulting in the disruption of *Samyak Dhatuparinama* (proper tissue metabolism). Then if the *Agni* is not corrected and *Amavisha* is formed which can be correlated with chronic inflammatory states.

From an Ayurvedic perspective, cancer may be linked to the prolonged presence and accumulation of *Amavisha*, which the body is unable to eliminate adequately. *Ama* exists in the body as *Linavastha* and cannot be expelled due to weakened bodily strength (*Sharira Shakti*). Its accumulation is further aggravated by impaired digestion (*Agnimandya*) and improper tissue metabolism (*Dhatu Parinama*), ultimately leading to emaciation and cancer cachexia. In many types of cancer, *Ama* closely resembles *Amavisha*, exhibiting highly toxic properties that contribute to disease progression¹⁵.

Atherosclerosis and Ama

Atherosclerosis is the process of plaque formation in the vascular intima of blood vessels, which is identified as a chronic vascular inflammation. Before, Atherosclerosis was considered as a lipid storage disease, because cholesterol accumulation happens in the plaques. In the following decades, research has highlighted inflammation as a key link between risk factors like

LDL, triglycerides, and changes in artery wall cells that attract immune cells. These immune cells accumulate within the lesions and produces complications¹⁶. Atherosclerosis involves a chronic, low-grade inflammatory response that draws innate and adaptive immune cells into the plaque, some of which recognize ApoB, the core protein of LDL particles¹⁴. LDL is oxidized by reactive oxygen species (ROS) in the intima, leading to its conversion into oxLDL and subsequent uptake by macrophages and oxLDL is the marker of plaque inflammation¹⁷.

Current atherosclerosis treatments primarily target traditional risk factors with lipid-lowering and glucose-lowering drugs, which also has anti-inflammatory effects to prevent and slow plaque formation and progression¹⁸. The MeOH bark extract of *Terminalia chebula* exhibited dose-dependent anti-hyperlipidaemic effects in high-fat diet-induced hyperlipidaemic rats, with a 600 mg/kg dose showing significant activity against high-cholesterol diet-induced hyperlipidemia¹⁹. According to Ayurveda, *Haritaki* (*Terminalia chebula*) has *Deepana* (metabolism-boosting) and *Sothahrit* (anti-inflammatory) properties, making it an effective anti-hyperlipidaemic agent. *Haritaki* possesses all six tastes except *Lavana* (salt). *Langhana* (depleting therapy) can be achieved by dominance of *Ushna* (hot), *Ruksha*(dry), *Laghu* (light) *Gunas* (properties). *Katu* (pungent), *Tikta* (bitter) *Rasa* and *Laghu*(light) *Ruksha*(dry) *Gunas* of *Haritaki* reduces the effect of *Kapha Medo Dushti* (vitiation of *Kapha* and *Medas*) along with neutralization of *Amavisha* through *Deepaniya* (improving digestion) property.

Rheumatoid arthritis and Ama

Rheumatoid arthritis (RA) is a chronic inflammatory disease with a multistep pathogenesis, beginning with autoimmunity, progressing to local inflammation, and ultimately causing bone destruction²⁰. The systemic effects of pro-inflammatory cytokines in RA influence metabolism, with the extent of metabolic changes and types of metabolites potentially serving as markers of cytokine-mediated inflammation. Evidence supports metabolomic analysis as a novel, non-targeted approach for identifying potential biomarkers in RA patients²¹.

Madhava Nidana describes *Amavata* as a condition caused by *Viruddhahara* (incompatible diet) and *Mandagni* (weak digestive power). As a result of *Mandagni* (weak digestion), *Ama* is formed in the body and, when combined with *Vata*, leads to *Srotorodha* (blockage of channels), which triggers inflammatory response in the body. Vitiated *Vata* and *Ama* accumulate in the joints, causing pain, swelling, stiffness, and restricted movement. *Jwara* (fever) is a classical feature of *Amavata*, indicating the presence of persistent low-grade inflammation in *Amavata* patients. Ayurvedic management

focuses on *Deepana* (enhancing metabolism), *Pachana* (improving digestive power), *Langhana* (lightening therapy), *Snehana* (oleation), *Swedana* (sudation), and *Shodhana* (purification) to reduce inflammation and restore balance. By addressing the root cause through metabolic correction and detoxification, Ayurveda aims to manage *Amavata*, by reducing inflammation and preventing disease progression²². From an Ayurvedic perspective, Rheumatoid Arthritis may be conceptually correlated with *Amavata*, as both conditions are characterized by chronic inflammation, joint pain, swelling, stiffness, and progressive functional impairment. The role of *Ama* in initiating and sustaining inflammation in *Amavata* may parallel the inflammatory and immune-mediated mechanisms observed in Rheumatoid Arthritis.

Diabetes and Ama

In 2022, 14% of adults aged 18 and older were living with diabetes—a significant increase from 7% in 1990. Evidence suggests that oxidative stress and inflammation contribute to insulin resistance which is the key feature of type 2 diabetes. They activate stress kinases such as c-Jun N-terminal kinase and nuclear factor-κB kinase, which interfere with insulin receptor substrate-1 (IRS-1) and disrupt insulin signaling. Moreover, these factors reduce adiponectin production in adipose tissue, further impairing insulin function²³. Insulin reduces inflammation by inducing nitric oxide release, which dilates blood vessels and limits leukocyte adhesion and infiltration. Both basic and clinical evidence support metformin's anti-inflammatory effects; it reduces proinflammatory cytokine secretion in liver cells and macrophages and is associated with lower CRP levels²⁴.

Prameha is a multisystem disorder marked by the vitiation of *Agni*, an imbalance in the *Tridoshas*, and disruption of nearly all *Dhatus* (body tissues) and *Ojas* (essence of tissues). Etiological factors, including the vitiation of *Kapha Dosha*, lead to increased *Kleda* (excess moisture content) production, which in turn results in *Ama* formation and *Srotorodha* (blockage of channels). Additionally, diminished *Dhathvagni* (abnormal metabolism) and the involvement of *Medas* are observed in *Prameha*. The formation of *Ama* due to *Agnimandya* (weak digestive fire) in the early stages clearly illustrates the role of inflammation in the pathogenesis of *Prameha*²⁵. From an Ayurvedic perspective, Type 2 Diabetes Mellitus may be conceptually correlated with *Prameha*, particularly in its chronic metabolic and inflammatory manifestations. The involvement of *Agnimandya*, *Ama* formation, *Meda Dushti*, and *Srotorodha* in *Prameha* parallels the metabolic dysfunction, insulin resistance, and chronic low-grade inflammation observed in Type 2 Diabetes Mellitus.

Anaemia and Ama

The pathophysiology of Anaemia of inflammation (AI) is characterized by increased iron acquisition and retention within macrophages of the reticuloendothelial system. Concurrent intestinal iron absorption is suppressed, with consequently reduced serum iron concentrations thus limiting iron availability for erythropoiesis²⁶.

In *Panduroga*, weakened *Bhutagni* and *Dhathvagni* (decreased metabolism) correlates with reduced absorption of factors essential for erythropoiesis, as well as with disruptions in liver function related to iron metabolism. Although food is composed of the *Panchamahabhutas* (five elements), even with proper intake, impaired *Bhutagni* prevents these five elements from being absorbed.

Discussion

Based on the severity of *Ama*, treatment approaches include *Deepana Pachana* (improving metabolism), *Langhana* (a type of fasting), and *Shodhana* (purificatory therapies)²⁷. *Amapachana* refers to the process of digesting and eliminating *Ama*, which is the toxic residue produced from impaired digestion. When the digestive fire is weak, *Ama* accumulates and can lead to various disorders. *Deepana* is the practice of stimulating *Agni* therapeutic interventions and fasting, thereby enhancing the body's natural ability to eliminate toxins. Together, *Amapachana* and *Deepana* work synergistically to clear *Ama* and restore metabolic equilibrium. *Langhana* involves dietary restrictions, such as fasting and engaging in mild physical activity in order to gradually stimulate and support the digestive system. *Langhana* not only facilitates the gradual breakdown and elimination of accumulated *Ama* but also promotes overall metabolic balance. By giving the body a period of rest, *Langhana* helps to detoxify and reset the digestive process. *Deepana pachana*, *Langhana* and importance of *Satmya Ahara* can be compared with anti-inflammatory diet of current practise.

Anti-inflammatory diet includes a traditional Mediterranean diet, the Dietary Approaches to Stop Hypertension (DASH) diet, and traditional Okinawan, Nordic, or Mexican diets. It is a holistic lifestyle method that encompasses regular physical exercise, socialization, proper rest and a consumable diet that is fresh, seasonal and regional²⁸.

Recent studies suggests that an imbalance in microbial populations and dysbiosis is closely linked to obesity. Several mechanisms have been proposed to explain the potential role of gut microbiome and obesity. Latest research which

compared the gut microbiome in adults with obesity concluded that gut microbiota range in obese persons is significantly diminished compared to control group²⁸.

A RCT conducted on obese younger adults concluded that an energy restricted anti-inflammatory diet is effective in the management of body weight, BMI, visceral and total adipose tissue. The cardiometabolic and inflammatory parameters also showed significant improvement. This suggests the role of inflammation in the pathogenesis of obesity²⁹. Greater adherence to the Mediterranean diet has been associated with a lower incidence of prostate cancer and reduced disease aggressiveness³⁰.

Ventil et al. explain and analyse the links between cancer and metabolic syndrome, findings that emphasizes the approach of Ayurveda and other traditional systems of medicine by demonstrating that diseases cannot be viewed solely as a series of defective genetic and biochemical steps. Instead, the connections between inflammation, metabolic syndrome, and cancer suggest that even seemingly distinct diseases may arise from fundamental aberrations in metabolism, homeostasis, and immune function³¹.

Swati et al. conducted a study on 256 individuals, investigating inflammatory markers such as ESR and CRP. Using a specially prepared questionnaire, subjects were classified into *Pravara* (high), *Madhyama*(moderate), and *Avara* (minimum) *Amalakshana* groups. The study concluded that elevated inflammatory markers were observed during the *Ama* state, with statistically significant differences in the mean ESR and CRP levels among the three groups³².

Charaka recommended a combined approach of *Samsodhana* (cleansing therapies) and *Samana* (palliative treatments) for *Prameha* patients with obesity. This treatment protocol includes specific dietary preparations with *Laghu* (light) and *Ruksha* (dry) qualities, which help support metabolic health. Additionally, the prescribed *Vihara* (lifestyle regimen) incorporates various physical exercises designed to reduce accumulated *Medas*, thereby addressing its involvement in *Prameha*³³.

The treatment of *Panduroga* involves *Deepana Pachana*, which restores digestive power and neutralizes *Ama*. By enhancing *Agni*, *Deepana Pachana* ensures that nutrients are efficiently processed and absorbed, thereby promoting the restoration of health and overall vitality. This approach addresses the root cause of *Panduroga*, offering a foundational strategy for rebalancing metabolism and improving systemic health³⁴.

*Langhana*³⁵ is the first line of treatment of *Amavata* in order to neutralize *Ama*. The intensity of *Langhana* depends upon the *Rogibala* (patient's strength). In the initial phase, treatment often begins with *Deepana Pachana* using agents with *Katu-Tikta Rasa* (pungent and bitter drugs) to stimulate the digestive fire and help break down *Ama*. By implementing *Langhana*, *Agni* is restored, thereby enhancing the digestion and elimination of *Ama*. This approach not only alleviates the immediate symptoms associated with *Ama* accumulation but also targets the root cause, preventing further toxin formation. Combined with *Deepana-Pachana* and dietary interventions, *Langhana* helps to restore the metabolic balance and supports overall systemic health.

Conclusion

In Ayurveda, *Ama* is the toxic, undigested metabolic waste that accumulates in the body due to poor digestion and weak *Agni* (digestive fire). It is considered the root cause of many chronic diseases, as it creates blockages, disrupts normal bodily functions, and triggers immune responses. Inflammation is often measured through inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukins (IL-6, IL-1 β), and tumour necrosis factor-alpha (TNF- α). These markers indicate systemic inflammation, which is linked to conditions like and autoimmune disorders, cancer, cardiovascular diseases etc.

By correlating *Ama* with chronic low-grade inflammation, oxidative stress, and immune dysfunction, an integrative approach can be developed for diagnosis and management. Future research should focus on establishing standardized biomarkers for *Ama* and incorporating Ayurvedic principles into modern healthcare for holistic disease management.

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