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Review

Health perspectives of a bioactive compound curcumin: A review

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ABSTRACT

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a is an important consituitents present in *Curcuma longa* L. (turmeric) rhizome. It is also a lipophilic molecule that rapidly permeates cell membrane. Curcumin has been used as pharmacological traditional medicinal agent in Ayurvedic medicine for ~6000 years. Being chemopreventive agent, curcumin has been found to modulate multiple molecular pathways through several mechanisms, *e.g.* induction of apoptosis, inhibition survival signals, and prevention from reactive oxidative species (ROS). Curcumin significantly caused reduction in lung cancer stem cells markers (CD133, ALDHA1, CD44, Nanog, and Oct4) and the number of CD133-positive cells as well as efficiently decreased the tumorsphere formation, inhibited proliferation, and induced apoptotic cell death. It also suppressed the activation of both Wnt/β-catenin and Sonic Hedgehog pathways. Curcumin has been also reported to diminish renal hypertrophy, reduce mesangial matrix expansion, and cause a lower level of albuminuria. It also inhibited the upregulated protein and mRNA expressions of collagen IV and fibronectin in the renal cortices as well as significantly reduced the mature interleukin-1β, cleaved caspase-1, and NLRP3 protein levels in the renal cortices of db/db mice as well as in HK-2 cells. It also ameliorated the defective insulin signalling pathway by upregulating insulin-like growth factor (IGF)-1R, IRS-2, PI3K, p-PI3K, Akt and p-Akt protein expression while downregulating IR and IRS-1. Besides, curcumin lowered the heart MDA and DNA fragmentation levels, increased concentration of SOD, catalase, and gluathione levels, decreased the percentage of TUNEL-positive cells and γH2AX protein expression, while it lowered the percentage (%) of capspase 3 positive cells and improved the percentage of Bcl-2 positive cells. The current review article presents effective role of curcumin against cancer, diabetes, oxidative stress, cardiovascular, obesity, and aging.

1. Introduction

Cucumin (1,7-bis(4-hydroxy-3methoxyphenyl)-1,6-heptadien-3,5-dione) is also known diferuloylmethane is yellowish polyphenol, which mostly purified from the rhizome of *Curcuma loga* L as well as from some others members of the genus. *Curcuma loga* L has been used in tredational system in Asian countries as a medicinial herb for numerous pathologies due to its anti-radical, anto-inflammatory, anti-mutagenic, anti-microbial, and anti-cancer activities (Pulido-Moran, Jorge Moreno, Ramirez-Tortosa, & Ramirez-Tortosa, 2016). In advanced colon cancer (Cca) patients, curcumin treatment significantly lowered the forkhead box protein (Foxp) 3 positive Treg frequency and enhanced the frequency of Th1 cells. Treating with curcumin repressed the Foxp3 gene transcription in Tregs, the Tregs were then converted into Th1 cells. The results also revealed that Foxp3 bound T-bet to prevent IFN-γ expression in $CD4^+$ T cells, which was abolished by treating with curcumin (Xu, Yu, & Zhao, 2017). Curcumin decreased *N*-nitrosodiethylamine (DEN)-induced hepatocarcinogenesis through regulating the oxidant stress enzymes (T-SOD and CAT), liver function (ALT and AST), LDHA, AFP level, and COX-2/PGE2 pathway. Furthermore, curcumin attenuated metabolic disorders *via* increasing concentration of glucose and fructose, and decreasing levels of glycine and proline, and mRNA expression of GLUT1, PKM, and FASN. Docking study on curcumin molecule pointed out to a strong affinity with key metabolic enzymes such as GLUT1, PKM, FASN, and LDHA (Qiu et al., 2017). (see Fig. 1)

Curcumin-loaded magnetic hydrogel nanocomposite in the treatment of heart hypertrophy reduced the malondialdehyde (MDA) levels, enhanced superoxide dismutase (SOD), and glutathione peroxidase (GPx) enzymes activities. It also reduced the expression of three heart

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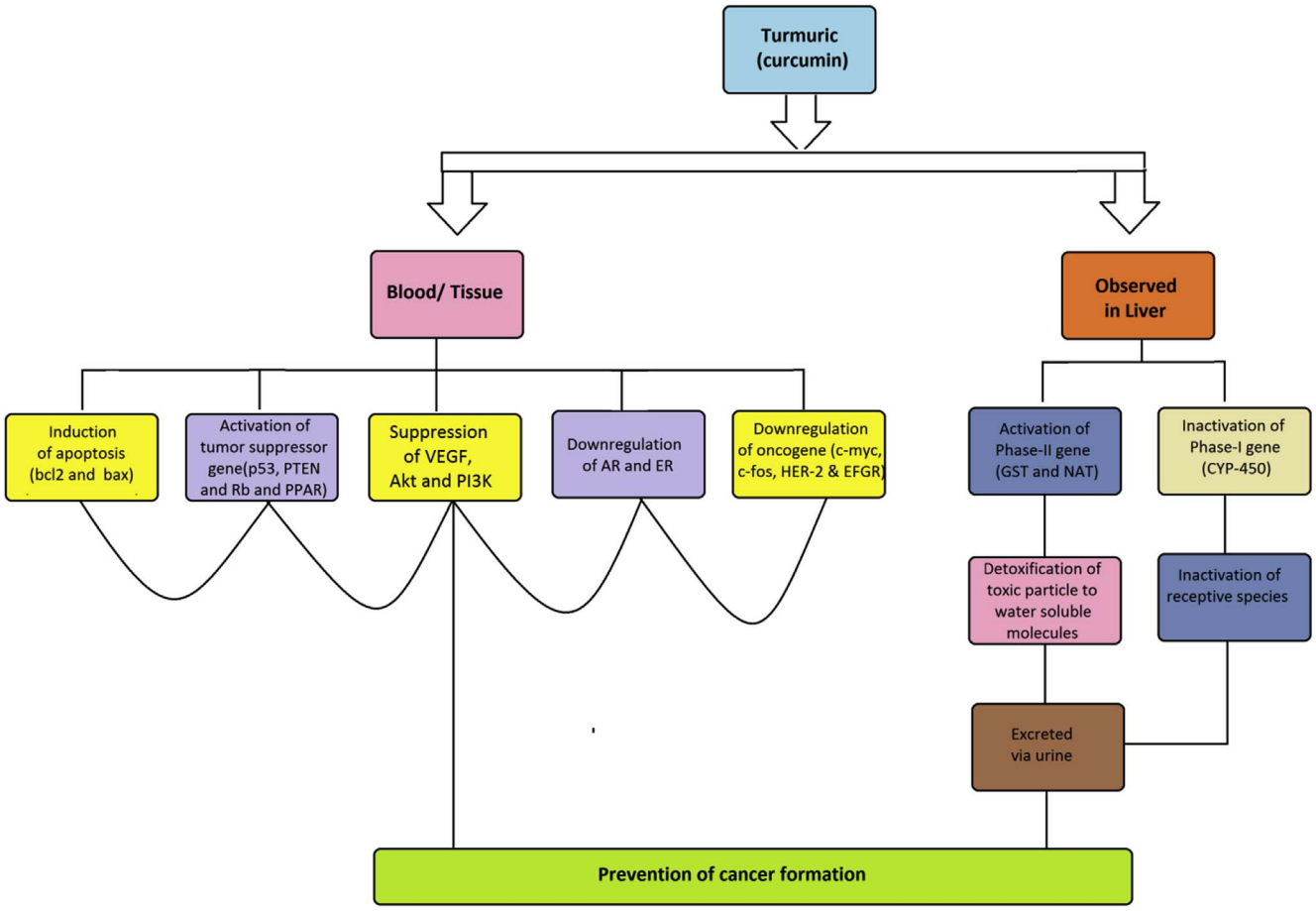

Fig. 1. Turmeric/curcumin shows a significant role in cancer prevention *via* induction of apoptosis, activation of tumour suppressor gene and phase II gene, and inactivation of oncogene, hormonal receptor gene, and angiogenesis and phase-I gene.

failure markers, atrial natriuretic peptide (ANP), B type natriuretic peptide (BNP), and beta major histocompatibility complex (β-MHC) in cardiac tissue (Namdari & Eatemadi, 2017). The molecule attenuated norepinephrine (NE)-induced cardiac cell death and modulation of apoptosis in H9c2 cardiomyocytes (Manghani, Gupta, Tripathi, & Rani, 2017). Recently, curcumin has been found to have a preventive role against spinal cord ischemia-reperfusion (IR) *via* decreasing the elevated MDA level, enhancing the concentrations of SOD, GPx, and lowering nitric oxide (NO) levels (Akar et al., 2017). Curcumin attenuated hydrogen peroxide (H_2O_2)-induced apoptosis in H9c2 cardiomyoblasts *via* causing a dose-dependent induction of heme oxygenase-1 (HO-1) protein expression. It also reduced the cleaved caspase-3 (CC3) protein expression level and enhanced the Bcl-2/Bax ratio. Moreover, curcumin has anti-apoptotic function throughupregulating HO-1 protein through the PI3K/Akt signaling pathway (Yang et al., 2017). In depression and diabetes, curcumin was reported to upregulate the phosphorylation of insulin receptor substrate (IRS)-1 and protein kinase B (Akt) in the liver, enhanced insulin sensitivity, and reversed the metabolic abnormalities and depressive-like behaviors. Moreover, curcumin increased the hepatic glycogen content by inhibiting glycogen synthase kinase (GSK)-3β and prevented gluconeogenesis by inhibiting phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase) (Shen, Wei, Li, Qiao, & Li, 2017). Encapsulating curcumin with 10 or 50 mg/kg caused up to 37% reduction in the glucose levels in streptozotocin diabetic rats, significantly decreased levels of inflammatory cytokines, and prevented 8-oxo-2′-deoxyguanosine (8-oxo-dG) in pancreatic tissue (Ganugula et al., 2017).

2. Health perspectives

2.1. Anticancer

Epithelial-mesenchymal transition (EMT) is associated with embryonic growth and also as initiation and growth of epithelim originated malignant tumors. The extra-cellular measured protein kinase 5 in benzidine expected bladder cancer groth. In human normal urothelial cells (SV-HUC-1), curcumin effectually weakened benzidine made urocystic EMT by inhibiting ERK5/AP-1 pathway (Liu, Wang, et al., 2017, Liu, Liu, et al., 2017). In castration-resistant prostate cancer (CRPC) cells, curcumin induces apoptosis and autophagy whereas at apoptosis- and autophagy-inducing concentrations, curcumin enhanced the expression levels of transferrin receptor 1 (TfR1) and iron regulatory protein 1 (IRP1) (Yang et al., 2017).

In another study (Ebrahimifar et al., 2017), after AGS cells treated with a combination of curcumin and paclitaxel (300 nm) or methotrexate (100 μm) or vincristine (5 nm), the cell viability was significantly decreased after incubation of AGS cells with curcumin. Combination with curcumin (15–50 μm) significantly increased cytotoxicity of all three agents. Group of researchers (Ali et al., 2017; Baghbani & Moztarzadeh, 2017) investigated that curcumin derivative (*Z*)-3-hydroxy-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one (DK1) efficiently induced apoptotic cell death, caused cell cycle arrest at G2/M phase, which is accompanied by upregulating p53, p21 proteins, down regulating PLK-1 subsequently promote phosphorylation of CDC2 in breast cancer cell MCF-7 and normal cell MCF-10A. Moreover, curcumin derivative also enhanced the glutathione concentrations andreactive oxygen species, whereas it increased the cytochrome c and