



Review Article

BASIC TENETS OF SANDHIGATAVATA W.S.R. OSTEOARTHRITIS AND ASSESSMENT OF PHARMACOLOGICAL BASIS OF TRAYODASHANGA GUGGULU: A CLASSICAL AND CONTEMPORARY OVERVIEW

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ABSTRACT

Sandhigatavata is comparable to osteoarthritis of modern medicine. It is a kind of articular degenerative disorders that can affect any joints but generally observed weight bearing joints. It is prevalent since antiquity and commonly exists among elderly age group. Osteoarthritis is the second most common rheumatologic problem and it is the most frequent joint disease with a prevalence of 22% to 39% in India. It is predominant in females as compared to male. Variety of herbal and herbo-mineral formulations are mentioned in Ayurvedic lexicons for its management, *Trayodashanga guggulu* is one of them. In this concern, we have laid down an emphasis in brief on *Sandhigatavata* and trying to explore the classical and contemporary pharmacological aspects of *Trayodashanga guggulu* for its management.

INTRODUCTION

Osteoarthritis (OA) is a common clinical condition in old age population for which patients seek complementary treatment.^[1] Due to the limitations of conventional medicine, patients are increasingly turning to alternative therapies including Ayurveda. Osteoarthritis has a clinical similarity to *Sandhigatavāta* of Ayurveda, which is defined in the context of *Vātavyādhi*.^[2] *Sandhigatavāta* is initiated due to inappropriate nutrition, lifestyle, old age and other associated risk factors, which results deterioration of body tissues (*Dhātuksaya*). It may lead to aggravates *Vāta* (the humour responsible for all bodily motions) and reduces *Śleṣaka Kapha* (synovial fluid present in joints).

The exacerbated *Vāta* results in joint tissue destruction and it may lead to joint deterioration, discomfort, and inflammation. In old age, there is a

rise in *Vāta Doṣa*, *Vasti* (medicated enema) therapy is regarded as superior one and is the therapy of choice for vitiated *Vātapradhana* (*Vāta* dominating) diseases.^[3] Considering the role of *Vridhāvasthā* (elderly age group) and *Vātadoṣa*, *Trayodaśāṅga Guggulu* has been chosen as drug of pharmacological assessment due to its *Vedāsthāpaka*, *Rasāyana* and *Vātaśamaka* properties.

Musculoskeletal Diseases (MSDs) constituted the second largest contribution to worldwide disability, according to the 2016 Global Burden of Disease (GBD) research. The burden of MSDs varies by age group, however between 20% and 33% of individuals worldwide suffer with a painful MSD^[4]. OA accounts for 50% of all MSDs. Globally, 9.6 percent of men and 18% of women over the age of 60 suffer from symptomatic OA, with the knee being the most often afflicted joint^[5].

Osteoarthritis (OA) is a common chronic joint disease that may rise gradually as human life expectancy increases.^[6] Numerous studies have shown a link between OA and genetic, biochemical, and biomechanical variables.^[7] OA is a degenerative joint disease that affects cartilages and the tissues that surround them. It advances slowly and is frequently accompanied by pain and restricted joint movement.^[8] Thus, OA not only diminishes the quality of life of

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patients, but also increases certain social and economic burden.

Once considered a non-inflammatory type of arthritis, OA is now understood to be associated with an excessive inflammatory response.^[9] Numerous studies have established that the primary mechanisms behind the inflammatory response are intimately linked to the formation of free radicals and the establishment of oxidative stress.^[10] Notably, oxidative stress has a role in OA development.^[11]

The majority of current treatments for OA include intra-articular injection, oral drugs, physical, alternative, and surgical measures.^[12] Numerous medications have been shown to be useful in alleviating pain in people with OA, including analgesics such as non-steroidal anti-inflammatory medicines (NSAIDs), corticosteroids such as glucocorticoids; hyaluronic acid, and local anaesthetics.^[13,14] However, its clinical applicability has been limited due to adverse effects. As a result, it is critical to do research on novel therapeutic agents for the treatment of OA.

Disease Review

In Ayurveda treatises, the disease can be understood by obtaining chiasmic view into the bottomless description of *Vāta-Vyādhi*. *Vātavyādhi* is a group of *Vātika* disorders.^[15] *Sandhigatavāta* is described in the classical texts of Ayurveda under *Vātavyādhi*. It is specially occurring in *Vṛiddhāvasthā* where *Dhātukṣaya* takes place, which leads *Vātaprakopa*. *Vāta* and *Asthi* have *Āsraya-Āsrayī Saṁbandha*, which means *Vāta* takes shelter in *Asthi*. Aggravated *Vāta* reduce the *Sneha*, from *Jānu Sandhi* by its opposite qualities to *Sneha*. Due to diminution of *Sneha*, *Khavaigunya* occur in *Asthi* and *Sandhi*, which is responsible for the production of *Sandhigatavāta*.

Pathophysiology (Samprāpti)

The *Samprāpti* of *Vāta Vyādhi* in general is applicable to *Sandhigatavāta*, as no separate *Samprāpti* is given in the texts. According to *Ācārya Caraka*, the *Rikta Srotas* in the body gets filled with *Anila* that is *Balwān (Prakupita)* and leads to the production of various *Sarvāṅga* and *Ekāṅga Roga*.^[16] *Cakrapāṇi* ^[17] commenting on the word '*Riktani*' says; *Snehādi Guṇasūnya* i.e., the *Srotas*, which is devoid of *Sneha Guṇas* gets filled with *Prakupita Vāta* and produces either *Sarvāṅga* or *Ekāṅga Roga*. *Sandhigatavāta* may

be an *Ekāṅga Roga* or *Sarvāṅga Roga* i.e., involved single or multiple joint.

Sandhigatavāta is a type of *Vāta Vikāra*, where the *Dūṣita vāta* involves the *Sandhi* and hence, the nomenclature- *Sandhigatavāta*. In *Sandhigatavāta* early pathology starts with accumulation of *Vāta* specially *Vyāna Vāyu*, which is aggravated by different factors and takes it up to the *Prasara* stage. The *Khavaigunya* of *Sandhi* leads its *Sthānasamśraya* of vitiated *Vātadoṣā* and provides its interaction with associated structures of joints (*Dūṣyas*). The *Prakopa* of *Vāta* in the body takes place due to two causes i.e., a) *Āvaraṇa* and b) *Dhātukṣaya*. *Sandhigatavāta* is commonly seen in the obese persons. It may be due to *Āvaraṇa* of *Kapha* and *Meda*. *Sandhigatavāta* being a degenerative disease and mainly occurs in the old age, which may also be considered due to the pure *Dhātukṣaya*. In such type of disorders *Caraka* mentioned that the *Kha-vaigunya* is mainly due to empty *Srotasa*.^[16] According to *Cakrapāṇi*^[17] this means the diminution of *Śleṣaka Kapha* specially its *Sneha guṇa* in the involved joint. In *Vṛiddhāvasthā*, *Vāta Doṣa* is dominant due to natural ageing process and *Kapha Doṣa* decreases. So, obviously *Sandhigatavāta* is more likely to occur in *Vṛiddhāvasthā*. Further in *Vṛiddhāvasthā*, the functioning of *Dhātvaṅni* becomes irregular, which may lead to *Anuloma Kṣaya* of *Dhātus*.

Osteoarthritis (OA) is the most prevalent kind of arthritis globally, affecting any joint in the body. In middle-aged and older persons, symptomatic OA is a significant source of disability and participation limitation. In a healthy joint, cartilage covers the bones' surfaces and aids in their movement. When cartilage is destroyed, the entire joint's tissues become more active in an attempt to heal the injury. However, the healing processes are not always effective, resulting in symptoms. It can be characterized and diagnosed in a variety of ways, including pathological abnormalities, imaging changes, physical indications, and co-occurring symptoms.^[18] The cervical and lumbo-sacral spines, hip, knee, and first metatarsal phalangeal joints (MTP) are typically damaged by osteoarthritis. OA structural alterations are practically ubiquitous in the aged, according to cadaveric research. Many people with OA don't have symptoms, the incidence of symptomatic OA is more important than the frequency of structural abnormalities.^[19]

Table 1: Contents of Trayodaśāṅga Guggulu ^[20]

Name	Latin Name	Family	Parts Used
<i>Babūla</i>	<i>Acacia arabica</i>	Leguminoceae	Bark
<i>Aśwagandhā</i>	<i>Withania somnifera</i>	Solanaceae	Root

<i>Haūber</i>	<i>Juniperus communis</i>	Cupressaceae	Seed
<i>Gudūcī</i>	<i>Tinospora cordifolia</i>	Menispermaceae	Stem
<i>Śatāvarī</i>	<i>Asparagus racemosus</i>	Liliaceae	Tuber
<i>Gokshur</i>	<i>Tribulus terrestris</i>	Zygophyllaceae	Root
<i>Vidhārā</i>	<i>Argyrea speciosa</i>	Convolvulaceae	Seeds
<i>Rāsnā</i>	<i>Pluchea lanceolata</i>	Compositae	Root
<i>Śatapuṣpā</i>	<i>Foeniculum vulgare</i>	Umbelifereae	Root
<i>Karchura</i>	<i>Curcuma zedoaria</i>	Zingiberaceae	Bark
<i>Ajwayan</i>	<i>Trachyspermum Ammi</i>	Umbelifereae	Satva
<i>Śūṅṭhī</i>	<i>Zingiber officinale</i>	Zingiberaceae	Rhizome
<i>Guggulu</i>	<i>Commiphora mukul</i>	Burseraceae	gum resin
<i>Ghrita (ghee)</i>	-	-	-
<i>Devadāru</i>	<i>Cedrus Deodara</i>	Pinacea	Stem/Bark

Table 2: Ayurvedic pharmacodynamics & classical indication of individual herb of *Trayodaśāṅga guggulu*^[21,22]

Drugs	Rasa	Guṇa	Vīrya	Vipāka	Doṣakarma	Relevant therapeutic uses
Ābhā	<i>Tikta, Kaṣāya</i>	<i>Laghu, Rūkṣa</i>	<i>Śīta</i>	<i>Kaṭu</i>	<i>Kapha -hara</i>	<i>Asthi-snadhi gata Vāta, Bhagna</i>
Śūṅṭhī	<i>Kaṭu</i>	<i>Laghu, Snigdha</i>	<i>Ūṣṇa</i>	<i>Madhura</i>	<i>Vāta Kaphaśāmaka</i>	<i>Dīpana, Āmadośahara, Pācana, Anulomana</i>
Gudūcī	<i>Tikta, Kaṣāya</i>	<i>Laghu</i>	<i>Ūṣṇa</i>	<i>Madhura</i>	<i>Tridoṣa-śāmaka</i>	<i>Sāṅgrāhika, Dīpana, Balya, Rasayana, Raktaśodhaka, Jwarghna</i>
Aśwagandhā	<i>Tikta, Kaṭu, Madhura</i>	<i>Laghu, Snigdha</i>	<i>Ūṣṇa</i>	<i>Madhura</i>	<i>Vāta-Kaphaśāmaka</i>	<i>Śoṭha-nāśaka, kṣayanāśaka, Balya, Rasāyana.</i>
Śatāvarī	<i>Madhura, Tikta</i>	<i>Gurū, Snigdha</i>	<i>Śīta</i>	<i>Madhura</i>	<i>Vāta-pitta-śāmaka</i>	<i>Rasāyana, Balya, Medhya, Viṣaghna</i>
Rāsnā	<i>Tikta</i>	<i>Gurū</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Kapha -vāta-śāmaka</i>	<i>Āma-pācaka, Vedanāśāmaka, Viṣaghna, Rasāyana</i>
Devadāru	<i>Tikta</i>	<i>Laghu, Snigdha</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Vātahara, Kapha hara</i>	<i>Śoṭha, Vibandhanāśaka, Āma-Vātahara</i>
Gokshuru	<i>Madhura</i>	<i>Gurū, Snigdha</i>	<i>Śīta</i>		<i>Tridoṣa-śāmaka</i>	<i>Balya, Brumhana, Vṛsya</i>
Vidhārā	<i>Tikta, Kaṣāya, Kaṭu</i>	<i>Laghu, Snigdha</i>	<i>Ūṣṇa</i>	<i>Madhura</i>	<i>Kapha -vāta-śāmaka</i>	<i>Balya, Āmavāta-hara, Śoṭhahara, Rasāyana</i>
Hapuṣā	<i>Tikta, Kaṣāya, Kaṭu</i>	<i>Guru, Mṛdu</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Vātaśāmaka, Kapha śāmaka</i>	<i>Lekhana, Śoṭhhara, Agnidīpaka</i>
Śatapuṣpā	<i>Tikta, Kaṭu</i>	<i>Laghu, Rūkṣa, Tikṣṇa</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Kaphvātaśāmaka</i>	<i>Vedanāśāmaka, Śoṭhahara, Dīpana</i>

Guggulu	<i>Tika, Katu, Madhura, Kasaya</i>	<i>Laghu, Tikṣna, Snighda, Picchila, Suksma, Sara</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Tridosahara</i>	<i>Vedanasthapana-Nadibalya- Vātasamaka</i>
Yavānī	<i>Tikta, Kaṭu</i>	<i>Laghu, Rūkṣa, Tikṣṇa</i>	<i>Ūṣṇa</i>	<i>Kaṭu</i>	<i>Kapha-vātasāmaka</i>	<i>Vedanāsāmaka, Śothahara, Anulomana</i>

Table 3: Contemporary pharmacological Evidences of Trayodaśāṅga guggulu

Selected Trial Drug	Contemporary Pharmacological evidences
<i>Ābhā (Acacia nilotica)</i>	Anti-inflammatory in chronic systemic inflammation ^[23] , anti-cancer ^[24] , hepatocellular protective effect ^[25] , strong anti-oxidant ^[26] , free radical scavenging activity ^[27]
<i>Śūṅṭhī (Zingiber officinale)</i>	Anti-obesity and weight lowering effect ^[28] , analgesic ^[29] , alleviates neuropathic pain by inhibiting neuro-inflammation ^[30] , anti-hyperalgesic potency in chronic pain ^[31] , anti-osteoarthritic effects ^[32] , role in the prevention of ageing and degenerative diseases ^[33] , therapeutic efficacy in knee OA ^[34]
<i>Guḍūcī (Tinospora cordifolia)</i>	Antiosteoporotic ^[35] , chondroprotective ^[36] , osteoprotective and osteoblast stimulatory ^[37] , analgesic and anti-inflammatory ^[38] , osteogenic and antiosteoporotic ^[39] , immunomodulatory and other multifaceted use ^[40] , effective as alternative to glucosamine and celecoxib ^[41] .
<i>Aśvagandhā (Withania somnifera)</i>	Anti-inflammatory and anti-arthritic ^[42,43] , anxiolytic and stress relieving, ^[44] chondroprotective, ^[45] anti-osteoarthritic effect ^[46] , anti-osteoporotic effect ^[47] , anti-hyperalgesic, analgesic ^[48] .
<i>Śatāvārī (Asparagus recemosus)</i>	Anti-inflammatory ^[49] , antioxidant ^[50] anti-stress ^[51] , anti-depressant; antioxidant and hepatoprotective ^[52]
<i>Rāsnā (Pluchea lanceolata)</i>	Protective against cognitive deficits ^[53] , rejuvenating and anti-inflammatory effect ^[54]
<i>Karcūra</i>	Anti-inflammatory activity, ^[55] antioxidant activity, ^[56] hepatoprotective activity, ^[57] immunomodulatory effect. ^[58]
<i>Devadāru (Cedrus Deodara)</i>	Anti-inflammatory and analgesic, ^[59] anti-oxidant, anti-obesity, ^[60] anti-depressant, free radical scavenging ^[61] .
<i>Vidhārā (Argyrea speciosa)</i>	Ameliorative potential against neuropathic pain ^[62] , analgesic and anti-inflammatory, ^[63] anti-obesity ^[64] , anti-stress, ^[65] anti-arthritic ^[66]
<i>Hapuṣā (Juniperus communis)</i>	Anti-arthritic, ^[67] anti-inflammatory, ^[68] anti-nociceptive ^[69]
<i>Śatapušpā (Anethum sowa)</i>	anti-inflammatory on topical use, ^[70] anti-spasmodic, ^[71] anti-oxidant and carminative ^[72]
<i>Ajamodā (Carum roxburghianum)</i>	Gut relaxation and antispasmodic ^[73] , anti-bacterial activity, ^[74] anti-cancer, ^[75]
<i>Yavānī (Trachyspermum ammi)</i>	Anti-arthritic ^[76] , analgesic on topical use ^[77] , anti-inflammatory ^[78] , anti-rheumatic potential ^[79]
<i>Gokṣuru (Tribulus terrestris)</i>	Analgesic, ^[80] anti-inflammatory & anti-oxidant activity, ^[81] anti-arthritic activity ^[82] , immunomodulatory effect ^[83] , diuretic ^[84] , absorption enhancer ^[85]

DISCUSSION

Probable Mode of Action of *Trayodaśāṅga a Guggulu*^[86]

Trayodaśāṅga, a *Guggul* is an Ayurvedic formulation of 13 herbs, including *Guggulu*, that has been prepared in ghee. Constituents such as *Śatāvri*, *Ashwagandha*, and *Gudūcī* are rejuvenators that strengthen *Dhatu*. *Śunthī* and *Ajamodā* is booster of *Jatharāgni*, whereas *Babūla* focuses on *Asthidhātvaṅni* and thus maintain the integrity of bone and joints.

Ghee's has *Yogavāhi* characteristic aids in the drug's absorption and penetration^[87]. Thus, *Trayodaśāṅga guggulu* has a direct effect on the aetiology of *Sandhigatavāta*, aids in the disintegration of *Samprapti*, and balances the vitiated *Vāta Doṣa*.

According to Ayurvedic principles, *Agnimāndya* always results in *Anuloma Dhātuksaya*, which results in *Vātavyādhi*. *Agnimāndya*, as a *Vātavyādhi*, is critical in *Sandhigatavāta*. *Agnimāndya* is rectified by *Dīpana-Pācana dravya* such as *Śunthī*, *Ajamodā*, and *Śatapushpā*, which also serve as *Vātānulomaka*, *Vātaśāmaka*, and *Vedanāsthāpaka* properties respectively. *Dhātuksaya rodhaka*, *Dhātuvardhaka*, and *Daurbalyanāśaka cikitsā* are the need of hours in patients having in *Sandhigatavāta* because *Mamsa* and *Asthidhātu ksaya*. *Aśwagandhā*, *Śatāvri*, *Gudūcī*, *Guggulu*, *Vridhdhārū*, *Babūla*, *Hapuṣā*, and *Goghṛta* acted as *Balya*, *Rasāyana*, and *Vayasthāpaka*, which are quite beneficial *Sandhigatavāta* in geriatric-prone patients^[88].

Generally, *Vātavyādhi Vātaprakopa*, *dhātuksīṅnata*, *Dhātu rūkṣata*, *Paruṣata*, and *Asthi Dhātuksaya* are discovered. *Trayodaśāṅga Guggulu*'s contents were mostly *Guru*, *Snigdha guṇatmaka*, *Madhur rasa*, *Madhur vipākī*, and *Ūṣṇa vīryātmaka*, all of which have characteristics that alleviate the above-mentioned symptoms. Thus, the components of *Trayodaśāṅga Guggulu* directly contributed to *Samprapti vighaṭana* through the specific qualities of each medication and the medicine as a whole.

Ayurvedic medicines have constituents that may be classified into four groups based on their mode of action.

- **Rasāyana and Balya:** *Aśwagandhā*, as well as *Guggulu* boosts the body's general vitality, promoting appropriate *Dhātupoṣaṇa*, and aiding in the prevention of degenerative processes of *Jānusandhi*.
- **Vātaśāmaka, Śūlapraśamana,** and **Śothahara:** The majority of Ayurvedic herbs fall under this category, and these herbs primarily aid to alleviate *Sandhiśūla*, *Sandhiśoṭha*, and *Sandhigrāha* among other conditions, by their unique impact on joints due to their unique *Guṇa* and *Karma*.

- **Āmapacana, Rocana, Dīpana:** *Ajamodā*, *Śatapushpā* and *Śunthī* along with others herbs, contribute to the maintenance of a healthy digestive system, which aids in the digestion of *Ama doṣa* in the body.

It has been well established for many years that reactive oxygen species are crucial in inflammatory processes, including various kinds of arthritis such as osteoarthritis. Cartilage degradation, the last stage of joint tissue degeneration, is caused by a combination of mechanical stress and biochemical causes, namely metalloproteinase and reactive oxygen species. Antioxidants, both enzymatic and non-enzymatic, maintain a balance of reactive oxygen species activity by blocking oxidative enzymes and scavenging free radicals. Thus, antioxidant therapy techniques for osteoarthritis have been proposed.^[89]

As the above data show, most of contents of *Trayodaśāṅga a Guggulu* have analgesic, antioxidant, anti-inflammatory properties. Contents like *Aśwagandhā* etc., which have anti-arthritic effect by their anti-inflammatory and/or antioxidant properties^[90,91] and it have shown different beneficial effects on adjuvant experimentally induced arthritis treatment. Now in modern medicine we know that one of the predisposing factors to osteoarthritis development is renal dysfunction.^[92] For this reason, *Gokṣhurū* (*Tribulus terrestris*) have beneficial effect in renal functioning.

CONCLUSION

No doubt contemporary medicine has found a way to minimise the intensity of pain and by adopting the knee transplant measures facilitate the quality of life up to some extent in OA patient but these are always associated with adverse events. As noted above, the (herbal) ingredients of *Trayodaśāṅga guggulu* are primarily supported by current documentation for their anti-arthritic, analgesic, and anti-oxidant properties; and for treating and preventing osteoarthritis. It is impossible to disregard the possibility that further alternative medications might be used in modern medicine as natural anti-inflammatory agents not only to prevent osteoarthritis development but also to manage osteoarthritis. Undoubtedly, further research is needed to prove the safety and effectiveness of these herbs to manage osteoarthritic joint pain and inflammation.

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