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Biological deeds of Curcumin

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Abstract: Curcumin is derived from the plant Curcuma longa and is the active ingredient of the spice turmeric. It has attracted a lot of attention due to its hopeful biological properties to treat cancer, Alzheimer's disease, HIV, chronic inflammations, oxidative stress, and cystic fibrosis. Curcumin underwent clinical trial for cancer owing to its major activity as an antitumor and chemo preventive agent.
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1. Introduction

Phytochemicals are naturally occurring substances found in plants. There has been considerable public and scientific interest in the use of phytochemicals derived from dietary components to combat human diseases, especially the two commonest killers in the developed world, cardiovascular disease and cancer. The dried ground rhizome of the perennial herb Curcuma longa Linn., called turmeric in English, haldi in Hindi and ukon in Japanese, has been used in Asian medicine since the second millenium BC [1]. Its utility is referred to in the ancient Hindu scripture, the Ayurveda. In addition to its aromatic, stimulant and colouring properties in the diet, turmeric is mixed with other natural compounds such as slaked lime and has been used topically as a treatment for wounds, inflammation and tumours. The pharmacology and putative anti-cancer properties of curcumin has been the subject of several review articles [2-3].

Curcumin is an oil-soluble pigment, practically insoluble in water at acidic and neutral pH, and soluble in alkali. Preparations of water-soluble curcumin by incorporation into various surfactant micellar systems (e.g. sodium dodecyl sulfate) have been reported [4]. In solutions the principal colouring components of curcumin exhibit keto-enol tautomerism and, depending on the solvent, up to 95 percent are in the enol form.

2. Molecular targets of curcumin

Accumulating evidence suggests that curcumin has a diverse range of molecular targets, which supports the notion that curcumin influences numerous biochemical and molecular cascades. Among its molecular targets are transcription factors, growth factors and their receptors, cytokines, enzymes, and genes regulating cell proliferation and apoptosis.

2.1. Curcumin interacts with numerous targets

Curcumin is apparently a highly pleiotropic molecule that interacts physically with its numerous targets. It binds to and inhibits the activity of enzymes, growth factor receptors, metals, albumin, and other molecules. It binds proteins such as P-glycoprotein [5], multidrug resistance proteins 1 and 2, glutathione [6].

2.2. Curcumin downregulates the activity of multiple kinases

A variety of tyrosine kinases are activated by mutations that contribute to the malignant transformation, growth, and metastasis of human cancers. Accordingly, protein kinases involved in key growth signaling cascades are good candidate targets for novel chemo preventive approaches to treat many human cancers. For example, most human cancers over express epidermal growth factor receptor (EGFR) and HER2/neu, which ultimately stimulates the proliferation of cancer cells [7].

Curcumin regulates activities of several enzymes that mediate tumor growth In addition to directly regulating the expression of candidate genes, curcumin also appears to effectively regulate the activities of enzymes that control tumor growth and proliferation. Curcumin blocks fibrosis in anti-Thy1 glomerulo nephritis through its up regulation of hemoxygenase-1 (HO-1) gene expression, suggesting that it has anti fibrotic effects in glomerular disease [8].

3. Biological activities of curcuminoids

Curcuminoids from turmeric and their derivatives have been shown to possess a wide range of biological activities including antioxidant, anti-inflammatory, anticancer, antimicrobial, neuro protective, cardio protective and radio protective effects etc.

3.1. Curcumin is extremely safe and well tolerated

The potential use of curcumin in chemo preventive or therapeutic settings has raised the obvious issues of toxicity and tolerance.

3.2. Neuroprotective effects and medicinal use in Alzheimer's disease (AD)

The pathogenesis of neurodegenerative diseases such as Alzheimer or Parkinson is multi-factorial with a complex combination of genetic components and environmental factors. Toxic reactions, including inflammation, glutamatergic toxicity, dysfunction of mitochondrial activity and ubiquitin/proteasome system, the activation of apoptosis pathways, the elevation of iron and nitric oxide and the alteration of the homeostasis of antioxidants/oxidation are involved in the pathogenesis of neurodegenerative diseases [9].

3.3. Antitumor-activity

The effect of curcuminoids and cyclocurcumin examined on the proliferation MCF-7 human breast tumor cells. DMC is a better inhibitor than CUR and BDMC due to the presence of both phenolic hydroxyl groups, methoxyl groups and the diketone moiety. Cyclocurcumin had no effect on MCF-7 cell proliferation suggested that the diketone system of curcuminoids appears to be the part of the molecule involved in the antiproliferative effect of curcuminoids [10].

3.4. Antioxidant activity

Curcuminoids possess powerful antioxidant activity as demonstrated in many chemicals in vitro tests and in several in vivo trails. These compounds could be used in food systems to enhance the shelf life due to their good antioxidant capacity.

3.5. Curcumin has potential as palliative therapy for cancerous skin lesions

External sebaceous neoplasms (e.g., actinic keratosis, superficial basal cell carcinoma, and external genital warts) have traditionally been treated topically with corticosteroid creams. In a study [11], curcumin's efficacy when applied as either an ethanol extract of turmeric or as an ointment to external cancerous skin lesions was evaluated in 62 patients. Regardless of the application, curcumin provided remarkable symptomatic relief that was in many cases relatively durable (lasting several months) and in all cases (except for a single adverse reaction in one subject) extremely safe.

3.6. Cardio protective effects

CUR has extensive cardio protective effects against diabetic cardiovascular complications, cardiac hypertrophy and myocardial infarction. CUR is associated with cytokine-cytokine receptor interaction, ECM-receptor interaction, focal adhesions and colorectal cancer. The idiopathic pulmonary arterial hypertension is a complex disease that mainly affects pulmonary arterial circulation.

3.7. Radio protective or radio sensitizing effect

Curcuminoids are well antioxidant polyphenols with radio modulatory properties, radio protecting non-cancerous cells while radio sensitizing tumor cells.

3.8. Anti-angiogenic and anti-proliferative activities

The anti-angiogenic effects of Ar-turmerone were evaluated in human microvascular endothelial cells, zebrafish and Matrigel plugs mouse models. Ar-turmerone significantly inhibited the proliferation, tube formation and motility of HMEC-1 cells at noncytotoxic concentrations. It exerted anti-angiogenic activity by down-regulation of Angiopoietin-2 and Tie-2 expression in zebrafish. It significantly inhibited the blood vessel growth, confirmed by the in vivo studies using Matrigel plugs mouse model. Ar-turmerone can be used as a potential anti-angiogenic agent [12].

3.9. Anti-inflammatory and antirheumatic activity

Rheumatoid arthritis is a frequent complication in the elderly, and most treatments aim at reducing the temporary symptoms attributable to the underlying inflammatory activity [13]. The need for new treatment approaches has led to the recent introduction of potent disease-modifying antirheumatic drugs (DMARDs), whose clinical benefits are unfortunately offset by their high cost and frequently undesirable side effects. Curcumin has been considered as an alternative.

Biological activities of various curcuminoid formulations Curcuminoids and their analogs are often a source of biological activities such as drugs or drug templates with limited toxicity and high activity.

4. Nutraceutical applications of curcuminoids

Food plant extracts, with medicinal values and lesser side effects are a source of chemically diverse compounds. Curcuminoids, present in C. longa, an established food and medicinal plant, are known for their hypoglycemic property. CUR was found to be a very effective in antagonizing the S9-mediated mutagenicity of several food-derived heterocyclic amines. The structural activity relationship between CUR and its naturally occurring derivatives DMC,

BDMC and other structural related natural and synthetic analogs of CUR, namely tetrahydrocurcumin, dibenzoylmethane, dibenzoylpropane, vanillin, ferulic acid, isoferulic acid and caffeic acid by Ames Salmonella/reversion assay against different classes of cooked food mutagens [14].

Conclusions

Curcuminoids are the promising natural compound with a large variety of therapeutic properties, particularly biological targets and interactions, linked to numerous diseases. Unfortunately the clinical applications of curcuminoids are restricted by their poor solubility, low absorption and bioavailability, high metabolism rate. To overcome these limitations, curcuminoids and their derivatives have been modified and attached with lipids, micelles, nanoparticles, liposome and metal complexes.

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