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Curcumin: A Multiple Edged Sword in the Prevention of Cancer

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Abstract

Cancer is a major public health problem and is accompanied by gradual accumulation of epigenetic and genetic alterations that disturbs cellular homeostasis. The current approach for the treatment of cancer is potentially based on the use of chemotherapeutic agents. Despite significant advances in the therapeutic modalities, these anti neoplastic drugs exert low therapeutic response, associated with side effects and are also expensive. Thus, there is urgent necessity of pharmacological agents which may attenuate anticancer agents associated disadvantages. Curcumin, a polyphenolic compound is one such natural remedy which is potentially qualified as a multiple edged sword due to its broad biological activity. Earlier studies have reported that curcumin acts as an anti-inflammatory, anti-proliferative and anti-metastatic agent without showing any deleterious effects. The current review summarizes the understanding the role of curcumin as a potential drug to control the development and progression of cancer.

Keywords: Cancer; Curcumin; Anti neoplastic drugs

Abbreviations: PTEN: Phosphatase and Tensin Homolog Deleted on Chromosome Ten; VEGF: Vascular Endothelial Growth Factor; NF- κB: Nuclear Factor-Kappa B; Akt: Protein Kinase B; Bcl2-xL: B Cell Lymphoma-Extra Large; C-myc: C-Mycproto-Oncogene; PI3K: Phosphatidylinositol-4,5-Bisphosphate 3-Kinase

Introduction

Carcinogenesis is a mechanistically complex process and comprises a series of genetic variations that disrupt the balance between cellular and molecular signal cascades [1]. It accounts for a significant proportion of the global cancer burden in terms of morbidity and mortality. The majority of causes of carcinogenesis is attributable to lifestyle, diet, and genetic factors, there has been increasing awareness and focus on its prevention or treatment [2]. The present treatment regimens include surgical resection, radiation and chemotherapy. The use of anti neoplastic therapies remains the most effective and standard treatment for patients with metastatic cancer. The efficacy of these chemotherapeutic regimens has been observed limited, with recurrence common. Moreover, the current approach for the treatment of cancer is generally expensive, exhibits side effects and also changes the normal functioning of genes. Therefore, there is dire need for the development of a safe and effective mode of therapeutic strategies to control the development and progression of cancer.

Some traditional medicinal plants are safe, effective and affordable to control the progression of tumor cells. Curcumin, an important constituent of the spice turmeric (*Curcuma longa*), is one such regimen that is safe, inexpensive, and efficacious. Turmeric powder is yellow pigmented and has been extensively used in Ayurveda medicine for the treatment of various diseases such as asthma, bronchial hyperactivity, allergy and hepatic disease. Turmeric powder has numerous curcuminoids that include curcumin (77%), demethoxycurcumin (17%), and bisdemethoxy curcumin (3%). Curcumin is a polyphenol (1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) and has been designated as an alternative approach in the prevention of cancer [3,4]. Extensive research and clinical studies conducted in the last decades have demonstrated that cancer development comprises the dysregulation of multiple cellular signaling pathways. It has been reported that curcumin play a novel role in the prevention and treatment of cancer through the modulation of diverse molecular targets including

genes regulating cell proliferation and apoptosis, angiogenesis, transcription factors, growth factors and their receptors [5,6].

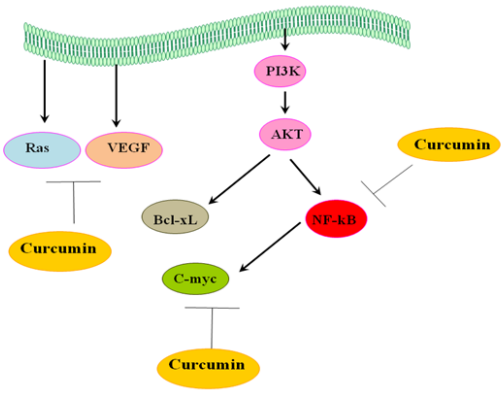

Figure 1: The representative image of diverse molecular targets regulated by curcumin in cancer. Vascular endothelial growth factor (VEGF); Nuclear factor-kappaB (NF- κB); Protein Kinase B (Akt); B cell lymphoma-extra large (Bcl2-xL); C-mycproto-oncogene (C-myc); Phosphatidylinositol-4, 5-bisphosphate 3-kinase (PI3K).

However, an understanding the mechanism of action of curcumin in the modulation of various molecular pathways might provide a novel insight to develop therapeutic strategies to manage the various types of cancers (Figure 1). Apoptosis is a series of complex biochemical events which involves the activation of various molecules and leads to the initiation of cell death [7]. Any aberrant activation in apoptosis contributes to cancer initiation, progression and treatment failure, thus plays an important role in cancer development and therapy. The apoptotic signaling pathway proceeds via the activation of pro-apoptotic proteins and inactivation of anti-apoptotic proteins such as members of Bcl-2 family [8]. Any agent that can selectively induce apoptosis in tumor cells is potentially promising approach in cancer therapy [9]. Earlier studies have reported that curcumin induces the activation of apoptosis in various cell lines such as colon, breast, prostate and stomach cancer cell lines [10-12]. Infact, curcumin activates the process of apoptosis through activation of caspase-3, cytochrome c release, and down regulation of bcl-2 in tumor cell lines by inhibiting various genes [13-16].

Tumor suppressor genes, particularly p53 have been identified as a guardian of genome which regulates various cellular and molecular pathways and, thereby inhibits cancer development and its progression. Earlier research studies have reported that curcumin can regulate the process of apoptosis and cell proliferation by up regulating p53 expression in cancer cells [17,18]. Another tumor suppressor gene, phosphatase and tensin homolog deleted on chromosome ten (PTEN) have been also observed to increase curcumin induced cytotoxicity [19]. Angiogenesis is a complex process which plays a vital effect in tumor cell invasion. The angiogenic factor, vascular endothelial growth factor (VEGF) expression have been found to be up regulated in tumors and also associated with metastatic potential [20]. Research studies have reported that curcumin is an inhibitor of VEGF expression in different types of cancers and therefore, considered as an anti angiogenic agent [21].

The transcription factor, Nuclear factor-kappa B (NF- κB) plays an important role in immune, inflammatory response and is constitutively expressed in almost all cancer types. An important study demonstrated that curcumin is involved in the suppression of NF-κB activation and the expression of various oncogenes regulated by NF-κB, including c-jun, c-fos, c-myc, NIK, MAPKs, ERK, ELK, PI3K, Akt, CDKs, and iNOS [22,23]. In this regard, curcumin has been considered as an anticancer, antioxidant, and anti-inflammatory agent. Moreover, an inactivation of an oncogene is a safe route in the prevention of carcinoma. It has been reported that curcumin shows a significant effect in cancer prevention through the down regulation of proto oncogenes such as N-myc, ras and fos [24,25]. Several other investigations have reported that curcumin shows the effect of anti proliferative and anti migratory via inhibiting various important signaling pathways such as EGFR, PI3 K/Akt and MAPK pathway [26-31]. From these observations, curcumin has established as an attractive strategy for the prevention of various types of cancers through the activation or inactivation of various genetic pathways.

Conclusion

Overall, the present review article highlights that use of curcumin provides an effective therapeutic treatment for the prevention of cancer by modulating diverse molecular pathways.

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