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Review Article

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SEPARATION IDENTIFICATION OF BIOACTIVE COMPOUNDS AND PREPARATION OF A HERBAL TOPICAL FORMULATION OF CURCUMIN

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ABSTRACT

Curcumin is one of the main active ingredients of roots or rhizomes of *curcuma longa*. The roots are found to be medicinally valuable.[1] The molecules has many potent therapeutic activities like antioxidant, ant-inflammatory, ant0icancer, antibacterial, wound healing, anti-viral, hepatoprotective, neuroprotective. It may help in the treatment of inflammation and muscle pain brought on by exercise, improving recuperation and performance in athletes.[2] Additionally, those without medical diagnoses may benefit from a very low dosage of the complex.[3] Its anti-inflammatory and antioxidant properties are responsible for the majority of these advantages.[5] Curcumin's low bioavailability, which seems to be mostly caused by poor absorption, fast metabolism, and rapid elimination, prevents it from providing the health advantages when consumed alone.[6] Bioavailability can be increased by a number of factors.

KEYWORDS: Curcumin, ant-inflammatory, anticancer, antibacterial activity, turmeric powder.

INTRODUCTION

Curcuma longa has been traditionally used in Asian countries as a medical herb due to its antioxidant, anti-inflammatory, antimutagenic, antimicrobial, and anticancer properties. Curcumin, a polyphenol, has been shown to target multiple signalling molecules while also demonstrating activity at the cellular level, which has helped to support its multiple health benefits.[3] It has been shown to benefit inflammatory conditions, metabolic syndrome, pain, and to help in the management of inflammatory and degenerative eye conditions. In addition, it has been shown to benefit the kidneys. While there appear to be countless therapeutic benefits to curcumin supplementation, most of these benefits are due to its antioxidant and anti-inflammatory effects.[4] Despite its reported benefits via inflammatory and antioxidant mechanisms, one of the major problems with ingesting curcumin by itself is its poor bioavailability, which appears to be primarily due to poor absorption, rapid metabolism, and rapid elimination. Several agents have been tested to improve curcumin's bioavailability by addressing these various mechanisms. Most of them have been developed to block the metabolic pathway of curcumin in order to increase its bioavailability. For example, piperine, a known bioavailability enhancer, is the major active component of black pepper and is associated with an increase of 2000% in the bioavailability of curcumin. Therefore, the issue of poor bioavailability appears to be resolved by adding agents such as piperine that enhance bioavailability, thus creating a curcumin complex.[3-4]

Curcumin is being recognized and used worldwide in many different forms for multiple potential health benefits. For example, in India, turmeric—containing curcumin—has been used in curries; in Japan, it is served in tea; in Thailand, it is used in cosmetics; in China, it is used as a colorant; in Korea, it is served in drinks; in Malaysia, it is used as an antiseptic; in Pakistan, it is used as an anti-inflammatory agent; and in the United States, it is used in mustard sauce, cheese, butter, and chips, as a preservative and a colouring agent, in addition to capsules and powder forms.[17] Curcumin is available in several forms including capsules, tablets, ointments, energy drinks, soaps, and cosmetics. Curcuminoids have been approved by the US Food and Drug Administration (FDA) as "Generally Recognized as Safe" (GRAS), and good tolerability and safety profiles have been shown by clinical trials, even at doses between 4000 and 8000 mg/day and of doses up to 12,000 mg/day of 95% concentration of three curcuminoids: curcumin, bisdemethoxycurcumin, and demethoxycurcumin.[5]

It is the purpose of this review to provide a brief overview of the plethora of research regarding the potential health benefits of curcumin. Due to the extent of the literature, we have chosen to focus on the benefits associated with some common health conditions and on benefits in healthy people rather than to review the extensive literature related to cancer and other disease states. For a comprehensive review of curcumin's effects on cancer.[6] Soluble in organic solvent such as acetone, ethanol, methanol, dimethyl formamide and DMSO. The solubility of curcumin in these solvents is approx: 1mg/ml & in acetone it is at least 20 mg/ml. Insoluble in cold water and ethers. Curcumin, a yellow pigment from *Curcuma longa* is a major component of turmeric with immune-modulating, anti-inflammatory, wound-healing, antibacterial, antitumor, anti- carcinogenic, and antioxidant properties. This agent has shown some significant effect on psoriasis with properties related on numerous receptors to which curcumin binds. These include 5-LOX, xanthine oxidase, thioredoxin reductase, COX-2, *p*-glycoprotein, GST, PKA, PKC, cPK, PK, Ca^{2}+- dependent protein kinase (CDPK), glutathione and reduce oxidative stress. Furthermore, curcumin appears to inhibit the production of cytokines that can lead to inflammation. This may include tumor necrosis factor (TNF), intetleukin-6 and induced suppression of phosphorylase kinase activity which correlates with the resolution of human psoriasis. Testing in animal models and humans.[8] The clinical trials has revealed that the bioavailability of curcumin is low, owing to its poor absorption across the gut, inadequate tissue distribution , rapid metabolism, and its subsequent elimination from the body. Use of turmeric supplement for long duration is seem to lead to digestive problems and potentially causing complications to people suffering from gallbladder disease. High turmeric doses acts as blood thinner and can also lead to stomach upset with children being more susceptible to dietary turmeric supplements and medication side effects.[8]

Fig: No. 1 Curcumin.

Besides curcumin being low absorption into the blood stream, the other documented problems with this product is that it is not advisable to use repeatedly without food in the stomach because it tends to effect upsets to the stomach if taken on empty stomach. To maximize its absorption, it is recommended that patient accompany curcumin with fatty foods or preferably used at the same time wish fish oil supplement. Curcumin, the active compound found in turmeric, is renowned for its various bioactive properties. Here are some key bioactive compounds and their potential health benefits.

Health Benefits

Anti-inflammatory: Curcumin inhibits pro-inflammatory cytokines and enzymes like COX-2 and LOX, which can help reduce inflammation.[12]

Antioxidant: It scavenges free radicals and enhances the body's antioxidant defenses, protecting cells from oxidative stress.[11]

Anticancer: Curcumin has been shown to influence multiple signaling pathways involved in cancer cell proliferation, apoptosis, and metastasis. It may inhibit the growth of various cancer types, including breast, prostate, and colorectal cancers.[11]

Neuroprotective: Potentially beneficial in neurodegenerative diseases like Alzheimer's by reducing amyloid plaque formation.

Demethoxycurcumin

Anti-inflammatory and Antioxidant: Similar to curcumin, it helps in reducing inflammation and oxidative stress.

Anticancer Activity: Studies indicate it may inhibit cancer cell growth and induce apoptosis.

Bisdemethoxycurcumin

Cytotoxic Effects: It may possess anticancer properties, particularly against certain types of cancer cells.[11]

Anti-inflammatory: It can help modulate inflammatory responses.

Turmerones

Neuroprotective Properties: Ar-turmerone has been linked to promoting neural stem cell growth and potential use in treating neurological conditions.

Anti-inflammatory Effects: These compounds may also help reduce inflammation and improve overall health.

Phenolic Compounds

Antioxidant Effects: They enhance the body's ability to combat oxidative stress, potentially lowering the risk of chronic diseases.

Vitamins and Minerals

- **Vitamins**: Includes vitamin C and E, which have antioxidant properties.
- **Minerals**: Manganese, iron, and potassium, which support various bodily functions.

Mechanisms of Action

Antioxidant

Antioxidant and anti-inflammatory properties are the two primary mechanisms that explain the majority of the effects of curcumin on the various conditions discussed in this review. Curcumin has been shown to improve systemic markers of oxidative stress. There is evidence that it can increase serum activities of antioxidants such as superoxide dismutase (SOD). A recent systematic review and meta-analysis of randomized control data related to the efficacy of supplementation with purified

curcuminoids on oxidative stress parameters—indicated a significant effect of curcuminoids supplementation on all investigated parameters of oxidative stress including plasma activities of SOD and catalase, as well as serum concentrations of glutathione peroxidase (GSH) and lipid peroxides. It is noteworthy to point out that all of the studies included in the meta-analysis utilized some sort of formulation to overcome bioavailability challenges, and four out of the six used piperine. Curcumin's effect on free radicals is carried out by several different mechanisms.[12] It can scavenge different forms of free radicals, such as reactive oxygen and nitrogen species (ROS and RNS, respectively); it can modulate the activity of GSH, catalase, and SOD enzymes active in the neutralization of free radicals; also, it can inhibit ROS-generating enzymes such as lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase. In addition, curcumin is a lipophilic compound, which makes it an efficient scavenger of peroxyl radicals, therefore, like vitamin E, curcumin is also considered as a chain-breaking antioxidant.[13]

Anti-Inflammatory

Oxidative stress has been implicated in many chronic diseases, and its pathological processes are closely related to those of inflammation, in that one can be easily induced by another. In fact, it is known that inflammatory cells liberate a number of reactive species at the site of inflammation leading to oxidative stress, which demonstrates the relationship between oxidative stress and inflammation. In addition, a number of reactive oxygen/nitrogen species can initiate an intracellular signaling cascade that enhances pro-inflammatory gene expression. Inflammation has been identified in the development of many chronic diseases and conditions. These diseases include Alzheimer's disease (AD), Parkinson's disease, multiple sclerosis, epilepsy, cerebral injury, cardiovascular disease, metabolic syndrome, cancer, allergy, asthma, bronchitis, colitis, arthritis, renal ischemia, psoriasis, diabetes, obesity, depression, fatigue, and acquired immune deficiency syndrome AIDS. Tumor necrosis factor α (TNF-α) is a major mediator of inflammation in most diseases, and this effect is regulated by the activation of a transcription factor, nuclear factor (NF)-κB. Whereas TNF-α is said to be the most potent NF-κB activator, the expression of TNF-α is also regulated by NF-κB.[13] In addition to TNF-α, NF-κB is also activated by most inflammatory cytokines; gram-negative bacteria; various disease-causing viruses; environmental pollutants; chemical, physical, mechanical, and psychological stress; high glucose; fatty acids; ultraviolet radiation; cigarette smoke; and other disease-causing factors. Therefore, agents that downregulate NF-κB and NF-κB–regulated gene products have potential efficacy against several of these diseases. Curcumin has been shown to block NF-κB activation increased by several different inflammatory stimuli.[14] Curcumin has also been shown to suppress inflammation through many different mechanisms beyond the scope of this review, thereby supporting its mechanism of action as a potential anti-inflammatory agent. The molecule has many potent therapeutic activities like antioxidant, anti-inflammatory, anticancer, anti-diabetic, antibacterial, wound healing, antiviral and antifungal, hepatoprotective, neuroprotective.[15]

Side Effects

Curcumin has a long established safety record. For example, according to JECFA (The Joint United Nations and World Health Organization Expert Committee on Food Additives) and EFSA (European Food Safety Authority) reports, the Allowable Daily Intake (ADI) value of curcumin is 0–3 mg/kg body weight. Several trials on healthy subjects have supported the safety and efficacy of curcumin. Despite this well-established safety, some negative side effects have been reported. Seven subjects receiving 500–12,000 mg in a dose response study and followed for 72 h experienced diarrhoea, headache, rash, and yellow stool. In another study, some subjects receiving 0.45 to 3.6 g/day curcumin for one to four months reported nausea and diarrhea and an increase in serum alkaline phosphatase and lactate dehydrogenase contents.[16]

Preparation Steps

Step 1: Extraction of Curcumin

- **Turmeric Powder**: Start with high-quality turmeric powder.
- **Solvent Extraction**: Use ethanol or another suitable solvent to extract curcumin from turmeric.
  - Mix turmeric powder with the solvent.
  - Stir and let it sit for a few hours.
  - Filter to obtain the curcumin-rich extract.[17]

Step 2: Formulation

- **Oil Phase**: Heat the carrier oil gently and add the emulsifier (if making a cream).
- **Water Phase**: Heat water (if applicable) and mix in any soluble additives.
- **Combine Phases**: Slowly add the water phase to the oil phase while stirring continuously to form an emulsion.
- **Incorporate Curcumin**: Add the extracted curcumin to the mixture, ensuring it is well dispersed. Using a high-shear mixer can help achieve a uniform blend.[17]

Step 3: Cooling and Thickening

- Allow the mixture to cool.
- If needed, add thickeners gradually to achieve the desired consistency.

Step 4: Incorporating Additives

- Add any essential oils, preservatives, or additional beneficial ingredients once the mixture has cooled to prevent degradation of volatile compounds. Curcumin, a bioactive compound found in turmeric, has gained attention for its anti-inflammatory and

antioxidant properties. When formulating a topical preparation, several factors should be considered, including solubility, stability, and absorption through the skin.[17] Here's a basic overview of potential formulations:

1. **Creams and Lotions**

- **Base:** Emulsifying agents (e.g., cetyl alcohol, stearyl alcohol) mixed with water and oil phases.
- **Curcumin Incorporation:** Disperse curcumin in a small amount of a suitable solvent (like ethanol or propylene glycol) before adding it to the oil phase.
- **Additives:** Consider including ingredients like aloe vera or vitamin E for added benefits.[19]

2. **Gels**

- **Base:** Use a gel-forming agent like carbomer or hyaluronic acid.
- **Curcumin Incorporation:** Dissolve curcumin in a small volume of alcohol or another suitable solvent before mixing it into the gel.
- **Preservatives:** Ensure stability with suitable preservatives.[17]

3. **Ointments**

- **Base:** Use a hydrocarbon base (e.g., petroleum jelly) or a mixture of waxes and oils.
- **Curcumin Incorporation:** Heat the base gently to dissolve curcumin before allowing it to cool.
- **Texture:** Adjust the texture with emulsifying wax or other thickening agents.[20,21]

4. **Transdermal Patches**

- **Matrix System:** Incorporate curcumin into a polymer matrix (like ethylene-vinyl acetate).
- **Release Modifiers:** Use materials that control the release of curcumin, enhancing penetration.
- **Adhesives:** Ensure the formulation adheres well to the skin.
- **Stability:** Curcumin is sensitive to light and heat; use opaque containers and store in cool conditions.
- **Bioavailability:** Use techniques like nanoemulsion or liposomes to enhance skin absorption.
- **PH:** Maintain a skin-friendly pH (around 5-6) for optimal stability and skin compatibility.[16]

Formulation Example: Curcumin Gel

1. **INGREDIENTS**
   - Curcumin: 1-5%
   - Carbomer: 0.5-2%
   - Triethanolamine: to adjust pH
   - Distilled water: q.s. (quantity sufficient to 100%)
   - Preservative: as needed
2. **METHOD**
   - Disperse carbomer in water and hydrate.
   - Dissolve curcumin in a small volume of ethanol and mix.
   - Combine both phases, adjust pH with triethanolamine, and add preservatives.[20,21]

CONCLUSIONS

Curcumin has received worldwide attention for its multiple health benefits, which appear to act primarily through its anti-oxidant and anti-inflammatory mechanisms. These benefits are best achieved when curcumin is combined with agents such as piperine, which increase its bioavailability significantly. Research suggests that curcumin can help in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia. It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing recovery and subsequent performance in active people. In addition, a relatively low dose can provide health benefits for people that do not have diagnosed health conditions. Recent research has provided the scientific basis for "traditional" curcumin and confirmed the important role of curcumin in the prevention and treatment of diabetes and its associated disorders. Further, multiple approaches are also needed to overcome limited solubility and poor bioavailability of curcumin. These include synthesis of curcuminoids and development of novel formulations of curcumin, such as nanoparticles, liposomal encapsulation, emulsions, and sustained released tablets.

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