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A REVIEW ON ANTIMICROBIAL ACTIVITIES OF TRIPHALA AND ITS CONSTITUENTS

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ABSTRACT

An infection is the detrimental colonization of a host organism by a foreign replicator. Infectious diseases remain the first cause of premature death throughout the world. Search of new natural compounds with pharmacological properties is a field of interest widely growing, especially for the management of infectious diseases such as meningitis, tuberculosis, malaria, hepatitis, AIDS etc. Dietary intake of foods or plant based extracts with antioxidant properties were shown to have beneficial effects on human health and improve immune functions against these diseases. Triphala is an Ayurvedic herbal formulation which contains equal proportion of fruits of Terminalia bellerica Roxb. (Bibhitaki), Terminalia chebula Retz. (Haritaki) and Emblica officinalis Gaertn. (Amalaki). It is a well known phytomedicine with known antioxidant, antibacterial, antifungal, antiviral, antiparasitic and anti-inflammatory activities. It has been used in the traditional medicines either alone or in combination with other plants for treatment of various health ailments. The most traditional usage of Triphala is to improve digestion, correct constipation, tone gastrointestinal tract and reduce oxidative stress. This review summarizes the current knowledge about the antimicrobial effects of Triphala and its constituents in counteracting oxidative stress as well as inflammatory mechanisms, using in vitro and in vivo models of acute and chronic infectious diseases.

KEYWORDS: Triphala, T. bellerica, T. chebula, E. officinalis, Infectious disease, Antimicrobial activity.

1. INTRODUCTION

Infectious diseases are the leading cause of death worldwide, and the numbers of deaths from infectious diseases are increasing day by day. Of all infectious disorders pneumonia, diarrhea, tuberculosis and malaria have been the leading causes of death.[1] According to recent literature 50,000 men, women and children are dying every day due to these diseases.[2] This translates into approximately 50,000 preventable deaths per day.[1,3] If present trends continue, 4·4 million people will still die in 2030.[1] Microbes that cause illness are also known as pathogens. The most common pathogens are bacteria and viruses**,** though a number of other microorganisms, including some kinds of fungi and protozoa, also cause disease (Table 1). An infectious disease is termed communicable if it is easily transmitted from one person to another. There is also strong evidence that microbes may contribute to many non-infectious chronic diseases such as some forms of cancer and coronary heart disease.[4] In the human host, a microorganism causes disease by either disrupting a vital body process or stimulating the immune system to mount a defensive reaction. An immune response against a pathogen, which can include high fever, inflammation and other damaging symptoms, may be more destructive than the direct damage caused by the microorganism.[5]

Antibiotics are a type of antimicrobials used to treat various infections and are used specially against bacteria. Several such agents are also effective against a number of fungi, protozoa, some are toxic to human and animals even when given in therapeutic dosage. Antibiotics are not effective against viruses and may be harmful when taken inappropriately. Promoting appropriate use of natural or synthetic antibiotics and preventing the spread of drug resistant bacteria are key issues in tackling the public health problem of antimicrobial resistance. Resistant microorganisms are able to survive attack by antimicrobial drugs, so that standard treatments become ineffective and infections persist, increasing the risk of spread of these microorganism to others hosts. Multidrug resistance (MDR) creates serious challenges to the medicinal field and infections caused by MDR bacteria.[6] Target based drug resistance to the antibiotics have also been reported. Recent studies also indicate that synthetic drugs are emerging as drugs of abuse for college students and young military personnel.[7] Nowadays, people suffering from the side effects of antimicrobial resistance are trying to find alternative solution in natural products. Medicinal plants provide a wealth of antimicrobial agents. Herbs are used to treat various infectious diseases worldwide. Interestingly, some herbs have antimicrobial activity against bacterial pathogens in addition to their flavoring effects.[8] From the earliest times, herbal spices are added for improving taste which naturally and safely

renew shelf life of food products. Bacterial pathogens are sensitive to extracts from many traditional plants.[9] Therefore, the natural plants have been used as antimicrobial agents which provide a promising safe solution. Natural products have certain advantages besides being cheap to produce; they are biodegradable and readily available. Herbal medicines are also used as dietary supplements and are produced without added artificial ingredients.[10]

Table:1. Microbial infectious diseases and their annual case numbers

Type of micro organism	Name of Microorganism	Disease name	Effect of disease	Annually reported cases
Bacteria	Haemophilus influenza	meningitis	brain damage, hearing loss or learning disabilities	4,100
	Shigella dysenteriae	Shigellosis	dysentery (diarrhea with blood), fever, abdominal pain, rectal tenesmus	300,000
	Clostridium perfringens	gas gangrene	skin injury, sudden pain, feeling of heaviness, a low-grade fever, apathetic mental status, necrosis	3000
	Bacillus anthracis	anthrax	fever, chills, nonproductive cough, chest pain, headache, myalgias, and malaise	20,000 to 100,000
	Mycobacterium leprae	Leprosy (a rare disease)	anesthesia, weakness, paralysis, muscular atrophy, skin lesions, affects mucous membrane & peripheral nerves	108
	Borrelia burgdorferi	syphilis	arthritis, brain damage, and blindness.	100,000
	Borrelia burgdorferi	lyme	irregular heartbeat, eye & liver inflammation (hepatitis), apoptosis, severe fatigue.	30,000
	Vibrio cholera	cholera	watery diarrhoea, vomiting and leg cramps, can quickly result in dehydration and death	> 500 000
	Clostridium tetani	tetanus	impairs in motor neurons, muscle stiffness and spasms	49,000
	Mycobacterium tuberculosis	tuberculosis	cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats	9.6 million
	Bordetella pertussis	pertussis	runny nose, sneezing, mild cough, low-grade fever.	32, 971
	Solmonella typhi	typhoid fever	poor appetite, abdominal pain, headaches, fever, intestinal bleeding.	724.6
	Yersinia pestis	plague	enlarged and painful lymph nodes, fever, chills, headaches, and weakness.	1,000 to 3,000
	Streptococcus pyogenes	scarlet fever	sore throat, fever, and a characteristic red rash	1000
	Rickettsia parkeri	rickettsioses	fever, headache and skin rashes	579
Fungi	Aspergillus niger	aspergillosis	fever, bloody cough, chest or joint pain, headaches or eye symptoms, nose bleed,	3.5 million

			facial swelling, skin lesions	
	Blastomyces dermatitidis	blastomycosis	fever, chills, cough, and discomfort or pain in the muscles, joints and chest pain	1.5 million
	Candida albicans	candidiasis	veginal itching, swelling and irritation.	7,000 to 28,000
	Histoplasma capsulatum	Histoplasmosis	Ch chills, cough, chest and joint pain, muscles s stiffness, shortness in breathing	144,462
	Pneumocyctis firovecii	pneumocyctis pneumonia	fever, mild and dry cough, rapid breathing, fatigue, major weight loss, chest pain during breathing	4.9 milliom
	Sporothrix schenckii	sporotrichosis	nodule formation, shortness of breath, cough, and fever.	1000
	Trichophyton rubrum	Ringworm	itchy, red, raised, scaly patches around the outside normal skin	>10,000
Protozoa	Entamoeba histolytica	amoebiasis	loose stools, stomach pain and stomach cramping	100,000
	Giardia lamblia	giardiasis	diarrhea, gas, greasy stool, stomach or abdominal cramps, nausea	19,888
	Trypanosoma brucei	African sleeping sickness	fever, severe headaches, irritability, fatigue, swollen lymph nodes, aching muscles and joints.	300 000
	Leishmania donovani	leishmaniasis	ulcers of skin, mouth, fever, low red blood cells, enlarged spleen and liver	20 000 to 30 000
	Toxoplasma gondii	Toxoplasmosis	fever, muscle aches, fatigue, swollen lymph glands.	20,000
	Plasmodium falciparum	malaria	high fever, profuse sweating, headache, vomiting, diarrhea, anemia	438 000
	Babesia microti	babesiosis	fever, chills, sweats, headache, body aches, loss of appetite, nausea, fatigue.	99, 226
	Trichomonas vaginalis	Trichomonias (STD)	vaginal itching and discharge, painful urination, swelling in the groin	100,000
Virus	Human papillioma virus (HPV)	HPV infections	formation of warts including genital, common, plantar, flat, dark color of skin, chances of cervical cancer	12,900
	Varicella Zoster virus.	Chicken pox	fever, rash of itchy inflamed pimples which turn to blisters and then loose scabs	100,000
	Human Immunodeficiency virus	AIDS	fever, chills, joint pain, muscle ache, sore throat, sweats enlarged glands, a red rash, tiredness, weakness, weight loss.	1.4 – 1.7 million
	Herpes	Hepatitis C	fatigue, abdominal pain, nausea, loss of appetite, or yellow jaundice. Jaundice	>350 000
	Chlamydia trachomatis	Chlamydia	lack of hunger, vomiting, belly aches, itchiness, feverish, muscle and joint pain.	> 20 million
	Influenza	Flu	fever, cough. sore throat. runny nose, muscle or body aches, headaches, fatigue vomiting and diarrhea.	250,000 to 500,000
	Herpes virus	Viral meningitis	headache, dislike of bright lights, neck stiffness, fever and nausea/vomiting.	36,000

Triphala is an Indian tridoshic herbal formulation consisting of fruits of T. bellerica (TB), T. chebula (TC) and E. officinalis (EO) in 1:1:1 ratio (Fig. 1). Recipe for this traditional herbal supplement is described in the traditional Indian texts, the Charaka and Susruta Samhita. According to Ayurveda the resultant formulation was shown to promote health, immunity and longevity when used in a recommended manner.[11] Triphala corrects constipation, act as restoratives for gastrointestinal tract and also detoxifies the whole body and improves digestion and assimilation.[12] Triphala and its constituent's acts as cardiotonic, control blood pressure, improve blood circulation and reduce cholesterol level and helps in improving body's defense system.[14] Triphala and its constituents have shown antioxidant, anti-inflammatory, hepatoprotective[15,16] etc. that make them one of the most commonly used traditional medicines. Triphala is known to give a long life and is invigorating to whosoever takes it, as it works slowly and gently and may be taken over long periods of time without any side effect. Triphala and its constituents also showed strong antimicrobial activity against different microorganism (Table 2,3,4). Many active antimicrobial compounds were isolated from it by FT-IR and GC-MS analysis.[14]. Analysis of fruits of TB, TC and EO has shown significant microbial inhibition.[17] This review aims to give an overview of the recent scientifically tested antimicrobial activities of Triphala and its constituents which may be used as a good preventive/remedy against infectious diseases.

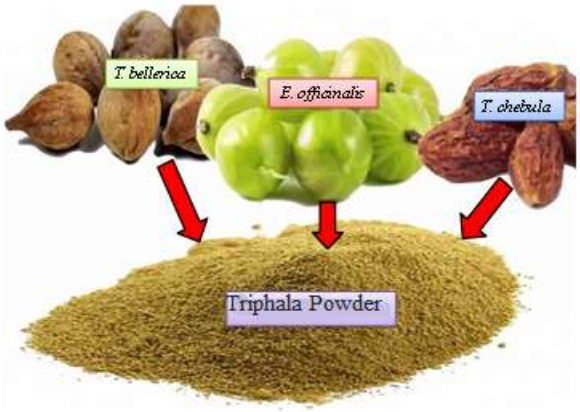

Figure 1. Triphala and its constituents

2. Ethanomediccal use of Triphala and its constituents

The combined use of different plant extracts is useful in decreasing drug resistant problems.[18] Triphala contains various phenolic and nonphenolic compounds[19] effective against both pathogenic and non pathogenic bacterial strains.[20] Triphala was found to be effective against enteric bacterial pathogens and enterococcoi.[21] It has shown broad

spectrum antimicrobial activity against some resistant bacterial isolates. Triphala and its constituents are also reported effective against human pathogenic bacteria.[22] Aqueous and ethanolic extract of Triphala and its ingredients have shown promising effects against the growth of bacterial strains isolated from the HIV infected patients.[23] Use of Triphala as mouthwash effectively reduced the number of mutant streptococci in saliva.[24] The bacterial isolates isolated from the wounds also showed sensitivity towards the extracts of Triphala when tested in vitro.[25] Additionally, Triphala and its constituents are reported to possess antifungal and antiprotozoal activity (Table 3,4). Ingredients of Triphala showed significant inhibitory activity at lowest IC_{50} values against human immunodeficiency virus-1 reverse transcriptase (Table 4)

2.1. T. bellerica (TB)

TB is a large deciduous tree which belongs to family combretaceae. It is generally known as felleric mycobalane in English and locally as Baheda. It is laxative, astringent, analgesic, antipyretic and antiemetic in nature whereas seeds are rich in oil and have narcotic properties.[26,27] In Ayurveda fruits and its kernel are said to possess medicinal value. Fruits of TB contain different tannins, flavonoids and other phenolic compounds[27,28] that may responsible for various biological activities. As per literature Ayurvedic plant parts are good in cold, cough, chronic diarrhea, dysentery and helps to increases appetite.[29] TB leaf showed good in vitro antioxidant against different reactive oxygen species.[15] The fruits are regarded as an excellent expectorant and strong rejuvenator against microbial infections.[30] Antimicrobial activity of TB fruit against a wide variety of pathogenic bacteria, yeast and fungi has been reported. TB fruit showed significant efficacy against virulence factors of respiratory and mammary glands infectious disease pathogens.[31] TB possesses antifungal compounds, that were shown promising challenge against fetal fungal diseases caused by cryptococcal pathogen.[32] Besides antibacterial and antifungal TB also have good activity against protozoa and virus (Table 4). TB showed potential to inhibits Hepatitis B surface antigens binding ability and HBV-DNA enzyme. It has also demonstrated trypanocidal activity against the related organism Trypanosma evansi (Table 4)

2.2. T. chebula (TC)

It is top listed Ayurvedic medicinal plant belonging to family Comcretaceae. TC is very rich source of tannins, phenolics, fatty acids and triterpenoid.[33,34] The leaves were found to contain polyphenols such as punicalin, punicalagin, terflavins B, C, and D. The plant is also

found to contain phloroglucimol and pyrogallol, along with phenolic acids such as ferulic, p-coumaric, caffeic and vanillic acids. The powder of the dried fruits of TC is used for the various therapeutic purposes to promote longevity. Due to strong antioxidant and in vivo wound healing capacity and significant medicinal properties,[15,16] TC is also known as the "King of Medicine" in Tibet.[35] TC exhibited antibacterial activity against a number of both Gram-positive and Gram-negative human pathogenic bacteria (Table 2). Ellagic acid isolated from TC showed good inhibiting potential against coliforms forming infectious pathogens.[36] The ethanolic extract of TC fruits demonstrated a strong antimicrobial activity against multidrug-resistant uropathogenic bacteria and phenolics were found to be responsible for this antibacterial activity. In vitro assessment of TC fruit, bark and leaves showed significant antifungal and antiviral activities (Table 3,4). Seed and fruit pericarp of TC have a potential against multi drug resistance parasite plasmodium falciparum to combat against malaria (Table 4).

2.3. E. officinalis (EO)

It is a large tree belonging to Euphorbeacae family, and is commonly known as Indian gooseberry in English and locally as Amla. It is well known that all parts of Amla plant are used to treat a range of diseases but most significant is the fruit. Fruit is used either alone or in combination with other plants to treat many common ailments such as cold, fever, peptic ulcer, dyspepsia and as digestive aid as well as serious diseases like cancer and cardiovascular disease.[37] The fruit of EO is also known for significant antimicrobial phenolic compounds.[37]It contains many active phytochemicals including flavonoids. It is one of the richest sources of vitamin C that were responsible for antioxidant, anti-inflammatory and antimicrobial activities. Gallic acid and tannic acid are the major phytoconstituents of EO and has strong antimicrobial potential.[38] In vitro assessment of EO fruit and leaf showed 100 percent antibacterial, antiprotozoal and antifungal activities. It has good antioxidant and anticancer activity and showed strong squabble against infectious diseases.[15,16] In more than 150 literatures cited in last 5 years little in vitro and in vivo studies of Triphala and its ingredients against infectious diseases caused by virus and protozoa were found. Thus Triphala and its constituents is emerging herbal warrior against infectious microorganisms.

3. Phytochemical of Triphala and constituents

Phytochemical analysis of Triphala and its constituent plants revealed the presence of a variety of antioxidant compounds such as phenolics, flavonoids, tannins, alkaloids, terpenoids, vitamins, glycosides, fatty acids and phytosterols.[27,39] Epidemiological studies have shown that many of these antioxidant compounds are responsible for antimicrobial activities to a greater or lesser extent. Antioxidant activity of phenolic compounds has been correlated to their chemical structures. Structure activity relationships of some phenolic compounds were thoroughly studied.[40]

3.1. Flavonoids

Flavonoids are ubiquitous in photosynthesising cells and are commonly found in fruit, vegetables, nuts, seeds, stems, flowers etc. Plant samples containing high concentrations of flavonoids are frequently reported to show better antibacterial activity.[41] For centuries, preparations containing these compounds as the principal physiologically active constituents have been used to treat human diseases. Increasingly, this class of natural products is becoming the subject of anti-infective research and many research groups have isolated and identified the structures of flavonoids possessing antibacterial, antifungal and antiviral activities.[42] Owing to the widespread ability of flavonoids to inhibit spore germination of plant pathogens, they have been proposed for use against human fungal pathogens.[43] FT-IR analysis of extract of TB revealed the presence of alkaloids, phenol, tannins and flavonoids.

The flavonoid, 7-hydroxy-3,4-(methylenedioxy) flavan, isolated from TB fruit, has also been shown to possess activity against C. albicans. Inhibition of HIV-1 entry into cells expressing $CD4^+$ and chemokine co-receptors[44] and antagonism of HIV-1 reverse transcriptase by the flavone O-glycoside have been demonstrated by Li and colleagues[45]. Phytochemical analysis of TC showed promising activity of flavonoid against Gram positive bacteria and also showed good antifungal activity. Rutin and quercetin were isolated through HPTLC method from TC exhibit anti-inflammatory, antihepatotoxic, antiulcer and antimicrobial activities.[46]

3.2. Tannins

Tannins were identified as another large class of phenolics present in Triphala and its constituents. These are generally subdivided into hydrolyzable and condensed tannins. Hydrolyzable tannins contain a central core of polyhydric alcohol such as glucose and hydroxyl groups, which are esterified either partially or wholly by gallotannins or

ellagitannins. In TC 33% of total phytoconstituents are hydrolysable tannins that are responsible for pharmacological activities.[47] These tannins contain phenolic carboxylic acids such as gallic acid, ellagic acid, chebulic acid and gallotannins. Ellagitannins such as punacalagin, casurarinin, corilagin, terchebulin, chebulanin, neochebulinic acid, chebulagic acid and chebulinic acid have been reported in literature as antimicrobials.[35] Tannins isolated from TB, TC and EO[48,49] have shown many biological and pharmacological activities.

8.3. Terpenoids

Terpenoids are naturally occurring organic chemicals that are under investigation for antibacterial, antiviral and other pharmaceutical functions**.** Terpenoids were found to exhibit antimicrobial activity[50]. GC-MS analysis of bark of EO showed very promising terpenoid compound such as lupeol and betulin.[51]

8.4. Phenolics

Phenolics are either direct or indirect antioxidants. They exhibit beneficial regulatory effects on signalling pathways. Antimicrobial action of phenolic acids against pathogens is hyperacidification of the plasma membrane.[52] This hyperacidification would alter cell membrane potential, making it more permeable, as well as affecting the sodium potassium ATPase pump implicated in ATP synthesis.[53] Antimicrobial phenolic compounds were isolated from TC, TB and EO through reverse phase chromatography, HPLC and confirmed by NMR and ESI-MS.[54]

8.5. Glycosides

Many bioactive glycosides have been reported such as alkyl, amino, cardiac or steroidal, cynogenic, terpenoidal etc. The alkyl glycoside agents have a particular utility in teeth cleaning preparations due to their improved activity against gram-positive bacteria.[55] Aminoglycoside antibiotics display concentration-dependent bactericidal activity against gram negative aerobes, some anaerobic bacilli and drug resistant staphylococci.[56] They require only short contact time and are most effective against susceptible bacterial populations that are rapidly multiplying. The inhibitory action of cardiac glycosides on active Na^+ and K^+ transporter has been reported.[57] Glycosides were isolated from TC, TB and EO revealed presence of antibacterial, antioxidant and other pharmacological activities.[58,59,60]

Table 2. Antibacterial activities of Triphala, T. bellerica, T. chebula and E. officinalis

Baterial Name	Plant Name (strain name)[reference]			
	Triphala	T. bellerica	T. chebula	E. officinalis
Bacillus subtilus	NCIM 2718[61]	ATCC6059[62] ATCC 6633[63]	MTCC 441[35] MTCC 1790[64] MTCC 121[65]	MTCC 2274[66]
Escherichia coli	ATCC 25922[61] EC1211[67] ATCC 8739[67]	Enteropathogen[68] uropathogen[68] ATCC 25922[62] NCIM 2931[63]	ATCC 25922 [69] MTCC 1687[70] ATCC 8739[71] HM626200[72] MTCC 2124[73] MTCC 7410 [73] MTCC 46[74] MTCC 452[75] MTCC 448[76] K-12[77]	MTCC 730 [66] ATCC 25922[62] ATCC 9637[66] MTCC 723[78] MTCC 443[79] ATCC 632[80]
Klebsiella pneumonia	ATCC 70063[61] KP1221[67] MTCC 4030[14]	NCIM 2719[63] MTCC 4030[81]	ATCC 14380[35] MTTC 6644[70] ATCC 12657[71] MTCC 3384[73] MTCC 7407[65] ATCC 70060[69] MTCC 4030[74]	ATCC 43816[82] ATCC 15380[62] MTCC 4030[66] MTCC 2405[78] MTCC 106[79] ATCC 31488[80]
Pseudomonas aeruginosa	ATCC 27853[83] PA1231[67] MTCC 1934[14]	ATCC25619[68] ATCC 27853[63,68] MTCC 1934[81]	ATCC 43495[77] ATCC 27853[35] ATCC 9027[71] HM626201[14] MTCC 1934[74] MTCC 7093[76] MTCC 2295[73] MTCC 424[75]	ATCC27853[79] MTCC 1934[80]
Staphylococcus aureus	ATCC 25923[61] ATCC 6538P[67] ATCC 29213[83,84] MTCC 3160[14]	ATCC 9144[68] ATCC 6538[62] MTCC 3160[81]	ATCC 25923[69] MTTC 737[70] ATCC 19615[70] HM626197[72] MTCC 7443 [72] MTCC 3160[65] MTCC 740[85] NCTC 6571[69] MTCC447[86] MTCC 87[75]	ATCC 25923[85] MTCC No.96[78] ATCC 12600[80] MTCC 3160[81]
Salmonella typhimurium	NR	NCTC8393[64] ATCC 13311[68] ATCC 23564[63,68]	SSFP 4S[35] MTCC 733[65,66] MTCC3216[77] MTCC 98[73,75]	NR
Streptococcus mutans	MTCC 890[88] DMST18777[89]	MTCC 890[90]	MTCC 497[85]	MTCC 890[91] ATCC 25175[92]
Proteus mirabilis	NR [62]	NCIM 2241[63]	MTCC 3310[74]	NCIM2241[62]

			MTCC 425[73] HM626199[72]	
Proteus vulgaris	NR	NR	MTCC 742[65] MTCC 1771[77] MTCC 744[73] MTCC 426[75]	ATCC 12454[62] MTCC 0426[66]
Staphylococcus epidermidis	NR	ATCC 12228[63]	MTCC 3615[35] ATCC 12228[71] MTCC435[75]	NR
Bacillus cereus	NR	ATCC 14579[62] ATCC11778[63]	NR	NR
Lactobacillus Acidophilus	MTCC 447[93]	NR	ATCC 9361[85]	MTCC 10307[91]
Streptococcus pyogenes	ATCC 12204[83]	NR	NR	MTCC1925[94]
Enterococcus faecalis	EF1201[67]	NR	NR	MTCC 2729[94] MTCC 439[66,91] ATCC 35550[92]
Corynebacterium rubrum	NR	ATCC 14898[63]	NR	NR
Listeria monocytogens	NR	ATCC 19112[63]	NR	NR
Shigella dysenteriae	NR	ATCC 9361[62]	NR	NR
Salmonella paratyphi	NR	ATCC 9150[63]	NR	NR
Streptococcus pneumoniae	NR	UTI isolate[68]	NR	NR
Yersinia enterocolitica	NR	ATCC9610[68]	NR	NR
Acinetobacter sp.	NR	NR	HM626198[72]	NR
AgrobacteriumTumefaciens	NR	NR	MTCC 431[74]	NR
Bacillus amyloliqufaciens	NR	NR	MTCC 1488[95]	NR
Brevundimonas diminuta	NR	NR	ATCC 19146[77]	NR
Enterobacter aerogenes	NR	NR	MTCC 7325[65] MTCC 2822[74] MTCC 111[75] K-12[77]	NR
Helicobacter pylori	NR	NR	NCTC RSB6[77] NCTC 33098[77]	NR
Salmonella enteric	NR	NR	NR	MTCC735[93] ATCC23564[87] ATCC 13311[80]
Staphylococcus saprophyticus	NR	NR	NR	ATCC 35552[61]
Streprtococcus	NR	NR	NR	MTCC 0459[66]

faecalis				ATCC 8043[80]
Listeria seeligeri	NR	NR	NR	ATCC 35967[80]
Micrococcus luteus	NR	NR	NR	MTCC 1538[66]
Nocardia asteroids	NR	NR	NR	MTCC 274[79]
Pasteurella multocida	NR	NR	NR	MTCC 1161[78]
Erwinia carotovora	NR	NR	NR	MTCC 1428[85]
Klebsiella aerogenes	NR	NR	NR	ATCC 9621[80]
Alcaligenes faecalis	NR	NR	NR	ATCC8750[87] MTCC 5521[79]
Enterobacter cloacae	NR	NR	NR	ATCC 10699[62]
Vibrio cholera	NR	NR	NR[77]	NR
Streptomyces aureofaciens	NR	NR	MTCC 325[76]	NR

NR: Strain name not reported

Table 3. Antifungal activities of Triphala, T. bellerica, T. chebula and E. officinalis

Fungal Name	Plant Name (strain name)[reference]			
	Triphala	T. bellerica	T. chebula	E. officinalis
Aspergillus flavus	MTCC 277[14]	MTCC 277[82]	MTCC 277[74]	NR
Aspergillus Fumigates	NR[94]	NR	MTCC3216[97]	NR
Aspergillus niger	MTCC 282[14]	NR	MTCC 282[74]	MTCC 282[82]
Aspergillus Terreus	NR	NR	NR	NR
Aspergillus Versicolor	NR	NR	NR	NR
Candida albicans	NR	NR	MTCC 183[76] MTCC 227[85] MTCC 3017[73]	MTCC183[94] MTCC 854[91] ATCC 2091[92] MTCC 183[82]
Microsporum canis	NR	NR	NR	NR
Trichophyton rubrum	NR	NR	NR	NR
Candida glabrata	NR	MTCC 3019[76]	MTCC 3019[76]	NR
Cryptococcus neoformans	NR	MTCC 184[76]	NR	NR
Candida	NR	NR	MTCC 184[76]	MTCC 184[91]

tropicalis				
Saccharomyces cerevisiae	NR	NR	MTCC170[85]	NR

NR: Strain name not reported.

Table 4. Antiprotozoal and antiviral activities of Triphala, T. bellerica, T. chebula and E. officinalis

Activity Name	**Plant Name[reference]**			
1. Antiprotozoal	**Triphala**	**T. bellerica**	**T. chebula**	**E. officinalis**
Leishmanicidal	NR	[98]	NR	[99]
Plasmodial	NR	[100]	NR	[100]
Amoebic	NR	NR	[101,102]	NR
Helmintic	NR	NR	NR	[103,104]
2. Antiviral		NR	NR	
Influenza A virus	[105]	NR	NR	NR
Herpes simplex virus (HSV)	[106]	NR	NR	NR
Human cytomegalovirus	[107]	NR	NR	NR
HIV	NR	[108]	[109]	[110]
HBV	NR	[111]		NR
influenza A virus H3N8	NR	NR	[112]	NR
Encephalitis Virus	NR	NR	[113]	[113]
Human Enterovirus 71	NR	NR	[114]	NR
Hepatitis C virus	NR	NR	NR	[115]

NR: Antiprotozoal and antiviral activity not reported.

4. Toxicology

While Triphala and its constituents have many health benefits, there are some of the potential concerns and side effects to be aware of while using it. The major precaution to be taken while using Triphala is that it shouldn't be taken by pregnant women as it is believed to favor miscarriage. Triphala can moderate blood sugar level, so patients of diabetes should take it under medical supervision. In case of an overdose, it can lead to dehydration which happens due to increased cleansing process of colon. Side effects are most common amongst first time users. EO is often recommended for pregnant women and lactating mothers in India. But, the other two ingredients of Triphala, TB and TC may be harmful during pregnancy. So, if someone still likes to keep the antioxidant intake high whilst pregnant, she may switch to powdered EO instead of Triphala. Interestingly, EO is also believed to enhance fertility in both men and women. Higher doses of TB, TC and EO may trigger healing crisis.

5. Future consideration

Development of antimicrobial compounds from natural sources has great potential because they are easily available, economical and non-toxic in long term use. Since people consume

them in daily life, there is no need of clearance from regulatory authorities like the Food and Drug Administration (FDA) for their use in Ayurvedic formulations. Triphala and its constituents offers an inexpensive solution to more expensive modes of treatment for everyday issues like digestive and cold complaints, as well as for difficult conditions like microbial infection, inflammation including some forms of cancers. It is a natural, earth-friendly agricultural product which can be taken every day to improve health. In a world where general population reaches for digestive aids of all sorts, Triphala and its constituents still offers their benefits to those with less than healthy diets and lifestyles. Many in vitro antibacterial and antifungal studies of Triphala and its constituents have been reported. In comparison to antibacterial and antifungal activities, very few studies on antiviral and antiprotozoal activities are reported. As Triphala and its constituents are easily available and very cost effective, it may be a good source of phytomedicine against microbial infection, inflammation, cancer and other cardiovascular diseases. In future it can be explored further for other parameters such as inhibition of biofilm formation, microbial quorum sensing, and inhibition of microbial gene expression before recommending it for usage in routine clinical practice. Further in vitro as well as in vivo studies are required to explore the antiviral and antiprotozoal activities of TB, TC and EO. The methodology developed may be used for detection of new natural bioactive compounds.

6. CONCLUSION

Now a days, due to extensive use of antibiotics and vast majority of synthetic drugs, many multidrug resistant strains are developing specially in hospital environment. To overcome drug resistance and to avoid side effects associated with the commonly available antibiotics, there is need of an alternative treatment method to cure such infections by use of traditional medicinal herbs like TB, TC and EO which are potent antibacterial agents, clinically safer, economically cheaper and affordable. Present review builds a foundation for further in vitro and in vivo studies to understand the mechanism of antimicrobial action of Triphala and its constituents which may help in developing better therapeutic agents and healthy products.

Conflict of interest

The authors declare that they have no conflict of interest.

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