

A REVIEW OF THERAPEUTIC EFFECTS OF CURCUMIN'S BASED ON ITS ANTI-INFLAMMATORY PROPERTIES AND ANTICANCER ACTIVITIES IN UTTARAKHAND

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ABSTRACT

Curcumin, a polyphenolic compound derived from turmeric (*Curcumin longa*), is one such agent that has been extensively studied over the last three to four decades for its potential anti-inflammatory and/or anti-cancer effects. Curcumin has been found to suppress initiation, progression, and metastasis of a variety of tumors. These anti-cancer effects are predominantly mediated through its negative regulation of various transcription factors, growth factors, inflammatory cytokines, protein kinases, and other oncogenic molecules. It Inhibit the proliferation of cancer cells by arresting them at different phases of the cell cycle and/or by inducing their apoptosis. The current review focuses on the brief overview of the anti-inflammatory and anticancer activities of curcumin to prevent and treat the disease.

Keywords: Curcumin, Inflammation, Cancer, Anticancer agent, *Curcumin longa*.

INTRODUCTION

Turmeric (the common name for *Curcuma longa*) is an Indian spice derived from the rhizomes of the plant and has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. *Curcuma longa* is a perennial member of the Zingiberaceae family and is cultivated in India and other parts of Southeast Asia. Curcumin is a polyphenol (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione). Ayurvedic medicine clearly designates curcumin as an effective medicine for various disorders such as asthma, bronchial hyperactivity, allergy, anorexia, coryza, cough, sinusitis, and hepatic disease (Ammon *et al.*, 1991). Extensive research on curcumin over decades with approximately 6850 publications has provided

greater insight into its medicinal and health benefits. There are many reports of its anti-infectious (Chan *et al.*,2005), anti-oxidant (Sreejayan *et al.*, 1997, anti-inflammatory (Brouet *et al.*,1995; Dikshit *et al.*,1995), hepato-protective (Kiso *et al.*,1983), cardio protective (Venkatesan *et al.*,1998), thrombosuppressive (Srivastava *et al.*,1985), anti-arthritic (Deodhar *et al.*,1980), chemo-preventive, and anti-carcinogenic (Chen *et al.*, 2006, Chen *et al.*, 2006, Divya *et al.*, 2006) properties. Multiple therapeutic activities have been attributed to curcumin mostly because of its anti-inflammatory and anti-oxidant effects.



Fig.1. Extraction of curcumin and its chemical structure showing the metal binding reactive -diketone moiety

Active constituents

The bright yellow color of turmeric comes mainly from fat-soluble, polyphenolic pigments known as curcuminoids. Curcumin, the principal curcuminoid found in turmeric, is generally considered its most active constituent. Other curcuminoids found in turmeric include demethoxycurcumin and bisdemethoxycurcumin. The other constituents present in turmeric are volatile oils including tumerone, atlantone, and zingiberone and sugars, proteins, and resins the curcuminoid complex is also known as Indian saffron. Curcumin is a lipophilic polyphenol that is nearly insoluble in water but is quite stable in the acidic pH of the stomach (Fig. 1).

Absorption of Curcumin

Curcumin has multiple pharmacologic effects, but its poor bioavailability reduces their therapeutic effect which appears to be primarily due to poor absorption, rapid metabolism, and rapid elimination. Curcumin with all these positive qualities has only remained a potential candidate for cancer treatment over the years without seeing any proper usage because of its hydrolytic instability involving the β -diketone moiety in a cellular medium and its poor bioavailability. Since it is unstable in aqueous medium and undergoes rapid hydrolytic degradation thereby it limits its usefulness as anticancer drug. There are several components that can increase bioavailability. For example, piperine is the major active component of black pepper and, when combined in a complex with curcumin, has been shown to increase bioavailability by 2000%.

Anti-inflammatory mechanisms

The desirable preventive or putative therapeutic properties of curcumin have also been considered to be associated with its antioxidant and anti-inflammatory properties. The anti-inflammatory effect of curcumin is most likely mediated through its ability to inhibit cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS). COX-2, LOX, and iNOS are important enzymes that mediate inflammatory processes. Improper up regulation of COX-2 and/or iNOS has been associated with the pathophysiology of certain types of human cancer as well as inflammatory disorders. Because inflammation is closely linked to tumor promotion, curcumin with its potent anti-inflammatory property is anticipated to exert chemo

preventive effects on carcinogenesis. Hence, the past few decades have witnessed intense research devoted to the antioxidant and anti-inflammatory properties of curcumin.

Curcumin's anti-inflammatory properties and carcinogenesis

It is well understood that pro-inflammatory states are linked to tumor promotion. The anti-inflammatory, anti-oxidative, apoptosis inducing and anti-angiogenic abilities of curcumin are the main characteristics which are involved in its anti-tumoral activity. Preclinical cancer research using curcumin has shown to inhibit carcinogenesis in a number of cancer types including melanoma, carcinoma, colon, liver, pancreatic, ovarian and breast cancers.

Based on its distinct chemical properties, curcumin interacts with numerous extracellular and intracellular molecules that are actively involved in cancer initiation and progression, thereby inhibiting cancer progression (Anand *et al.*, 2008; Aggarwal *et al.*, 2009; Aggarwal *et al.*, 2006; Gupta *et al.*, 2011). Increasing evidence suggests that deregulated inflammatory pathways play a pivotal role in a multitude of chronic diseases, including cancer (Sethi *et al.*, 2012). The mechanism by which chronic inflammation drives cancer initiation and progression is via increased production of pro-inflammatory mediators, such as cytokines, chemokines, reactive oxygen species (ROS), over expression of oncogenes, cyclooxygenase (COX-2), matrix metalloproteinase (MMPs), intracellular signaling pathway mediators, transcription factors such as nuclear factor κ B (NF- κ B), signal transducer and activator of transcription 3 (STAT3), protein kinase B (AKT), and activator protein 1 (AP1) that drive tumor cell proliferation, transformation, invasion, metastasis, angiogenesis, chemoresistance, and radioresistance (Dibb *et al.*, 2004, Manning *et al.*, 2007; Balkwill *et al.*, 2001; Hanahan *et al.*, 2000, 2011; Lemmon *et al.*, 2010; Siveen *et al.*, 2014).

CONCLUSION

The *in vitro* and *in vivo* researches together with clinical trials conducted over the past few decades substantiate the potential of curcumin as an anti-cancer agent. At the molecular level, curcumin targets numerous pathways, highlighting its ability to inhibit carcinogenesis at multiple levels. Clinical trials with curcumin indicate safety, tolerability, non-toxicity (even up to doses of 8000 mg/day),

and efficacy. However, curcumin activity is limited by its poor bioavailability and some possible adverse effects. Nonetheless, curcumin has established itself as a safe and promising molecule for the prevention and therapy of not only cancer but also other inflammation-driven diseases.

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