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File: ■ Triphala (*Phyllanthus emblica*; *Terminalia chebula*; *Terminalia bellerica*) ■ Cancer Prevention and Treatment

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RE: Triphala in the Prevention and Treatment of Cancer - Review of the Evidence

Baliga MS. *Triphala*, Ayurvedic formulation for treating and preventing cancer: a review. *J Altern Complement Med*. 2010;16(12):1301-1308. doi:10.1089/acm.2009.0633.

Made from three fruits (amla [*Phyllanthus emblica*], chebulic myrobalan [*Terminalia chebula*], and belleric myrobalan [*Terminalia bellerica*]), *Triphala* is one of the most common Ayurvedic preparations. It is formulated in two variations: one uses equal portions of all three fruits; the other, one part chebulic myrobalan, two parts belleric myrobalan, and four parts amla. In Ayurveda, *Triphala* is a *tridoshic rasayan*, balancing and strengthening the three elements of human life: *vata*, *pitta*, and *kapha*. (See an explanation of these concepts from the Ayurvedic Foundation at: http://www.ayur.com/dosha/tridosha.html.) In practice, *Triphala* is used for gastric and digestive issues, cardiovascular problems, vision disorders, liver problems, and inflammation. It has been reported effective for anemia, jaundice, asthma, fever, chronic ulcers, leucorrhea, and pyorrhea. *Triphala* exhibits antibacterial, antimalarial, antifungal, antiallergic, and antiviral effects. *Triphala* is a cardiotonic and reduces myocardial necrosis and serum cholesterol. It is hepatoprotective, and has also been reported to have antiaging effects and to improve mental function. It further potentiates adrenergic function, important in stress recovery.

Studies performed since 2000 suggest that *Triphala* may be antioxidant, antimutagenic, antineoplastic, chemoprotective, radioprotective, and chemopreventive, with a possible role in cancer prevention and treatment. This article summarizes the recent findings.

In vitro studies found dose- and time-dependent cytotoxic effects of *Triphala* extracts and constituents on a variety of cultured cancer cell lines, while equal concentrations did not harm cultured normal cells. In several cancer cell lines, *Triphala* and its ingredients inhibited DNA synthesis, decreasing replication and proliferation. An extract of chebulic myrobalan was most effective, followed by *Triphala*, then amla, then belleric myrobalan.

Triphala treatment of two human breast cancer cell lines caused reproductive cell death. One line (MCF-7) was more sensitive to *Triphala* than the other (T47D). Apoptosis was induced in various cancer cell lines, again with no effect on healthy cells. MCF-7, a p53+/+ cell line, was more sensitive to apoptosis than T47D, a p53-/- cell line. Treatment

of MCF-7 cells with pifithrin *α*, an inhibitor of p53, reversed *Triphala*'s effects and, with similar observations in other cell lines, confirms the role of p53 in *Triphala*-induced apoptosis. Similarly, while *Triphala* increased intracellular reactive oxygen species (ROS) in some cancer cells compared with normal cells, pretreatment with antioxidants inhibited this effect. In some cell lines, *Triphala*-induced apoptosis was linked to phosphorylation of p53 at Ser-15 and ERK at Thr-202/Tyr-204. This effect was reversed with pretreatment of an antioxidant, N-acetylcysteine (NAC).

In cancer-bearing research animals, feeding *Triphala* significantly increased apoptosis, leading to tumor regression and decreased tumor volume. Animals fed *Triphala* showed no impaired movement or discomfort, suggesting absence of systemic or cognitive toxicity. *Triphala*'s chemoprotective potential is seen in coadministration with methotrexate, an antifolate often used as an anticancer and immunosuppressive drug. While very useful, methotrexate is an enterotoxin. Both *Triphala* formulas significantly restored intestinal brush border membranes in methotrexate-damaged rats. The 1:2:4 formula was more effective, with significant decreases in permeation clearance of phenol red, attenuation of histopathological changes, level of disaccharides in brush border membrane vesicles, and lipid peroxidation of intestinal mucosa over the equal parts formula. *Triphala* protected against ionizing radiation with peritoneal or oral dosing in animal studies. It was ineffective when administered after radiation. In two studies, mortality was delayed and reduced, and symptoms of radiation sickness decreased; in one, radiation tolerance increased by 1.4 Gy, giving rise to a dose reduction factor of 1.15. In the other, radiation-induced mortality decreased 60% in mice given 1g/kg body weight, with less oxidative stress, less DNA damage, and increased antioxidant defenses.

Triphala may also have chemopreventive effects. In preclinical studies, feeding *Triphala* reduced induced forestomach papillomagenesis in mice in a time- and dose-dependent manner. Feeding *Triphala* before, after, and during carcinogen exposure reduced tumor incidence by 77.77%. Longer term feeding brought further decreases. A 2.5% *Triphala* diet was more effective than the same percentage of any of the three fruits alone, suggesting a synergistic or additive effect.

Several mechanisms may contribute to *Triphala*'s anticancer effects, including free radical scavenging, increased antioxidant enzyme production, reduced cellular damage, inhibition of lipid peroxidation, and anti-inflammatory, antimutagenic, anticlastogenic, and immunomodulatory effects. All have been seen in preclinical studies. Most studies of *Triphala* and its ingredients have been in vivo. More animal, in vitro, and eventually human studies are needed to clarify its mode or modes of action and the contribution of each ingredient and its compounds to *Triphala*'s effects. In view of the considerable variation in the chemical composition of *Triphala*, the author recommends rigorous quality control regarding authenticity and quantification of active phytochemicals in the combination. *Triphala*'s apparent safety also argues for more study.

—Mariann Garner-Wizard

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