

# Therapeutic influence of some dietary articles on gut microbiota in the pathogenesis of rheumatoid arthritis (*Amavata*) – A review

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## Abstract

**Background:** *Amavata* is a chronic immune-inflammatory systemic disorder caused by the formation of *Ama* and its association with *Vata* at *Kaphasthana* (joints) and can be simulated with rheumatoid arthritis (RA). Published evidences show that treatment indicated in *Amavata* is effective in RA. Increased inflammatory status in RA is suggestive of gut dysbiosis involving gut microbiota (GM). **Aim:** The aim of the present study was to analyze the influence of diet on GM of RA patients based on *Pathya* (dietary advice) mentioned for *Amavata*. **Materials and Methods:** Laghutrayis such as Bhavaprakasha Samhita, Madhava Nidana and Sharangadhara Samhita, Bhaishajya Ratnavali and Nighantus (Sanskrit glossary) such as Raja Nighantu, Bhavaprakasha Nighantu and Yogaratnakara, Ashtanga Hridaya also different databases were reviewed for *Pathya* of *Amavata*. Different databases such as PubMed, Scopus, DHARA, Google Scholar, Science Direct were searched with research papers establishing the role of nonnutritive bioactive components in horse gram, barley, garlic, ginger, drumstick leaves, cow urine and buttermilk in the management of RA were also reviewed. It was found that *Pathya* influences on the GM by lowering or inhibiting inflammatory markers such as interleukin-6 (IL-6), 17 and leukotrienes through Bowman-Birk inhibitors and polyphenolic compounds. Among them, *Takra* is already a proven probiotic. *Gomutra* augments B and T lymphocytes, IL-1 and IL-2, strengthening the immune system. **Conclusion:** It was concluded that *Pathya Ahara* mentioned for *Amavata* have a direct link with GM of RA patients. Even though the pharmacological actions have been clinically proven/practised, this review creates evidence for its scientific basis.

**Keywords:** *Amavata*, Ayurveda, gut microbiota, microbiome, *Pathya*, rheumatoid arthritis

## Introduction

*Amavata* is an inflammatory systemic disorder caused by the formation of *Ama* (undigested or intermediate product of digestion or metabolism) and its association with vitiated *Vata* at *Kaphasthana* (joints) and can be simulated with rheumatoid arthritis (RA). Constant use of incompatible food articles and strenuous exercise immediately after consumption of fatty foods leads to indigestion. This results in the formation of *Ama*, which gets circulated throughout the body by *Vyana Vayu* (type of *Vata*, that is responsible for circulation). This then accumulates at *Shlesma Sthana* (especially at synovial joints), particularly at the site of *Shleshaka Kapha* (subtype of *Kapha* situated in the joints), leading to the manifestation of symptoms of the disease. According to Ayurveda for *Amavata*, *Shamana* (conservative) and *Shodhana* (biological purification of the body) treatments are advised, whereas

anti-inflammatory, analgesics, steroids and disease-modifying anti-rheumatic drugs are required for its management as per modern medicine.<sup>[1]</sup>

A wide research field has been brought about by the advancement of characterization and understanding of gut microbiota (GM) in autoimmune diseases like RA. Smoking, GM and periodontal bacteria are the most common factors in the development of RA. Hence, an increased inflammatory status has been associated with gut dysbiosis.<sup>[2]</sup>

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Recent clinical studies revealed that in autoimmune diseases like RA there are marked shift in the intestinal microbiota and a reduced commensal gut microbial community in comparison with healthy controls. Hence, to study the influence of diet in GM of RA (*Amavata*) and to analyze the role of selected *Pathya* (dietary regimen) in RA (*Amavata*) and thereby bringing a light toward the influence of GM in the management of RA, present review was undertaken.

## Materials and Methods

Classical textbooks such as Bhavaprakasha Samhita, Madhava Nidana and Sharangadhara Samhita, Bhaishajya Ratnavali and Nighantus (Sanskrit glossary) such as Raja Nighantu, Bhavaprakasha Nighantu, Yogaratnakara and Ashtanga Hridaya were reviewed to analyze the role of *Pathya* mentioned in the chapter of *Amavata* in the management of RA. Different databases such as PubMed, Scopus, DHARA, Google Scholar, Science Direct were searched using keywords like RA, GM, gut dysbiosis, immunomodulatory diet, probiotics, Prebiotics, nutraceuticals, horse gram, ginger, garlic, moringa, barley, yoghurt, cow urine, chick-pea, rice, bitter gourd, ash gourd and brinjal with the help of Boolean operators “AND,” “OR” and “NOT.” Filters like clinical trials, within 5 years and free full text were applied. Among those the research papers containing data regarding the role of GM, prebiotics, probiotics, immune-modulatory diet, nutraceuticals in RA were reviewed in detail.

## Outcomes and Discussion

Among 649 articles searched, 34 were found relevant. The articles pointing out the close association of GM in the etiopathogenesis of RA and the role of certain selected *Pathya* in regulating the changes that occurred in GM of RA were reviewed. A close relationship with the diet and commensal GM was found out from the literary search. From these reviewed articles, 7 wholesome items mentioned in the context of *Pathya* (wholesome) in *Amavata*, which are used commonly were selected. They are horse gram (*Kulattha*), barley (*Yava*), garlic (*Lashuna*), ginger (*Ardraka*), drumstick leaves (*Shigru*), cow urine (*Gomutra*) and buttermilk (*Takra*) and were grouped as the herbal origin and animal origin.

### Influence of diet on gut microbiota of rheumatoid arthritis patients

GM denotes an entire ecosystem inhabiting each organism, thus constituting a “superorganism.”<sup>[3]</sup> Energy as well short-chain fatty acids (SCFAs) synthesis from indigestible food and immune-boosting in the host plays an indispensable role with GM.<sup>[4]</sup> This reflection has paved for the curiosity in studying about GM as a possible source of origin for the autoimmune diseases. Study of various research articles revealed that there is a marked shift in the quantity of bacterial groups in the intestinal microbiota of RA patients.

The physiology of healthy intestinal barrier, its functional integrity and permeability regulation is controlled by GM

and the diet reaching the gut. It has been proved that the pathophysiology, prevention and management of RA are influenced by the diet. Functional foods or nutraceuticals are bioactive components of the diet that exerts beneficial effects along with nutritional supplies resulting in improved health when consumed habitually.<sup>[5]</sup>

Micronutrients such as vitamins and fatty acids and nonnutrients such as bioactive phytochemicals and probiotics are classified as nutraceuticals. The homeostasis of GM is maintained by the nutrients that reach the gut.<sup>[6]</sup> The bioavailability and effects of polyphenols on GM and reciprocally the regulation of GM by the polyphenols determines the equilibrium of intestinal microflora.<sup>[7]</sup>

The complex carbohydrates, such as oligosaccharides, which are slowly digestible are termed as prebiotics and affect human health and the gut microbiome.<sup>[8]</sup> Dietary poly and oligosaccharides can pass directly to the distal gut as they are resistant to upper gut metabolism. In the distal gut, they serve as a source of energy for GM. GM can metabolize complex carbohydrates and fats through fermentative processes to produce SCFAs such as butyrate, propionate and acetate. The by-products of fermentative reactions have significant effects on the gut environment and on the host, such as anti-inflammatory and immune-modulatory functions. For example, butyrate has a predominant role in the regulation of gut health by providing an energy source for colonocytes.<sup>[9,10]</sup>

Fiber, the most well-known nutrient and food component plays an important impact on GM. Dietary fiber also can increase the bacteria capable of producing SCFAs, thus benefitting the intestinal barrier structure.<sup>[11]</sup> The dietary fiber does not undergo metabolism in the small intestine as it is resistant against the chemical changes occurring in the small intestine. It gets degraded by fiber-degrading microbes in the colon, resulting in the production of SCFAs.<sup>[12]</sup> Studies pointed out that the production of SCFAs are increased when vegan and vegetarian diet is consumed. A noteworthy regular intake of foods of plant origin such as fruits, pulses vegetables and legumes helps in modulating GM.<sup>[13]</sup>

### Influence of *Pathya* (dietary regimen) mentioned in the treatment of *Amavata* for regulating gut microbiota of RA patients.

The importance of *Pathya* (dietary regimen) and *Apathya* (unwholesome) in Ayurveda can be deduced from the fact that *Charaka* has stated *Pathya* (wholesome) as a synonym for treatment. *Charaka* has stated that when *Srotas* (channels of circulation) are affected by aggravated and vitiated *Dosha*, *Pathya* (dietary regimen) helps to correct the *Srotas* and *Dosha* alleviation.<sup>[14]</sup>

The role of horsegram (*Kulattha*), barley (*Yava*), garlic (*Lashuna*), ginger (*Ardraka*), drumstick leaves (*Shigru*), cow urine (*Gomutra*), and buttermilk (*Takra*) were specifically reviewed for its potentiality in the management of gut dysbiosis thus bringing about an anti-inflammatory effect.

*Ahara* is the root cause for strength, complexion and vitality of living beings. It has the ability to promote health as well as to control the disease pathology.<sup>[15]</sup> *Pathya* for *Amavata* can be advised to be included in a regular diet in the form of different preparations. For example, *Kulattha* (horse gram), *Takra* (buttermilk), *Ardra* (ginger), *Lashuna* (garlic), *Gomutra* (cow urine), *Shigru* (moringa), *Shunthi* (dry ginger), *Patola* (snake gourd), *Chanaka* (chickpea), *Shali* (paddy/rice), *Yava* (barley), *Karavellaka* (bitter gourd), *Vartaka* (brinjal) bring about the effect of *Upashaya* (relieving symptoms and reversing pathogenesis).<sup>[16]</sup>

### Effect of horse gram in gut dysbiosis

*Kulattha* (*Macrotyloma uniflorum* Lam. or *Dolichos biflorus*) is commonly known as horse gram is a nutraceutical pulse variety. It contains 50%–70% of carbohydrates, especially starch, nonstarch polysaccharides (dietary fiber) and a significant number of oligosaccharides and nonnutritive bioactive substances such as phytic acid, phenolic acid, fiber and enzymatic inhibitor. Dietary oligo and polysaccharides do not get digested completely in the small intestine. These complex carbohydrates are transformed into butyrate (SCFAs) by GM in the large intestine through fermentative processes. Surprisingly 43.4% of total carbohydrates comprise of these resistant starches. Bowman–Birk inhibitor (BBI), a proteinase inhibitor present in horse gram has a potential anti-inflammatory activity against several degenerative and autoimmune disorders. Butyrate and other bioactive substance have a protective role against inflammatory reactions, which is a predisposal factor of gut dysbiosis.<sup>[17]</sup>

### Effect of barley in the maintenance of commensal gut microbiota

*Yava*, commonly known as barley (*Hordeum vulgare*), is a potential source of dietary fibers, prebiotic food, thus lowers markers of inflammation through gut mediated microbiota responses. SCFA like propionate, butyrate produced through gut fermentation acts as an anti-inflammatory. Studies proved that usage of barley-based food significantly caused the abundance of various bacterial diversity, mainly *Bifidobacterium* species and lactobacillus species, which belong to a healthy GM. It was also reported that dietary change can result in a rapid shift of microbiota in inflammatory and autoimmune conditions within a day.<sup>[18]</sup>

### Effect of garlic in gut microbiota of an inflammatory condition

*Lashuna*, commonly known as garlic (*Allium sativum* Linn.) contains compounds uracil, S-allyl cysteine, and diallyl sulfide. Among these diallyl, sulfide has proved to inhibit the activity of prostaglandins produces as a result of inflammatory reaction in RA.<sup>[19]</sup> Others were reported to inhibit the activity of the nuclear factor-kappa B and cyclooxygenase-2 genes involved in arthritis signaling pathways. Microbial stool analysis studies revealed that garlic intake results in a healthier firmicutes-to-bacteroidetes ratio, an upsurge in commensal bacterial lushness. Studies proved that garlic extract has a

potential role in GM and inflammatory status, thus regulating immunity.<sup>[2]</sup> Garlic maintains GM in equilibrium by protecting them from intestinal inflammation. Thus, garlic helps in the restoration of intestinal microflora by its prebiotic properties<sup>[2]</sup> and sources of intracellular hydrogen sulphide (H<sub>2</sub>S).<sup>[20]</sup>

### Effect of ginger in inflammatory pathology

*Ardra*, commonly known as ginger (*Zingiber officinale* Roscoe.) is used and known for its strong anti-inflammatory properties for centuries ginger has the capacity to destroy *Helicobacter pylori*, a bacterium which causes ulcer leading to gastric or/and intestinal permeability.<sup>[21]</sup> *H. pylori* can cause immunological instabilities leading to autoimmune disease pathogenesis.<sup>[22]</sup> Studies revealed that active principle of ginger called as gingerols has the potential to switch off inflammatory genes and can also suppress the action of leukotrienes (inflammatory molecule), thereby making it more effective than a conventional pain reliever. This indicates a significant role for ginger on GM in the pathogenesis of the inflammatory or autoimmune disease.

### Effect of moringa in the growth of probiotics

*Shigru*, commonly known as drumstick tree (*Moringa oleifera* Lam.), in the recent studies has shown that it's polyphenols could modify the gut microbial composition and was converted by them to bioactive compounds in a two-way relationship “polyphenols↔microbiota” which greatly influence host health. Phenolic compounds arrest the development of some pathogenic bacteria such as *Escherichia coli*, while they promote the growth of some probiotics such as *Lactobacillus*. *Moringa oleifera* leaf extract in a study showed that it could serve as a gut modulator in obesity-induced dysbiosis, thus proving a significant correlation between increased levels of bifidobacteria and reduced leakiness in the gut.<sup>[23]</sup>

### Cow urine as a bioenhancer

cow (*Bos indicus*) urine (CU) was also reviewed as it is used in Ayurveda treatments and is well known for its therapeutic properties.<sup>[24]</sup> Cow urine enhances the blastogenesis of B and T lymphocyte. It helps macrophages in augmenting phagocytosis by the production of interleukin-1 (IL-1), interleukin-2. Thus, it helps in preventing and controlling infections.<sup>[25]</sup> Cow urine is beneficial in fighting against bacterial and fungal infection. It acts as a bio-enhancer of some antimicrobial drugs.<sup>[26]</sup> The only animal product used as a bio-enhancer with the antimicrobial drugs is cow urine.<sup>[27]</sup> Studies revealed that the action of rifampicin against *E. coli* got added up to 5–7 folds when used along with *Gomutra* and about 3–11 times when used against gram-positive bacteria.<sup>[28]</sup>

### Buttermilk as a natural probiotic diet

*Takra* commonly known as buttermilk, is a natural probiotic diet as it contains abundant friendly bacteria for intestine, benefiting the state of homeostasis. The normally present bacteria, present in meals get destroyed due to acidic environment of the small intestine, whereas bacteria in yogurt/buttermilk cross over from these environments and reach the large intestine where

these probiotics digest prebiotics (food fibers) forms SCFAs, thereby strength to the immune system by increasing the formation of IgA named antibiotics. Thus, *Takra* detoxifies the body, cleanses intestines and replenishes the intestinal flora.

### Probable mode of action of *Pathya*

The seven *Pathya* of herbal and animal origin mentioned earlier have *Agnivardhaka* (digestive/metabolic stimulating) property due to their *Laghu* (easy to digest), *Ushna* (hot potency) and *Tikshna Guna* (helping for easy assimilation) and due to these *Guna* (attribute/property) they possess therapeutic action such as clearing of *Ama*, pacify *Kapha* and *Vata Dosha*. Thus, these drugs stimulate *Agni*, digest *Ama*, remove excessive *Kledaka Kapha* (subtypes of *Kapha* situated in the *Amashaya*), prevent further production of *Ama* (clear obstruction in channels of circulation) and transport *Pakwa Dosha* from *Shakha* (circulation) to *Koshtha* (cavities of body/hollow organs) for removal from the body. Increased salivary and gastric secretions by the use of *Katu Rasa* (pungent taste) are well known. Apart from this, they also improve the intestinal motility acting as *Vatanulomaka* (proper functioning of *Vayu*). According to *Ayurveda*, *Agni* is responsible for the subtle transformative processes associated with digestion called *Paka* or *Pachana Karma*, i.e., physiology of metabolism. Emerging studies put forward the presence of microbiome and microbiota in the human body. Thus, microbiota in the host acts as host-microbiota co-metabolic structure, which carries out various metabolic processes in the human body.<sup>[29]</sup> Hence, a direct correlation among the physiological aspects of both *Agni* and microbiota can be well-thought-out.

### Conclusion

The equilibrium of gut microbiota (GM) has role in the homeostasis of host immune mechanisms. Hence, when there is any alteration in GM, the immune mechanism is vulnerable to an inflammatory conditions like rheumatoid arthritis. Diet can thus play a major role in the modulation of GM in RA. The presence of BBIs in *Kulattha* (horse gram); bioactive components such as polyphenols and flavonoids in *Lashuna* (garlic); butyrate, SCFA in *Yava* (barley) controls etiopathogenesis of RA by restoring GM. *Shigru* (moringa), *Takra* (buttermilk), *Gomutra* (cow urine) and *Lashuna* (garlic) can inhibit inflammatory markers like IL-6, IL-17. Thus, dietary regimen has a direct link with GM of RA and specially dietary regimen mentioned as do's and dont's in the treatment of *Amavata* can be effective in the management of rheumatoid arthritis.

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### Conflicts of interest

There are no conflicts of interest.

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