

DRUG REVIEW OF TRIPHALADI GHRITA: AN AYURVEDIC FORMULATION IN THE MANAGEMENT OF KRIMI ROGA IN CHILDREN

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ABSTRACT

Worms are endoparasites residing in human beings. Diseases caused by helminthiasis are common and comprise very large group of infestations and infections in human beings. Worm infestations are present in people of all ages but children are much more prone to it as they are at the stage of beginners to learn how to cope with the parasitic enemies. Because of various side effects of modern medication use of herbal medication was increasing nowadays and also wide variety of plants possess broad spectrum anthelmintic property. So, Triphaladi ghrita may be useful in krimi roga in children. The ingredients of Triphaladi ghrita have effects like Krimighana, Shulaghna, Agnideepana, rechak. Constituent ingredients of Triphaladi ghrita are Vacha (*Acorus calamus*), Kampillaka (*Mallotus philippinensis*), Danti (*Baliospermum montanum*), Trivit (*Operculina*

turpentum), Amalki (*Emblica officinales*), Bibhitaki (*Terminalia bellirica*), Haritaki (*Terminalia Chebula*). This study offers an overview of pharmacological action of each ingredient on several systems. It offers thorough scientific evidence supporting method of action of each ingredient.

KEYWORDS: Worm infestation, Triphaladi ghrita, Vacha, Danti, Trivit, Kampillaka, Amalaki, Bibhitaki, Haritaki.

INTRODUCTION

Intestinal parasitic infestation is the most common paediatric complaint worldwide in both tropical and subtropical geographical areas. In developing countries like India, the important factors for spreading worm infestation are poverty, ignorance, lack of hygiene, maintenance of bad sanitation and use of uncooked food or improper washing of food materials.^[1] Helminthiasis being condition chiefly affecting GIT, it is a threat to health and future of a generation. Helminthiasis of children is often neglected by both parents and physicians because of lack of severity of symptoms until the infection becomes severe. More than 1.5 billion people or 24% of the world population are infected with soil transmitted helminth infections worldwide.^[2] Over 270 million pre-school age children and over 600 million school age children live in areas where these parasites are intensively transmitted.^[3] According to WHO 110 Million people were defecating in the open space resulting in high levels of environmental contamination and expose to the risk of worm infestations.^[5] Symptoms of krimi roga in children abdominal pain, fever, constipation, itching in anal region, teeth grinding, discoloration, vomiting, appetite loss, diarrhea.^[6] In Ayurveda various types of krimighana drugs have been described. One of them is Triphaladi ghrita as per Bhaisajya Ratnavali.

The details of constituent ingredients are as follows

Ingredients of formulation

Details of constituent of triphaladi ghrita

Sr No.	Ingredients	Botanical name	Family Name	Parts Used
1.	Vacha	<i>Acorus Calamus</i>	Araceae	Root
2.	Kampillaka	<i>Mallotus Philippinesis</i>	Euphorbiaceae	Glands and hair of fruit
3.	Danti	<i>Baliospermum montanum</i>	Euphorbiaceae	Root
4.	Trivit	<i>Operculina turpenthum</i>	Convolvulaceae	Root
5.	Amalaki	<i>Emblica officinalis</i>	Phyllanthaceae	Fruit
6.	Bibhitaki	<i>Terminalia bellirica</i>	Combretaceae	Fruit
7.	Haritaki	<i>Terminalia chebula</i>	Combretaceae	Fruit

Ayurvedic properties of ingredients of triphaladi ghrita

	Vacha ^[7]	Kampillaka ^[8]	Danti ^[9]	Trivit ^[10]	Amalaki ^[11]	Bibhitaki ^[12]	Haritaki ^[13]
Rasa	Katu, Tikta	Katu	Katu	Tikta	Katu, Tikta	Kashya	Katu, Tikta
Guna	Laghu, Snighda	Laghu, Ruksha	Guru, Tikshna	Laghu, Ruksha	Guru, Ruksha	Laghu, Ruksha	Laghu, Ruksha
Virya	Ushna	Ushna	Ushna	Ushna	Sheeta	Ushna	Ushna
Vipaka	Katu	Katu	Katu	Katu	Madhur	Madhur	Madhur

Vacha

Pharmacological actions

1. Immunomodulatory effects	Inhibition occurred for the proliferation of humans' mononuclear cells (from peripheral blood) in a culture with a mitogen (phytohemagglutinin or an antigen and the alcoholic extract. There was inhibition in the production of interleukin-2(IL-2) and tumour necrosis factor. However, lectins, which were constituent of another extract of rhizomes, had shown mitogenic action on T lymphocytes. ^[14]
2. Analgesic	The alcoholic fraction of rhizome is able to prevent 15.16% and 54.51% of the acetic acid induced writhing response with 250mg/kg and 500mg/kg of the extract respectively. The extract of rhizome at 100mg/kg oral intake for 14 days alongside vincristine is able to significantly reduce neuropathic pain as assessed by Von Frey hair tests as well as the sciatic functional index with a potency comparable to pregabalin(10mg/kg). ^[15]
3. Antibacterial effects	The rhizome showed antibacterial action (in terms of zone of inhibition of bacterial growth) in vitro against methicillin – resistant <i>Staphylococcus aureus</i> (MRSA) and strains of gram-negative bacteria (like <i>Escherichia coli</i> , <i>Shigella dysenteriae</i> , etc) which produces β - lactamase. These antibacterial actions were related to the presence of flavonoids and phenolic compounds in the rhizome. ^[16]
4. Anti-diarrhoea effects	There was increase in the time of onset of diarrhea and decrease in total number of faeces and number of wet faeces in comparison to the total weight of wet faeces prior consumption of the rhizome extract. ^[17]
5. Antifungal effects	In plants, β – asarone as an isolate of <i>Acorus gramineus</i> , completely inhibited mycelial growth of some pathogenic fungi whereas in other slight suppression was found. Calamus's leaves contain a class III haem peroxidase which, in the host's defence against pathogenic fungi, may inhibit hyphal growth of invasive pathogens in plants. ^[18]
6. Anti-inflammatory effects	The alcoholic extract showed moderate anti- proteolytic activity with the trypsin's induction of hydrolysis of bovine serum albumin (BSA). It has also exhibited the inhibition of β glucuronidase. ^[19]
7. Antioxidant effects	The rhizome extract has sufficient amounts of vitamin C and total polyphenolic compounds. It has the potential for increasing the antioxidants capacity and function in the brain due to the active anti -oxidant compound found in it i e α -asarone. ^[20]
8. Anti-spasmodic	It occurred through the blockage of calcium ion channels, a particular action with fraction of n-hexane. This fraction may contain constituents that are able to block calcium ion channels so that antispasmodic action results. ^[21]
9. Antitoxic effects	There was reduction in concentration of serum creatinine, low blood urea nitrogen and lesser activity of kidney ornithine decarboxylase. Renal oxidative diminished with prophylactic calamus. There was decrease in the content of glutathione,

10. Insect repellence	glutathione-S-transferase, glutathione reductase, lipid peroxidation and in generation of hydrogen peroxide. ^[22] Calamus oil extract has shown insecticidal property. Calamus is a potential larvicide. With exposure to an alcoholic extract of the roots, there was larvicidal action on housefly culex (<i>Culex quinquefasciatus</i>). ^[23]
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Kampillaka

Pharmacological activities

1. Purgative Activity and Anthelmintic activity	A significant purgative effect after an oral dose (120mg/kg) in rats was assessed from resins isolated from plant. Its effect was evaluated from the weight of faeces as well as from surface area of blotting paper soaked by liquid faeces. The anthelmintic effect on tapeworm was evaluated in albino rats, from the resin of the plant showed lethal effect of 35.69% and 78.21% respectively in small intestine in concentrations 60 and 120mg/kg respectively. ^[24]
2. Anti-Inflammatory and Immunoregulatory activity	Chalcones derivatives from the fruits of <i>M. philippinensis</i> and mallotophilippens C, D and E inhibit nitric oxide (NO) production and inducible NO Synthase (iNOS) gene expression by a murine macrophage like cell line, which was activated by lipopolysaccharide (LPS) and recombinant mouse interferon-gamma (IFN-gamma). Further investigations suggest the downregulations of cyclooxygenase-2 gene, interleukin- 6 gene, and interleukin-1b gene expression. The above results show that these chalcones have good anti-inflammatory and immunoregulatory effects. ^[25]
3. Hepatoprotective activity	Methanolic extract of <i>M. philippinensis</i> leaves decreases the CC14- Induced elevation in biochemical parameters (SGOT, SGPT, SALP, direct bilirubin, total bilirubin, and MDA) on pretreatment at doses 100-200 mg/kg and also reversed the functional and antioxidant parameters. Histopathological studies also suggest the hepatoprotective activity of plant. ^[26]
4. Antioxidant Activity and Antiradical activity	Different factors of bark and fruit of <i>Mallotus</i> were studied for its total antioxidant activity (TAA) and antiradical activity against DPPH on a Sephadex LH-20 column using ethanol and acetone water as mobile phase. Among different extracts, bark fraction showed the strongest antiradical activity (TAA value-5.27 mmol Trolox Equi/g) and reducing power. ^[27]
5. In vitro cytotoxic against human cancer cell	Glandular hair extract of <i>Mallotus</i> fruit powder was assayed against 14 human cancer cell lines among different fractions; 95% ethanolic extract showed the highest cytotoxic effect as compared to 50% ethanolic and aqueous portion. Further, the chromatographic analysis of the said fraction afforded a polyphenolic molecule rottlerin in <i>Mallotus</i> plant. ^[28]

Danti

Pharmalogical activities

1. Free radical scavenging activity	<p>Free radical scavenging potential of the aqueous extract (4,8,12,16,20 and 24mg/ml) of roots of <i>B. montanum</i> was evaluated by using diphenyl-picryl-hydroxyl (DPPH) assay and nitric oxide (NO) scavenging assay. Ascorbic acid was used as standard for the study. The results of study revealed significant free radical scavenging activity of the extract in dose dependent manner and comparable to the standard drug ascorbic acid.^[29]</p>
2. Anthelmintic activity	<p>The roots of <i>B. montanum</i> were evaluated for their anthelmintic activity against <i>Pheretima posthuman</i> and <i>Ascaridia galli</i> as test worms. Various concentrations (10-100mg/ml) of alcoholic and aqueous extract were tested in the bioassay, which involved determination of time of paralysis and time of death of the worms. Both the extracts exhibited significant anthelmintic activity at highest concentration of 100mg/ml. Piperazine citrate (10mg/ml) was included as standard reference and distilled water as control.^[30]</p>
3. Immunomodulatory activity	<p>In one study, different concentration (25,50 and 100mg/ml) of alcoholic extract of roots of <i>B. montanum</i> were studied for their effect on different in vitro methods of phagocytosis such as neutrophil locomotion and chemotaxis, immunostimulant activity of phagocytosis of killed <i>Candida albicans</i> and qualitative nitro blue tetrazolium test using human neutrophils. The results of this study revealed that the extract has stimulated chemotactic, phagocytic and intracellular killing potency of human neutrophils in dose dependent manner. The study exhibited stimulatory effect of the plant on cell-mediated immune system by increasing neutrophil function.^[31]</p>
4. Antimicrobial activity	<p>The crude ethanolic extract of leaves of <i>B. montanum</i> was evaluated for its antimicrobial potential by disc diffusion method. The various concentration (10,20,40) mg/ml of extract prepared in DMSO were screened using <i>Staphylococcus aureus</i>, <i>Pseudomonas aeruginosa</i>, <i>Escherichia coli</i> and <i>Candida albicans</i>. Ampicillin trihydrate (1mg/ml) and fluconazole (0.5mg/ml) served as reference control for the study.^[32]</p>
5. Hepatoprotective activity	<p>In one study, hepatoprotective activity of chloroform, alcohol and aqueous extract of roots of <i>B. montanum</i> was evaluated using paracetamol induced liver damage model in albino rats. Hepatotoxicity in rats was induced by paracetamol (2g/kg, p. o). All the extracts were administered orally to animals daily for seven days. Silymarin (200mg/kg) was given as reference standard. The alcohol and aqueous extract treated group of rats showed significant reduction in serum enzyme aspartate aminotransferase (AST), alanine</p>

	aminotransferase (ALT), alkaline phosphatase (ALP), γ -glutamyl transpeptidase and lipid peroxidase and increase in reduced glutathione (GSH) when compared to paracetamol treated groups of rats while chloroform extract showed moderate hepatoprotective activity. ^[33]
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Trivit

Pharmalogical action

1. Antidiarrheal activity	An experimental study was carried out by Shareef et al. to investigate the antidiarrheal potency of ethanolic root extract of OT through castor oil induced diarrhea model in mice. The root extract was administered orally in three different doses form. And it was observed that the ethanolic root extracts showed antidiarrheal effects in a dose dependent manner. ^[34]
2. Anti-inflammatory Activity	An experiment was conducted in the investigation of the anti-inflammatory potential of Ot root powder in formalin- induced edema in rats. In this root powder and its Ayurvedic polyherbal formulation (Avipattikar churna) were administered orally in rats at a dose of 100 mg/kg body weight. The results showed a remarkable reduction in formalin- induced edema volume, i.e. 36.45% and 27.11% respectively. ^[35]
3. Antihepatotoxic activity	The ethanolic extract of OT administered intraperitoneally at the dose of 100-2000mg/kg body weight which revealed significant hepatoprotective activity in a dose dependent manner. Here silymarin was employed as a standard drug and thus showed a significant increment in hepatoprotective efficacy. ³⁶
4. Anthelmintic Activity	OT possess the anthelmintic properties which helps in clearing of intestinal worms from body. Hence the use of this herb is quite effective in the treatment of various intestinal infections which are caused by bacteria, virus, protozoa and various other pathogens which may lead to serious digestive problems. ^[37]
5. Purgative activity	Purgative action of this herb is quite beneficial in various stomach disorders like flatulence, indigestion, and unsatisfactory bowel movements etc. Being purgative in nature OT is quite useful in arthritis and osteoarthritis. It helps to reduce the inflammation and swelling in joints. More over its anti-inflammatory properties help in pain reduction. ^[38]

Amalaki**Pharmacological actions^[39]**

1. Antioxidant Activity	<p>Vitamin C and low molecular weight hydrolysable tannins are abundant in Amalki fruit. Amalki becomes a good source of antioxidants as a result of these contents. Tannins like punigluconin, pedunculagin, embelicanin-A and emblicanin-b. The primary constituent of <i>E. officinalis</i> fruit is tannins, which have a significant potential for treating intestinal disease including diarrhea and dysentery. Tannins are also astringent in nature.</p> <p>A wide range of hepatotoxic substances, including heavy metals, ethanol, carbon tetrachloride ochratoxins, hexachlorocyclohexane and antitubercular medications, have been proven to be resistant to Amalaki.</p> <p>It has been proven that <i>E. officinalis</i> fruit extracts have a substantial immunomodulatory effect. Amalaki has mild cytoprotective and immunostimulant properties.</p> <p>Blood sugar levels are lowered by the fruit Amalaki's high Vitamin C content. It activates the Langerhans islets, a small collection of cells that release the hormone insulin.</p>
2. Intestinal disorders	
3. Hepatoprotective	
4. Immunomodulator	
5. Antidiabetic	

Bibhitaki**Pharmalogical action**

1. Antihelminthic activity	Terminalia bellirica is the key ingredient in "Triphala" formulation which is commonly used to treat digestive issues including worm infestations due to its anthelmintic properties. The anti-worm activity of Terminalia bellirica is due to its bioactive compounds like tannins, which can disrupt the worm's physiology and impair their ability to attach to the intestinal wall. ^[11]
2. Immunomodulatory Activity	A chemical agent that modifies the immune response or the functioning of the immune system is referred as immunomodulator. This is commonly known that macrophages gives role in different mechanism against the infection of host and used in destroying the tumor cells. <i>T. bellirica</i> fruit extract possess immunomodulatory activity which is proved by phagocytic and lymphocyte proliferation activity of fruit methanolic extract on the mouse. ^[12]
3. Hepatoprotective Activity	The protective effects of TB fruit extract and its active constituents against CCl ₄ in toxicity. Treatment with extract (50,100 and 200mg/kg) showed dose dependent recovery in parameters such as SGOT, SGPT and lipid peroxidase, glutathione but the effect of Galli acid is more reliable. ^[13]
4. Antioxidant Activity	The antioxidant activity is due to phenolics, flavonoids content of aqueous (AETB) and ethanolic extract (EETB) of fruits of <i>T. belerica</i> . The antioxidant activity was investigated by DPPH (1,1-diphenyl -1,2-picryl hydrazyl), ABTS (2,2-Azino-bis 3 ethyl benothiazoline-6 sulphonic acid, diammonium salt,

5. Antimicrobial Activity	superoxide, nitric oxide, reducing power and TAC (Total antioxidant capacity) ^[14] <i>T. bellirica</i> has shown potent action against infectious agents in vitro. Fruit extracts contains phenol, tannins, alkaloid and flavonoids. Alkaloids are mainly responsible for inhibiting the microorganisms by impairing the enzyme involved in energy productions, interfering with the integrity of cell membrane and structural component synthesis. In the fruit extract of <i>T. bellirica</i> have tannins which is useful in preventing the formation of microorganisms. ^[15]
6. Antispasmodic and Bronchodilatory Activity	<i>T. bellirica</i> fruit extract may promote the relaxation of spontaneous contractions in isolated rabbit jejunum and guinea pig ileum. In guinea pig trachea, TB relaxed the carbachol induced contractions. In which protective effect of TB against castor oil induced diarrhea. It also reserves the CCH and K ⁺ induced contractions in a pattern which is similar to that of dicyclomine. Carbachol may induce mediated bronchoconstriction also observed in rodents. ^[16]

Haritaki

Pharmacological action

1. Antiprotozoal activity	A combination of <i>T. chebula</i> and four other botanicals (<i>Boerhaviadiffusa</i> , <i>Berberis aristata</i> , <i>Tinospora cordifolia</i> and <i>Zingiber officinale</i>) had a maximum cure rate of 73% in experimental amoebic liver cure in hamsters and 89% in experimental caecal amoebiasis in rats showing its antiamoebic activity against <i>Entamoeba histolytica</i> . The acetone extract of <i>T. chebula</i> seeds showed anti plasmodium activity against plasmodium falciparum. ^[46]
2. Cardioprotective activity	Terminalia chebula extract pretreatment was found to ameliorate the effect of isoproterenol on lipid peroxide formation and retained the activities of the diagnostic marker enzymes in isoproterenol induced myocardial damage in rats. ^[47]
3. Antioxidant and free radical scavenging activity	The leaves, bark & fruit of Terminalia chebula possessed high antioxidant activity and phenolic were found to be responsible for this activity. Methanolic extract was also found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro. ^[48]
4. Anti-inflammatory activity	Aqueous extract of dried fruit of <i>T. chebula</i> showed anti – inflammatory activity by inhibiting inducible nitric oxide synthesis. Terminalia chebula in polyherbal formulation (Aller-7) exhibited a dose dependent anti-inflammatory effect against Freund's adjuvant induced arthritis in rats. ^[49]
5. Cytoprotective activity	The ethanolic extract of Terminalia chebula fruit exhibited a notable cytoprotective effect on the HEK-N/F cells. In addition its extract exhibited significant cytoprotective effect against UV induced oxidative damage. ^[50]
6. Antispasmodic activity	One of the numerous studies of Terminalia chebula

<p>7. Immunomodulatory activity</p> <p>Antiamoebic activity</p>	<p>demonstrated its antispasmodic properties by the reduction of abnol as intestinal spasms.^[51]</p> <p>Crude extract of Terminalia chebula stimulated cell-mediated immune response in experimental amoebic liver abscess in golden hamsters, aqueous extract of Terminalia produced an increase in humoral antibody titre and delayed type of hypersensitivity in mice.^[52]</p> <p>A combination of Terminalia chebula and four other botanicals (Boerhavia diffusa, Berberis aristate, Tinospora cordifolia and Zingiber officinale) had a maximum rate of 73% in amoebic liver abscess in hamsters and 89% in experimental caecal in humoral antibody (HA) titre and delayed type hypersensitivity in mice.^[53]</p>
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CONCLUSION

Antihelminth from natural sources may play key role in treatment of these parasitic infections. Because modern medicine use to treat worms are having side effects like hallucinations, skin rashes, nausea etc. Owing to the complex action of the polyherbal formulation, triphaladi ghrita may be more sensible choice for the secure and efficient management of krimi roga in children.

Conflict of interest

Nil.

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