



## PHYTOCHEMICAL AND PHARMACOLOGICAL ACTIONS OF TRIPHALA: AYURVEDIC FORMULATION - A REVIEW

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### ABSTRACT

Triphala is one of the most important and potent *Rasayana* drug used in Indian System of Medicine. Triphala is a *tridoshic rasyana* having a balancing and rejuvenating effect on the three constitutional elements that constitute 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. This review paper focuses on the phytochemical and therapeutic effect of triphala.

**Keywords:** Triphala, Rasayana, Immunomodulator, Antioxidant, AIDS.

### INTRODUCTION

Triphala is a well known polyherbal formulation from Ayurveda. It is a Rasayana Drug used in Indian System of Medicine (ISM)<sup>1</sup>. Triphala is a mixture of three fruits which is composed of dried fruits of *Emblica officinalis* Gaertn (Euphorbiaceae), *Terminalia bellerica* Linn (Combretaceae) and *Terminalia chebula* (Combretaceae) in equal proportions (1:1:1) as described in Ayurvedic Formulary of India<sup>2</sup>. Triphala is one of the Ayurvedic medicinal herbal formulations prescribed by most health care practitioners. It is gentle for people of all ages from children to seniors<sup>3</sup>. In Ayurveds Triphala is termed as a tridoshic rasayana and to have balancing and rejuvenating effects on the three constitutional elements that govern human life (Vata, Pitta and Kapha)<sup>4,5</sup>. It is used as colon tonic, laxative, eye rejuvenator, anti-inflammatory, antiviral etc<sup>3</sup>. Triphala has been tested as an antioxidant and also radioprotector in mice<sup>6,7</sup>. Triphala is employed to treat conditions like headache, dyspepsia, ascites and leucorrhoea. It is also used as a blood purifier that can improve mental faculties and possesses anti-inflammatory, analgesic, anti-arthritis hypoglycemic and anti-aging properties<sup>7-11</sup>. Triphala is claimed to have antiviral and antibacterial effect<sup>12</sup>. Triphala is prescribed for various symptoms of infections, fatigue, assimilation and infectious diseases such as tuberculosis, pneumonia, AIDS, periodontal diseases<sup>13</sup>. It is reported to reduce considerably the damage due to oxidative stress<sup>14</sup>. Triphala inhibits the growth of Gram positive and Gram negative bacteria<sup>15</sup>. Triphala is rich in gallic acid, Vitamin C, ellagic acid, chebulic acid, bellericanin,  $\beta$ -sitosterol and flavonoids<sup>7</sup>.

### PHYTOCHEMICAL CONSTITUENTS OF TRIPHALA

Phenolic acids, flavonoids and tannins are the most commonly found polyphenolic compounds in the plant extracts. HPLC analysis and Folin-Ciocalteu and Folin-

Denis method showed that triphala contains 38±3% polyphenols and 35±3% tannins. Triphala contains sufficient gallic acid and hence can be used as a marker compound for in-vivo studies. HPLC studies reveal the presence of four phenolics gallic acid (0.026% w/w), tannic acid (0.024% w/w), syringic acid (0.016% w/w) and epicatechin (0.013% w/w) along with ascorbic acid (0.036% w/w) in triphala. *E.officinalis* contained ascorbic acid (0.026%), gallic acid (0.081%), *T.bellirica* contained gallic acid (0.005% w/w), tannic acid (0.004% w/w) and ascorbic acid (0.023%), while *T.chebula* contained gallic acid (0.024% w/w), tannic acid (0.011% w/w), syringic acid (0.009% w/w) and epicatechin (0.0060% w/w) together with ascorbic acid (0.02%). Triphala contains numerous other phenols<sup>17</sup>.

### THERAPEUTIC USES/ EFFECTS OF TRIPHALA

#### Triphala as an anticancer drug

Triphala possesses cytotoxic effect on cancer cell lines. Gallic acid is the major component and suppression of growth of cancer cells may be due to gallic acid<sup>18</sup>. Viability of breast cancer cells (MCF-7) decreased when treated with increasing concentration of triphala. Cytotoxicity of normal breast epithelial cells was not affected when treated with similar concentration of triphala. Triphala increased intracellular Reactive Oxygen Species (ROS) in MCF-7 and MCF-95 cells. Triphala induced cytotoxicity in tumor cells but not in normal cells<sup>19</sup>. Triphala shows antimutagenic effect on Ames histidine reversion assay on *Salmonella typhimurium* against 4-Nitro-o-Phenylene Diamine (NPD), Sodium Azide, 2-aminofluorene (2AF). Water extract was found to be ineffective while chloroform and acetone extract showed inhibition of mutagenicity. 98.7% inhibition was observed with acetone extract against revertants induced by S9-dependent mutagens<sup>20</sup>. Triphala exhibits anticancer activity on two human breast cancer cell lines (MCF-7 and



T47 D) differing in p53 status. MCF 7 with wild type p53 was more sensitive to triphala than T47 D which is p53 negative. Exogenous addition of antioxidants, glutathione (GSH) and N-Acetyl Cysteine (NAC) inhibited anti proliferative ability of Triphala in MCF 7 and T47 D cells. Triphala induced dose and time dependent increase in intracellular reactive oxygen species in both the cell lines. The sensitivity of the cells to triphala depends on their p53 status<sup>21</sup>. Triphala inhibits the growth of human pancreatic cancer cells in cellular and in vivo model. Survival of cells was significantly reduced when capan-2 cells were exposed to triphala for 24 hours. Triphala when orally administered at dose of 50 mg/Kg or 100 mg/Kg suppressed growth of capan-2 pancreatic tumor xenografts<sup>22</sup>. Triphala has a chemoprotective role against 1,2 -Dimethylhydrazine, Dihydrochloride induced cancer, by decreasing lipid peroxidation activity of lactate dehydrogenase (LDH), increase in level of reduced glutathione (GSH); it prevents peroxidative damage<sup>23</sup>. Triphala reduces tumor incidence by increasing the antioxidant status of animals. Triphala reduces benzo(a) pyrene [B(a)P] induced forestomach papillomagensis in mice. It reduces tumor incidence by 77.77% in short term treatment and by 66.66% in long term treatment groups<sup>24</sup>.

Triphala possesses radioprotective effect and delays onset of mortality, reduced radiation sickness symptoms when interperitonally administered to  $\gamma$ - radiation subjected mice. Triphala exhibits protection at a dosage of 12.5 mg/Kg and is non-toxic up to a dosage of 240 mg/Kg<sup>7</sup>. Triphala reduces mortality by 60 % when fed at a dose of 1g/Kg body weight for 7 days prior to whole body  $\gamma$ -irradiation at 7.5 Gy followed by post-irradiation feeding for 7 days. There was an increase in xathine oxidoreductase activity and decrease in superoxide dismutase activity in the intestine of mice exposed to whole body  $\gamma$ -irradiation<sup>25</sup>.

#### Antioxidant Activity of Triphala

Triphala is effective in inhibiting  $\gamma$ -radiation induced damage in microsomal lipids and plasmid pBR 322 DNA. Triphala is rich in polyphenols (38±3%) and tannins (35±3%). Polyphenolic contents in triphala are responsible for the antioxidant and radioprotecting ability, reduce the oxidative stress by converting reactive oxygen free radicals to non-reactive products<sup>16</sup>. 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. Administration of Triphala (1g/Kg/body weight/48 days) prevents Cold Stress induced oxidative stress and elevation in LPO and Corticosterone levels. The antioxidant property can be correlated to prevention of cold stree induced oxidative stress<sup>26</sup>. Triphala and the individual ingredients of triphala effectively inhibit  $\gamma$ -radiation induced strand break formation in plasmid DNA. They inhibit radiation induced

lipid peroxidation and possess ability to scavenge free radicals like DPPH and superoxide. Triphala mixture is more effective as it possess combined activity of all the three ingredients<sup>27</sup>. Superoxide radical scavenging activity of triphala using xanthine and xanthine oxidase activity showed that in addition to reacting with superoxide radical, triphala also inhibited uric acid formation. Triphala is rich in phenols/polyphenols (38±3%), tannins (35±3%), flavonoids were absent. HPLC analysis revealed that gallic acid content was 73±5 mg/g and increased to 150±5mg/g upon acid hydrolysis<sup>28</sup>.

#### Triphala against Stress

Triphala supplementation has a protective effect against stress. Triphala administration for 48 days (1g/kg/animal body weight) prevents cold stress induced behavioral and biochemical abnormalities like increase in immobilization, with decrease in rearing, grooming and ambulation behavior, significant increase in lipid peroxidation (LPO) and corticosterone levels<sup>29</sup>. Triphala prevents noise-stress induced changes in antioxidant and cell mediated immune response in rats. Changes induced by noise stress at 100 dB for 4 hour/d/15 days were controlled by Triphala at 1g/Kg/body weight/48 days<sup>30</sup>.

#### Antimicrobial Activity of Triphala

Triphala controls dental plaque, gingival inflammation and microbial growth caused by *Streptococcus mutans* and *Lactobacillus*. Triphala controls plaque from baseline and its activity is comparable to commonly available mouthwash Chlorhexidine<sup>31</sup>. Ayurvedic formulations like Triphala Mashī exhibit antimicrobial activity attributed to phenolic compounds and tannins in triphala. The activity is comparable to that of triphala. It inhibits dose-dependent growth of gram positive and gram negative bacteria<sup>32</sup>. Triphala and its individual fruit components have a potent antibacterial action against a wide spectrum of bacterial isolates like *seudomonas aeruginosa*, *Klebsiella pneumonia*, *Shigella sonnei*, *Staphylococcus aureus*, *vibrio cholera*, isolated from HIV infected patients. 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<sup>33</sup>. 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.aerogens*. 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*<sup>34</sup>. 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<sup>35</sup>. Triphala possess antibacterial activity against pathogens like *Salmonella*, *Staphylococcus*, *Pseudomonas* and *E.coli*, *Bacillus* isolated from wounds of workers and students. Triphala Mashi formulation has lesser antibacterial activity as compared to Triphala<sup>36</sup>. Triphala inhibits growth of *Enterococci* which causes nosocomial bacteremia, surgical wound/urinary tract infections. Triphala exhibited a large zone of inhibition against *Enterococci*<sup>37</sup>.

### 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, uronic acid<sup>38</sup>. Collagen sponges incorporated with triphala when used to close wounds showed increase thermal stability, water uptake capability, faster wound closure, improved tissue regeneration. *Epigallocatechin* gallate interaction with collagen contributes to this quick wound healing activity<sup>39</sup>.

### Triphala as an immunomodulator

Triphala has an immunomodulatory activity when tested using carbon clearance test and Delayed Type Hypersensitivity (DTH) [Foot Pad Swelling] response. Triphala Mega extract when administered at 500 mg/Kg and 1000 mg/Kg orally showed an increase in carbon clearance index which reflects enhancement of phagocytic function of mononuclear macrophage and nonspecific immunity. There was an increase in DTH response or cell mediated immunity. Triphala mega extract had a stimulatory effect on T cells. The good immunomodulatory property of triphala could be attributed to flavonoids, alkaloids, tannins, saponin glycosides and phenolic compounds<sup>40</sup>. Triphala inhibited the stress induced by noise (4hour /day for 15 days). Triphala at a dose of 1g/Kg/day for 48 days, enhanced Avidity Index (AI), but neutrophil function like adherence, phagocytosis were not altered. Neutrophil function was enhanced in triphala immunized group with a decrease in corticosterone level. Neutrophil function was significantly suppressed followed by increase in corticosterone levels both in noise-stress and noise-stress immunized groups. The noise stress induced changes were significantly prevented in triphala administered group. Oral administration of triphala stimulates neutrophil functions in immunized rats and stress induced suppression in neutrophil function were prevented by triphala<sup>41</sup>.

### Triphala as anti-inflammatory

Triphala when topically administered prevents uveitis induced by intravitreal injection of lipopolysaccharide from *Escherichia 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. The treated groups showed not only significant reduction in severity of clinical signs and also reduction in aqueous humor levels

of inflammatory cell, protein content and TNF- $\alpha$  compared with that of the control group<sup>42</sup>.

### Triphala in Arthritis

The efficacy of triphala on monosodium urate crystals induced inflammation for gouty arthritis was compared with no-steroidal anti-inflammatory drug Indomethacin. Triphala treatment inhibited paw volume, levels of lysosomal enzymes, lipid peroxidation and inflammatory mediator tumour necrosis factor- $\alpha$ , $\beta$ -glucuronidase and lactate dehydrogenase level were reduced. Triphala exerted a strong anti inflammatory effect against gouty arthritis<sup>43</sup>. Triphala (1g/Kg/body weight) was evaluated for its antiarthritic effect against indomethacin (3 mg/Kg/body weight) in arthritis induced rats by Freund's adjuvant (0.1ml). Levels of lysosomal enzymes, tissue marker enzymes, glycoproteins and paw thickness increased in arthritis induced animals. The physical, biochemical changes observed in arthritic animals were altered significantly to near normal conditions after oral administration of Triphala<sup>44</sup>.

### Triphala in other disorders

Triphala ghrita offers protection against cataract. Triphala gritha at a dose of 1080 mg gives protection against delaying the onset and progression of cataract. The anticataract effect may be attributed to antioxidant activity of gallic acid, ellagic acid and ascorbic acid<sup>45</sup>. Triphala possess enteroprotective effect against methotrexate induced intestinal damage (12 mg/Kg, orally for 4 days to albino rats). Triphala formulations prepared by mixing 1:1:1 of *T.chebula*, *T.bellirica* and *E.officinalis* and 1:2:4 proportions of the three ingredients, both exhibited enteroprotective effect. Both the formulations at a dose of 540 mg/kg significantly restored the depleted protein level in brush border membrane of intestine, phospholipids and glutathione content and decreased the myeloperoxidase and xanthine oxidase level in intestinal mucosa. Triphala unequal formulation showed decrease in permeation clearance of phenol red, level of disaccharidase in brush border membrane vesicles and lipid peroxidation content of intestinal mucosa. Triphala unequal formulation exhibits more protection than equal formulation<sup>46</sup>. Triphala and Triphala Mashi at a dose of 200, 400, 800 mg/kg when administered to castor-oil induced diarrhoeal rats, exhibited an increase in first defecation time, cumulative fecal weight and intestinal transit time. Aqueous and alcoholic extracts of Triphala and Triphala Mashi are safe upto a dose of 1750 mg/Kg, when evaluated for acute oral toxicity<sup>47</sup>. Triphala when administered repeatedly is effective in treating haloperidol induced (1mg/Kg) catalepsy. In acute cases, the aqueous extract of triphala reduced cataleptic score after latency of 60 minutes. The effect of triphala on cataleptic score in both acute and chronic cases were comparable to that produced by standard drug scopolamine<sup>48</sup>. Triphala possess significant antidiabetic activity. Triphala causes normalization of Fasting Plasma Glucose (FPG) induced by high fructose



diet in rat model. Triphala/the individual ingredients possess significant antidiabetic activity<sup>49</sup>. Triphala is associated with hyperlipidemic effect on hypercholesteremic induced rats. There is a increase in total cholesterol, LDL (Low d.Lipoprotein) and VLDL (Very Low d.Lipoprotein) and free fatty acid in hypercholesteremic rats were reduced in triphala treated hypercholesteremic mice<sup>50</sup>. Triphala also possess an effective antiplaque activity. The ethonolic extract of the formulation has higher antioxidant activity and inhibits *Streptococcus mutans*. Triphala extract inhibits the bio-film formation and protects gum cells due to antioxidant activity<sup>51</sup>.

### CONCLUSION

Triphala is one of the most important rasayana drugs commonly used in Ayurvedic system of medicine. Bhavprakash Nigantu mentions triphala to be a mixture of equal proportions of three fruits namely; *Emblica officinalis* Gaertn (Euphorbiaceae), *Terminalia belerica* Linn (Combretaceae) and *Terminalia chebula* (Combretaceae)<sup>52</sup>. According to Charaka Samhita daily consumption of the rasayana drug triphala for a period of one year makes a person survive for hundred years without any illness. Triphala is an esteemed drug in India which has been prescribed for centuries to cure a wide range of ailments. 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<sup>53</sup>.

Triphala is effective in curing a wide range of ailments. Its potency as an anti-cancer drug, antibacterial, anti-inflammatory and in treatment of arthritis, stress, and cataract is all well studied and proven. As there is lot of adulteration and substitution in the herbal market more studies and parameters for Quality Control of the individual ingredients and the compound formulation triphala needs to be established and carried out so as to ensure reliability and reproducibility of the formulation.

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