Review Article

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A REVIEW ON SHADANGA GHRITA: AN AYURVEDIC FORMULATION FOR COMMON DIARRHOEA CAUSING ENTEROPATHOGENS

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ABSTRACT

Atisaar is a very commonly found disease in all age groups. It is colloquially called diarrhoea, a prevalent clinical feature of acute and chronic inflammation of the gastrointestinal tract. The line of treatment depends on the type and stage of the disease. In Ayurveda, Atisaar is classified based on the vitiation of Dosha, while in modern medical science, it is based on the type of causative organism. There are so many formulations used to treat diarrhoea in Ayurvedic texts. Lipid-based formulations of Shadanga Ghrita include ingredients such as Kutaj (*Holarrhena antidysenterica* Wall), Daruharidra (*Berberis aristata* DC), Pippali *(Piper longum* Linn), Shunthi *(Zingiber officinale* Rosc), Katuka (*Picrorhiza kurroa* Royle ex Benth), Laksha (*Laccifer lacca* Kerr.) and Go-ghrita. Different fractions of extracts of each drug and isolated phytochemicals have potent anti-bacterial and anti-diarrhoeal activities, as proven by many studies. Thus, a literary survey helps to understand the mode of action of this formulation and might be helpful in the calculation of dose for pre-clinical studies and clinical trials.

Keywords: Atisaar, Anti-bacterial, Anti-diarrhoeal, Shadanga Ghrita, Ayurveda.

INTRODUCTION

In Ayurveda, diarrhoea can be co-related with "Atisaar", which means *"ati"* (excess) and "saranam" (flow), a condition where watery stool passes in excess with high speed [1]. Diarrhoea is a significant health problem in developing countries such as India, which is defined as an increase in bowel frequency, fluidity, or volume and is characterized by increased bowel sound, movement, and abdominal pain [2]. Diarrhoea is commonly seen in children, especially those below 12 years of age [3]. Worldwide, more than 1 million people suffer from one or more episodes of acute diarrhea per year [4]. Acharya Charaka and Vagbhata classified diarrhoea based on Sharira Dosha and Mansika Nidana (Etiology) into six types of Vatika, Paitika, Kaphaja, Sannipataja, Shokaja, Bhayaja [5, 6]. Acharya Sushruta mentioned Amaja Atisaar instead of Bhayaja Atisaar [7]. Atisaar has mainly been associated with Agnimandya and Ama formation in traditional Ayurveda texts, contributing significantly to disease pathogenesis [1]. Shadanga Ghrita contains most of the ingredients with Katu (pungent), Tikta (bitter) Rasa, and Ushna Virya (hot potency), which possess Dipana and Pachana properties and help to break the samprapti of Atisaar. Go-ghrita is Madhura in Rasa, Sheeta in Virya, and Pitta- shamaka but Deepana in Karma [8].

In Ayurvedic texts, various formulations and treatment modalities have been described for the management of Atisaar and Shadanga Ghrita is one of the formulations mentioned in the renowned text Chakra Dutta, [9] indicated for Atisaar, which contains the most potent ingredients, namely Kutaj (*Holarrhena antidysenterica* Wall), Daruharidra (*Berberis aristata* DC), Pippali *(Piper longum* Linn), Shunthi (*Zingiber Officinale* Rosc*)*, Katuka (*Picrorrhiza kurroa* Royle ex Benth), Laksha (*Laccifer lacca* Kerr.) and Go-ghrita which are primarily accountable for their anti-bacterial, anti-inflammatory and anti-diarrheal activity to cure diarrhoea. Preparation of this oleaginous dosage form of Sneha Kalpana is described as subjecting Ghrita to a particular pattern of heat-treated with 1/4th part Kalka (paste) and 4th part of Kashaya (decoction) of drugs mentioned above in equal proportions. [10]

A literary review was conducted from Ayurvedic books and published research papers related to Shadanga Ghrita and Diarrhoea. Hindi, English and Botanical names were used as a keyword for the search. Information about anti-diarrheal pharmacological actions was selected for our study.

Drug Review

Shadanga Ghrita is a very common formulation used in Atisaar (diarrhoea) in Ayurveda. This formulation was first mentioned by Acharya Vrinda Madhava [11] (9 AD); afterwards, authors of Vangsen Samhita [12], Chakra Dutta [9], depicted the same formulation with word-to-word same verse. This is enough to say that it is a popular and effective medication for treating diarrhoea. This formulation was made of purified six herbs.

***Holarrhena antidysenterica* Wall.**

Holarrhena antidysenterica Wall is a deciduous laticiferous shrub considered a small tree. The tree grows up to three meters high, and it has a short stem with pale bark and several branches. Stem bark and seeds are used in various formulations in ISM Indian systems of medicine(ISM)[13] Synonyms- Vatsaka (found in Vatsa Desa), Girimallika (Kutaja tree grows in mountains and flowers are white like that of jasmine), Kalinga (commonly found in Kalinga region), Indravriksha (widely found in Mahendra Parvata Kshetra), Vrikshak (small tree), Chakrashakhi (plant grows gregariously), Mallikapushp (flowers are bright white like that of jasmine), Yavaphala (barley shaped seeds of *Holarrhena antidysenterica* Wall)[14].

Ayurvedic Pharmacological Properties of *Holarrhena antidysenterica* Wall: The drug is Tikta (bitter) and Kashaya (astringent) in Rasa, Laghu (light), Ruksha (dry) in Guna, Sheeta (cold) in Virya and Katu (pungent) in Vipaka, thus pacifying Kapha Dosha due to its Katu (pungent), Tikta (bitter) Rasa, Ushna Virya (hot potency) and Katu (pungent) Vipaka and pacifies Pitta Dosha due to its Tikta Rasa (bitter taste) and Vata Dosha due to Ushna Virya (hot potency). The seeds of *Holarrhena antidysenterica* Wall are Atisarahara (anti-diarrhoeal), Shoolahara (analgesic), Dipana and Pachana. [15].

Chemical Composition of *Holarrhena antidysenterica* Wall: The stem and bark of *Holarrhena antidysenterica* Wall contain Conessine, Isoconessine, Conessimine, Isoconessimine and Conarrhimine. The stem bark of *Holarrhaena antidysenterica* Wall contains Holarrifine, Kurchamide, Conessidine, Holarrhidine, Holarrhidine, Kurchenine, Holarrhessimine, Conkurchinine, Kurchamine, Kurchilidine, Neoconessine, Holadysenterine, Kurchessine, Lettocine, Holarrhimine, Holacine, Holafrine, Holacetine, Condamine, Pubamide, Holadiene, Pubescine, Holonamine, Regholarrhenine B, Regholarrhenine C, Regholarrhenine D, Regholarrhenine E, Regholarrhenine and the seeds contain Antidysentericine, conimine [16]. *Holarrhena antidysenterica* Wall is a rich source of other steroidal alkaloids such as kurchine, kurchimine, conessidine, holarrimine, conessidine, conkurchicine, etc. regholarrhimine [17]. Stem bark and seeds of *Holarrhena antidysenterica* Wall have been reported to contain several steroidal alkaloids, such as conanines, 3- aminoconanines, 20-aminoconanines, 3-aminopregnans, 3, 20-diaminopregnanes and their derivatives [18]. The seeds of *Holarrhena antidysenterica* Wall also contain steroidal alkaloids viz, conessine, isoconessimine, conessimin, norconessimine, holarrhimine and holarrhidine [14].

Pharmacological Action of *Holarrhena antidysenterica* Wall

Anti-bacterial activity: Kavitha *et al*. (2004), the alkaloids from the ethanolic extract of *Holarrhena antidysenterica* Wall seeds at 1.25, 2.5, 3.5 mg concentration exhibited anti-bacterial activity against the entheogenic pathogen *Escherichia coli* [19]. Mahatoe *et al*. (2013), the crude methanolic bark, seed and callus extract of *Holarrhena antidysenterica* Wall at 100% concentration showed significant inhibition zones against *Staphylococcus aureus*, *Salmonella typhimurium* and *Escherichia coli*. *Staphylococcus aureus* was found to be the most susceptible organism, but the maximum zone of inhibition was found in *Salmonella* (7.05 mm) and lowest in *Escherichia coli* (3.1mm) [17]. Gawhare *et al*. (2013) investigated the anti-bacterial activity of methanolic, ethanolic and aqueous extracts of *Holarrhena antidysenterica* Wall seeds against enteropathogenic *Escherichia coli.* Still, only methanolic extract with MIC value 2.0 gm/10ml showed significant anti-bacterial activity against enteropathogenic *Escherichia coli* [20]. Srivastava and Saxena (2015) studied the anti-bacterial activity of aqueous extract of *Holarrhena antidysenterica* Wall seeds at 40-80 mg/ml against *Escherichia coli*, *Staphylococcus aureus, Klebsiella pneumonia, Proteus mirabilis Pseudomonas aeruginosa, Salmonella typhi,* and *Vibrio cholera*. They exhibited significant anti-bacterial activity against *Escherichia coli, Salmonella typhi* and *Staphylococcus aureus* [13].

Anti-diarrheal activity: Kavitha *et al.,* (2004), the ethanolic extract of *Holarrhena antidysenterica* Wall seeds in castor oil-induced diarrhoea at 200, 400, 600, and 800 mg/kg body weight reduced defecation [19]. Daswani PG *et al*., (2012), the ethanolic extract of *Holarrhena antidysenterica* Wall seeds on castor oil-induced diarrhoea in rats reduced diarrhoea with a decrease in the number of wet faeces in pretreated rats at a dose of 200-800 mg/kg [21]. Further, Kumar Dushyant *et al*. (2013) studied the ethanolic extract of *Holarrhena antidysenterica* Wall seeds at 100, 200 and 400 mg/kg body weight against castor oil and *Escherichia coli* induced diarrhoea and found that diarrhoea was reduced significantly with *Holarrhena antidysenterica* Wall seed extract at 200 and 400 mg/kg body weight [22].

***Berberis aristata* DC**

It is a deciduous evergreen shrub found at an altitude of 7,000-10,000 ft., and the root, stem bark, and fruit of *Berberis aristata* DC are used in Ayurveda. Synonyms-Katamkateri (leaves are spiny toothed), Katankini (leaves are spiny toothed), Daruharidra (due to its yellow stem), Pachampacha (improves liver function) and Darvi (wood is an integral part of medicine [23]. Tree turmeric or Indian berberry [24].

Ayurvedic Pharmacological Properties of *Berberis aristata* DC: The drug is Tikta (bitter) and Kashaya (astringent) in Rasa, Laghu, and Ruksha in Guna, Ushna in Virya (potency), and Katu (pungent) in Vipaka thus pacify Kapha Dosha because of its Ushna Virya and Tikta Rasa (bitter) and pacifies Pitta Dosha because of its Tikta Rasa (bitter) [25].

Chemical Composition of *Berberis aristata* DC: Root of *Berberis aristata* DC contains Berberine, oxycanthine, epiberberine, palmatine, dehydrocaroline, jatrorhizine, karachine dihyrokarachine, taximaline, oxyberberine, aromoline and columbamine, pakistanine, methyl pakistanine, pseudopalmatine chloride and pseudoberberine chloride, secobisbenzlisoquinoline or simple isoquinoline. The principal alkaloid found in *Berberis aristata* DC is berberine with a yield of 2.23%, followed by palmatine [26]. It also contains hentriacontane, sitosterol and its glucoside, palmitic acid and oleic acid and saponin[23]. The stem bark of *Berberis aristata* DC contains oxyberberine, berbamine and aromoline [27]. Its bark also contains protoberberine and bis isoquinoline [28].

Pharmacological Action of *Berberis aristata* DC

Anti-bacterial activity: Sun D. *et al*. (1988) found that Berberine sulfate present in *Berberis aristata* DC at 30 µg /ml completely inhibited the growth of *Streptococci* and blocked adherence of these organisms to host cells [29]. Singh *et al.* (2007) reported that the hydro-alcoholic root extract of *Berberis aristata* DC at concentrations of 10,30 and 50 µg/disc showed broad anti-bacterial activity against *Micrococcus luteus, Bacillus subtilis, Bacillus cereus, Enterobacter aerogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus*, *Vibrio cholera, Escherichia coli* and *Salmonella typhi* [30]. Shahid *et al*. (2009) reported that the aqueous and alcoholic extracts of fresh *Berberis aristata* DC roots and aqueous extracts of dried roots at concentrations of 12.5, 25 and 50 µg/disc showed broad anti-

bacterial activity and the best action was demonstrated by alcoholic extracts at a concentration of 50 µg/disc against *Vibrio cholera* [31]. Saxena *et al*. (2014), various extracts from *Berberis aristata* DC showed significant zone of inhibition against *Staphylococcus aureus, Streptococcus epidermidis, Streptococcus mutans, Bacillus cereus, Klebsiella pneumoniae, Escherichia coli,* and Ethanol and methanol extracts exhibited maximum zones of inhibition 22 mm and 15 mm against *Staphylococcus aureus* and 12 mm inhibition against *Klebsiella pneumonia* [32]. Tamilsevi *et al*. (2014), the methanolic extract of *Berberis aristata* DC showed anti-bacterial activity against various pathogens such as *Nocardia sp.*, *Staphylococcus aureus*, *Streptococcus pneumonia, Pseudomonas aeruginosa, Staphylococcus, viridians,* and *Escherichia coli*. The highest antimicrobial activity was exhibited against *Escherichia coli* with a MIC of 23.20 mg/ml and the least against *Nocardia sp.* with a MIC of 6.00 mg/ml [33].

Anti-diarrhoeal activity: R B Sack *et al*. (1982), the berberine from the roots and barks of *Berberis aristata* DC showed the inhibition of secretory response of heat-labile enterotoxins of *Vibrio cholera* and *Escherichia Coli in* rabbit lighted intestinal loop model and showed clinical effectiveness in treating acute diarrheal disease [34].

Anti-inflammatory Activity: N. Rajput *et al*., (2004), the aqueous extracts of roots of *Berberis aristata* DC at a dose of 500–1000 mg/kg and the alcoholic extracts at a dose of 25-50 mg/kg was found to have a significant anti-inflammatory effect when compared with 10 mg Diclofenac sodium [35]. Shahid *et al*. (2009), the aqueous and alcoholic extracts of *Berberis aristata* DC at 50 mg/kg concentrations, showed promising activity in acute inflammation [29].

***Picrorhiza kurroa* Royle ex Benth**

It is a small perennial herb found at an altitude of 3000- 4300 meters. The Rhizome *(*Kanda) of *Picrorhiza kurroa* Royle ex Benth is used in Ayurveda. Synonyms- Katuka, Tikta (bitter taste of it), Kandruha (plant may be grown by stem cuttings), Shatparva (various nodules), Matsyashakla (rhizome resembles fish scales*),* Chakrangi (when cut the stem appears like a wheel), Krishnabheda (on breaking the rhizome, it becomes black powder) [36].

Ayurvedic Pharmacological Properties of *Picrorhiza kurroa* Royle ex Benth: The drug is Tikta (bitter) in Rasa (taste)*,* Laghu (light) and Ruksha in Guna, Sheeta (cold) in Virya (potency), and Katu (pungent) in Vipaka, thus pacifies Kapha and Pitta Doshas [37].

Chemical Composition of *Picrorhiza Kurroa* Royle ex Benth: The chemical constituents on the *Picrorhiza kurroa* Royle ex Benth rhizomes show Irridoid bitter substances, picroside I, Picroside II, Kutkoside; Kutkin, Picrorhizin. The roots also contain kutkin, kurrin, vanillic acid, kutkiol, kutkisterol, D-Mannitol, [36]. The rhizome of *Picrorihza kurroa* Royle ex Benth also reported containing Tannins, saponins, sterols/triterpenes, alkaloids, cucurbitacin glycosides, flavonoids, polyphenolic compounds, protein/amino acids, carbohydrates, and iridoid glycosides [38]. *Picrorrihza kurroa* Royle ex Benth's rhizome contains pikuroside, veronicoside, phenol glycosides, several cucurbitacin glycosides, and 4-hydroxyl-3-methoxyacetophenone [39]. *Picrorhiza kurroa* Royle ex Benth is known to have picroside-I and II as major bioactive compounds [40].

Pharmacological Action of *Picrorhiza kurroa* Royle ex Benth

Anti-bacterial activity: Vohra *et al*. (1972), the aqueous extracts of the root of *Picrorhiza kurroa* Royle ex Benth showed moderate activity against *Staphylococcus aureus* and marked inhibition against *Escherichia coli* [41]. Rathee *et al*. (2012), the Aqueous and Methanolic extracts of *Picrorhiza kurroa* Royle ex Benth at 10, 25, 50,100 mg/ml showed significant anti-bacterial activity against *Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus* and *Escherichia coli* [38]. Mohammed Rageeb *et al*. (2012) studied the ethanolic extracts of *Picrorhiza kurroa* Royle ex Benth (5mg, 10mg 15 mg, 20 mg /75 µl) against *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and the most susceptible microorganism was found *Escherichia coli* [42]. Sharma *et al*. (2012), the methanolic extracts of *Picrorihza kurroa* Royle ex Benth at 10 mg/ml, showed significant activity against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* when compared with Ciprofloxacin [43].

Anti-inflammatory activity: Salma *et al*., (2017), Apocynin, a Phyto-constituents of root extracts of *Picrorhiza kurroa* Royle ex Benth inhibited oedema at the rate of 29.8% and has been proven to possess anti-inflammatory properties [44].

***Piper longum* Linn**

It is an ascending or prostrate climber herb that needs support for its proper growth. The valuable part is root and fruit. Synonyms- Magadhi (abundantly available in Magadha Desa), Vaidehi (very common in Videha Desa), Upkulya (grows near or along the side of water streams), Ushna (causes are burning sensation in tongue), Tikshana (seeds are spicy) [45].

Ayurvedic Pharmacological Properties of *Piper longum* Linn: The drug is Katu (bitter) in Rasa (taste)*,* Laghu (light)*,* Snigdha (smooth), and Tikshana (sharp) in Guna, *Anushansheeta* (temperament neither hot nor cold) in Virya (potency) and Madhura (sweet) in Vipaka, thus pacifies Kapha Dosha due to Katu (pungent) Rasa (taste) and Vata Dosha due to Madhura Rasa (sweet taste). The root of *Piper longum Linn* is an appetizer, digestant and carminative [46].

Chemical Composition of *Piper longum* Linn: The fruit of *Piper longum* Linn contains many alkaloids such as piperine, together with methyl piperine, iperonaline, piperettine, asarinine, pellitorine, piperundecalidine, piperlongumine, piperlonguminine, refractomide A, pregumidiene, brachystamide, brachystamide-A, brachystine, pipercide, piperderidine, longamide and tetrahydropiperine, terahydro piperlongumine, dehydropipernonaline piperidine, piperine [47]. Fatty acids of crushed seeds of *Piper longum* Linn have been reported to contain palmitic, hexadecenoic, stearic, linoleic, oleic, higher saturated acids, arachidic, and behenic acids. Its fruit yielded Piperine, Pipernonaline, piperundecalidine, n-hexadecane, n-heptadecane, n-octadecane, n-nonadecane, n-eicosane, root yielded Piperine, Piperlongumine and piperlonguminine [48].

Pharmacological Action of *Piper longum* Linn

Anti-Amoebic Activity: Khan mohib *et al*., (2007), The methanolic extract and piperine of *Piper longum* Linn fruit against *Entamoeba histolytica* experimental caecal amoebiasis showed the methanol extract, and piperine of *Piper longum* Linn cured 90% and 40% of rats with caecal amoebiasis respectively [49].

Anti-bacterial activity: Ghoshal S *et al*. (1996), aqueous and methanolic extract of *Piper longum* Linn. Against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa* at 5 mg/ml, 7 mg/ml, and 10 mg/ml have been proven to show anti-bacterial activity against *Streptococcus aureus, Escherichia coli,* and *Pseudomonas aeruginosa* [50]. Trivedi M.N. *et al*. (2011) tested the aqueous and methanolic extracts of *Piper longum* Linn fruit at 5, 7, and 10mg/ml against *S. aureus Bacillus subtilis, Pseudomonas aeruginosa, and Escherichia coli.* The methanolic extract was more active against *S. aureus and E. coli* when compared with the standard drug Streptomycin 100 µg/ml [51]. Dinesha R. *et al.* (2015), the hot water extract of *Piper longum* Linn (at 90-106 µg/ml) exhibited significant inhibitory action against *Escherichia coli, Klebsiella pneumoniae, Proteus Vulgaris, Pseudomonas, Salmonella typhimurium, Streptococcus Sps, Staphylococcus aureus,* and *Vibrio cholera* when compared with the standard drug Streptomycin [52].

Anti-inflammatory Activity: Kumar *et. al,* (2009), the dried fruit oil of *Piper longum* Linn at 0.5 ml/kg, 1.0 ml/kg showed its anti-inflammatory activity in carrageenan rat paw oedema [53].

***Zingiber officinale* Rosc.**

It is a perennial herb with elongated leafy stems and horizontal tuberous rootstocks. The Kanda (rhizome) of *Zingiber officinale* Rosc is used in Ayurveda. Synonyms- Nagaram (it is available in shops), Avak Chatram (leaves spread out like umbrella), Shringver (horn-shaped rhizomes), Katubhadram (one of the best Katu Dravya), Utkatam (rhizome is robust), Ushnam (rhizome causes burning sensation), Maha-Aushadh (very efficacious drug), Vishvabheshaj (commonly used by public because of its quality and readily availability) [54].

Ayurvedic Pharmacological Properties of *Zingiber officinale* Rosc.: The drug is Katu (bitter) in Rasa (taste), Laghu (light) and Snigdha (smooth) in Guna, Ushna (hot) in Virya (potency,) and Madhura (sweet) in Vipaka, thus pacifies Vata Dosha because of its Ushna Virya (hot potency) and Madhura (sweet) Vipaka and pacifies Kapha Dosha because of its Katu (pungent) Rasa (taste) and Ushna Virya (hot potency). It is Dipana, Pachna (carminative), and Shoolhara (analgesic) in properties[55].

Chemical Composition of *Zingiber officinale* Rosc.: *Zingiber officinale* Rosc contains volatile oils such as terpenoids, alpha terpinene, alpha terpineol,4-terpineol, terpinolene, gamma terpinolene, cineole, beta eudesmol, nerol, trans-nerolidol, borneol, elemol, tau-muurolol, 2-decanol, fenchol, linalool, plinol, camphenol, butanal, germacrone, 2-heptanone, (z)-citral, 2-nonanone, beta-cyclocitral, 2-undecanone, beta-ctronellal, crypton, 6-methyl-5-hepten-2-one, hexanal, zingiberene, isoeugenol etc., Gingerol, a mixture of 3-methoxy-4-hydroxyphenyl functional group, it also contains a variety of amino acids, including aspartic acid, serine, glutamate, valine, lysine, threonine, cysteine etc. [56]. *Zingiber officinale* Rosc has been reported to have Aromatic oil (1-4%), Starch (40-60%), Fat (10%), Fibre (5%), Camphene, Phellandrene, Zingiberine, Cineol, Borneol, Gingerol, Gingerin (Oleoresin). *Zingiber officinale Rosc* oil contains monoterpene hydrocarbons, sesquiterpene hydrocarbons oxygenated mono and sesquiterpene phenyl propanoids [54]. Hasan *et al*, (2012), *Zingiber officinale* Rosc contain Sesquiterpene hydrocarbons was found as major constituent other constituent found are zingiberene (9%, 6%), β-bisabolene (4%, 5%), α-farnesene (11%, 7%), β-sesquiphellandrene (9%, 13%), monoterpene hydrocarbons which is α-curcumene (14%, 0%) and phenolic compounds which are gingerol (25%, 23%) and shogaol (18%, 25%)[57].

Pharmacological Action of *Zingiber officinale* Rosc.

Anti-diarrhoeal Activity: Poonam G. Daswani *et al*, (2010), the decoction of *Zingiber officinale* Rosc reduced the bacterial colonization of Hep-2 cells and disclosed its anti-diarrhoeal action by affecting bacterial and host cell metabolism [58].

Anti-bacterial Activity: S.P. Malu *et al*., (2008), n-hexane and ethyl acetate extract of *Zingiber officinale* Rosc exhibited anti-bacterial activity at 1.0%, 0.5%, 0.25% and 0.125% against *Staphylococcus epidermis, Coliform bacillus* and *Streptococcus viridian's* [59]. Hiba Ali Hasan *et al*., (2012), methanol and n-hexane extracts of *Zingiber officinale* Rosc at 50, 25, 12.5, 6.25, and 3.1 mg/ml, when compared with standard drug streptomycin (10µg/disc) exhibited significant anti-bacterial activity against *Staphylococcus epidermidis, Proteus sp., Escherichia coli, Enterococcus sp., Pseudomonas fluorescent* [57]. Mohmoud Rafieian- Kopaei *et al*. (2016), hydroalcoholic extracts of *Zingiber officanle* Rosc against *Staphylococcus aureus, Pseudomonas aeroginosa,* and *Listeria monocytogenes* at 52**,** 52, 416, and 52 µg/ml respectively showed significant anti-bacterial activity [60]. U. Santo Grace et al., (2017), ethanolic extracts of *Zingiber officinale* Rosc at different concentrations as 5µ/l, 10µ/l, and 15µ/l showed anti-bacterial activity against *Streptococcus aureus* [61]. Further, Rampogu *et al.* (2018) revealed that gingerenone-A and 6 shogaol were found in *Zingiber officinale* Rosc at 25, 50, and 75 µg/ml showed an inhibitory effect on *Staphylococcus aureus*. The minimum zone of inhibition was observed at 25 µg/ml [62]. Qian-Qian Mao *et al*., (2019), methanolic extract of *Zingiber officinale* Rosc at 2000 mg/kg body weight showed significant anti-bacterial effect against *Pseudomonas aeruginosa* [63].

Anti-inflammatory Activity: Qian- Qian Mao *et al.,* (2019), *Zingiber officinale* Rosc, and its active components have been proven to exhibit anti-inflammatory effects mainly in inflammatory bowel disease [63].

***Laccifer lacca* Kerr.**

Lac is a slick serum secreted by a scale insect species *Laccifer lacca* Kerr. These insects suck the liquor of several plants and bushes and secrete Lac as a protective covering. *Laccifer lacca* Kerr looks like tiny spots on plants having no limbs and covered with slick serum [64]. It is a natural commercial resin of animal origin, secretion by a scale insect. The resin of *Laccifer lacca* Kerr. is used in Ayurveda. Synonyms- Laksha, Vrikshamaya, lac [65].

Ayurvedic Pharmacological Properties of *Laccifer lacca* Kerr.: Lac is Kashaya (astringent) in Rasa (taste), Laghu (light) and Snigdha (smooth) in Guna, sheeta (cold) in Virya (potency), and Katu (pungent) in Vipaka, thus pacifies Kapha and Pitta Doshas. Atisaarhara (anti-diarrhoeal) and Pravahikahara (anti-dysenteric) in properties [65].

Chemical Composition of *Laccifer lacca* Kerr.: *Laccifer lacca* Kerr contains aleuritic acid as the main constituent (35% of resin) and Butolic acid, laccaic acid [64]. The major constituents present in *Laccifer lacca* Kerr is the resin (68-90%), dye (2-10%), wax (5-6%), mineral matter (3-7%), albuminous matter (5-10%), water (2-3%) [64].

Pharmacological Activity of *Laccifer lacca* Kerr.

Anti-bacterial Activity: Suddhasattya Dey *et al*. (2018), among various extracts of *Laccifer lacca* Kerr, the methanolic extracts and ethyl acetate extract exhibited 18mm zone inhibition against

E. coli and 15mm zone of inhibition against *Staphylococcus aureus* [67].

Ghrita (Go-Ghrita)

Ghrita is animal fat that remains liquid or semi-solid at room temperature. There are four types of Sneha described in Ayurveda; among them, Ghrita is the best. It has the most crucial property, which is known as Sanskaranuvartana. It is appetizing and Satmya for every individual since their childhood [68]. Ghrita is lipophilic, and due to this property, it facilitates the transportation of ingredients of formulation to the target organ and final delivery inside the cell because the cell membrane also contains lipids [69].

Ayurvedic Pharmacological Properties of Go-Ghrita: Ghrita is Madhura (sweet) in *Rasa* (taste), Guru (heavy), Snigdha (smooth) and Mridu (soft) in Guna, Sheeta (cold) in Virya (potency) and Madhura (sweet) in Vipaka and thus pacifies Vata, Pitta and Kapha Doshas and possesses Dipana and Pachana (carminative) properties[8].

Chemical Composition of Go-Ghrita: Ghrita contains Triglycerides (97.098%), di-glycerides (0.25-1.4%), Monoglycerides (0.16-0.0038%), ketoacid glycerides (0.015-0.018%), glycerylesters (0.011-0.05%), free fatty acids (0.1-0.44%), phospholipids (0.2-1.0%), sterols (0.22-0.41%), butyric acid (4.5-6.0%), caprylic acid (0.9-1%), lauric acid (6-7%), myristic acid (21-23%), palmitic acid (19-19.5%), Arachidic acid (0.5-0.8%), oleic acid (27-27.5%) [68].

DISCUSSION

Diarrhoea remains a significant public health problem in developing countries. Acute infective diarrhoea is widely prevalent and is an essential factor contributing to morbidity and mortality, especially in children below five years. It is generally a symptom of gastrointestinal infection usually caused by *Staphylococcus aureus, Streptococcus aureus, Vibrio cholera, Salmonella typhimurium,* and *Escherichia coli.*

Anti-bacterial properties of *Berberis aristata* DC have been proved by ethanolic, methanolic, aqueous, and hydro-alcoholic root extracts against *Micrococcus luteus, Bacillus subtilis, Bacillus cereus, Enterobacter aerogenes, Klebsiella pneumonia, Staphylococcus aureus, Streptococcus aureus, Vibrio cholera, Salmonella typhimurium, and Escherichia coli*. Ethanolic and methanolic extracts showed maximum activity. Anti-diarrhoeal and anti-bacterial properties of *Berberis aristata* DC have been proved by the phytochemicals berberine, oxycanthine, berbemine, and palmatine present in the bark of *Berberis aristata* DC. Anti-inflammatory activity of *Berberis aristata* DC was proved by the aqueous and alcoholic extracts at 50 mg/kg body weight.

Anti-bacterial properties of *Zingiber officinale* Rosc *were* proved by n-hexane, ethyl acetate, ethanolic, methanolic and hydro-alcoholic extracts against *Staphylococcus epidermis, Proteus sp. Escherichia coli, Enterococcus sp., Pseudomonas florescent, Staphylococcus aureus, Coliform bacillus, Pseudomonas aeruginosa* and *Streptococcus viridians.* The significant anti-bacterial activity was displayed by methanolic, ethanolic, and n-hexane extracts, while aqueous extract displayed no activity. The phytochemicals gingerenone-A, shogaol-6 and gingerol, have shown anti-bacterial properties.

The phytochemical piperine present in *Piper longum* Linn. had proved its anti-bacterial properties displayed by its methanolic and aqueous extracts against *Staphylococcus aureus, Bacillus subtilis, Streptococcus aureus, Klebsiella pneumoniae, Vibrio cholera, Salmonella typhimurium, and Escherichia coli.*

Anti-bacterial properties of *Picrorhiza kurroa* Royle ex Benth were proved by its ethanolic, methanolic, and aqueous extracts against *Bacillus subtilis, Micrococcus, Staphylococcus aureus, Streptococcus aureus, Vibrio cholera, Salmonella typhimurium, and Escherichia coli.* Methanolic and aqueous extracts displayed significant anti-bacterial activity. The phytochemical apocynin present in it exhibited its anti-inflammatory properties.

Anti-bacterial properties of *Holarrhena antidysenterica* Wall have been proved by ethanolic, methanolic, and aqueous extracts against *Staphylococcus aureus, Salmonella typhimurium,* and *Escherichia coli.* Ethanolic and methanolic extracts displayed significant anti-bacterial activity compared to aqueous extract. The anti-diarrhoeal activity of *Holarrhena antidysenterica Wall* had proved by the ethanolic extract. The phytochemical conessine present in the seed of *Holarrhena antidysenterica* Wall had established its anti-bacterial and anti-diarrhoeal activity.

Anti-bacterial properties of *Laccifer lacca* Kerr have been proved by methanolic and ethyl acetate extract against *Escherichia coli* and *Streptococcus aureus.* The phytochemicals laccaic acid, butolic acid and aleuritic acid present in the resin of *Laccifer lacca* Kerr had proved anti-bacterial properties of *Laccifer lacca* Kerr.

There has not been any previous research study conducted on Go-ghrita related to its anti-bacterial and anti-diarrhoeal activity. But it may be used in processing because it is the simplest natural way to increase the shelf life of drugs.

CONCLUSION

Shadanga Ghrita is one of the essential Ayurvedic formulations indicated for diarrhoea. It is described in Ayurveda, Atisaar mainly occurs due to Agnimandya and Ama formation. Dipana and Pachana drugs interrupt the Samprapti of Atisaar. Some of the drugs present in this formulation are Sheeta in Virya, and some of them are Ushna in Virya. Sheeta Virya is Stambhana that controls Pakvaatisaar, and the action of Ushna Virya (hot potency) is Shoshanakarma which controls Amatisaar. Most of the ingredients present in this formulation are Katu, Tikta in Rasa, Ushna Virya, and Katu in Vipaka and hence possess Dipana and Pachana properties. Because of these properties, the drugs mentioned above can break the pathogenesis of Atisaar.

Based on the research done individually on its ingredients, it has been proven that all the drugs present in Shadanga ghrita possess anti-bacterial, anti-diarrhoeal properties. Their anti-bacterial property is significantly effective in controlling various pathogens causing diarrhoea, and therefore it helps speed up the treatment of Atisaar. Maximum anti-bacterial activity has been found in ethanolic and methanolic extracts of most drugs (herbs) used in Shadanga Ghrita. So Ghrita-based formulation is an effective way to formulate organic compounds soluble extraction and concentration of active principle of medicine.

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