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BENEFICIAL ROLE OF CURCUMIN IN DISEASES TREATMENT

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ABSTRACT: Curcumin regulates cellular signaling pathway related to cancer growth, inflammation and apoptosis and due to biological activities can be target DNA, RNA, and enzymes. Also, curcumin has an inhibitory effect against MARK, P53, β-catenin, and AKT. It can be considered as a promising agent to treat many diseases, but it is important that should be acceptably carried out cellular targeting with curcumin. Here, we reviewed the beneficial effects of curcumin in the treatment of diseases. Our review study was confirmed that curcumin has a potential effect in diseases treatment, but there is a dire need for an increase of its bioavailability to the promotion of its efficacy. We suggest that should be design the methods for increase of cellular targeting by curcumin in further studies.

INTRODUCTION: Curcumin is considered as a phenolic compound with therapeutic properties including anti-inflammation, antioxidant and anticancer [1]. In previous studies, it has been found that it is a safe compound for the body following its administration in patients with cancer and healthy individuals. Its therapeutic effects are more than its side effects [2, 3]. However, despite having such a beneficial effect on human biological, it has not very high bioavailability in human due to poor absorption and fast metabolism [4, 5].

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In animal and human, major amount of curcumin is excreted as urine and feces and is absorbed only a small portion of curcumin that combines with glucuronide and sulfate to create its conjugated forms in the liver. These events lead to the reduction of plasma concentrations of free curcumin [2, 5, 6, 7, 8, 9].

Also, curcumin is an insoluble compound in the water at neutral and basic conditions due to the production of phenolate that leads to poor availability in aqueous systems [10, 11]. Using nanoparticles can increase cellular uptake and stability of curcumin so that solid lipid nanoparticles promote the distribution and stability of curcumin in aqueous solutions that lead to improvement of the anticancer effect of curcumin [12]. Also, silica nanoparticle can be a suitable delivery system for curcumin because it has been

demonstrated that silica nanoparticle increases the anti-tumor properties of curcumin [13]. In this study, we reviewed the beneficial effect of curcumin on the treatment of diseases.

Review Method: Here, we searched paper related to the role of curcumin treatment of diseases with keywords such as curcumin and cancer, curcumin and Parkinson's diseases, curcumin and Alzheimer disease, curcumin and histone acetyltransferase (HAT), curcumin and diabetes in databases include a web of science, PubMed and Scopus. Then, the papers were fully read and summarized here.

Curcumin Beneficial Effects in Diseases Treatment: According to a study Yallapu *et al*., 2014, PLGA or poly (lactic-co-glycolic acid) combined with curcumin leads to a reduction of tumor cells growth (prostate cancer). Poly (lactic-co-glycolic acid) combined with curcumin had a pivotal role in the inhibition of beta-catenin expression in tumor cells. Also, it led to inhibition of anti-apoptotic proteins (Mcl-1, Bcl-xL) through suppression of STAT3 and AKT phosphorylation. Down-regulation of miR21 and up-regulation of miR-205 also were showed after treatment with poly (lactic-co-glycolic acid) combined with curcumin. Given that these effects poly (lactic-co-glycolic acid) combined with curcumin can be considered as a promising agent to treat cancer due to good delivery into tumor cells [14]. Thiolated chitosan nanoparticle can promote the anticancer effect of curcumin because it increases curcumin bioavailability. Also, treatment of mice with colon cancer by curcumin loaded with thiolated chitosan nanoparticle led to dramatical reduction of cancer cells [15].

Kumar *et al*., 2014 examined that treatment of ovarian cancer cells (SKOV-3) with the curcumin-loaded polymer of 2-hydroxymethyl methacrylate resulted in a decrease of cancer cells by arresting of the cell cycle in G0/G1 and induction of apoptosis [16]. It has been reported that curcumin-combined silica nanoparticle conjugated with hyaluronic acid results in cytotoxic effects on human colon carcinoma (colo-205) that is due to appropriate delivery of curcumin into cancer cells through silica nanoparticle conjugated with hyaluronic acid [17]. Curcumin-loaded PLGA-PEG nanoparticle has anti-tumor effects against breast cancer (cell line MCF-7) due to obvious reduction of cancer cells followed by treatment with curcumin-loaded PLGA-PEG nanoparticle [18]. The effect of polysorbate 80-coated cerasomes to deliver curcumin in mice with Parkinson's disease was confirmed promotion of cross of the blood-brain barrier and subsequently improvement of mice with Parkinson's disease [19]. Curcumin and piperine coated with glycerol monooleate easily pass the blood-brain barrier and prevent the formation of alpha-synuclein oligomers. Also, curcumin and piperine coated with glycerol monooleate reduce the effect of rotenone as a Parkinson's disease inducer. Curcumin and piperine coated with glycerol monooleate is an important factor in the reduction of oxidative stress, apoptosis and autophagy pathway and ultimately protect dopaminergic neurons against damage [20].

A research group was found that amine-functionalized mesoporous silica nanoparticle could be a good delivery system for curcumin to abrogation of Parkinson's disease complications because the administration of curcumin-loaded amine - functionalized mesoporous silica nanoparticle leads to the reduction of alpha-synuclein accumulation [21]. Mathew *et al*., 2012 designed a water-soluble nanoparticle (PLGA nanoparticle conjugated with Tet-1 peptide) for transferring of curcumin. Based our their study, curcumin-loaded-PLGA nanoparticle conjugated with Tet-1 peptide prevented the accumulation of amyloid beta and had an antioxidant effect and not cytotoxic effect, therefore, it can be very effective in the treatment of Alzheimer's disease [22]. It has been showed improvement of memory and reduction of amyloid plaques in mice with Alzheimer's disease after treatment with highly stabilized curcumin nanoparticle according to study conducted by Kin Cheng *et al*., 2013. Meanwhile, the presence of high level of curcumin in plasma indicated an enhancement of its pharmacokinetic characteristic using the nanoparticle [23].

Curcumin-loaded PLGA nanoparticle is effective in neural stem cell differentiation at rat's hippocampal and subventricular. Injection of this compound into hippocampal leads to neurogenesis induction through the expression of genes related to cell growth and proliferation (reelin, nestin and Pax6) and differentiation of neurons, such as neurogenin,

neuro D1, neuregulin, neuroligin and Stat3. These events ultimately result in improvement of learning and memory due to the destruction of beta-amyloid [24]. The curcumin-coated magnetic nanoparticle has diagnostic value for Alzheimer's disease because it is a non-invasive diagnostic procedure by MRI and reduces PET disadvantages [25]. Curcumin-loaded PLGA nanoparticle is a good agent against Alzheimer's disease due to it protects neurons against oxidative stress by up-regulation of expression of genes like APOE, APOJ, TRX, GLRX REST that indicate its high uptake in neurons [26]. Curcumin inhibits histone acetyl-transferase, the main reason for cardiac hypertrophy and heart failure, and prevents hypertrophy [27, 28]. Furthermore, curcumin protects the heart against damage caused by ischemia/ reperfusion [29, 30].

In cells, curcumin leads to proteasome-dependent degradation of histone acetyltransferase. This event is the main reason for inhibition of histone acetyltransferase by curcumin. Curcumin is a selective inhibitor of histone acetyltransferase [28]. By the mechanism, curcumin prevents the excessive increase of ratio heart weight to body weight [31]. Retinopathy occurs in diabetes due to the inability of the body for the elimination of free radicals and pro-inflammatory molecules such as NF-κB, VEGF, and IL1β. Curcumin prevents progression of diabetes retinopathy by inhibition of free radicals formation and reduction of inflammation [32].

CONCLUSION: The use of herbal medicines is increasing in recent years. Thus, efforts to review and revive herbal medicines are reasonable so that to understand their effect mechanism lead to achieving new strategies to treat many diseases. Curcumin is the most important component of turmeric. However, its low bioavailability has limited its healing properties. Today, it has been proposed several mechanisms to increase its bioavailability that can improve its absorption. For example, nanoparticles can significantly increase curcumin effectiveness. In this review study, we showed that to apply strategies for the promotion of curcumin bioavailability lead to increase of its efficacy in the treatment of diseases; therefore we suggest that design further studies based on this view.

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