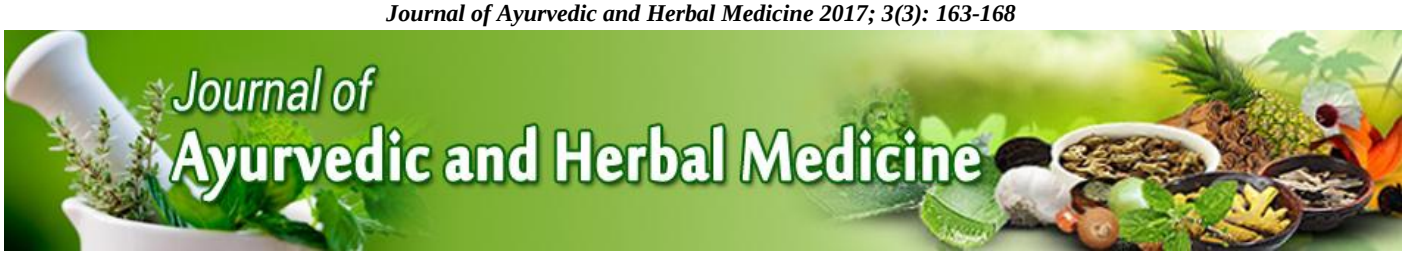

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Review on *Trisama*- an unexplored ancient Ayurvedic formulation

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ABSTRACT

Indian system of medicine has a longstanding history of using medicinal plants for the prevention and treatment of various health ailments. *Trisama* is an ancient Ayurvedic preparation can be prescribed for a wide range of disorder but not popular as many other Ayurvedic herbal formulations. *Trisama* is preparing by mixing the *Sunthi* (*Zingiber officinale* Linn.), *Haritaki* (*Terminalia chebula* Retz.), and *Guduchi* (*Tinospora cordifolia* Willd Meirs) in equal proportion. It is credited with diverse beneficial therapeutic effects mainly as *Shothhara* and *Amapachana* and reported to possess many pharmacological properties due to its common *Usna Virya* and *Madhur Vipaka* of the individual ingredients. The reported pharmacological effects of its ingredients are anti-oxidant, anti-inflammatory, anti-pyretic, analgesic, anti-microbial, hypolipidemic, cardioprotective, gastroprotective, cytoprotective effects etc. The bioactive components responsible for these therapeutic potential are mainly due to the presence of major important phytoconstituents such as phenolics components like gingerols, gingerdiols and gingerdione, shogaols, zingiberine, giloin, berberine, tinosporin, tinosporin acid and gallic acid. The present review focuses on summarizing the formulation details by their Ayurvedic properties, phytoconstituents and pharmacological activity. The review suggests that, *Trisama* formulation is easily available, economical, palatable and more beneficial for human health.Hence, it may be popularize among general Practitioner as an important Ayurvedic medicine in the form of *churna* (powder) and *kwatha* (decoction) for the treatment of *Sotha* and metabolic disorders.

Keywords:*Ayurveda, Guduchi, Haritaki, Sunthi,Trisama*.

INTRODUCTION

Medicinal plants, as source of remedies, are widely used as alternative therapeutic tools for the prevention or treatment of many diseases. Out of all the plants that have proved useful for humanity, a few are distinguished by their astonishing versatility. The term *Triphala* and *Trikatu* in Ayurvedic literature usually used to indicate three ingredients[1].This is also called as *Samatraya* (three ingredients in equal quantities). In classics, another group of three drugs mentioned with the name *Trisama* is a compound Ayurvedic formulation composed of three ingredients in equal quantity. They are as *Sunthi(Zingiber officinale* Linn.), *Haritaki* (*Terminalia chebula* Retz.), and *Guduchi* (*Tinospora cordifolia* Willd Meirs). The use of drug is mentioned in form of *Trisama*, an Ayurvedic remedy for the treatment of metabolic, inflammatory and digestive disorders. It provides a comprehensive account of Ayurvedic properties, important pharmacological studies and chemical constituents.

Individual content of *Trisama* are also widely used in many Ayurvedic formulations as well as in single for many ailments but most importantly to treat inflammatory and metabolic disorders. Scientific studies carried out in the past two decades on individual content have validated many of the ethno-medicinal claims and researches have shown to possess anti-oxidant, anti-inflammatory, anti-pyretic, anti-bacterial, wound healing, anti-carcinogenic, hypoglycemic, anti-cancer, radioprotective, chemopreventive, cardiovascular, cytoprotective, anti-arthritic, anti-microbial, immunomodulatory, gastro protective and hypolipidemic effects. *Trisama* is an important Ayurvedic formulation in many disorders but not explored by physician in clinical practice. It is need of present era, to find out scientific evidence of such useful unexplored formulation mentioned in Ayurvedic classics hence, thought worthwhile to carryout extensive review on *Trisama* and its ingredients.

Rasapanchaka of *trisama*

Sunthi

Rasa- Katu; Guna- Tiksna, Usna, Guru; Veerya- Ushna; Vipaka- Madhura; Prabhava- Tridoshashamaka; Karma-Vatahara, Kaphahara, Rochana, Dipana, Bhedana, Svarya, Hrdya, Vrisya

Haritaki

Rasa- Kashaya, Tikta, Madhura, Katu, Amla; Guna- Laghu, Ruksha; Veerya- Ushna; Vipaka- Madhura; Prabhava- Tridoshashamaka especially *Vatashamaka; Karma- Shothahara, Vedanasthapana, Vranashodhana, Vranaropana, Deepana, Pachana, Anulomana, Mridurechana, Grahi, Shonitasthapana, Kaphaghna, Srotah-shodhana, Vrishya, Garbhashayashothahara, Mootrala, Rasayana.*

Guduchi

Rasa- Tikta, Kashaya; Guna- Guru, Snigdha; Veerya- Ushna; Vipaka- Madhura; Prabhava-Tridoshashamaka; Karma-Vedanasthapana, Deepana, Pachana, Pittasaraka, Anulomana, Sangrahi, Raktashodhaka, Kaphaghna, Vrishya, Balya, Pramehahara, Mootrajanana, Dahaprashamana, Rasayana.

CHEMICAL CONSTITUENTS

***Sunthi*:** The constituents of ginger are numerous and vary depending on the place of origin and whether the rhizomes are fresh or dry. The primary pungent agents (phenylalkylketones or vanillylketones) of ginger are gingerol, with other gingerol analogues such as the shogoals, paradol and zingerone also found in high levels in rhizome extracts. The major pharmacological activity of ginger appears to be due to gingerol and shogaol. Phenylalkylketones or vanillylketones of ginger include 6-gingerol 8-gingerol and 10-gingerol, 6-shogaol, 8-shogaol, 10-shogaol and zingerone. 6-paradol, 6 and 10-dehydrogingerdione and 6- and 10-gingerdione have also been identified [2].

***Haritaki*:** It contains several phytoconstituents like tannins, flavonoids, sterols, amino acids, fructose, resin, fixed oils etc., however, it is fairly rich in different tannins (approximately 32% tannin content). Few hydrolysable tannins like terflavin B, C, and D, punicalagin and punicalin, terflavin & terchebulin with novel tetraphenyl carboxylic acid (terchebulic acid) moiety.+ Further, tannin content of *T. chebula* largely depends on its geographic location. The chief components of tannin are chebulic acid, chebulinic acid, syringic acid, chebulagic acid, gallic acid, corilagin and ellagic acid [3]. Phytochemicals like anthraquinones, ethaedioic acid, sennoside, 4, 2, 4 chebulyl-d glucopyranose, terpinenes and terpinenols have also been reported to be present [4]., Recent studies shows that *T. chebula* contains more phenolics than any other plant [5]. like 1,6-di-*O*-galloyl-D-glucose, punicalagin, 3,4,6-tri-*O*-galloyl-D-glucose, casuarinin, chebulanin, corilagin, neochebulinic acid [6]. From leaves of *Terminalia chebula,* a new triterpene, 2-α-hydroxymicromeric acid, maslinic acid and 2 -α- hydroxy ursolic acid were isolated [7].

***Guduchi*:** Numerous constituents belonging to different chemical classes such as alkaloid, terpenoid, lactone, glycoside, steroid, phenolics, aliphatic compounds, lignan, and polysaccharide have been isolated and characterized from different parts of *T. cordifolia* like Tinosponone and tinocordioside [8], sesquiterpene glucoside tinocordifolioside [9], sesquiterpene tinocordifolin [10] have been isolated and reported from the stem of *Tinospora cordifolia*. The new clerodone furano diterpene named columbin [11], tinosporaside [12], immunological active arabinolactone [13], cordioside, furano diterpene [14], magnoflorine [15] and several glycosides, alkaloids; Jetrorrhizine, palmitine, berberine, tembeterine, phenyl propene, disaccharides, cordifolioside A, B and C [16] have been isolated from *Tinospora cordifolia*. Other compounds isolated as choline, tinosporic acid, tinosporal, tinosporone, 20-β-hydroxy ecdysone [17], cordifolioside D & E and palmatoside C and F [18, 19]. Especially Leaves are rich in protein, calcium, and phosphorus [20]. Methanol extract of leaves is rich in flavanoids, alkaloids and glycosides [21].

PHARMACOLOGICAL ACTIVITY

Sunthi

Anti-coagulant effects: *Z. officinale* has been shown to inhibit platelet aggregation and to decrease platelet thromboxane production *in-vitro* [22]. (8)-Gingerol, (8)-shogaol, (8)-paradol, and gingerol analogues (1 and 5) exhibited antiplatelet activities. However, its *in-vivo* effects has not been well studied [23].

Anti-emetic effects: The components in ginger that are responsible for the antiemetic effect are thought to be the gingerols, shogaols, and galanolactone and diterpenoid [24]. Recent animal models and *in vitro* studies have demonstrated that, ginger extract possesses antiserotoninergic and 5-HT3 receptor antagonism effects, which play an important role in the etiology of postoperative nausea and vomiting [25].without affecting the gastric emptying time in a randomized, placebo controlled, crossover trial of 16 healthy volunteers given with ginger (1g orally) [26].

Anti-inflammatory effects: *Z. officinale* has a long history of use as an anti-inflammatory and many of its constituents have been identified as having anti-inflammatory properties [27]. *Z. officinale* has been found to inhibit prostaglandin biosynthesis [28] and interfere with the inflammatory cascade and the vanilloidnociceptor [29].

Anti-nociceptive effects: (6)-shogaol has produced anti-nociception and inhibited the release of substance P in rats, seemingly via the same receptor to which capsaicin binds. However, it was observed to be 100 times less potent and to elicit half the maximal effect of capsaicin [30].

Anti-oxidant effects: *In vitro*, *Z. officinale* has been shown to exhibit anti-oxidant effects [31]. (6)-gingerol appears to be the anti-oxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress [32].

Gastrointestinal effects: The active components of ginger are reported to stimulate digestion, absorption, relieve constipation and flatulence by increasing muscular activity in the digestive tract. In addition, (6) shogaol, generally more potent than (6)-gingerol, has inhibited intestinal motility in intravenous preparations and also facilitated gastrointestinal motility in oral preparations. Ginger extract has also been reported to inhibit the growth of *Helicobacter pylori* in vitro. However, observed a significant increase in the exfoliation of gastric surface epithelial cells following the consumption of six gram or more of ginger (after examining gastric aspirates in ten healthy volunteers) [33].

Immunomodulatory effects: In vitro evidence indicates that, *Z. officinale* has immunomodulatory effects and is an effective anti-microbial and antiviral agent [34].

Effects on lipid: Buccal ingestion of ginger extract has been shown to have hypocholesterolemic, hypolipidemic, and anti-atherosclerotic effects in cholesterol fed rabbits and in rats. Inhibition of LDL oxidation and attenuated development of atherosclerosis has also been observed in apo-lipoprotein E-deficient mice [35].

Weight loss effect: Spiced foods or herbal drinks, such as those that contain ginger, have the potential to produce significant effects on metabolic targets, such as satiety, thermo genesis, and fat oxidation [36].

Anti-arthritic effect: A study investigated the anti-arthritic effects of *Z. officinale* and its bioactive constituents. A well characterized crude ginger extract was compared with a fraction containing (6)-gingerol and their derivatives to inhibit joint swelling in an animal model of rheumatoid arthritis, streptococcal cell wall induced arthritis. Both extracts demonstrated the anti-inflammatory activity in rat. The crude dichloromethane extract containing essential oils and more polar compounds, was more efficacious, when normalized to (6)-gingerol content, in preventing, both joint inflammation and destruction in rat [37].

Cardiovascular effects: In vitro studies indicate that, gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardio tonic properties at higher doses [38].

Haritki

Anti-bacterial activity: *T. chebula* exhibited anti-bacterial activity against various gram positive and gram negative bacteria such as *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa* suggestive of its broad spectrum antimicrobial activity [39]. Another study revealed that gram positive organisms inhibited on larger extent as compare to gram negative organisms [40]. The gallic acid and ethyl ester showed effects on methicillin resistant *Staphylococcus*. *T. chebula* is well efficient against *Helicobacter pylori*, a bacterium responsible for gastritis, ulcer and stomach cancers [41]. Water extract of fruit of *Terminalia chebula* reported as inhibitor of urease activity of *Helicobacter Pylori*[42].

Anti-amoebic & anti-protozoal activity: *T. chebula* shows invivo anti-amoebic activity against *Entamoeba histolytica* in experimental caecal amoebiasis [43]. The acetone extract of *T. chebula* seeds showed anti-plasmodial activity against *Plasmodium falciparum*[44].

Anti-fungal activity: An aqueous extract of *T. chebula* exhibit anti-fungal activity against a number of dermatophytes and yeasts; It is effective against the pathogenic yeast *Candida albicans* and *dermatophytes epidermophyton, Floccosum, Microsporum gypseum and Trichophyton rubrum*[45].

Anti-viral activity: Afruit extract of *T. chebula* showed inhibitory effects on Human Immunodeficiency Virus-1 reverse transcriptase [46]. A study proved that *T. chebula* fruits contain four human HIV-type 1 integrase inhibitors such as gallic acid and three galloyl glucoses, and suggested that galloyl moiety had a major role for inhibition of the 3'-processing of HIV-1 integrase by these compounds [47]. The aqueous extract of *T. chebula* execute the most prominent Anti-HBV activity by decreasing the level of extracellular HBV virion DNA at concentration ranging from 64 to 128 µg [48].

Anti-diabetic effects: Methanolic extract & chloroform extract of *T. chebula* significantly reduced the blood sugar level in normal and alloxan diabetic rats [49]. *T. chebula* fruit and seeds also exhibited dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in short term and long term study [50].

Hypolipidemic and hypocholesterolemic effects: *T. chebula* extract showed hypolipidemic activity in experimentally induced atherosclerosis & cholesterol induced hypercholesterolemia in rabbits [51], *Triphala* (*T. chebula*, *T.belerica*, *E.officinalis*) formulation was found to have hypolipidaemic effects on the experimentally induced hypercholesteremic rats [52]. The *Vara Asanadi kwath* (Polyherbal decoction) showed significant reduction in hyperlipidemia in high fat diet induced hyperlipidemic rats [53].

Cardioprotective effects: Ethanolic extract of *T. chebula* fruits was verified in isoproterenol induced myocardial damage in rats. It was documented that pretreatment with *T. chebula* extract had cardioprotective effect [54].

Hepatoprotective effects: Ethanolic extract of *T. chebula* fruit showed strong hepatoprotective activity [55]. It also showed similar property against anti-tuberculosis drug Rifampicin, Isoniazid and Pyrazinamide (combination) induced liver toxicity due to its prominent anti-oxidative and membrane stabilizing activities [56].

Anti-nociceptive effects: Ethanolic extract of *T. chebula* fruits showed a potential drug for bioactivity guided isolation of natural analgesic agents in the management of chronic pain [57].

Cytoprotective effects: Gallic acid and chebulagic acid, isolated from fruit extract of *T. chebula*, blocked cytotoxic T lymphocyte (CTL)-mediated cyto-toxicity [58]. It exhibited the inhibition of duodenal ulcers and appeared to exert a cytoprotective effect on the gastric mucosa *in vivo*[59].

Anti-arthritic effects: Hydro-alcoholic extract of *T. chebula* produced a significant inhibition of joint swelling as compared to control in both formaldehyde-induced and CFA-induced arthritis in rats. *T. chebula* could be used as a disease-modifying agent in treatment of rheumatoid arthritis [60]. Study shows that acetone extract of *T. chebula* fruits have better effect on controlling CFA induced arthritis showing the definite effect in reducing the inflammatory components [61]. Aqueous extract of dried fruit of *T. chebula* showed anti-inflammatory by inhibiting inducible nitric oxide synthesis [62].

Gastro enteric effects: *T. chebula* displaced potential anti-ulcerogenic activity in ethanol & cold restraint stress induced ulcer method in rat [63]. Intragastric administration of the crude drug to rats, at a dose of 1.5 g/l for 15 days, reduced the number of gastric ulcerations induced by pentagastrin and carbachol [64]. The methanolic extract of *T. chebula* showed significant reduction in gastric volume, free acidity & ulcer index in pylorus ligation and ethanol induced ulcer model rats [65]. A study showed purgative action of an oil obtained from *T. chebula*[66].

Anti-helminthic effects: Ethyl acetone and ethanol extracts of dried leaves and seeds of *T. chebula* showed complete inhibition by ovicidal and larvicidal activities tested invitro [67].

Anti-caries effects: Aqueous extract of *T. chebula* strongly inhibited the growth, sucrose induced adherence and glucan induced aggregation of *Streptococcus* mutants. Mouth rinsing with a 10% solution of the extract inhibited the salivary bacterial count and glycolysis of salivary bacteria for up to 90 min of post rinsing [68].

Wound healing effect: Topical administration of an alcoholic extract of the leaves of *Terminalia chebula* shows healing of dermal wound [69].

Anti-cancer effect: Methanolic extract of *Terminalia chebula* fruit and its phenolics content chebulinic acid, tannic acid and ellagic acid showed most growth inhibitory effect on several malignant cell lines [70] and prophylactic treatment with methanolic extract showed chemopreventive activity on nickel chloride induced renal oxidative stress and toxicity in rats [71].

Guduchi

Anti-diabetes effects: The stem of *T. cordifolia* is widely used in the therapy of diabetes by regulating the blood glucose in traditional folk medicine of India. It has been reported to mediate its anti-diabetic potential through mitigating oxidative stress (OS), promoting insulin secretion and also by inhibiting gluconeogenesis and glycogenolysis, thereby regulating blood glucose [72]. Alkaloids, tannins, cardiac glycosides, flavonoids, saponins, and steroids as the major phytoconstituents of *T. cordifolia* have been reported to play an anti-

diabetic role. The isoquinoline alkaloid rich fraction from stem, including, palmatine, jatrorrhizine, and magnoflorine have been reported for insulin-mimicking and insulin-releasing effect both *in vitro* and *in vivo* study [73].

Anti-toxic effects: *T. cordifolia* extracts have been reported to scavenge free radicals generated during aflatoxicosis [74]. *T. cordifolia* stem and leaves extract has shown hepatoprotective effect in albino male mice against lead nitrate induced toxicity. Oral administration of plant extracts prevented the occurrence of lead nitrate induced liver damage [75].

Anti-arthritic and anti-osteoporotic effects: A single or synergistic formulation of *T. cordifolia* with *Z. officinale* have been reported in rheumatoid arthritis treatment in traditional medicine [76]. *T. cordifolia* has been reported to affect the proliferation, differentiation and mineralization of bone like matrix on osteoblast model systems in vitro and hence, finds potential application as an anti-osteoporotic agent. Alcoholic extract of *T. cordifolia* has been shown to stimulate the growth of osteoblasts, increasing the differentiation of cells into osteoblastic lineage and also increasing the mineralization of bone like matrix [77]. Ecdysteroids isolated from the plant have been reported of protein anabolic and anti-osteoporotic effects in mammals. Beta-Ecdysone (Ecd) from *T. cordifolia* extracts have been reported to induce a significant increase in the thickness of joint cartilage and induce the osteogenic differentiation in mouse mesenchymal stem cells [78].20-OH-β-Ecd isolated from *T. cordifolia* has been reported of its anti-osteoporotic effects thus, highlighting the role of *T. cordifolia* in the treatment of osteoporosis and osteoarthritis [79].

Anti-HIV effects: Extract of *T. cordifolia* has been shown to demonstrate a decrease in the recurrent resistance HIV virus thus, improving the therapeutic outcome [80]. Anti-HIV effects of *T. cordifolia* extract was revealed by reduction in eosinophil count, stimulation of B-lymphocytes, macrophages and polymorph nuclear leucocytes and hemoglobin percentage thus, revealing its promising role of application in management of the disease [81].

Anti-cancer effects: The anti-cancer effects of *T. cordifolia* are mostly studied in animal models. *T. cordifolia* has been shown to possess a radio protective role by significantly increase in body weight, tissue weight, testis body weight ratio and tubular diameter and inhibit the harmful effects of sub lethal gamma radiation on testis in male swiss albino mice. In pre-irradiating mice, it significantly affected radiation induced rise in lipid peroxidation and resulted in the decline of GSH concentration in testis [82]. Pretreatment of HeLa cells by *Guduchi* have been shown to decrease the cell viability, increase LDH and decrease in GSH-S transferase activity [83].

Anti-microbial effects: Methanol extracts of *T. cordifolia* have been reported to have potential against microbial infections [84]. The anti-bacterial activity of *T. cordifolia* extract has been assayed against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteusvulgaris*, *Salmonellatyphi*, *Shigellaflexneri*, *Salmonellaparatyphi*, *Salmonellatyphimurium*, *Pseudomonasaeruginosa*, *Enterobacteraerogene* and *Serratiamarcesenses* (Gram-positive bacteria) [85]. Extract has been reported of immunostimulant properties on macrophages [86]. Intra mammary infusion of hydro-methanolic extracts of *T. cordifolia* treatment showed enhanced phagocytic activity of polymorphonuclear cells in bovine subclinical mastitis [87].

Antipyretic effects: Studies have shown insignificant antipyretic effects in the hexane and chloroform soluble fractions of the stem of *T. cordifolia* [88].

Anti-inflammatory effects: The water extract of the stem of *T. cordifolia* has been checked for anti-inflammatory activity in albino rats. It has significant anti-inflammatory response evoked by carrageenan when administered orally and intraperitoneally [89].

Memory enhancing effects: Study has shown that *T. cordifolia* helps in cognitive enhancement by immunostimulation and synthesis of acetylcholine. Thus, contributing increased choline level which shows that, it has memory enhancing property for learning and memory in normal and memory deficits animals [90].

DISCUSSION

Trisama is an important and highly effective Ayurvedic formulation but not widely practiced as many other Ayurvedic formulations. It can be used in many diseases due to its beneficial popular ingredients like *Sunthi*, *Haritaki* and *Guduchi*. All the ingredients have common *Madhur vipaka* and *Ushna virya* by their Ayurvedic *rasapanchak*. As per classical concept, pharmacological action of drugs is interpreted on the basis of their Ayurvedic properties. Pharmacokinetics of drug deals with *Rasa*, *Virya* and *Vipaka* which supersede one another in order. *Rasa* is the perception of taste. *Vipaka* (transformation) is always a process and not the active ingredients of drug. It deals with the synergistic actions of various drugs. The *virya* (potency) is the active principle by which drug act on living system. Therefore, we can predicts there effect from the properties of formulation. The ingredients of *Trisama* shows various types of pharmacological activities such as anti-inflammatory, anti-arthritic, anti-cancer, anti-emetic, anti-coagulant, anti-tussive, cardiovascular, anti-microbial etc. Many important potential phytoconstituents are available in *Trisama*, like phenolics components, gingerols, gingerdiols and gingerdione, shogaols, zingiberine, giloin, berberine, tinosporin, tinosporin acid and gallic acid which are responsible for above stated therapeutic potential of test drug. So, on the basis of above finding we can predict the immense use of *Trisama* in number of disease according to their phytoconstitiuents.

Trisama is *mishraka varga* which is explained in classical literature like *kashyap samhita* in *Shothhara* chapter. Others literature like *Yogchintamani* also described use of *Trisama* in the gutika dosage form. Hence, after going through its different utility in the form of medicines in routine practices, it may be used in many of the disorders by general Practitioner.

CONCLUSION

Trisama is group of three *dravyas* predominated by its *Usna Virya* and *Madhur Vipaka.* Its individual ingredients used in many types of Ayurvedic formulations and have diverse pharmacological activities such as anti-inflammatory, anti-arthritic, anti-cancer, anti-emetic, anti-coagulant, anti-tussive, cardiovascular, anti-microbial and in metabolic disorders etc. The *Trisama* formulation is easily available, economical, palatable and more beneficial for human health. Hence, it may be popularize among general Practitioner as an important Ayurvedic medicine in the form of *churna* (powder) and *kwatha* (decoction) for the treatment of *Sotha* andmetabolic disorders.

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