

Curcumin Reviewed as a Nontoxic Potential Adjuvant in Resistant Head and Neck Cancers

By: HerbClip, American Botanical Council

Wilken R, Veena MS, Wang MB, Srivatsan ES. Curcumin: a review of anti-cancer properties and therapeutic activity in head and neck squamous cell carcinoma. *Mol Cancer*. February 7, 2011;10:12. doi:10.1186/1476-4598-10-12.

Turmeric (*Curcuma longa*) root is traditionally used for digestive ills and for inflammation and arthritis treatment in Ayurvedic medicine.¹ The most investigated compound isolated from turmeric root, curcumin, has been previously shown to have anticancer activity.¹⁻³ This review details the state of the anticancer research surrounding curcumin and addresses what is known about its molecular mechanisms of action. The authors specifically focus the review around head and neck squamous cell carcinoma (HNSCC), the sixth most common cancer worldwide, and discuss curcumin's suitability as an adjuvant to current chemotherapy used to treat this form of cancer.

The authors provide a broad outline of the basic chemistry of curcumin. As a polyphenol, its structure accounts for its antioxidant activity; particularly, curcumin prevents lipid peroxidation and scavenges a multitude of macrophage-generated reactive oxygen species. Previous studies also report that, in general, curcumin downregulates the macrophages' response to oxidative stress. In terms of anti-inflammatory activity, work has shown that curcumin suppresses the activation of transcription factor nuclear factor-kappa B (NF-κB), which activates many inflammation-related genes such as cyclooxygenase-2, inducible nitric oxide synthase, and interleukin(IL)-1 and IL-8. The authors' own work, as well as that of other researchers, shows an increase in NF-κB expression in HNSCC and other cancers.

The authors mention that previous studies link the lower number of colon cancer patients in India with a curcumin-rich diet. They include a multitude of details about the many mechanisms of the anticancer activity of curcumin. For example, in addition to suppressing the activation of NF-κB, curcumin also limits the expression of another major transcription factor associated with cancer via inflammation and other pathways, activator protein 1 (AP-1). The authors continue with a brief but concise explanation of the cell cycle and its regulation in order to illustrate how curcumin suppresses the expression of cyclin D1 which is known to alter the cell cycle in many types of cancers. In addition, the authors describe curcumin's ability to induce apoptosis in tumor cells through the cell cycle and other apoptosis pathways.

The process of a cell's digestion of its components, known as autophagy, is also well explained; the current state of research suggests that autophagy is employed by cancer cells and that the disruption of autophagy in normal cells leads to cancer. The authors describe the mechanisms by which curcumin induces autophagy in various cancer cells and mention possible future research for the role curcumin may play in autophagy in general.

The authors also describe how angiogenesis, the growth of new blood vessels central to tumor development, is an ongoing target for cancer therapies. Curcumin suppresses angiogenesis signaling molecules like vascular endothelial growth factor in tumor models

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and cells through various metabolic pathways, and has been shown to inhibit metastatic processes and proteins in breast cancer cells in vitro.

Lastly, the authors finish the review discussing curcumin's anticancer effects specifically in HNSCC. For example, the authors mention the effectiveness of curcumin against HNSCC cell lines in vitro, in particular through the inhibition of NF- κ B, and continue to thoroughly describe the molecular mechanisms behind this activity. They especially mention their own work and detail an example of how curcumin's anticancer activity is via a different pathway than the molecularly-targeted chemotherapy compound cetuximab, adding weight to the idea of utilizing curcumin as an adjuvant. Additionally, work from the authors' lab shows an increase of curcumin's bioactivity when paired with cisplatin, a platinum-based chemotherapy compound. Also, when used in conjunction with radiation, greater tumor suppression was observed than when either radiation or curcumin were used singly.

Although curcumin has shown anticancer activity in vivo, the authors mention the problems researchers have had with low oral bioavailability. Possible solutions include pairing curcumin with piperine to slow the compound's breakdown, as well as the use of liposomes, phospholipids, and nanoparticles as alternative delivery systems for intravenous therapy. The liposomal pairing has been especially successful, with tumor suppression measured in vivo without any toxic effects detected in serum and liver.

In this review, the authors make a convincing case on the necessity for alternative therapies and adjuvants for HNSCC treatment, as current chemotherapies, radiotherapy, and/or surgeries result in serious adverse side effects or permanent problems. In addition, the authors demonstrate how curcumin's bioactivity is broadly diverse in terms of molecular mechanisms, suggesting a strong future of therapeutic use. The authors' inclusion of tables and clear diagrams depicting various cell processes help the reader in understanding these mechanisms. This review is both current and thorough; it is especially recommended for those involved in cancer research or treatment and those interested in the broad spectrum of anticancer potential of this well-studied natural product.

—Amy C. Keller, PhD

References

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