Review Article

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ANTI-INFLAMMATORY AND ANTI-MICROBIAL ACTION OF TRIPHALA GUGGULU: A REVIEW

Neelam Rawat [1]*, Yadevendra Yadav [2], Shuchi Mitra [3], Usha Sharma [3], Khem Chand Sharma [4]

[1] PG Scholar, PG Department of Rasa Shastra and Bhaishajya Kalpana Uttarakhand Ayurved University, Rishikul Campus Haridwar, Uttarakhand, India

[2] Assistant Professor, PG Department of Rasa Shastra and Bhaishajya Kalpana Uttarakhand Ayurved University, Rishikul Campus Haridwar, Uttarakhand, India

[3] Associate Professor, PG Department of Rasa Shastra and Bhaishajya Kalpana Uttarakhand Ayurved University, Rishikul Campus Haridwar, Uttarakhand, India

[4] Professor and HOD, PG Department of Rasa Shastra and Bhaishajya Kalpana Uttarakhand Ayurved University, Rishikul Campus Haridwar, Uttarakhand, India

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***Corresponding author**
E-mail: neelamrawat1415@gmail.com

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ABSTRACT

Triphala Guggulu, an Ayurvedic herbal formulation, consists of dried powder of fruits of three plants commonly known as Triphala: *Emblica officinalis* Gaertn. (Euphorbiaceae), *Terminalia bellerica* Roxb. (Combretaceae) and *Terminalia chebula* Retz. (Combretaceae) along with *Piper longum* Linn. (Piperaceae), combined with the oleo-gum resin of *Commiphora wightii* Arnott. Bhandari (Burseraceae). It is mentioned in the Ayurvedic Formulary of India (AFI) taken from Sharngadhar Samhita for several therapeutic uses. This formulation is indicated in the treatment of Bhagandara (fissure-in-ano), Gulma (Benign growths), Shotha (Inflammation) and Arsha (Piles) by Acharya Sharangdhara Mishra in his book. This review article aims to evaluate all the experimental work done on the anti-inflammatory and anti-microbial action of constituents of Triphala Guggulu. A review of all research work was done from the Central Council of Research in Ayurvedic Sciences (CCRAS) database of medicinal plants and online research journals. The outcome of this study shows that all Triphala Guggulu ingredients can work as anti-inflammatory and antibacterial activity against a wide range of microbes. Thus, Triphala Guggulu is an effective formulation to cure infectious wounds and normalize gut motility, beneficial in health conditions such as Piles, Fistula, Inflammation etc.

Keywords: Anti-Inflammatory, Guggulu, Triphala, Ayurveda

INTRODUCTION

Triphala Guggulu is an official Ayurvedic formulation as per the Ayurvedic Formulary of India[1]. It is indicated in the treatment of Bhagandara (fissure-in-ano), Gulma (Benign growths), Shotha (Inflammation) and Arsha (piles) by Acharya Sharangdhara. It consists of Guggulu, an oleo-gum-resin of *Commiphora wightii* (Arn.) Bhandari as a base along with other fruit powders of Pippali (*Piper longum* Linn.) and Triphala, i.e., fruits of Amalaki *(Emblica officinalis* Gaertn*).,* Haritaki *(Terminalia chebula* Retz.), and Vibhitaki (*Terminalia bellirica* Roxb). This formulation was firstly mentioned in Sharangdhara Samhita, and the formulation methodology was adopted in the official Ayurvedic pharmacopoeia of the Government of India, Ayurvedic Formulary of India (AFI) in Volume II[2]. The main constituent of this formulation is Guggulu which contains biologically active steroids, viz. *E* and *Z* guggulsterones[3]. The three fruits, Haritaki, Vibhitaki and Amalaki, when combined in equal ratio, constitute "Triphala", a well-recognized preparation of Ayurveda[4]. Contents of Triphala mentioned above have gallic acid as a standard marker and are rich in tannins[5,6]. Also, Piperine in *P. longum* is a well-known bioavailability enhancer and biomarker[7]. Guggulu has been used to treat various disorders such as obesity, osteoarthritis, rheumatoid arthritis, gout, facial paralysis, sciatica, faecal impaction, haemorrhoids, liver disorders, inflammation, cyst, cervical lymphadenitis, coronary thrombosis, diabetes, urinary calculus, and skin diseases[8,9]. Many commercial polyherbal anti-inflammatory formulations contain Guggulu as the chief ingredient [10]. In addition, Triphala also possesses many biological activities, including antimutagenic[11], radioprotective[12], immunomodulatory[13], anticancer [14,15,16] anti-inflammatory[17] and antioxidant activities[18]. Hence, this article aims to highlight its constituents' anti-inflammatory and anti-microbial action, a basic requirement to treat the indicated diseases.

Shotha vis-a-vis Inflammation

"Shotha" (Inflammation) is an extensive term for both local and internal organ swellings and inflammations. Charaka Samhita has described Shotha (Inflammation), its classification, symptomatology, complications, and management, but its surgical aspect is well defined in Sushruta Samhita. According to Acharya Sushruta, "Shopha" (Inflammation) is localized swelling in any part of the body involving the skin and the underlying flesh, which may be even or uneven, massive, and knotty or nodular in consistency[19]. Inflammation is a colloquial term both for Shotha and Shopha.

Shotha (Inflammation) is a disease which may appear in any part of the body encompassing Twak (Skin) and Mamsa (Muscle tissues) due to derangement of dosha (body humour)[20]. In it, Vata

is the prominent dosha which vitiates the Pitta and Kapha Doshas, due to which these vitiated and deranged doshas come in the periphery and get localised between the Twaka (Skin) and Mamsa (Muscles) by vitiating the Rasa (nutrient fluids), Rakta (blood) and Mamsa (Muscle tissues) dhatus (structural entities) and hence obstructing the Rasavaha, Raktavaha, and Mamsavaha Strotas (channels); resulting in the pathogenesis of Utsedha (swelling) which is associated with Vedana (pain), Lalima (redness), Ushma (heat), Gaurav (heaviness) and Lomharsha (horripilation). Acharya Sushruta has mentioned that there is no pain without the involvement of Vata Dosha, no Paka without the participation of Pitta Dosha, and no suppuration without the involvement of Kapha Dosha [21]. Regarding the classification, Charaka has mentioned three types of Shotha; Vataja, Pittaja and Kaphaja[22,] while Sushruta has mentioned six types of Shopha, viz, Vataja, Pittaja, Kaphaja, Sannipattaja, Raktaja and Agantuja[23].
Inflammation is termed a response of the immune system to harmful stimuli, such as pathogens, damaged cells, toxic compounds, or irradiation[24], which removes that injurious or external stimuli and initiates the healing process[25]. The five cardinal signs of inflammation are rubor (redness), tumour (swelling), calor (heat), dolour (pain) and functio-lasea (loss of function). Depending upon an individual's immunity and response duration, inflammation can be classified as acute or chronic. Acute inflammation is of short span (lasting less than two weeks), resolves quickly, represents the early body reaction, and is usually followed by healing. On the other hand, chronic inflammation is of a much longer duration[26]. At the tissue level, inflammation is a reactionary response due to infection or injury of local immune, vascular, and inflammatory cell[27]. Other important microcirculatory events during the inflammatory process include vascular permeability changes, leukocyte recruitment and accumulation and inflammatory mediator release[28]. People with low immunity and adverse environmental conditions are at high risk of infections due to endogenous (dysfunctional immune system) and external factors (i.e., comorbidities, drugs). Infections can induce disease relapses and be characterized by a severe clinical outcome, representing a frequent cause of death. Furthermore, the stimulation of systemic inflammation also gets induced by the infectious pathogens[29]. Thus, Inflammation is linked with a broad spectrum of Infectious as well as non-communicable disorders (NCD) like - allergies, and cardiovascular dysfunctions etc[30].

Components of Triphala Guggulu

Triphala Guggulu is widely used for the treatment of Shotha (Inflammation), Arsha (Piles), Bhagandar (Fistula-in-ano) and Gulma (Benign Growth). Each ingredient possesses properties which alleviate inflammation and pain, one of the significant symptoms of these diseases. Here, experimental work on each of the constituents' anti-inflammatory and anti-microbial action has been discussed.

***Commiphora wightii* (Arnott) Bhandari**

Guggulu plays a vital role in the traditional system of Indian medicine. It consists of vivid phytochemicals like steroids, aliphatic sterols, ferulates, di and triterpenoids, diterpenoids, triterpenoids, steroids, long chain and guggulsterone - I, II and III [32].

Anti-inflammatory activity: In one study, oral administration of aq. resin, stem bark, and methanolic extract of *Commiphora wightii* (Arn.) Bhandari showed anti-inflammatory activity by decreasing carrageenan-induced paw oedema period of 5 hours at the dose level of 500 mg/kg BW, oral[32]. Several studies of Guggulu confirmed its anti-inflammatory and antiarthritic activities [33-39]. In inflammation induced by Freund's adjuvant, crystalline steroid from petroleum ether extract showed the inhibition of full development of the primary lesions in adjuvant arthritis and severity of secondary lesions compared with the untreated control group[40]. Guggulosomes prepared using guggul by bath sonication, and trituration methods showed better anti-inflammatory effect and efficacy than ibuprofen. Also, both had a synergistic effect [41].

Myrrhanol A and Myrrhanone A from guggul-gum resins showed a potent anti-inflammatory effect on adjuvant-induced air pouch granuloma of mice more than hydrocortisone and 50% extract of crude resin.

Another experiment determined that Emulgel, a biphasic herbal formulation containing *Commiphora wightii* (Arn.) Bhandari exhibited good anti-inflammatory activity and was found to be comparable with marketed tacrolimus ointment. Also, E and Z Guggulsterones were found to decrease the level of inflammatory mediators such as MMP-2, nitric oxide and PGE-2[42]. Guggulosomes prepared using guggul exerts significant anti-inflammatory activity at 5 hours against carrageenan injection. Also, the proteasomal formulation of guggulu lipids holds immense potential for the development of topical herbal anti-inflammatory formulation as compared to topical NSAIDS[43]. A steroidal compound isolated from petroleum ether extract of *Commiphora wightii* (Arn.) Bhandari on rat paw oedema showed much more anti-inflammatory potent than its resin fraction[44].

Anti-microbial activity: A study on the volatile oil of *Commiphora wightii* (Arn.) Bhandari suggested it to be highly effective against *Rhyzopertha dominica*. Also, its ethanolic extract exhibited the best antibacterial activity at 5 mg/ml against multidrug-resistant *Klebsiella pneumoniae*[45]. Various studies revealed significant antibacterial activity of an active compound, 5(1-methyl,1-aminoethyl)-5-methyl-2-octanone, of the methanolic extract against guggulu gum Gram-positive and moderate activity against Gram negative bacteria[46-48]. Alpha pinene found in Guggulu acts as an anti-fungal and anti-microbial agent[49]. Eugenol (mono terpenoid) has antioxidant properties and is an anti-microbial agent[50]. Mansumbinoic acid also acts as an anti-inflammatory and anti-bacterial agent[51]. Alpha terpineol has strong anti-microbial activity[52].

In a new study on the essential oils, a wide range of inhibiting activity against Gram-positive and Gram-negative bacteria was exhibited by chloroform extract, and seven sesquiterpenoids compound isolated from the oleo-gum resin of guggulu[53].

***Terminalia chebula* Retz.**

Haritaki contains high amounts of phenolic intensifies, including ellagic acid, gallic acid and chebulic acid[54].

Anti-inflammatory activity: An aq. extract of dried fruit of *Terminalia chebula* Retz. showed anti-inflammatory effect by inhibiting inducible nitric oxide synthesis[55]. Also, a dose-dependent anti-inflammatory effect was exhibited by *Terminalia chebula* Retz. against Freund's adjuvant-induced arthritis in rats in a polyherbal formulation named Aller-7[56]. Yang *et al*. demonstrated the anti-activity of 12 bioactive mixes from the concentrate of *Terminalia chebula* Retz. organic products against inflammation through restraint of COX-2 and iNOS exercises[57]. Also, a single dose administration of 400 and 600 mg/kg body weight (b.w), ethanolic extract of *Terminalia chebula* Retz., at p.o for 3 hours significantly decreased the number of writhes in acetic acid-induced mice[58]. In the experiment of 1% formalin-induced

right dorsal hind paw oedema in mice and carrageenan-induced paw oedema in rats, oral administration of aq. extract of *Terminalia chebula* Retz., a dose of 150, 300, and 600 mg/kg, bw significantly inhibit the licking response in the early and late phases. Topical administration of *Terminalia chebula* Retz., a dose of 1, 2, and 4 mg/ear significantly inhibit EPP (ethyl phenyl propiolate) induced ear oedema but not the AA-induced ear oedema in rats[59]. In acetic acid-induced writhing in rats, oral administration of methanolic extract of *Terminalia chebula* Retz., at the dose of 1000 mg/kg, bw, showed the highest reduction of 63.1% of writhing from 14.1 to 5.2 then the 300, 500 mg/kg, bw. This effect is due to the inhibition of both COX and LOX pathways by chebulagic acid, resulting in decreased generation of inflammatory mediators[60].

Anti-microbial activity: A study on aq. extract of the fruit of *Terminalia chebula* Retz. by Disc Diffusion Method against microbes like *Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermis, Escherichia coli, Shigella flexneri* and *Pseudomonas aeruginosa* showed significant anti-microbial activity[61]. Testing crude ethyl acetate and ether extract against common pathogenic bacteria (*Staphylococcus aureus, Proteus vulgaris* and *Escherichia coli*) and fungal strains (*Aspergillus niger* and *Candida albicans*), extracts of *Terminalia chebula* Retz. were found to be active against almost all tested pathogenic strains[62].

Antibacterial potency of the extract of *Terminalia chebula* Retz. Standard growth inhibitory Assay methods were tested in which all extracts showed varying degrees of strain-specific antibacterial potential, among which ethanol extract showed superior activity against *Escherichia coli* and hot aq. extract against *Staphylococcus aureus*[63-65]. Strong antibacterial activity was demonstrated by ethanedioic acid and ellagic acid isolated from the butanol fraction of *Terminalia chebula* Retz. fruit extract against intestinal bacteria, *Clostridium perfringens* and *Escherichia coli* [66].

In a study, aq. extracts of *Terminalia chebula* Retz. were compared with standard drugs, i.e., Gentamycin tetracycline was tested against six medically important bacterial strains, gram-positive (*Bacillus subtilis, Bacillus aureus* and *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa*). Results showed a more significant effect of aq. extract against gram-negative than gram-negative bacteria[67]. Aq. extract of *Terminalia chebula* Retz. reportedly showed antifungal activity against several dermatophytes (e.g., *Microsporum gypseum, Floccosum, Epidermophyton* and *Trichophyton rubrum*) and yeasts (e.g., *Candida albicans*)[68].

Ethanol extract of *Terminalia chebula* Retz. fruit showed potent antibacterial activity against multidrug-resistant uropathogenic *Escherichia coli,* and phenolics were responsible for this antibacterial activity[69].

***Terminalia bellerica* Roxb.**

Its fruit rind is one of the important contents of Triphala (three fruits)[70]. It contains various phytochemicals like tannins, chebulinic acid, gallic acid, ethyl gallate and glycoside[71].

Anti-inflammatory activity: In a study, the aq. extract of *Terminalia bellerica* Roxb. decreased a total number of writhing at the dose of 9, 18 and 36 mg/kg, bw, oral in acetic acid-induced Swiss albino mice[72]. Also, the methanolic extract showed a reduction in paw oedema of 50%, 55.88% and 61.76% at the respective dose of 50, 12 and 300 mg/kg, bw, oral in carrageenan-induced paw oedema in rats[73].

At the dose of 100–400 µg/ml in lipopolysaccharide (LPS) induced RAW264 murine macrophage cells by MAPK/NF-kB pathway and enhanced antioxidant defence capacity via Akt/AMPK/Nrf2 pathway, anti-inflammatory activity was shown by *bellerica* extract (TBE)[74].

Anti-inflammatory activities of *Terminalia bellerica* Roxb. extract was evaluated in the carrageenan-induced paw oedema model, in which inhibition of paw oedema was compared to control group, observed at different doses of 100, 200 and 400 mg/kg at 1, 3, and 5 hours and comparable efficacy of anti-inflammatory activity were shown for indomethacin at 200 mg/kg[75].

Table 1: *Rasa panchaka* (Ayurvedic Pharmacodynamic property) of *Triphala Guggulu* [31]

Ingredients	Rasa (Taste)	Guna (Attribute)	Virya (Potency)	Vipaka (Action)	Doshakarma (Action on body humour)
Haritaki *Terminalia chebula* Retz.	Panchrasa (Lavana i.e., salt absent)	Laghu (Light) Ruksha (Dry)	Ushna (Hot)	Madhura (Sweet)	Tridoshahar esp. Vatahar
Vibhitaki *Terminalia bellirica* (Gaertn.) Roxb.	Kashaya (Astringent)	Laghu (Light) Ruksha (Dry)	Ushna (Hot)	Madhura (Sweet)	Tridoshahar esp. Kaphahar
Amalaki *Emblica officinalis* Gaertn.	Panchrasa (Lavana i.e., salt absent)	Guru (Heavy) Ruksha (Dry) Sheet (Cold)	Sheeta (Cold)	Madhura (Sweet)	Tridoshahar esp. Pitta-shamak
Pippali *Piper longum* Linn.	Katu (Pungent)	Laghu (Light) Snigdha (Soft) Tikshna (sharp)	Anushna Sheet (Neither cold nor hot)	Madhura (Sweet)	Kapha-Vatashamaka
Guggulu *Commiphora wightii* (Arnott) Bhandari	Tikta (Bitter) Katu (Pungent)	Laghu (Light) Ruksha (Dry) Tikshna (sharp) Vishad (vivid) Sukshma (Micro) Sara (old) (mobile) Snigdha (Soft Pichchila (Fresh) (lubricous)	Ushna (Hot)	Katu (Pungent)	Tridoshahar, Kapha-Vata har

Table 2: Dosha Karma and action of ingredients of *Triphala Guggulu*

Ingredients	Karma (Action)	Roghaghnta (Therapeutic Indication)
Terminalia chebula Retz.	Deepan (Carminative) Anuloman (Regulation of Vata dosha) Shothahar (Anti-inflammation) Vedanasthapan (Analgesic) Rasayana (Rejuvenation) Krimighna (Anthelmintics) Kushthaghna (Anti-leprosy) Vranashodhan (Wound cleaning) Vranaropana (Desiccant) Lekhana (Scraping) Gulmahar (Anti- Benign growth) Arshohar (Anti-piles) Medhya (Nootropic) Vrishya (Aphrodisiac)	Vrana (Wound) Udarroga (GIT disorders) Arsha (Piles) Krimirog (Worm infestation) Shool (Pain) Vatavyadhi (Disorders of Vata) Mukhroga (Oral diseases) Prameha (Diabetes) Anaha (Bloating) Gulma (Tumour) Vibandha (Constipation) Shotha (Inflammation) Raktvikar (Blood disorders) Hriddaurbalya (Cardiac disorders)
Terminalia bellirica (Gaertn.)Roxb.	Deepan (Carminative) Shothahar (Anti-inflammation) Vedanasthapan (Analgesic) Krimighna (Anthelmintics) Jwaraghna (Antifebrile) Bhedana (Cathartics) Rechana (Purgation) Anuloman (Regulation of Vata dosha)	Shotha (Inflammation) Krimirog (Worm infestation) Charmarog (Skin diseases) Shwitra (Leukoderma) Arsha (Piles) Vibandha (Constipation Kasa (Cough) Shwasa (Dyspnoea) Vrana (Wound) Pravahika (Dysentery)
Emblica officinalis Gaertn.	Deepan (Carminative) Anuloman (Regulation) Rasayana (Rejuvenation) Kushthagna (Anti-leprosy) Vrishya (Aphrodisiac) Jwaraghna (Antifebrile) Dahaprashman (Mitigation of burning sensation) Medhya (Nootropic) Balya (Tonics)	Arsha (Piles) Daha (Burning) Shotha (Inflammation) Charmarog (Skin diseases) Hridrog (Heart disease) Yakshma (Weakness) Kushtha (Leprosy) Daha (Burning sensation) Udararoga (GIT disorders) Amlapitta (Hyperacidity) Kasa (Cough) Shwas (Dyspnoea)
Piper longum Linn.	Deepan (Carminative) Vatanuloman (Regulation) Rasayana (Rejuvenation) Krimighna (Anthelmintics) Kushthagna (Anti-leprosy) Jantughna (Anti parasitic) Jwaraghna (Antifebrile) Balya (Tonics) Vrishya (Aphrodisiac)	Shotha (Inflammation) Gulma (Tumour) Pandu (Anaemia) Raktvikara (Blood disorders) Aamvata (Rheumatoid Arthritis) Krimirog (Worm infestation) Kushtha (Leprosy) Kasa (Cough) Arsha (Piles) Rajorodh (Amenorrhoea) Ajeerna (Indigestion)
Commiphora wightii (Arnott) Bhandari	Deepan (Carminative) Anulomana (Regulation) Shothahar (Anti-inflammatory) Vedanasthapan (Analgesic) Rasayana (Rejuvenation) Krimighna (Anthelmintics) Kushthaghna (Anti-leprosy) Jantughna (Anti parasitic) Vranashodhan (Wound cleaning) Vranaropana (Desiccant) Varnya (Skin whitening) Hridya (Cardiac) Arshoghna (Anti Piles)	Sandhivaat (Gout) Aamvaat (Rheumatoid Arthritis) Charmarog (Skin diseases) Arsha (Piles) Medoroga (Fat metabolism disorders) Kshaya (Weakness) Vrana (Wound) Krimi (Worm infestation) Gridhrasi (Sciatica) Shotha (Inflammation) Shleepada (Vata vyadhi) Vatvyadhi (Vata disorders) Nadishool (Nerve disorders) Granthi (Node) Kushtha (Leprosy) Pandu (Anaemia) Prameha (Diabetes) Ardita (Hemiplegia of face)

Anti-microbial activity: A study reported that crude methanolic extract of *Terminalia bellerica* Roxb fruits and its various organic fractions elicited both *in-vitro* and *in-vivo* antioxidant activity and antibacterial activity[76].

In an experiment, the antimicrobial activity of *Terminalia bellerica* Roxb. against nine human microbial pathogens was seen. The highest zone of inhibition was shown at 4 mg conc. of aq. extract of dried fruit of *Terminalia bellerica* Roxb. against *Staphylococcus aureus.* Except for *Escherichia coli* (entero-pathogen) and *Pseudomonas aeruginosa*, the remaining pathogens also showed high sensitivity to the methanol extract. Thus, proving the broad-spectrum antimicrobial activity of *Terminalia bellerica* Roxb. dry fruit[77].

In a study using the agar well diffusion method, antimicrobial activity was evaluated against Gram-positive or negative bacteria such as *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus cereus, Pseudomonas aeruginosa, Salmonella spp*, *Escherichia coli* and *Azotobacter spp* etc. Ethanolic extracts showed good activity against the tested bacterial isolates compared to methanol, chloroform or aqueous extract[78].

The aq. leaf extract exhibited significant activity against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Shigella flexneri, Salmonella typhi* and fungal isolates – *Aspergillus niger*, Mucor species, *Aspergillus fumigatus*, *Rhizopus* species and *Aspergillus flavus,* compared with chloroform and petroleum ether extract respectively[79].

***Emblica officinalis* Gaertn.**

Emblica officinalis Gaertn. contains chemical constituents such as vitamin C, minerals, amino acids, tannins, phyllembelic acid, phyllemblin, rutin, curcuminoids, emblicol and some phenolic compounds[80,81].

Anti-inflammatory activity: Previous studies reported that *Emblica officinalis* Gaertn. has antimicrobial[82], antioxidant[83,84], anti-inflammatory[85], analgesic and antipyretic[86,87] and antiulcerogenic[88] activities. It has been reported to be used for anti-inflammatory and anti-pyretic treatments by the rural population[89].

In a study, *Emblica officinalis* Gaertn. exhibit anti-inflammatory activities in carrageenan-induced acute and cotton pellet-induced chronic inflammation in Sprague-Dawley rats by reducing paw volume in acute inflammation and the granulomatous tissue mass and plasma extravasation in chronic inflammatory condition[90].

Also, the aq. extract of *Emblica officinalis* Gaertn. has reported an inhibitory effect on the synthesis and release of inflammatory mediators in rats[91]. The potential anti-inflammatory efficacy was shown by the water fraction of *Emblica officinalis* Gaertn. fruits butanol extract against indomethacin-induced gastric ulcer[92].

In the inflammation model induced by lipopolysaccharide-induced RAW264.7 macrophages, various solvent extracts of *Emblica officinalis* Gaertn. such as ethyl acetate and petroleum ether inhibit NO secretion and cytokines (TNF-alpha, IL-1beta, IL-6) in RAW264.7 macrophages[93].

In another such study, ethanolic extract of the leaves was examined against the carrageenan-induced mice model. The oedema volume was comparatively higher in groups with ethanolic extract given[94].

On examination of Aller-7, a poly-herbal formulation containing *Emblica officinalis* Gaertn., it exhibits potent anti-inflammatory activity against compound 48/80-induced paw oedema in both Balb/c mice and Swiss Albino mice and carrageenan-induced paw oedema in Wistar albino rats and an approximately 63% inhibitory effects and good trypsin inhibitory activity[95].

Anti-microbial activity: Various studies have demonstrated the potent antimicrobial properties of *Emblica officinalis* Gaertn and antifungal activity *in vitro*. *Emblica officinalis* Gaertn. has an antimicrobial activity due to the presence of flavonoids (quercetin), ascorbic acid, gallic acid, alkaloids (phyllantine**,** phyllantidine) and hydrolysable tannins (emblicanin A and B)[96]. Tannin has antimicrobial properties by enzyme inhibition, substrate deprivation, cell wall inhibition by inhibiting oxidative phosphorylation, metal ion deprivation, etc[97]. *Emblica officinalis* Gaertn. is active against various bacteria, including *Staphylococcus aureus, Escherichia coli, Mycobacterium tuberculosis, Salmonella typhosa* and *Candida albicans*[98].

A study using an agar well diffusion test showed that 100% (v/v) APE extract exhibited a more enhanced antibacterial activity against Gram-positive *Staphylococcus aureus* than Gram-negative *Escherichia coli* [99,100]. Methanolic seed extract at a 200 mg/ml dose showed the highest activity against *Escherichia coli*, *Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa*, *Enterococcus spp*[101].

Another study noted higher antibacterial action of *Emblica officinalis* Gaertn. for Gram-positive bacteria while limited effectiveness for countering fungi[102-104]. The extracts of EO exhibited an increased zone of inhibition (ZOI) when tested for *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Bacillus cereus, Vibrio cholerae* and *Candida albicans*[105]. Antimicrobial effectiveness for Gram-positive, Gram-negative bacteria and fungal agents reflects the usage of the fruit of *Emblica officinalis* Gaertn. as a remedy for different microbial diseases[106].

***Piper longum* Linn.**

Pippali (*Piper longum* Linn.) fruit contains volatile oil, alkaloids, isobutyl amides, lignans and esters. Piperine, the prime constituent of fruit, is reported to have significant anti-inflammatory activity[107,108].

Anti-inflammatory activity: In a study, Piperine showed anti-inflammatory action on Carrageenan-induced oedema, accountable to the release of various biochemicals, viz. histamine, 5-HT, various kinins etc., in the initial phase and release of prostaglandin-like substances in 2 to 3 hours in the second phase[109,110].

It is seen that the fruit decoction showed anti-inflammatory activity against carrageenan-induced rat paw oedema[111].

Another study reported considerable suppression of oedema formation against carrageenan-induced paw oedema in rats by both the varieties of Pippali. Where chhoti variety produced highly significant pedal oedema suppression, which is almost equal to the effect of the standard drug at 24 hours and more effective than the standard drug at 48 hours of formaldehyde injection. And the most remarkable point was that the chhoti variety at 200 mg/kg produced more inhibition of oedema than the standard anti-inflammatory drug, Diclofenac Sodium[112].

Anti-microbial activity: According to a study, it was proposed that *Piper longum* Linn. can be a promising source of antimicrobial agents where it could be used against certain antibiotic-resistant specific bacteria and fungi[113].

Comparing various extracts of *Piper longum* Linn. with streptomycin exhibited excellent antibacterial activity against bacterial pathogens, such as *Staphylococcus albus, Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli and Bacillus megaterium* and a fungus, *Aspergillus niger*[114]. In an experiment, all *Piper longum* Linn extracts showed inhibitory activity regarding Metronidazole[115]. Both the root and fruit of *Piper longum* Linn possess anti-amoebic activity approximately to the same extent[116].

The n-butanol soluble fraction, hexane fraction, and ethanolic extract of both *Piper longum* Linn roots and fruit containing Piperine exhibit anti-amoebic activity against *Entamoeba histolytica*[117].

Drug	Chemical constituents responsible for anti-inflammatory activity
Guggulu	Naringenin[32] Diayangambin[33] 1,8-Cineole[34] Mansumbinoic Acid[35] Myrrhanol[36] E-Guggulsterone And Z-Guggulsterone[37] Ellagic acid[38]
Haritaki	Tannins Like Chebulic Acid, Chebulagic Acid, Chebulinic Acid, Corilagin, Gallic Acid, Gallotannins and Ellagic Acid[54]
Vibhitaki	Tannins, Chebulinic Acid, Gallic Acid, Ethyl Gallate and Glycoside[71]
Amalaki	Gallic Acid and Fisetin[118]
Pippali	Piperine, Volatile Oil, Alkaloids, Iso butylamides, Lignans and Esters[107,108]

DISCUSSION

Triphala Guggulu was firstly mentioned in Chakra Dutta, where it is primarily indicated in Vranashotha (Wound inflammation). Triphala Guggulu is also shown in various diseases such as Shotha (Inflammation), Arsha (Piles), Bhagandar (Fistula-in-ano), Gulma (Tumour), Vranashotha (Wound inflammation), Vrana (Wound) in different classical texts. It also works as an effective formulation for wound healing. The wound is a cardinal feature in diseases like Piles, Fistula, Fissure-in-ano etc. In these diseases, wounds often persist to chronicity where chances of multiple microbial infections increase rapidly and frequently. Infection is a significant complication/hindrance in the management of wounds.

In Ayurveda, Vata dosha is the prominent factor which vitiates Pitta and Kapha dosha resulting in the manifestation of Shotha (Inflammation). All the five mentioned constituents of this formulation are mostly Tridoshahar in its doshkarma properties. Also, most drugs possess Madhur Vipaka (Sweet Action) and Ushna Virya (Hot potency), which contributes to the alleviation of prominent Vata Dosha, leading to Shotha Prashaman or Anti-inflammatory action. In addition, most drugs possess Jantughna or Krimighna karma, i.e., anti-microbial properties. Another constituent of this preparation, Triphala itself, is a wonder drug formulation. It has been proven to be an excellent drug of choice in inflammation and has free radical scavenging properties contributing to reducing inflammation and infections. Rasayana Karma of *P. Longum* Linn also employs the efficacy of this formulation. The primary ingredient of the Triphala Guggulu is Guggulu, renowned as one of the best-known Shothahara dravya (Anti-inflammatory drugs) in Ayurveda, used mainly in all inflammatory conditions.

Contents of Triphala Guggulu exhibit remarkable anti-microbial action. Methanolic and Ethanolic Extract of *Commiphora wightii* (Arnott) Bhandari has significant anti-microbial activity against Gram-positive and negative bacteria. Aq. extract of *Terminalia chebula* Retz. showed a significant anti-bacterial as well as anti-microbial action. Ethanolic Extract of *Terminalia bellerica* (Gaertn.) Roxb. showed a wide range of susceptibility against multiple bacteria. Additionally, its aq. leaf extract is also effective. 100 % APE of *Emblica officinalis Gaertn.* exhibit anti-bacterial action against both strains, whereas methanolic extract against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae,* and *Enterococcus*. Both aq. and alcoholic extracts of fruits and its root exhibit a significant anti-microbial action against several bacteria and a fungus. In addition, *Piper longum* Linn is an excellent activity potentiator of another active pharmaceutical agent or drug. Inflammation always precedes Infection. Various experiments performed on *Commiphora wightii* Arnott Bhandari had concluded that both aq. and alcoholic extracts at a dose of 500 mg/kg b.w. significantly reduced Oedema. Ethanolic and Methanolic extract of *Terminalia chebula* Retz. at the dose of 400, 600, and 1000 mg/kg respectively reduced no. of writhes in which highest reduction of 63.1 %, i.e., from 14.1 to 5.2 writhes was seen in case of methanolic extract. In *Terminalia bellerica* (Gaertn.) Roxb. and *Emblica officinalis* Gaertn. both aqueous and alcoholic extracts were found to be effective. Extracts of *Piper longum* Linn at a dose of 200 mg/kg showed more inhibition than the standard drug, Diclofenac Sodium.

CONCLUSION

Thus, this review article focuses on experimental work on the anti-inflammatory and anti-microbial activity of the ingredients of Triphala Guggulu. It is directly indicated in Shotha (Inflammation), in which not only Guggulu (*Commiphora wightii* Arnott Bhandari) but also Triphala (*Terminalia chebula* Retz., *Terminalia bellerica* Gaertn. Roxb. and *Emblica officinalis* Gaertn.) and Pippali (*Piper longum* Linn.) contribute to its anti-inflammatory action. Also, all its constituents exhibit a notable potent anti-microbial activity making it an ideal drug of choice in inflammatory and infectious diseases. No experimental work has been done on the anti-inflammatory and anti-microbial action of Triphala Guggulu as an individual formulation. Further, clinical studies should be conducted on this popular and potent formulation to validate its anti-inflammatory and anti-microbial activity. Thus, there is a scope for further research on its properties and mode of action.

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