JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2024/35468

SHORT REVIEW

A Review Article on the Role of Ingredients of *Kshara Vasti* (Medicated Enema) on Gut Microbiota of Rheumatoid Arthritis Patients

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Abstract

Kshara Vasti (medicated enema) is an important treatment in the management of *Amavata* which is correlated with Rheumatoid Arthritis (RA). The ingredients of *Kshara Vasti* have the property to act against *Ama* which is a root cause of the development of the disease. The main aim of this review is to study the role of ingredients of *Kshara Vasti* on the gut microbiota of RA patients. Jaggery, tamarind and rock salt have been proven to have a positive effect on the gut microbiome by enhancing the abundance of health-promoting species. Cow's Urine (CU)/Cow Urine Distillate (CUD) enhances the bioavailability and efficacy of a drug with which it is co-administered. *Anethum sowa* has a significant impact on caecal microbiota. The production of Short-Chain Fatty Acids (SCFAs) by Gut Microbiota (GM) may be a probable mode of action for the suppression of inflammatory conditions like RA. Each constituent in *Kshara Vasti* has a positive impact on modulating gut microbiota.

Keywords: *Amavata, Ayurveda,* Gut Microbiota, *Kshara Vasti, Niruha Vasti,* Rheumatoid Arthritis

1. Introduction

Amavata can be correlated to Rheumatoid Arthritis due to its clinical presentation and it can be managed by Ayurveda treatments. Chakradatta has emphasised that the line of treatment should focus on normalising *Agni* and *Ama Pachana* and eliminate thus vitiated *Ama* and *Vata*. Thus, here *Kshara Vasti* is taken to review its role on GM of RA as Pharmacomicrobiomics is an emerging area to deal with the variations in microbiota profile in relation to drugs. *Kshara Vasti* is mentioned in *Chikitsa Sutra* described by Chakradatta of *Amavata. Kshara Vasti* comprises of *Saindhava (Rock salt), Guda (Jaggery), Chincha (Tamarind Paste), Shatahva (Anethum sowa)* and *Gomutra* (Cow urine)[1,2].

Gomutra which has *Kshara Guna* is used in this *Vasti* in a maximum dose, about two-thirds of the total amount. *Kshara Guna*, because of its *Lekhana* and *Vishoshana* properties helps in counteracting *Ama* due to its opposite qualities and thus breaks the *Samprapti* of *Amavata*[3]. But it must be kept in mind that it may further vitiate *Vata*. Thus, keeping this view in mind, 30ml *Sahacharadi Taila* is added along with *Kshara Vasti.* Hence *Sahacharadi Taila* was added to avoid further *Vata Prakopa* due to *Kshara Vasti.* There is evidence of variation and composition in microbiota with respect to bioavailability of drugs like Disease Modifying Anti-Rheumatic Drugs used for RA[4]. Biomedicine has already shown some examples like methotrexate which needs the presence of microbiota to transform a chemical constituent to its active form even though clarity has to be proven yet in its mechanism[5]. The role of diet in modulating GM of RA is gaining importance and has even been recognised

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Article Received on: 27.10.2023 Revised on: 21.02.2024 Accepted on: 27.02.2024

as a potential interventional management in many diseases including RA[6,7]. Keeping this view, the main objective of the review is to analyse each ingredient of *Kshara Vasti* based on its action on the GM of RA.

2. Materials and Methods

Samhitas and *Nighantus* were reviewed to analyse the role of each content of *Kshara Vasti* mentioned in *Amavata Chikitsa* for its management. Different databases like PubMed, Scopus, DHARA, Google Scholar, Science Direct were searched using keywords like Rheumatoid Arthritis, Gut Microbiota, Gut Dysbiosis, Tamarind, Jaggery, Bagasse, Sugarcane, *Anethum sowa, Anethum graveolens,* Cow Urine, Short Chain Fatty Acids (SCFAs), Rock Salt with the help of Boolean operators 'AND', 'OR' and 'NOT'. Filters like clinical trials, within 5 years and free full text were applied. Among the research papers containing data regarding the role of sugarcane, bagasse, jaggery, cow urine, *Anethum Sowa* and rock salt in GM and RA were reviewed in detail. Hence, this review article was undertaken to analyse the role of ingredients of *Kshara Vasti* on the gut microbiota of RA patients.

2.1 Methods

Most relevant 44 papers were reviewed to analyse the role of *Kshara Vasti* in GM of RA patients. The immune system gets hampered due to alteration in gut microbiota and this leads to inflammatory conditions like RA. The microbiota in the colon produces SCFAs, as a result of fermentation of resistant dietary fibres. These microbial products are mainly acetate, propionate and butyrate, which are utilised by the host. The hosts are prone to inflammatory diseases like RA when there is less production of SCFAs or when there is a reduction in the bacterial populations which produce these metabolites. There is evidence for the pathogenesis of inflammatory conditions due to low butyrate and propionate-producing bacteria[8,9,10].

Bacteroidetes are the major producers of propionate from resistant carbohydrates and help in the fermentation of important peptides. It was found low carbohydrate diet does not cause decreased propionate proportion among faecal SCFAs. Succinate, the precursor of propionate obtained from the fermentation of resistant starch, is produced by abundant bacteroidetes, especially *Prevotella copri*[11]. Butyrate produced as a result of the fermentation of resistant starch has been shown to possess an analgesic effect in humans by inhibiting visceral sensitivity due to the composition of the microbiota[12]. Butyrate acts as an energy source for colonocytes and thus plays a major role in regulating gut health[13,14]. The effect of nutrients like polyphenols which reach the intestine along with its bioavailability decide the integrity of the gut barrier and maintenance of the gut microbiota at an equilibrium[15,16].

Pathya Ahara mentioned in the context of *Amavata* was found to have a positive impact on GM, as its anti-inflammatory effect would be due to its effectiveness in managing gut dysbiosis. The presence of Bowman-Birk Inhibitors (BBI) in *Kulattha* (*Macrotyloma uniflorum* Lam. or *Dolichos biflorus*), bioactive components like polyphenols and flavonoids in *Lasuna* (*Allium sativum* Linn.), butyrate, a SCFA in *Yava (Hordeum vulgare*), controls ethiopathogenesis of RA by restoring GM *Shigru (Moringa oleifera* Lam), *Takra* (buttermilk), *Gomutra* (Cow's Urine) and *Ardrak (Zingiber officinale* Roscoe) can inhibit inflammatory markers like IL-6, IL-17 and can increase the abundance of commensal GM[17].

So along with diet, *Kshara Vasti* (medicated enema) which is administered directly into the gut i.e. site of GM should be a major target when modulation of GM of RA is planned. The action of *Kshara Vasti*is is decided by the ingredients present in it. *Saindhava Lavana* (rock salt), *Guda* (jaggery), *Chincha* (tamarind), *Gomutra*,(cow's urine) and *Shatapushpa* (*Anethum sowa)*[18] makes *Kshara Vasti* a *Tikshna* as well as *Amaharayukta* (alleviates *Ama*) (Table 1)

Table 1. Ingredients of *kshara vasti*

Ingredients	Quantity	Approximate Weight
Saindhava lavana (Rock Salt)	1 *Aksha*	12gm
Guda (Jaggery)	2 *Pala*	100gm
Satapushpa (*Anethum sowa*)	1 *Aksha*	12gm
Chincha (*Tamarindus indica*)	2 *Pala*	100gm
Gomutra	8 *Pala*	400gm

2.2 Method of Preparation of *Kshara Vasti*[19]

12 gm of *saindava* was taken in *Khalva Yantra* and made into fine powder.100gm g*uda* was taken in another vessel, 100ml of water was added to it, melted, filtered added to *Khalva yantra* and triturated till it became a homogenous mixture. *Sahacharadi thaila* 30ml was added to it to avoid *Vata kopa* and made a homogenous mixture. 12 gm of *Satapushpa kalka* was added and triturated well and made a homogenous mixture. 100gm of *chincha* (as *kalka dravya*) was taken in another vessel and 50ml water was added, squeezed well, filtered, added to the *Khalva* and triturated. 400ml fresh *Gomutra* was added as *Avapa* and mixed well until it became a homogenous mixture.

2.2.1 Jaggery

In *Kshara Vasti* jaggery is used instead of honey. Here, one-year-old jaggery should be taken and the properties are *Ishat kshara* (slightly alkaline), *naati sheeta* (not too cold potency), *laghu (*easily digestible*), pathyatama* (best among wholesome), *anabhishyandi* (does not obstruct channels), *agnivardhaka* (kindles metabolism) *vatakaphahara* (reduces vitiated *vata* and *kapha*). It acts as *mootra shodhaka* (purifies urine), *rakta shodhaka* (purifies blood and its components) and *hrudhya* (tasty)[20].

Jaggery in melted form along with *saindhava* (rock salt) makes the mixture nearly an isotonic one and these substances cause some irritative changes in the colon either due to its retention for a few minutes or by a stimulating effect. It might also help in extending the drug potential to cellular levels. Jaggery is melted in a minimal amount of water and it should not be made thick after melting, as its *sara guna* may tend to get reduced as per clinical observations.

Jaggery has various health benefits as it is the least processed sugar which has the capability to retain most of its phytochemicals. Sugarcane contains polyphenols, phenols, phenolic acids, coumarins, flavonoids, stilbenes etc. The phenolic content was found to be higher than 4mg/g in dry bagasse and studies proved its significant results in acting against pathogenic bacteria and viruses. The possible action of the polyphenolic compound provides a bacteriostatic mechanism of sugarcane bagasse[21].

The polyphenols present in the diet are utilised by the gut bacteria to produce SCFAs and other phenolic acid metabolites which are beneficial in maintaining health. It has been proved already, that phenolic compounds and dietary fibres play a potential role in GM in maintaining health and management of disease[22]. The enrichment of pathogenic bacteria can be attenuated by the action of phenolic acids which in turn does not produce any kind of harmful effects over commensal or probiotic microorganisms. Stilbenes, a type of phenolic compound, mainly found as resveratrol in dietary intake was evidenced for increased *Lactobacillus* and *Bifidobacterium* after intake for 20 days. Its intake also suppressed the development of pathogenic *E. coli* and Enterobacterial population and thus administration of resveratrol was found to be effective in modifying gut dysbiosis. Sugarcane fibres contain certain polyphenols which remain resistant during digestion and get broken down to release polyphenols during colonic fermentation by the microbiota to maintain a healthy gut and thereby prevent diseases. Sugarcane fibres when treated on healthy human beings revealed a strong shift in the microbial composition and structure at 24 hours and a much higher abundance at 48 hours with a higher abundance of bacterial family capable of fermenting resistant carbohydrates. Bacteroidetes (Bacteroidaceae and Porphyromonadaceae), Firmicutes (Lachnospiraceae and Ruminococcaceae) and Actinobacteria (Bifidobacteriaceae) were found to produce a higher number of Carbohydrate-Active-Enzymes (CAZymes) which have a stimulated potential to digest polysaccharides in the human colon[23].

Fatty acids derived from sugarcane have already been proven for their anti-inflammatory effects in mice models in RA[24]. A potential prebiotic effect has been proven for xylo-oligosaccharides derived from sugarcane due to its capacity to produce butyrate and increase in abundance of Bifidobacterium adoloscentis which is a health-promoting species[25]. So, we can assume that jaggery-produced sugarcane used in *Kshara Vasti* may have a potential impact on GM of RA but the mechanistic action of jaggery in the homogenous mixture of *Kshara Vasti* has not been proven yet.

2.2.2 Chincha (Tamarind Paste)

Tamarind paste is used as *Kalka Dravya* (paste form) in *Kshara Vasti. Pakwa chincha* (ripe tamarind) has *amla rasa* (sour taste), *vata-kaphashamaka* (reduces

vitiated *vata* and *kapha dosha), ruksha* (dry), *deepana* (kindles metabolism*), sara* (mobility) and *ushna* (hot) properties. These properties make it useful for the diseases of *amavata* and *kapha rogas*. *ruksha guna* (dry attribute) and *ushna virya* (hot potency) help in counteracting the *ama* (morbid matter) hence achieving a*ma pachana*[26].

The polysaccharides present in tamarind have a prebiotic potential associated with SCFA production thereby modulating GM composition[27]. These polysaccharides in tamarind were found to be stable during digestion in the upper gastrointestinal tract and most of its glycosidic bonds get disrupted during colonic fermentation which is degraded by colonic microbiota to produce SCFAs with an increased molar proportion of propionic and butyric acid. The SCFAs thus produced have an inhibitory role over pathogenic microbiota at the genus level and they augment the growth of beneficial bacteria including *Lactobacillus, Firmicutes* etc. This acts as an anti-inflammatory as well as helps in maintaining intestinal barrier integrity[27]. Studies have already proven the antinociceptive activity of Tamarind pulp through activation of the opioidergic mechanism at both the peripheral and central levels[28].

So, correlating the *gunas* and *karmas* of *chincha* with GM, we can conclude that tamarind which is used as a *kalka dravya* in *Kshara Vasti* helps in reducing the clinical signs and symptoms of RA by modulating the gut microbiome in such patients.

2.2.3 Cow Urine (CU)

In *Kshara Vasti, Gomutra* (CU) is the chief content used as *avapa dravya,* which owing to its *katu rasa* (pungent taste), *katu vipaka* (pungent effect after digestion), *ushna virya* (hot potency), *laghu* (light to digest), *ruksha* (dry), *tikshna guna* (sharp nature) pacify the *kapha*. The *ruksha guna* (dry attribute) of CU is very much helpful in diseased conditions like *amavata, kapha and medhoja vyadhies*. It is considered useful for *Kshara Vasti* owing to its *tridoshahara, agnideepana, ama pachana, srotovishodhana* and *vatanulomaka* properties[29,30].

CU is the only animal product which has proved its bio-enhancing or bio-potentiator activity, i.e., it has the ability to enhance the bioavailability and efficacy of a drug with which CU is co-administered[30]. Because of its bio-enhancing potential along with anti-fungal, anti-microbial and anti-cancerous drugs, CU has been granted US patents. Some studies claim that Cow Urine Distillate (CUD) is more effective than CU, CUD augments the effect of rifampicin, tetracycline and ampicillin by faster transportation across the gut wall by 2-7 folds[32]. Similarly, it improves the bioavailability of rifampicin, ampicillin and clotrimazole. CUD has the capacity to inhibit pathogenic gram-positive bacteria like *Staphylococcus aureus* and *Pseudomonas aeruginosa*[33]. Augmented BandT lymphocyte blastogenesis, IgG, IgA and IgM antibodies in mice were seen due to the administration of CUD. CU also increases the phagocytic activity of macrophages and thus it helps in preventing and controlling infections. Hence CU is an influential and harmless immunomodulator which increases humoral as well as cell-mediated immunity[34]. Considering hygienic conditions, CU has been replaced by CUD these days for all therapeutic conditions in clinical practice, Thus, we can say that it may be because of the same reason CU is used widely in Ayurveda formulations and treatments like *Kshara Vasti.*

2.2.4 Anethum sowa Roxb.ex Flem or Anethum graveolens Benth

Shatapushpa is a plant with a wide range of chemical constituents with many pharmacological effects. *Anethum sowa Roxb.ex Flem* or *Anethum graveolens Benth.* of Umbelliferae or Apiaceae family is called *Shatapushpa, Shatahwa and Mishi* in Sanskrit and is commonly known as 'Dill' seeds. *Shatapushpa* is a *Vata Kapha shamaka* and *Pitta vardhaka* drug due to its *katu -tikta rasa, tikshna –snigdha guna* and *ushna veerya*[35]. As it has proved for its anti-inflammatory properties, its seeds are used externally as well as internally for rheumatic complaints. *Shatapushpa* (*Anethum sowa*) is commonly used in *Vasti Karma* (medicated enema) as a *Kalka Dravya*. *Acharya Charaka* has included *Shatapushpa* in *Asthapanopaga* and *Anuvasanopaga Mahakashaya Ganas*[36].

Anethum sowa has stimulant, carminative, anti-microbial, anti-inflammatory and anti-bacterial properties. Seeds and seed oil being the most useful part of *Anethum sowa* contains tannins, flavonoids, essential oils like eugenol, carvacrol, carvon, D-limonene, thymol, anethole, umbelliferones, phenolic acids etc.[37].

Tannins in the form of dietary articles improve nutrition and control gastrointestinal diseases. Tannins are polyphenolic compounds which have a significant impact on caecal microbiota. The prebiotic activity of tannins stimulates the production of probiotic bacteria, thereby increasing the abundance of Bifidobacterial species[38].

The influential role of flavonoids in intestinal microbiota has been confirmed by many studies. The result of an *in-vitro* study using mice gut microflora suggested that intestinal microbiota can transform flavonoids but they are not necessary for absorption of flavonoids[39].

Eugenol, carvacrol, D-limonene etc are the Essential Oils (EO) present in *Anethum graveolens Benth.* or *Anethum sowa Roxb. ex Flem*. Even though EO has demonstrated a positive impact on intestinal microbiota, most of the EO molecules are quickly assimilated into the small intestine. So, it does not reach up to the level of the large intestine where bacteria are found in excess. EO acts as bacteriostatic as well as bactericidal as it can control and modulate bacterial growth. It can also penetrate and damage the cell membrane of pathogenic bacteria thus making the membrane unstable, thereby acting as bactericidal. Orally administered eugenol in mice, increased intestinal mucus secretion, making a thick epithelial layer which is associated with positive impacts of microbiota in intestinal mucosa. Oral intake of limonene in mice enhanced *Lactobacillus* as well as *Bifidobacterium* growth[40].

Kshara Vasti being directly administered into the large intestine may thus have an impact on the GM of RA. Even though each of the contents of *Kshara Vasti* has some kind of impact on GM in accordance with the research in biomedicine, the mechanistic action of a homogenous mixture of all contents remains unclear.

2.2.5 Rock Salt

Saindhava lavana, or rock salt, is said to be the best type of salt in Ayurveda and is advised for regular usage. *Lavana* being one among *Shadrasa* has the *gunas* of *Sookshma, Snigdha, Laghu, Vishyandi, Tikshna*, *Ushna*, *Vataghna*, and *Anabhishyandi*; also has the *gunas* of *Sheeta Virya* and *Madhura Vipaka*. It also functions as *Deepana, Paachana and Tridoshagna*, and promotes proper *Vatanulomana* (evacuation of bowel and bladder). Because of the *Sukshma Guna*, it can facilitate the drug's entry into the micro-channels. *Saindhava* combined with *Madhu* can dissolve *Kapha* and thus it can be easily eliminated. Like this, it may eliminate the morbid *Dosa Sanghata* by liquefying it and breaking it into tiny pieces due to its *Ushna* and *Tikshna* properties, respectively. In addition, *Saindhava* breaks apart *Madhu'sPichcchila*, *Bahula*, and *Kashaya* qualities and unites closely with them to create a homogenous composite. When *Saindhava* is absent or present in insufficient amounts, *Ayoga* results, and when it is present in excess, *Daha* and *Atisara* occur. Honey and Saindhava Lavana together maintain glucose and electrolytes, thereby preventing dehydration[41-43].

Regular salt normally increases *Pitta Dosha*, whereas *Saindhava Lavana*, being *Sheeta Virya* helps to balance *Pitta*. It relieves *Kapha* and balances *Vata* due to its *Rasa Pradhanyata*[44].

A study conducted in rats proved higher levels of SCFAs, mainly acetate, propionate and isobutyrate were found in faecal samples of high salt diet-fed rats than controls (normal salt diet). Even though the study was on high salt diet modulating GM and SCFA production in a hypertensive rat model, we could understand that SCFA levels were elevated in high salt diet-fed rats when compared to normal salt diet-fed rats, from which we can conclude even normal salt diet produce positive correlation in SCFA production. So, there are potential mechanistic effects on immune modulation and gut barrier that may account for correlations between salt and microbial variation but remain unclear[45].

NaCl (Sodium chloride) appears to induce microbial restoration by increasing the quantity of probiotic bacteria that promote health. Thus, sodium supplementation might have a favourable impact on the intestinal microbiome by increasing the abundance of health-promoting probiotic strains such as Lactobacillaceae[46].

Jaggery being the least processed sugar retains much of the phytochemicals that are present in sugarcane juice, and has potential prebiotic due to its capacity to produce butyrate and increase in abundance of *Bifidobacterium adoloscentis* which is a health-promoting species. The polysaccharides present in tamarind have a prebiotic potential associated with SCFA production thereby modulating GM composition. CU/CUD enhances the bioavailability and efficacy of a drug with which it is co-administered and it also acts as an immunomodulator.

Anethum sowa being anti-inflammatory, contains tannins, flavonoids etc which has a significant impact on caecal microbiota. The prebiotic activity of tannins stimulates the production of probiotic bacteria and helps in maintaining gut integrity. Rock salt supplementation might have a favourable impact on the intestinal microbiome by increasing the abundance of health-promoting probiotic strains.

3. Conclusion

Kshara Vasti is one of the prime treatment modalities in the management of Rheumatoid Arthritis. Even though it has already been proven for its clinical efficacy in RA, the role of *Kshara Vasti* in GM of RA has not been studied yet. The pharmacomicrobiomics of each constituent of *Kshara Vasti* is known to have a positive impact on modulating GM. The SCFAs like butyrate and propionate are produced as a result of the digestion of jaggery, tamarind and rock salt by GM but it is still unclear how *Vasti* (medicated enema) being a homogenous emulsion acts over GM of RA. The production of SCFAs by GM may be one of the probable modes of action for the suppression of inflammatory conditions like RA. Hence studies should be initiated to find the possible mechanism of action of *Kshara Vasti* over the gut microbiota of RA patients.

4. Acknowledgements

We would like to thank Amrita School of Ayurveda, Amritapuri, Amrita Vishwa Vidyapeetham for all the facilities provided. We would also like to thank AYUSH COE for the fellowship as the initial part of this work was a part of the Student Fellowship Program, AYUSH Center of Excellence (supported by the Ministry of Ayush, Government of India), Center for Complementary and Integrative Health, Interdisciplinary School of Health Sciences, Savitribai Phule Pune University (SPPU), Pune. We would also like to thank Dr. Girish Tillu for the valuable suggestions for writing this review.

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