INTRODUCTION

Triphala is a well known polyherbal formulation from Ayurveda. It is a Rasayana Drug used in Indian System of Medicine (ISM)¹. Triphala is a mixture of three fruits which is composed of dried fruits of Emblica officinalis Gaertn (Euphorbiaceae), Terminalia belerica Linn (Combretaceae) and Terminalia chebula (Combretaceae) in equal proportions (1:1:1) as described in Ayurvedic Formulary of India². 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 seniors⁵. In Ayurveds Triphala is termed as a tridoshic rasayana and having a balancing and rejuvenating effect on the three constitutional elements that govern human life (Vata, Pitta and Kapha)⁴.يبنوجود. It is used as colon tonic, laxative, eye rejuvenator, anti-inflammatory, antiviral etc⁵. Triphala has been tested as an antioxidant and also radioprotector in mice⁶.⁷. 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 properties⁵¹¹. Triphala is claimed to have antiviral and antibacterial effect⁹.¹⁰. Triphala is prescribed for various symptoms of infections, fatigue, assimilation and infectious diseases such as tuberculosis, pneumonia, AIDS, periodontal diseases¹¹. It is reported to reduce considerably the damage due to oxidative stress¹². Triphala inhibits the growth of Gram positive and Gram negative bacteria¹³. Triphala is rich in gallic acid, Vitamin C, ellagic acid, chebulic acid, bellericanin, β-sitosterol and flavonoids⁷.

PHYTOCHEMICAL CONSTITUENTS OF TRIPHALA

Phenolic acids, flavonoids and tannins are the most commonly found polyphenolic compounds in the plant extracts. HPLC analysis and Folin-Ciocalteau 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 (0.099% w/w) and epicatechin (0.006% w/w) together with ascorbic acid (0.02%). Triphala contains numerous other phenols¹⁷.

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 acid¹⁸. 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-7and barel-95 cells. Triphala induced cytotoxicity in tumor cells but not in normal cells¹⁹. 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 mutagens²⁰. Triphala exhibits anticancer activity on two human breast cancer cell lines (MCF-7 and
Triphala possesses radioprotective effect and delays onset of mortality, reduced radiation sickness symptoms when interperitonally administered to γ-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. Triphala reduces mortality by 60 % when fed at a dose of 1g/Kg body weight for 7 days prior to whole body γ-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 γ-irradiation.

**Antioxidant Activity of Triphala**

Triphala is effective in inhibiting γ-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. 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 stress induced oxidative stress. Triphala and the individual ingredients of triphala effectively inhibit γ-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. 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.

**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. 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.

**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 commercially available mouthwash Chlorhexidine. Ayurvedic formulations like Triphala Mashi 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. 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 cholaera*, 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. 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*. 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. 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. Triphala inhibits growth of Enterococci which causes nosocomial bacteremia, surgical wound/urinary tract infections. Triphala exhibited a large zone of inhibition against Enterococci.

**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. 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.

**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 medicated immunity. Triphala mega extract had an stimulatory effect on T cells. The good immunomodulatory property of triphala could be attributed to flavonoids, alkaloids, tannins, saponin glycosides and phenolic compounds. 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.

**Triphala as anti-inflammatory**

Triphala when topically administered prevents uveitis induced by intravital injection of lipopolysaccharide from Enteric bacteria. 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-α compared with that of the control group.

**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-α,β-glucuronidase and lactate dehydrogenase level were reduced. Triphala exerted a strong anti-inflammatory effect against gouty arthritis. 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.

**Triphala in other disorders**

Triphala ghrita offers protection against cataract. Triphala ghrita 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.

Triphala possesses 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 mycolperoxidase 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. 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 up to a dose of 1750 mg/Kg, when evaluated for acute oral toxicity. 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. 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. 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 hypercholestermine rats were reduced in triphala treated hypercholesteremic mice. Triphala also possess an effective antiplaque activity. The ethononic extract of the formulation has higher antioxidant activity and inhibits Streptococcus mutans. Triphala extract inhibits the biofilm formation and protects gum cells due to antioxidant activity.

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). 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.

Triphala is effective in curing a wide range of ailments. Its potency as an anti-cancer drug, antibacterial, anti-inflammatory and in treatment of arithritis, 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.

REFERENCES

26. Dhanalakshmi S, Srikumar R, Manikandan S, Parthasarathy NJ, Devi RS. Antioxidant Property of Triphala on Cold Stress Induced