

ORIGINAL ARTICLES

## Therapeutic Uses of *Triphala* in Ayurvedic Medicine

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### Abstract

**Aim:** The aim of this article is to review the current literature on the therapeutic uses and efficacy of *Triphala*. Herbal remedies are among the most ancient medicines used in traditional systems of healthcare such as Ayurveda. *Triphala*, a well-recognized and highly efficacious polyherbal Ayurvedic medicine consisting of fruits of the plant species *Emblica officinalis* (*Amalaki*), *Terminalia bellerica* (*Bibhitaki*), and *Terminalia chebula* (*Haritaki*), is a cornerstone of gastrointestinal and rejuvenative treatment.

**Methods:** A search of the PubMed database was conducted.

**Results:** In addition, numerous additional therapeutic uses described both in the Ayurvedic medical literature and anecdotally are being validated scientifically. In addition to laxative action, *Triphala* research has found the formula to be potentially effective for several clinical uses such as appetite stimulation, reduction of hyperacidity, antioxidant, anti-inflammatory, immunomodulating, antibacterial, antimutagenic, adaptogenic, hypoglycemic, antineoplastic, chemoprotective, and radioprotective effects, and prevention of dental caries. Polyphenols in *Triphala* modulate the human gut microbiome and thereby promote the growth of beneficial *Bifidobacteria* and *Lactobacillus* while inhibiting the growth of undesirable gut microbes. The bioactivity of *Triphala* is elicited by gut microbiota to generate a variety of anti-inflammatory compounds.

**Conclusions:** This review summarizes recent data on pharmacological properties and clinical effects of *Triphala* while highlighting areas in need of additional investigation and clinical development.

**Keywords:** Ayurveda, anti-inflammatory, immunomodulating, microbiota, antioxidant, antimicrobial

### Introduction

HERBAL REMEDIES REPRESENT some of the most ancient medicines in healthcare and are historically considered among the most powerful means of maintaining human health and homeostasis. Ayurveda, a Sanskrit word meaning the knowledge of life or the science of perfect health, is the traditional system of personalized medicine from India, which emphasizes disease prevention and health promotion. *Triphala* (Sanskrit; tri=three and phala=fruits) is a well-recognized and revered polyherbal medicine consisting of dried fruits of the three plant species *Emblica officinalis* (Family Euphorbiaceae), *Terminalia bellerica* (Family Combretaceae), and *Terminalia chebula* (Family Combretaceae) that are native to the Indian subcontinent. It is classified as a

*tridoshic rasayana* in Ayurvedic medicine as it promotes longevity and rejuvenation in patients of all constitutions and ages.

The formula consists of the fruits *Amalaki* or the Indian Gooseberry, *Bibhitaki*, and *Haritaki* of the three plants generally in equal proportions and has been used in traditional medicine in India for over 1000 years according to the writings of the great physician Charak in a foundational text of Ayurveda called the *Charaka Samhita* as well as in another key text called the *Sushruta Samhita*. According to Charak, taking the *Triphala Rasayana* (*Triphala* with honey and ghee) daily has the potential to make a person live for one hundred years devoid of old age and diseases.<sup>1</sup> The physician Sushrut indicated that the formula is useful for treating ulcers and wounds.<sup>2</sup>

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As both Ayurveda and Western medicine agree that health and disease begin in the gut,<sup>1,3</sup> *Triphala* represents an essential foundational formula as it promotes efficient digestion, absorption, elimination, and rejuvenation. Numerous references in well-respected Ayurvedic medical texts make clear that *Triphala* is revered as a multiuse therapeutic and perhaps even panacea historically.<sup>1,2</sup>

### Ayurvedic Classification

*Triphala* is classified as a tridoshic *rasayana*, meaning that the energetics are appropriate for *Vata*, *Pitta*, and *Kapha* or all types of patients. Charak describes *rasayanas* as having the qualities of supporting strength and immunity.<sup>1</sup> Given these qualities and the tonic energetics, *Triphala* can be considered for use in the very young, the infirmed, and the elderly. Other classical Ayurvedic classifications attributed to the formula are *shukrala*, digestive, mild laxative at normal doses, bowel tonic at low dose, purgative at high doses, carminative, expectorant, antispasmodic, and bronchodilator. In addition, myriad other uses are described both in the Ayurvedic medical literature and anecdotally.

### Ayurvedic Pharmacology

*Dravya guna* or Ayurvedic pharmacology describes the attributes of herbs. The *rasa* or taste of *Triphala* is sweet, sour, pungent, bitter, and astringent; the only taste not contained within the formula is salty. The *virya*, or potency and action, is neutral, and the *vipaka*, or postdigestive effect of the formula, is sweet. *Triphala* has a *prabhava*, meaning special action or trophism, for all doshas (energetics and mind-body types) and thus is balancing for all *doshas* and constitutions. The *gunas*, or qualities, of *Amalaki* are heavy and dry, and both *Haritaki* and *Bhibitaki* are considered light and dry.<sup>4</sup>

### Therapeutic Uses and Studies

Ayurvedic medicine uses *Triphala* as a pillar of gastrointestinal treatment; however, the complexity of the three *rasayanas*, or rejuvenative herbs, in the formulation allows for many applications. Moreover, studies have validated a number of potential uses of *Triphala*, which include free radical scavenging, antioxidant, anti-inflammatory, immunomodulating, appetite stimulation, gastric hyperacidity reduction, dental caries prevention, antipyretic, analgesic, antibacterial, antimutagenic, wound healing, anticariogenic, antistress, adaptogenic, hypoglycemic, anticancer, hepatoprotective, chemoprotective, radioprotective, and chemopreventive effects.<sup>4</sup> *Triphala* may also promote proper digestion and absorption of food, reduce serum cholesterol levels, improve circulation, relax bile ducts, prevent immunosenescence, maintain homeostasis of the endocrine system, and increase production of red blood cells and hemoglobin.<sup>4</sup>

The major constituents of the formula are the tannins, gallic acid, ellagic acid, and chebulinic acid, which are potent antioxidants that may account, at least in part, for the observed immunomodulatory activity of the formula.<sup>5-7</sup> *Triphala* also contains other bioactive compounds such as flavonoids (e.g., quercetin and luteolin), saponins, anthraquinones, amino acids, fatty acids, and various carbohydrates.<sup>6</sup> In addition, *Triphala*-derived polyphenols such as chebulinic acid are also transformed by the human gut microbiota into bioactive metabolites, which have demonstrated potential *in vitro* to prevent oxidative damage.<sup>8</sup>

### *Triphala* in gastrointestinal health

*Triphala* is perhaps most well known for its use in general gastrointestinal health. Animal studies have shown that both aqueous and alcohol-based extracts of *Triphala* prevent diarrhea.<sup>9</sup> *Triphala* also induces enteroprotective effects, which are likely due, at least in part, to the high antioxidant content. In a rodent model, *Triphala* replenished depleted protein in the intestinal villi of the brush border as well as glutathione and phospholipid levels; the formula simultaneously decreased myeloperoxidase and xanthine oxidase levels in intestinal epithelium.<sup>10</sup> In rats, *Triphala* exerted a gastroprotective effect on stress-induced ulcer.<sup>11</sup> One human clinical trial that investigated the use of *Triphala* in patients with gastrointestinal disorders reported that treatment reduced constipation, mucous, abdominal pain, hyperacidity, and flatulence while improving the frequency, yield, and consistency of stool.<sup>12</sup> *Triphala* also reduced colitis in a mouse model, and the treatment effect was attributed to antioxidant effects and high levels of flavonoids contained in *Triphala*.<sup>13</sup>

### Stress-reducing potential of *Triphala*

Stress-induced disorders such as anxiety represent the leading causes of adult disability worldwide.<sup>14</sup> Stress is a state of disharmony caused by perceived threat that is counteracted by an adaptive response to reestablish homeostasis and is associated with many chronic diseases. Animal studies have shown that *Triphala* protected against cold-induced stress and reversed stress-induced behavioral alterations and biochemical changes such as increased lipid peroxidation and corticosterone levels.<sup>15</sup> *Triphala* also prevented noise-induced stress.<sup>16</sup> In rats, *Triphala* prevented the noise-induced metabolic changes by mediating the antioxidant and cell-mediated immune response, and it was hypothesized that the biological mechanism is related to its antioxidant properties.<sup>6,16-19</sup> Modern humans experience high levels of stress, thus adaptogenic treatments are needed more extensively in clinical practice.

### Antiobesogenic and antidiabetic potential of *Triphala*

Deregulation of eating behavior is common in industrialized countries. Studies have demonstrated the potential of *Triphala* as a therapeutic agent for weight loss and reduction of body fat. In an animal study, *Triphala* was administered for 10 weeks to diet-induced obese mice.<sup>20</sup> *Triphala* treatment decreased the percentage of body fat, body weight, and energy intake. *Triphala* also decreased total cholesterol, triglycerides, and low-density lipoprotein cholesterol in the experimental group compared with the control group. In a 12-week, double-blind, randomized placebo-controlled trial, human subjects treated with *Triphala* lost ~5 kg compared with the placebo control group.<sup>21</sup> Mean fasting blood sugar and fasting serum insulin levels were also reduced in the treated compared with control subjects. Given the global obesity epidemic, more treatment options are necessary to reduce the associated healthcare burden.

*Triphala* exerts hypoglycemic effects. Patients with type 2 diabetes are likely to have high postprandial blood glucose levels, especially after consuming carbohydrates. Elevated blood glucose results from the breakdown of carbohydrates by the digestive enzymes, *alpha*-amylase and *alpha*-glucosidase,

and the reduced ability of cells to take in glucose from the blood. Past studies report that *Triphala* may exert actions similar to diabetic pharmaceutical drugs by inhibiting digestive enzymes and may decrease absorption of glucose through inhibition of glycolytic enzymes, thereby reducing blood glucose levels. One study demonstrated the inhibitory potential of *Triphala* on pancreatic glycolytic enzymes, namely *alpha*-amylase and *alpha*-glucosidase, which break down larger polysaccharides into glucose molecules that enter the blood stream.<sup>20</sup>

The role that *Triphala* plays in inhibiting starch digestion and absorption, thereby decreasing postprandial hyperglycemia, is similar to that of diabetes pharmaceutical drugs, such as miglitol and acarbose, which also target these glycolytic enzymes. In addition, *Triphala* decreased serum glucose levels in normal and alloxan-induced diabetic rats.<sup>22</sup> A clinical study of noninsulin-dependent diabetes mellitus patients revealed that supplementation with 5 g of *Triphala* powder for 45 days significantly lowered blood glucose levels.<sup>23</sup> Both fasting and postprandial blood glucose were reduced, which may be due to active ingredients such as sorbitol. Constituents in *Triphala*, including ellagitannins and gallotannins, also enhance both PPAR- $\alpha$  and - $\gamma$  signaling, which increase insulin responsiveness and glucose uptake without inducing adipogenesis.<sup>24</sup> These polyphenols may also promote decreased blood glucose and insulin levels in diabetic patients.

*Triphala* may also protect diabetics and those predisposed to diabetes through inhibition of glycation enzymes. Elevated blood glucose can cause severe damage through the process of glycation, in which sugar molecules compromise protein molecules in the body, which may in turn lead to nerve damage or blindness. Due to the presence of tannins, *Triphala* extract was found to effectively inhibit protein glycation *in vitro*.<sup>25</sup> *Triphala* may also prevent glycation through promotion of lower blood glucose levels. As diabetes is the most prevalent endocrine disease globally, increased access to complementary hypoglycemic therapies for integrative care is needed.

#### *Triphala and cardiovascular health*

Cardiovascular disease is a leading cause of mortality and morbidity worldwide, and hypercholesterolemia is an important risk factor. Animal studies have reported the hypercholesteremic effects of *Triphala*. In one study, *Triphala* reduced the total cholesterol, low-density lipoprotein, very low-density lipoprotein, and free fatty acid levels in rats fed an atherogenic diet for 48 days.<sup>26</sup> Another study in rats fed an atherogenic diet revealed that *Haritaki*, one of the herbs in *Triphala*, induced hypolipidemic effects in the herb-treated group. A reduction in total cholesterol, triglycerides, and total protein and elevation of high-density lipoprotein cholesterol were found in the herb-treated group compared with control group.<sup>27</sup> *Triphala* is a powerful herb to address imbalances in the gastrointestinal tract and cardiovascular system and should be more widely studied in the context of these common diseases.

#### *Antimicrobial potential of Triphala*

Overadministration of antibiotics has led to widespread drug resistance, thus it is becoming imperative that clinical researchers discover alternative and adjunctive antimicrobial

agents with high efficacy. Both *Triphala* water decoctions (12%) and ethanol extracts (14%) have demonstrated antibacterial activity *in vitro* against bacterial isolates derived from patients infected with human immunodeficiency virus<sup>28</sup>; the ethanol extracts were reported to have greater *in vitro* antimicrobial action against these species compared with the aqueous extracts, which may indicate lower solubility of the aromatic antibiotic compounds.

In addition, other studies report that these extracts also exert broad-spectrum antimicrobial action against antibiotic-resistant bacteria isolated from human subjects. The aqueous extracts (1:6) have demonstrated greater efficacy compared with the ethanol extracts (1:6) on pathogenic bacteria such as *Escherichia coli* and *Staphylococcus aureus*.<sup>29</sup> *In vitro*, ethanol extracts of *Triphala* (100 mg/mL) components exhibited specific antimicrobial activity against multidrug-resistant clinical bacterial isolates.<sup>30</sup> Thus, *Triphala* was reported to exert antibacterial effects on both gram-positive and gram-negative species *in vitro* and demonstrated potential for further investigation as a complementary or adjunct antimicrobial therapy.

In addition to antimicrobial effects against oral bacteria, *Triphala* has also demonstrated the potential to eradicate enteric pathogens *in vitro*. One study tested the effects of *Triphala* aqueous extract (200 mg/mL) against enteric bacterial pathogens *in vitro* and found that *Triphala* possesses strong antibacterial effects against *Staphylococcus epidermidis* and *S. aureus* and moderate effects against *Proteus vulgaris*, *Pseudomonas aeruginosa*, and *Salmonella typhi*.<sup>30</sup> In addition to antibacterial effects, *Triphala* is also known to exhibit antifungal properties. *Triphala* exerts antifungal action against *Aspergillus* species and has been reported to inhibit the fungus by up to 37.96% *in vitro*. In particular, the aqueous extracts (1:1) of fresh fruits were found to be more effective than dry fruits.<sup>31</sup> Thus, the formula represents a promising antimicrobial candidate in need of further study.

*The Potential of Triphala in Oral Care:* *Triphala* has been used traditionally in Ayurvedic medicine as an antimicrobial agent.<sup>32</sup> Numerous controlled clinical trials have shown that *Triphala* significantly reduces the abundance of oral bacteria, dental plaque, and gingivitis in human subjects.<sup>33–38</sup> For example, *Triphala* is effective against *Enterococcus faecalis*, one of the most difficult to eliminate oral pathogens that are commonly isolated in chronic periodontitis. One study revealed that *Triphala* (5 mg/mL) in 10% dimethyl sulfoxide (DMSO) was equally or more effective at eliminating *E. faecalis in vitro* compared with NaOCl, a common irrigant used during root canals.<sup>39</sup> *Triphala* was more effective than 0.5% and 1% NaOCl solution, but equally effective as 2.5% and 5% solutions.

In addition, another group reported that *Triphala* in 10% DMSO was more effective than 5.25% NaOCl solution against *E. faecalis* biofilms on *ex vivo* tooth substrate and suggested the extract as an alternative in the context of clinical root canal irrigation.<sup>40,41</sup> A study using human primary teeth *ex vivo* revealed that *Triphala* suspended in 10% DMSO (1:3) exhibited significant antibacterial activity compared with control as well as higher antibacterial activity compared with 3% NaOCl.<sup>42</sup> *In vitro* studies using *Triphala* ethanol extract have reported similar antimicrobial effects against *E. faecalis* compared with 2.5% NaOCl.<sup>43</sup> Thus, *Triphala* may represent a potential therapy to eliminate

*E. faecalis* as more side-effects and larger risk are associated with NaOCl solution treatment.

Dental caries, or cavities of the teeth, is a common infection associated with humans. Examining the use of *Triphala* as an oral antimicrobial agent, one study reported that *Triphala* dissolved in 10% DMSO exhibited a significant antibacterial effect *ex vivo* on extracted human mandibular premolars against *Streptococcus mutans*, which is one of the most prevalent oral pathogens responsible for dental cavities.<sup>44</sup>

Human clinical trials using *Triphala* water decoction as a mouthwash report that it exerts comparable efficacy compared with chlorhexidine gluconate germicidal mouthwash in the prevention of dental caries.<sup>45,46</sup> For example, a study in human subjects revealed that *Triphala* (6%) mouthwash promoted a significant reduction in oral streptococcus colonies. Oral streptococcus levels were measured after using a 6% *Triphala* mouthwash or 0.2% chlorhexidine mouthwash twice per day for 48 h and for 7 days; Streptococcus levels were reduced by 17% and 44%, respectively, in the *Triphala*-treated group.<sup>33</sup> The researchers concluded that *Triphala* was as effective as 0.2% chlorhexidine mouthwash given that the results of the *Triphala* treatment were similar to the chlorhexidine-treated group. Another double-blind human clinical trial also reported significant reductions in oral streptococcus levels at 5 and 60 min after rinsing with 15 mL aqueous *Triphala* extract (10%) mouthwash.<sup>47</sup>

In addition, a double-blind, randomized human clinical trial reported that *Triphala* (10%) mouthwash is effective against dental plaque and gingivitis in teenagers.<sup>48</sup> The study reported *Triphala* as equally effective in antiplaque and antigingivitis activity compared with chlorhexidine. Moreover, a clinical study in children on the effects of *Triphala* (0.6%) mouthwash on dental plaque, gingival inflammation, and microbial growth also compared its efficacy with a commercially available chlorhexidine mouthwash. The results indicated that both the germicidal chlorhexidine (0.1%) and *Triphala* mouthwash were equally effective in reducing plaque and increasing gingival health after 9 months; however, *Triphala* was more effective than chlorhexidine in reducing microbial cell counts.<sup>49</sup> A double-blind, randomized clinical trial in young adults also compared the efficacy of *Triphala* (0.6%) and chlorhexidine (0.12%) mouthwash for 21 days and reported a similar reduction in both plaque and gingival scores for both the *Triphala*- and chlorhexidine-treated groups.<sup>50</sup> *Triphala* mouthwash treatment has also shown promise to reverse precancerous oral lesions associated with tobacco use in young adults.<sup>51</sup>

In periodontal diseases, matrix metalloproteinases (MMPs) degrade extracellular matrix proteins in a spectrum of processes that include tissue remodeling such as the connective tissue destruction observed in periodontitis. *Ex vivo Triphala* studies using extracted gingival tissue have demonstrated a greater reduction of MMP-9 activity in patient-derived white blood cells treated with *Triphala* compared with patient-derived cells treated with the standard antibiotic drug.<sup>52</sup> In treated tissue extracts, *Triphala* (1.5 mg/mL) reduced MMP-9 activity by 77%, while doxycycline (300 µg/mL) reduced MMP-9 activity by 59%. Thus, MMP inhibitors are important adjunctive therapies in periodontitis treatment and *Triphala* may represent a candidate to investigate in greater detail in this context. In addition, given the observed effectiveness of *Triphala* mouthwash compared with standard treatment, ad-

ditional clinical trials should be performed to identify the potential for integration in dentistry.

#### Radioprotective effects of *Triphala*

Studies have concluded that *Triphala* may help prevent and reverse DNA damage and mutagenesis.<sup>53</sup> The prevention of DNA damage is important given that it is often an initiating event in carcinogenesis. Research in animal models and *in vitro* has shown that *Triphala* is effective in prevention of mutagenesis induced by both chemical- and radiation-induced damage.<sup>54-56</sup> An *in vitro* study found that *Triphala* eliminated reactive oxygen species in HeLa cells exposed to ionizing X-radiation or bleomycin, both of which generate DNA strand breaks through the generation of reactive oxygen species.<sup>57</sup> In addition, gamma-radiation-induced plasmid DNA strand break was inhibited by *Triphala in vitro*. The *rasayana* formulation also inhibited radiation-induced lipid peroxidation in rat liver microsomes and demonstrated the ability to scavenge free radicals such as superoxide. Importantly, the high levels of phenolic compounds such as gallic acid were attributed to the free radical scavenging activity.<sup>56</sup>

In animal models, *Triphala* intervention reduced radiation-induced mortality by 60% in mice fed *Triphala* for only 7 days before whole-body gamma-irradiation.<sup>54</sup> *Triphala* reversed the increased xanthine oxidoreductase and decreased the superoxide dismutase activity that was observed post-irradiation. Treatment with *Triphala* also prevented DNA damage in murine white blood cells and spleen cells post-irradiation. *Triphala* may play a protective role against oxidation, even when administered after exposure.

In addition, other animal studies have reported significantly reduced acute intestinal damage after ionizing radiation exposure in groups fed *Triphala* (1 kg/g) for at least 5 days before radiation treatment.<sup>58</sup> Moreover, studies have demonstrated that *Triphala* feeding before gamma-radiation exposure reduced radiation sickness and mortality in mice.<sup>59</sup> *Triphala* was reported to scavenge hydroxyl, superoxide anion, and nitric oxide free radicals in a dose-dependent manner *in vitro*.<sup>59</sup> *Triphala* aqueous extract feeding for 5 days before exposure was also reported as protective against gamma-radiation in mice at a dose of 10 mg/kg, which was 1/28 of the calculated LD50 dose.<sup>60</sup> Thus, the antioxidant and free radical scavenging activities of *Triphala* were concluded to serve a role in its protective effect against ionizing radiation. Human clinical trials to further elucidate the mechanisms of radioprotective action and clinical utility are required.

#### Antineoplastic activity of *Triphala*

*Triphala* has been investigated as a potential antineoplastic agent.<sup>61</sup> Numerous studies have been performed in this context and have shown that *Triphala* exerts an antineoplastic effect on many cancer cell lines, including those of the breast, prostate, colon, and pancreas.<sup>62-64</sup> Data in cell lines show that *Triphala* has a differential modulatory effect on normal and cancer cell lines. *Triphala* induces cytotoxicity in cancer cells, which showed increases in intracellular reactive oxygen species, but not normal cells. Excised tumor tissue from *Triphala*-fed mice compared with controls suggested that apoptosis induction may have mediated reduced tumor growth.<sup>65</sup>

Preclinical studies using *in vitro* and *in vivo* models report that *Triphala* inhibits cancer growth in both cell and *in vivo*

models and the effects are mediated through the ERK and p53 pathways.<sup>63</sup> In addition, methanol extract of *Triphala* suppressed proliferation and induced p53-independent apoptosis in human colon cancer stem cells.<sup>64</sup> *Triphala* suppressed the expression of oncogenes, c-Myc and Cyclin D1, and thus Wnt pathway signaling to reduce proliferation and resistance to apoptosis. *Triphala*-induced apoptotic induction occurred through the intrinsic mitochondrial apoptotic signaling pathway. Moreover, one clinical trial reported that *Triphala* powder treatment in healthy humans increased cytotoxic T cells and NK cells in the experimental group compared with the control group.<sup>66</sup> Thus, *Triphala* shows potential as an antineoplastic agent and thus should be systematically explored for potential as an adjunct therapy in the management of colon and other cancers.

#### Antioxidant activity of *Triphala* and eye health

Antioxidant effects of *Triphala* have the potential to help maintain eye health. *Triphala* is a rich source of vitamin C and flavonoids. One study used *Triphala* as a pretreatment in selenite-induced cataracts in mice. *Triphala* significantly restored glutathione levels in eye lenses. *Triphala* also increased the activities of antioxidant enzymes, such as superoxide dismutase, catalase, glutathione-S-transferase, and glutathione peroxidase, in the lenses of the experimental group when compared with the control group. While 100% of the mice in the control group developed cataracts, only 20% of the mice pretreated with *Triphala* developed cataracts. This effect may be linked to the antioxidant activity of *Triphala*.<sup>67</sup>

#### Anti-inflammatory effects of *Triphala*

Chronic inflammation is deleterious and affects most major chronic health conditions. *Triphala* has shown promise as an anti-inflammatory agent. In one study, *Triphala* performed better or equivalent when compared with standard drug treatment for a variety of biochemical measurements of inflammation.<sup>19</sup> In addition, *Triphala* significantly reduced inflammatory markers as well as bone and cartilage degradation in arthritic rats.<sup>68</sup> In this study, *Triphala* extract was significantly more effective than the nonsteroidal anti-inflammatory drug, indomethacin, in ameliorating arthritic and inflammatory effects. *Triphala* reduced expression of inflammatory mediators such as IL-17, COX-2, and RANKL through inhibition of NF- $\kappa$ B activation. Another study found that *Triphala* increased antioxidant levels and decreased lipid peroxidation in the tissues of arthritic rats.<sup>69</sup>

In lipopolysaccharide-stimulated macrophages, *Triphala* treatment suppressed production of inflammatory mediators (such as TNF $\alpha$ , IL-1 $\beta$ , IL-6, MCP-1, VEGF, NO, and PGE2), intracellular free radicals, inflammatory enzymes (such as iNOS and COX-2), and lysosomal enzyme release.<sup>70</sup> Chebulagic acid, a constituent in *Triphala*, was found to inhibit COX and 5-LOX, which are both major enzymes involved in inflammation and carcinogenesis.<sup>71</sup> *Triphala* also increased antioxidant activity in mice after induction of nephrotoxicity from bromobenzene. *Triphala* ameliorated nephrotoxic effects by upregulating antioxidant enzymes, superoxide dismutase, glutathione-S-transferase, and glutathione peroxidase. Lipid peroxidation and markers of kidney dysfunction were reduced in the

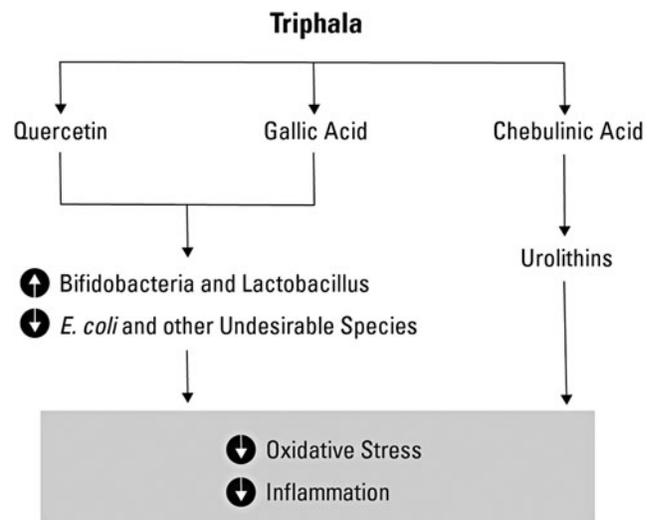
*Triphala*-treated group compared with controls.<sup>72</sup> The anti-inflammatory effects of *Triphala* should be investigated in greater detail.

#### Antiaging effects of *Triphala*

*Triphala* extract exerted highly protective antiaging effects on human skin cells *in vitro*. *Triphala* extract affects gene expression of human skin cells, stimulating collagen-1 and elastin-synthesizing genes and antioxidant genes responsible for the cellular antioxidant, SOD-2. *Triphala* extract was found to inhibit melanin production and hyperpigmentation due to the presence of protective phytochemicals. Furthermore, *Triphala* extract exhibited significant free radical scavenging activity on hydrogen peroxide-induced cell damage and senescence.<sup>73</sup> These results demonstrate potential dermal antiaging effects of *Triphala*, such as increasing collagen and elastin, increasing cellular antioxidants, and decreasing hyperpigmentation.

#### Variable efficacy of herbal therapies

A number of factors, including variability in herbal source, processing, bioavailability, digestion, and absorption of herbal components, cause the true efficacy of herbs on human health to be highly variable. This variability is known to be at least partially due to inherent variation in the gut microbiota that act on the ingested components of herbal remedies and transform them into compounds with increased bioabsorption and bioactivity. These features have confounded the true efficacy of herbal remedies as it pertains to the maintenance of human health and/or the ability to reverse chronic disease states.



**FIG. 1.** The bioactivity of *Triphala* is elicited by gut microbiota. The phytochemicals in *Triphala* promote the growth of beneficial gut microbes such as *Bifidobacteria* and *Lactobacillus* species while inhibiting the growth of less desirable and potentially more inflammatory gut residents such as *Escherichia coli*. The enzymatic activity of lactic acid bacteria degrades tannins in *Triphala* such as gallic acid. *Triphala*-derived polyphenols such as chebulinic acid are also transformed by the human gut microbiota into metabolites such as urolithins, which have the potential to prevent oxidative damage and inflammation. Illustration by Victor Hewitt; used with permission.

The increased popularity of herbal remedies such as *Triphala* has led to dramatic improvements in the processing of crude plant materials that serve to maximize the absorption of otherwise poorly absorbed plant components. Despite these improvements, these preparations still display pronounced variability in efficacy, which is likely related to the natural variation in composition of gut microbiota species that catalyze the biotransformation of herbal components. This response variability is not unique to herbs and, in fact, may be the case for virtually all health-promoting compounds ingested by humans (e.g., polyphenolic compounds derived from plants).

#### Triphala and the gut microbiome

It is known that phytochemicals in *Triphala* such as quercetin and gallic acid promote the growth of *Bifidobacteria* and *Lactobacillus* species while inhibiting the growth of undesirable gut residents such as *E. coli*.<sup>17,74–76</sup> In addition, the lactic acid bacteria possess enzymatic activity (e.g., tannase) to degrade plant tannins such as gallic acid contained in *Triphala*.<sup>77–79</sup> For example, *Triphala*-derived polyphenols such as chebulinic acid are transformed by the human gut microbiota into metabolites such as urolithins (Fig. 1), which have the potential to prevent oxidative damage.<sup>8</sup> The authors speculate that the bioactivity of *Triphala* is elicited by the gut microbiome to generate a widened spectrum and abundance of anti-inflammatory compounds.

*Triphala*-induced benefits in both the elderly and persons of all ages may be enhanced by coadministration of specific probiotic species. Thus, probiotic formulations consisting of bacterial species capable of mediating the increased digestion, bioabsorption, and bioactivity of *Triphala* may increase and make more uniform the response and impact of *Triphala* treatment on human populations. Further studies are required to determine the full effect of *Triphala* on gut microbiota and the potential of specific probiotics to increase the efficacy of the herb.

#### Conclusions

*Triphala* is a powerful polyherbal formula with myriad efficacious therapeutic uses for maintaining homeostasis as well as the prevention and treatment of disease. Many scientific studies have reported evidence-based validation of various traditional uses of *Triphala*. It provides therapeutic value for multiple pathologies. Additional government funding allocations and support are needed for further and ongoing studies to validate its therapeutic uses in human clinical trials and to define the biological mechanisms relevant to this plant-based medicine. More widespread education of the general public and medical providers on clinical Ayurvedic medicine and complementary therapies such as *Triphala* is warranted to increase awareness of these treatments for both clinical and healthy populations.

#### Author Disclosure Statement

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