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Review

Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies

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ABSTRACT

Curcumin, a hydrophobic polyphenol, is the principal constituent extracted from dried rhizomes of *Curcuma longa* L. (turmeric). Curcumin is known as a strong anti-oxidant and anti-inflammatory agent that has different pharmacological effects. In addition, several studies have demonstrated that curcumin is safe even at dosages as high as 8 g per day; however, instability at physiological pH, low solubility in water and rapid metabolism results in a low oral bioavailability of curcumin. The phytosomal formulation of curcumin (a complex of curcumin with phosphatidylcholine) has been shown to improve curcumin bioavailability. Existence of phospholipids in phytosomes leads to specific physicochemical properties such as amphiphilic nature that allows dispersion in both hydrophilic and lipophilic media. The efficacy and safety of curcumin phytosomes have been shown against several human diseases including cancer, osteoarthritis, diabetic microangiopathy and retinopathy, and inflammatory diseases. This review focuses on the pharmacokinetics as well as pharmacological and clinical effects of phytosomal curcumin.
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1. Introduction

The use of nutraceuticals and functional foods for the prevention and treatment of human diseases has become

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extensively popular over the recent decades. In this context, natural products have an indispensable role as drugs, supplements and lead compounds used in pharmaceutical industry, owing to their multimechanistic biological actions, sustainable availability and safety. It is well-known that plants are the wealthiest source of bioactive natural products and many macro- and micro-nutrients [1–3]. Curcumin is a herbal polyphenolic compound that is extracted from the famous spice turmeric [2,4–6]. Several studies have confirmed that curcumin possesses various biological and pharmacological properties including antioxidant, anti-inflammatory, immunomodulatory, anti-microbial, anti-ischemic, anti-carcinogenic, hepato-protective, nephro-protective, hypoglycemic, and antirheumatic activities [7–18]. This compound also shows various therapeutic effects against several diseases such as cancer, anxiety and depression, metabolic syndrome, hypertriglyceridemia, osteoarthritis and non-alcoholic fatty liver disease [7,11,13,19–25]. In particular, curcumin's capacity to regulate the expression and/or activity of several molecular targets can explain its potential utility in cancer chemoprevention and chemotherapy [4,5] (Fig. 1). Various animal [26,27] and human studies [28–31] have shown that curcumin is safe and could be tolerated even at very high doses [29,30]. In spite of its appreciated pharmacological effects and safety, curcumin has not been approved as a drug, and the bioavailability of curcumin has been argued as a potential reason limiting complete translation of *in vitro* benefits into clinical conditions [32,33].

Hitherto, several drug delivery strategies have been tested to improve the bioavailability of curcumin including solid dispersions, complexation with cyclodextrins, copolymeric micelles, polymeric nanoparticles, lipid-based nanoparticles, liposomes, and microemulsions [34]. Phytosomal delivery system has also emerged as a promising strategy to enhance the systemic bioavailability of curcumin. Phytosomes are complexes of phospholipids, mainly phosphatidylcholine, with polyphenolic compounds [35]. Marczylo et al. investigated whether formulation of curcumin in the form of phosphatidylcholine phytosomes increases the oral bioavailability or changes the metabolism of curcumin [36]. Their results suggested that concentrations of curcumin and its metabolites were five folds higher in rat plasma following administration of phytosomal versus unformulated curcumin [36]. In contrast, curcumin concentrations in the gastrointestinal mucosa following ingestion of the phytosomal formula were relatively below those seen with the unformulated curcumin [37], suggesting a higher rate of systemic absorption with phytosomal curcumin. Apart from pharmacokinetic evaluations, several studies have tested the pharmacological and therapeutic effects of curcumin in different diseases [38,39]. This review provides a concise summary of the pharmacokinetic properties of curcumin and different approaches used so far for the bioavailability enhancement of this phytochemical, with a particular focus on phytosomal curcumin and its reported effects in animal and human studies.

2. Pharmacokinetic properties of curcumin

Pharmacokinetic and bioavailability studies of curcumin have indicated its low intestinal absorption and rapid clearance from the body [40]. Metabolism, absorption, biodistribution and excretion of curcumin in rodents have been reported in several studies [41–43]. The overall findings imply that curcumin has a low absorption and rapid clearance following oral use. In a primary research, a dose of 1 g/kg curcumin was administered to rats and resulted in about 75% excretion of curcumin in feces, whereas poor amounts were found in urine [41,44]. In another research, absorption of curcumin was reported to be 60% after oral use in rats [45]. A radiotracing study with ^{3}H-radiolabeled curcumin confirmed that curcumin is transformed during its intestinal absorption [44,46].

Gutierres and colleagues investigated curcumin levels in rat plasma. In addition, they assessed alterations of insulin sensitivity and glucose tolerance in streptozotocin-diabetic rats treated with curcumin-enriched yoghurt [47]. Their results indicated that the elimination half-life of curcumin was 8.64 ± 2.31 (IV) and

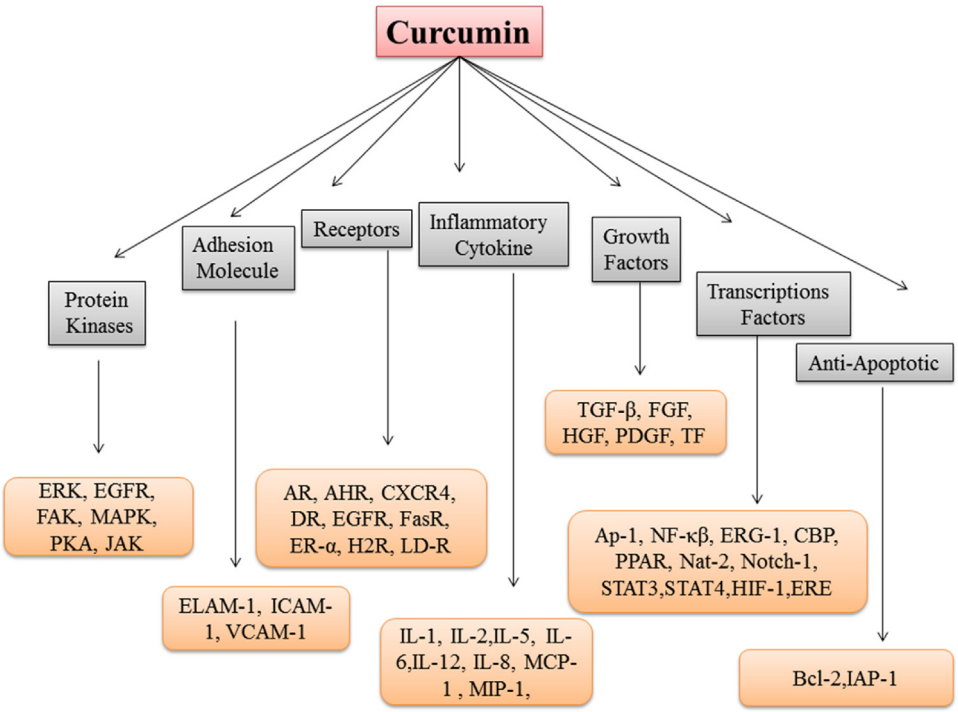

Fig. 1. Pathways regulated by curcumin.

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