



E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2016; 5(3): 23-27
Received: 05-03-2016
Accepted: 06-04-2016

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Pharmacological and therapeutic effects of triphala – A literature review

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Abstract

Triphala (tri = three and phala = fruits), is an ayurvedic preparation composed of three equal proportions of herbal fruits native to the Indian subcontinent: viz. *Terminalia chebula*, *Phyllanthus emblica*, and *Terminalia bellerica*. Triphala is a tridoshic rasayana having a balancing and rejuvenating effect on the three constitutional elements that govern the human life. Triphala is rich in antioxidants, possess antibacterial, anti-viral and anti-cancer properties. Triphala is also known to cure cataract and effective in the treatment of Acquired immune deficiency syndrome (AIDS). Triphala is rich in polyphenols, Vitamin C and flavonoids. This review paper focuses on the therapeutic effect of triphala. Triphala is a polyherbal formulation and the mechanism of action of polyherbals/herbal drugs and their extracts differ in many respects from that of the synthetic drugs or single substances. In ayurvedic terms, triphala, used in moderation, is said to have a beneficial effect on all three doshas—vata, pitta, and kapha. Triphala contains several compounds that have been proposed to be responsible for its claimed health benefits, including gallic acid, chebulagic acid, chebulinic acid etc. Triphala has a combination of both nutritional as well as blood and liver cleansing activities. It has little function as a demulcent or lubricating laxative. It possesses anthroquinones that help to stimulate bile flow and peristalsis. The nutritional aspect of triphala in the form of its high vitamin C content, presence of linoleic oil and other important nutrients make it more of a tonic. Triphala possess free radical scavenging, antioxidant, anti-inflammatory, antipyretic, analgesic, antibacterial, antimutagenic, wound healing, anti-cariogenic, antistress, adaptogenic, anti-diabetic, hypoglycaemic activity and so on. All these characters make “Triphala” one of the most valuable herbal preparations in the world.

Keywords: Triphala, Therapeutic effects, Ayurveda, Rasayana drug, Herbal formulation, Anti-Cancer, Anti-diabetic, Antioxidant, Anti-inflammatory

Introduction

In ayurveda, triphala is a well known poly herbal formulation. In Indian system of medicine (ISM) it is a rasayana drug [1]. Triphala is a mixture of the dried powders of three fruits such as *Emblca officinalis* Gaertn (Euphorbiaceae), *Terminalia bellerica* Linn (Combretaceae) and *Terminalia chebula* (Combretaceae) in equal proportions. Triphala is one among the ayurvedic medicinal herbal formulation mostly preferred by medical practitioners [2]. It can be used by all people irrespective of their age. In ayurveda it is described as a tridoshic rasayana that can balance and rejuvenate the three constitutional elements that govern human life ie; vata, pitta and kapha. It has various applications in medical field like laxative, eye rejuvenator, anti-inflammatory, antiviral and so on. It is also effective in headache, dyspepsia, ascites, leucorrhoea, also used as a blood purifier and possess anti-inflammatory, analgesic, anti-arthritis, hypoglycemic and anti-aging properties. Triphala is claimed to have antiviral and antibacterial effect [3]. Triphala is prescribed for fatigue, assimilation, reduces oxidative stress and infectious diseases such as tuberculosis, pneumonia, AIDS, periodontal diseases etc [4]. Triphala is reported to reduce considerably the damage due to oxidative stress [5]. Studies show that it inhibits the growth of Gram-positive and Gram-negative bacteria [6]. The recent studies proves that the triphala is rich in gallic acid, vitamin C, ellagic acid, chebulic acid, bellaricanin, beta – sitosterol and flavanoids [7].

Various studies prove that triphala possess various pharmacological and therapeutic activities.

Pharmacological and Therapeutic effects of Triphala Triphala as an anticancer drug

Triphala possess a cytotoxic effect to cancer cell lines. Suppression of the growth of cancer cells may be due to its major component gallic acid [8].

It was observed that an increased concentration of triphala decreased considerably the viability of breast cancer cells (MCF-7) without affecting the normal breast epithelial cells. Triphala resulted in an increase in the intracellular Reactive Oxygen Species (ROS) in MCF-7 cells. Triphala induced cytotoxicity in the tumor cells but not in the normal active cells [9]. Triphala shows antimutagenic effect on Ames histidine reversion assay on *Salmonella typhimurium* against 4, Nitro-o-phenylene Diamine (NDP), Sodium Azide, 2-aminofluorene (2AF). Chloroform and acetone extract shows inhibition of mutagenicity while the aqueous extract was found to be ineffective. 98.7% inhibition was observed with acetone extract against revertants induced by S9-dependent mutagens [10]. Triphala exhibits anticancerous activity on two human breast cancer cell lines (MCF-7 and T47 D differing in p53 status [11]. MCF 7 possessing wild type p53 was more sensitive to triphala than T47 D which is p53 negative. The anti proliferative ability of triphala was inhibited by the exogenous addition of antioxidants, glutathione, (GSH) and N-acetyl cysteine in MCF7 and T47 D cells. Triphala induced dose and time dependent increase in intracellular reactive oxygen species in both the cell lines. P53 status determines the sensitivity of cells to triphala. Triphala inhibits the growth of human pancreatic cancer cells in cellular and *in vivo* model. When capan-2 cells were exposed to triphala for 24 hours its survival capacity was significantly reduced. Triphala when orally administered at a dose of 50 mg/kg or 100 mg/kg suppressed the growth of capan-2 pancreatic tumor xenografts [12]. 1,2-Dimethylhydrazinedihydrochloride is a highly toxic and carcinogenic compound which affects the vital organs including liver. Triphala has a chemoprotective role against 1,2-dimethylhydrazine, dihydrochloride induced cancer, by decreasing the lipid peroxidation activity of lactate dehydrogenase (LDH), increasing the level of reduced glutathione (GSH); and preventing the peroxidative damage [13]. By increasing the antioxidant status of animals' triphala can reduce the incidence of tumor. Triphala reduces benzo (a) pyrene [B(a)P] induced for stomach papillomatosis in mice. It reduces tumor incidence by 77.77% in short term treatment and by 66.66% in long term treatment groups [14]. Triphala possesses radioprotective effect and delays onset of mortality, reduced radiation sickness symptoms when intraperitoneally administered to Y- radiation subjected mice. Triphala exhibits protection at a dosage of 12.5 mg/kg and is non-toxic upto a dosage of 240 mg/kg. Triphala reduces mortality by 60% when fed at a dose of 1g/kg body weight for 7 days prior to the whole body Y- radiation at 7.5 followed by the post irradiation feeding for 7 days. There was an increase in xanthine oxidase reductase activity and decrease in superoxide dismutase activity in the intestine of mice exposed to whole body Y- radiation [15].

Antioxidant activity of Triphala

Triphala is effective in inhibiting Y-radiation induced damage in microsomal lipids and plasmid pBR 322 DNA. Triphala is very rich in polyphenols and tannins. By converting reactive oxygen free radicals to non-reactive products, polyphenolic contents in triphala are responsible for the antioxidant and radioprotection ability. Triphala significantly prevents cold-stress induced oxidative stress. Cold-stress induced oxidative stress is measured by Lipid peroxidation (LPO), enzymatic superoxide dismutase (SOD), catalase (CAT) non-enzymatic (vitamin C) antioxidation status etc [16]. Administration of triphala (1g/kg/body

weight/48 days) prevents cold stress induced oxidation stress and elevation in LPO and corticosterone levels. The antioxidant property can be correlated to the prevention of cold stress induced oxidative stress. Triphala and the individual ingredients of triphala effectively inhibit Y-radiation induced strand break formation in plasmid DNA. They inhibit radiation induced lipid peroxidation and possess the ability to scavenge free radicals like DPPH and superoxide. Instead of individual ingredients triphala mixture is more effective as it possess combined activity of all the three ingredients. Superoxide radical scavenging activity of triphala using xanthine and xanthine oxidase activity had shown that in addition to reacting with superoxide radical, triphala also inhibited uric acid formation. Phenols or polyphenols and tannins are profusely found in triphala. Gallic acid content was also found in HPLC analysis. The antioxidant activities were determined by 1,1- diphenyl-2-picryl-hydrazyl (DPPH) method and inhibition of lipid peroxide formation induced by Fe²⁺-ascorbate system. They were found to strongly correlate with total polyphenol contents [17]. Mallotusin and mucic acid 1, 4-lactone 3-O-gallate were reported to have antioxidant activity [18]. Triphala has been found to be an excellent scavenger of hydroxyl radicals and nitric oxide radicals and is capable of increasing the capacity to tolerate non-specific stress in experimental animals [19]. TPL was also effective in preventing superoxide-induced haemolysis of red blood cells [20].

Triphala against stress

Stress has been reduced by the supplementation of triphala. Cold stress induced behavioral and biochemical abnormalities like increase in immobilization, with increase in rearing, grooming and ambulation behavior, significant increase in lipid oxidation (LPO) and corticosterone levels can be prevented by triphala administration for 48 days. Triphala prevents noise-stress induced changes in antioxidant and cell mediated immune response in rats.

Triphala in wound healing

The ointments prepared from triphala extracts show significant wound closure *in vivo*. The granulation tissue shows reduced bacterial count, increase in collagen, hexosamine and uronic acid. Collagen sponges incorporated with triphala when used to close wounds showed increased thermal stability, water uptake capability, faster wound closure, improved tissue regeneration etc. *Epigallocatechin gallate* interaction with collagen contributes to this quick wound healing activity. Triphala has also shown *in vitro* wound healing activity [21]. In one study, an infected wound was dressed with triphala (methanol extract). The study revealed that matrix metalloproteinases expression was correlated well with reduction in the inflammatory phase, thus confirming the efficacy of the dressing [22]. Another study had shown *in vitro* activity of triphala against wound pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Streptococcus pyogenes*. Reduction of matrix MMP expression was observed in the treated group by gelatin zymography [21].

Antimicrobial activity of Triphala

Triphala shows inhibitory activity on microbial growth caused by *Streptococcus mutans* and *Lactobacillus*. Ayurvedic formulations like triphala mashi exhibit antimicrobial activity attributed to phenolic compounds and tannins in triphala. It

inhibits dose dependent growth of gram positive and gram negative bacteria. Triphala itself and its individual fruit components have a potent antibacterial action against a wide spectrum of bacterial isolates such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Shigella sonnei*, *Staphylococcus aureus*, *Vibrio cholerae*, isolated from HIV infected patients. Triphala churna also possess antibacterial activity against various pathogens. Its acetone, ethanol and methanol extract possess high antibacterial potential against a wide range of bacteria *S.epidermidis*, *S.aureus*, *Staphylococcus*, *Pseudomonas* and *E.coli*. Triphala mashi formulations has lesser antibacterial activity as compared to triphala. Triphala and its individual components showed antibacterial effect on both gram –positive and gram-negative bacteria, which suggests the ingress of active phytochemicals through both the bacterial cells walls. Triphala churna has antibacterial activity against various bacterial pathogens. Aqueous extract has activity against *S.epidermidis*, *S.aureus*, *P. vulgaris*, mildly antibacterial against *S. typhimurium*, *B.subtilis* and negligible/no inhibitory effect against *E.coli* and *E. aerogenes*. The acetone, ethanol and methanol extracts of triphala churna possess highest antibacterial potential against *S.epidermidis*, *S.aureus*, *P. vulgaris* and no antibacterial activity against *E.coli*, *E. aerogenes* and *P. aeruginosa* [23]. The three fruits constituting triphala show potent antibacterial activity against *E.coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Staphylococcus epidermidis*, *Salmonella typhii*, *Salmonella typhimurium*, *Enterobacter aerogenes*. Daily intake of triphala controls enteric infections in human beings [24]. Triphala possess antibacterial activity against pathogens like *Salmonella*, *Staphylococcus*, *Pseudomonas*, *E.coli* and *Bacillus* isolated from wounds of workers and students. Triphala Mashi formulation has lesser antibacterial activity as compared to Triphala [25]. Triphala was found to be effective against enteric bacterial pathogens and enterococci. It has shown broad spectrum antimicrobial activity against some resistant bacterial isolates. Triphala and its constituents are also reported effective against human pathogenic bacteria [26].

Antidiabetic activity of Triphala

The oral administration of triphala extract in dose of 100 mg /kg reduced the blood sugar level in normal and in alloxan (120 mg/kg) diabetic rat significantly within 4 hours and continued daily administration of the drug produced a sustained anti-diabetic effect. Some studies have investigated the possible anti-diabetic properties of combination of triphala in animal models, one in a high fructose diet induced and another in alloxan diabetic rats [27, 28]. The results of these studies show that the administration of the extracts reduced the blood sugar level. They were found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals *in vitro* [27].

Analgesic, antipyretic and ulcerogenic activities of Triphala

The analgesic, antipyretic and ulcerogenic activities of triphala were compared with the non – steroidal anti-inflammatory drug Indomethacin on the experimental models in mice and it was found that triphala at both the dose levels produced excellent analgesic and antipyretic effect, without any gastric damage. The evaluated anti-ulcer efficacy of the polyherbal formulation NR-ANX-C (composed of the extracts from *Withania somnifera*, *Camellia sinensis*, *Ocimum*

sanctum, shilajith and Triphala) presume that the cytoprotective, antisecretory and antioxidant properties of NR-ANX-C were responsible for its anti-ulcer activity [29]. In a previous study, the anti-ulcer efficacy of polyherbal formulation was evaluated with the potent antioxidant activity in aspirin and pyloric ligation induced gastric ulcers in rats. The efficacy of the polyherbal formulation NR-ANX-C (composed of the extracts from *Withania somnifera*, *Camellia sinensis*, *Ocimum sanctum*, shilajith and triphala) was evaluated in terms of antioxidant potential as assessed in terms of protection from lipid peroxidation and the antiulcer activity as seen by the area of gastric lesions, gastric juice volume, gastric pH, total acidity and total adherent gastric mucus content. Several studies presume that the cytoprotective, anti-secretory and antioxidant properties of NR-ANX-C were responsible for its anti-ulcer activity. These findings suggest the potential for use of NR-ANX-C as an adjuvant in the treatment of gastric ulcer [30].

Anti-inflammatory activity of Triphal

Triphala when topically administered prevents uveitis induced by intravitreal injection of lipopolysaccharide from *E.coli*. The inflammation of anterior segment in control groups was significantly higher than in triphala treated groups. Triphala exhibits a protective effect in endotoxin –induced uveitis. One study indicated that gallic acid is a selective inhibitor of COX-2. Being a small natural product with selective and reversible inhibition of COX-2, gallic acid would form a lead molecule for developing a potent anti-inflammatory drug [31].

Triphala as an immune modulator

Triphala possess an immunomodulatory activity when tested using carbon clearance test and Delayed Type Hypersensitivity (DTH) response. The good immunomodulatory property of triphala could be attributed to flavonoids, alkaloids, tannins, saponins, glycosides and phenolic compounds. A study by Srikumar *et al* have shown that administration of triphala enhanced phagocytosis, phagocytic index, antioxidant activities and decreased corticosterone levels in animal exposed to noise stress.

Anti obesity activities of Triphala

An Anti-obesity study which evaluated the herbal formulation triphala in mice showed that the body weight was found to be reduced when compared with the control animals [32]. Gallic acid is a phenolic compound of triphala which is selected as a bioactive marker due to its easy availability and its anti-obesity property [33]. Accordingly, a randomized, double-blind, placebo controlled, clinical safety and efficacy trial at Shahed University in collaboration with Endocrinology and Metabolism Research Institute (EMRI) has been conducted for evaluation of the activity of triphala in obesity implementation (unpublished data).

Conclusion

Triphala (tri = three and phala = fruits), include the Arabized “Atrifal” and the Chinese term “San-Teng”. This preparation is composed of three equal proportions of herbal fruits: *Terminalia chebula*, *Phyllanthus emblica*, and *Terminalia bellerica*. Triphala is a tridoshic rasayana having a balancing and rejuvenating effect on the three constitutional elements that govern the human life. Triphala is rich in antioxidants, possess antibacterial, anti-viral, anti-cancer property. Triphala is also known to cure cataract and effective

in treatment of Acquired immune deficiency syndrome (AIDS). Triphala is rich in many polyphenols, Vitamin C, and flavonoids. Triphala is a polyherbal formulation and the mechanism of action of polyherbals/herbal drugs and their extracts differ in many respects from that of the synthetic drugs or single substances. In ayurvedic terms, triphala, used in moderation, is said to have a beneficial effect on all three doshas—vata, pitta, and kapha. It is most well-known for its gentle effects on the bowels, improving peristalsis and cleansing toxic build up of wastes; but ayurveda also views triphala as a nourishing supplement known for its ability to rejuvenate healthy tissues, allowing one to age gracefully and that is why triphala is also termed as 'nectar of life.

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