REVIEW ARTICLE

Beyond Curry: Turmeric's Formulation Journey in Pharmaceutical Sciences

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Abstract

Turmeric, one of the most effective herbal remedies, belongs to the *Zingiberaceae* family. Most of the studies have shown that *curcumin* is the main cause of the majority of the positive effects of turmeric. It is good for a number of things and has antioxidant qualities helpful for diseases, such as leukemia, diabetes, allergy symptoms, arthritic conditions Alzheimer's illness, and other persistent, hard-to-treat conditions illnesses are all examples. This review's objective was to offer a succinct summary of the most recent information on *curcumin*'s effects. In international journals, such as PubMed/Medline, Science Citation Index, and Google Scholar, they searched for recent literature concerning turmeric. Turmeric's usefulness in treating a variety of illnesses, especially those brought on by oxidative stress, such as cancer, diabetes, and inflammatory conditions, has been supported by recent studies. It also contains anti-HIV, anticoagulant, and hepatoprotective properties. The spice *curcumin* shows considerable potential as a medicine. It is remarkably non-toxic as well. The creation of modern pharmaceuticals based on *curcumin* should be addressed for the treatment of many diseases since the global landscape is evolving toward the use of non-toxic plant products with traditional medicinal properties. To do so, further study on turmeric is needed to investigate uncharted areas and their real-world therapeutic applications that may be used for the benefit of humanity, phroprotective qualities that aid in the battle against AIDS. Curcuma longa is the scientific name for turmeric. It has protective, renal, and antimicrobial benefits.

Key words: Formulations of turmeric, *in-vivo* effects, pharmacology, phytochemistry, treatment outcomes

INTRODUCTION

Since the birth of civilization, medicinal plants have been a dependable source for creating new medications and treating illnesses. An exhaustive review of the literature indicated that the plant turmeric, curcuma longa L. (*Zingiberaceae* family), is frequently used in herbal medicine and is thought to have a variety of pharmacological activities. Around the world, tropical and subtropical regions support the growth of turmeric. It is extensively cultivated in Asian nations, namely, China. The plant, which is native to China and India, has a short stem and can grow as tall as one meter. The oldest known medical practice known to man is the use of herbs as medicine, and it has been practiced throughout history in all societies.[1] Due to its advantageous qualities in Asian nations, such as India, Bangladesh, and Pakistan, in addition to being used as a spice, free radicals, to which we are continuously exposed in contemporary life, have the potential to harm any cell in the body that they come into touch with and have dangerous consequences.[2] Turmeric (Zarchooveh in Iran) is the name given to it. Ongoing use for its medicinal and taste qualities.[3] For example, diabetic wounds, rheumatism, inflammation, gastrointestinal, cough, coryza, anorexia, and sinusitis disorders are all claimed to be treated by traditional medicine's powder. Due to their great efficacy, high specificity, and low toxicity profiles, biopharmaceuticals are at the top of the pharmaceutical industry.[4]

CHEMICAL COMPOSITIONS OF TURMERIC

Curcumin I (60%) makes up the majority of the coloring matter, with smaller levels of *curcumin* III, *curcumin* II, and

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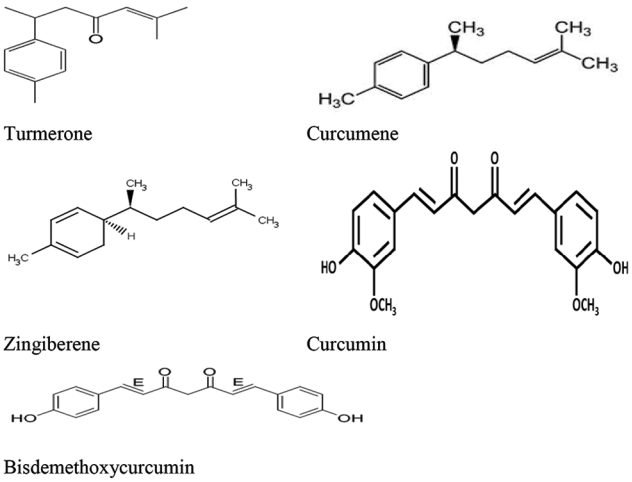
dihydro*curcumin*. The volatile oil also contains mono- and sesquiterpenes such as zingiberene (25%), -phellandrene, sabinene, turmerone, ar-turmerone, borneol, and cineole.



- Turmeric contains 5% volatile.
- Turmeric contains resin.
- Abundant Zingiberaceous granules of starch
- Curcuiminoids are yellow coloring compounds.
- *Curcumin* is the primary component of *Curcumin*oids.

PHARMACOLOGY OF TURMERIC

There are a number of medicinal and pharmacologic uses for turmeric. The following are turmeric's most significant medicinal and phytopharmacological qualities.

Antioxidant activity

It has been demonstrated that *curcumin* works well to scavenge oxygen-free radicals. It has antioxidants that resemble Vitamins C and E. Hemoglobin or lipids may be shielded from oxidation by it. Reactive oxygen species (ROS) generation, which includes the nitrite radical, can be considerably reduced. Superoxide anions and H_2O_2 are produced by active macrophages. Demethoxy*curcumin* and bisdemethoxy*curcumin*, two of its constituents, are antioxidants as well.[4] Every single type of cell in the human body has the potential to change malignantly and become cancer of that particular cell type; some cancers are more common than others.[5] Better cellular, protein, and medicinal molecule adhesion is the result of nanofibers' high surface area to volume quotient and, as a result, increased surface energy when compared to bulk materials.[6]

Effects on the heart and prevention of diabetes

Specifically, turmeric protects the heart through platelet aggregation, decreasing lipid peroxidation, anti-diabetic action, as well as antioxidant activities. In a study with 18 atherosclerotic rabbits, turmeric extract was given orally at doses ranging from 1.6 to 3.2 mg/kg/day. This resulted in lower plasma levels of cholesterol and triglycerides as well as decreased susceptibility of LDL to lipid peroxidation. The cholesterol-lowering effects of turmeric may be brought on by enhanced liver activity and decreased intestinal absorption of cholesterol. Turmeric components may reduce platelet aggregation by increasing prostacyclin synthesis and reducing thromboxane production. In diabetic rats, blood glucose levels are lowered by both turmeric and ginger. In addition, turmeric reduces diabetes complications. More clinical research in this area is needed to discover the optimal dosages for cardiovascular protection and cholesterol or glucose-reducing activities.[7]

Inflammation and edematous conditions

An intraperitoneal injection of 4 mg of total turmeric extract was used in a comparative study to assess the systemic absorption and therapeutic benefits of oral treatment. In an animal study where, rheumatoid arthritis was produced by a streptococcal cell wall, *curcumin*oids/kg/day for 4 days before the introduction of arthritis decreased joint inflammation in both the acute (75%) and chronic (68%) phases. Rats were given four days before the onset of arthritis and a 30-fold greater dose of the *curcuminoid* formulation was administered. When 4 mg of total turmeric extract (TTE) is injected intraperitoneally, the extract is administered straight into the peritoneal cavity, which is the region of the abdomen that contains different organs. This quantity decreased the inflammation in joints by 48%.

Antimicrobial activity

Numerous pathogenic fungus, bacteria, and parasites have been proven to be inhibited by turmeric's antimicrobial properties. In chicks with Eimeria maxima infection, a study demonstrated that meals with 1% turmeric reduced intestinal lesions while increasing weight gain.[8] Another animal study discovered that using turmeric oil topically to guinea pigs for 7 days after treatment inhibited the growth of dangerous fungus and dermatophytes.[9] The effectiveness of *curcumin* against Plasmodium falciparum and Leishmania major organisms has also been demonstrated.[10]

NUTRITIONAL COMPONENT

Turmeric contains a lot of fiber and carbohydrates. In addition, despite having certain proteins and lipids, it is free of cholesterol. It is one of the nutritionally dense foods since it also provides adequate levels of pyridoxine, Vitamin C, potassium, calcium, magnesium, and phosphorus organic food.[11]

MOLECULAR CONSTITUENTS

Each of the various molecular components of turmeric has different biological properties. One example is that there are at least 20 antimicrobial compounds and 14 of its components have been shown to have cancer-preventive characteristics. Furthermore, 12 of its molecules are anticancer, while the remaining 12 are anti-inflammatory. At least, 10 of its molecular components are also antioxidants. Figure 2. provides the medicinal effects along with the important mechanisms of turmeric. Nuclear factor-B (NF-B) and STAT3 (signal transducer and activator of transcription) nuclear factor of activated T-cells are known as NFAT, and nuclear factor erythroid 2-related factor 2 is known as Nrf2.mutation with sensitivity to heat with Z filaments; glutathione; nitric oxide synthase; and GSH: angiotensin-converting enzyme.

MEDICINAL USES OF TURMERIC

1. Anti-cancer effects
2. Natural anti-inflammatory
3. Powerful antioxidant
4. Prevents heart diseases
5. Treat or prevent's diabetes

Turmeric antibacterial properties and acne

Acne is largely caused by Propionibacterium acnes, the most common bacteria on human skin. When treating severe acne, azelaic acid is often used with antibiotics such as clindamycin and erythromycin. Researchers do, however, continue to investigate new antimicrobial drugs as antibiotic resistance increases.

Turmeric anti-inflammatory properties and acne

According to a 2017 article from Trusted Source, "According to research, *curcumin* may help treat inflammatory and oxidative diseases." Several preliminary studies have shown that the *curcumin* in turmeric may reduce inflammation in humans. There have not been any significant clinical investigations on turmeric's capacity to treat or prevent acne, although some evidence suggests that its anti-inflammatory characteristics may possibly be helpful in this condition.

FORMULATIONS OF TURMERIC

Curcumin has been subjected to a number of chemical changes, such as the use of liposomes, nanoparticles, micelles, phospholipid complexes, polymers, and adjuvants, in an effort to increase its solubility, bioavailability, targeted administration, and ADME profiles.[12–27] Among the many CUR formulations and delivery methods described in the literature,[28] liposomes, lipid-based nanoparticles, polymeric nanoparticles, micelles, microemulsions, and metal-based nanoparticles are only a few examples. Image of turmeric mentioned in figure 1

One of the several *curcumin* formulations is the phytosomal formulation of *curcumin* (Meriva), which is a mixture of *curcumin* and phosphatidylcholine.[28-57] Phospholipids are added to a hydroalcoholic extract of turmeric rhizomes under reflux conditions to create Meriva.[21] Compared to incomplete *curcumin*, Meriva has superior pharmacokinetic and bioavailability characteristics.[21] Numerous research have been carried out to determine whether phytosomal *curcumin* is effective at treating conditions, such as cancer, inflammatory disorders, and diabetes.[58] The findings refer to the higher dispersion capacities of the phytosomal *curcumin* formulation. Formulation of Turmeric and its uses are mentioned in Table 1.[28,29]

USE OF TURMERIC IN DAY-TO-DAY LIFE

It can heal wounds

Turmeric's *curcumin* can hasten wound healing by lowering oxidation and inflammation. Furthermore, it slows your body's response to cutaneous wounds. As a result, your wounds will recover faster. Turmeric has been found in research to be good for collagen and tissue. The journal Life Sciences recommends using *curcumin* as part of an ideal formulation to treat skin lesions.

It may be beneficial to your psoriasis

Turmeric's anti-inflammatory and antioxidant characteristics may help your psoriasis by lowering flare-ups and other symptoms. According to the National Psoriasis Foundation, it can be taken orally or as a supplement. Before attempting it, the organization recommends seeing a specialist about the appropriate dosage.

It might lessen acne scars

Try using a face mask with turmeric if you want to lessen acne and any scars that may follow. The skin can be relaxed and your pores can be targeted by the anti-inflammatory effects. Scarring may also be lessened with turmeric. If you have acne on your face, this combination of products may help.

It has been connected to scabies treatment

A mixture of turmeric and neem, an Indian herb, was successful in treating scabies in an early trial. Tiny mites are the cause of the skin rash-producing condition known as scabies.

Figure 1: Turmeric

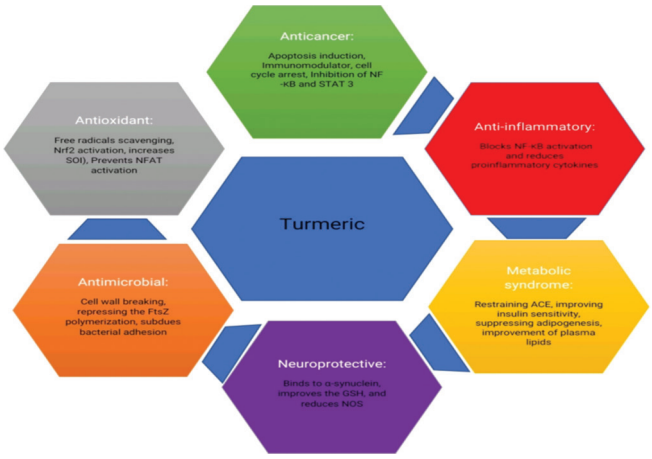


Figure 2: Pharmacological properties of turmeric

It may be beneficial for a variety of other dermatological disorders

Studies on turmeric's potential to treat various skin problems are insufficient to draw firm conclusions. However, eczema, alopecia, lichen planus, and other skin conditions may benefit from its use.

A study published in Phytotherapy Research suggests more investigation into turmeric's impact on various skin diseases. The study of turmeric as a skin care product remedy is gaining popularity.

Risk of using turmeric for your skin

Using turmeric presents a number of risks. When using turmeric, you need to use caution, being mindful of the type of substance you consume, the quantity, and any possible conflicts with other prescriptions you may be taking. Turmeric has a limited bioavailability. This shows that your metabolism quickly burns it off and that your body does not absorbs much of it.

Table 1: Formulation of turmeric and its uses

Formulation of turmeric	Uses
Nishamalaki (combination formulation of turmeric of Indian gooseberry)	Used in the treatment of Madhumeha (diabetes mellitus)
Gynoveda Haidro Khanda (powder/churn)	It is used in treatment of skin allergies, itching
Amrut Turmeric *curcumin* complex plus (tablets)	Helps with joint problem, relieves pain, has anti-inflammation and antioxidant properties
Organic India Turmeric formulation (tablets)	It protects the body against the ravages of inflammation
Himalaya Turmeric 95TM with *curcumin* (capsules)	It promotes the circulations and immune activity around joints and muscles to support flexibility and movement
Shridhenu high *curcumin* Haldi tablets	Anti-inflammation and anti-oxidant
Zeroharm Holistic *curcumin* NCM-100	Used in cancer, aging, arthritis and inflammation
Patanjali *curcumin* Gold 95 (tablet)	Used in joint pain management, antiseptic, helps to purify blood

CRITICAL ANALYSIS OF THE *IN VIVO* EFFECTS OF NON-CURCUMENOIDS

Numerous research supports the effectiveness of non-curcuminoids. According to a recent study, turmeric extract as a whole is superior to curcuminoids alone. According to these clinical investigations, curcumin is also particularly effective in treating a variety of cancers, including pancreatic, colorectal, breast, head, and neck.[59] There have even been published clinical experiments, some of which are still continuing, investigating the safety and therapeutic effectiveness of curcumin-free molecules.[60] Among these is β-elemene, a green drug derived from C. longa that is currently the subject of extensive research and is recognized as the most advantageous compound for medical use by the State Pharmacy of China and the Ministry of Health of the People's Republic of China. Its main application is against various cancers, such as esophageal squamous cell carcinoma, liver, brain, and non-small-cell lung cancer (NSCLC).[61] β-elemene used in combination was shown safe and effective in previous studies by means of controlled and randomized clinical trials. In these studies, about 1467 patients were split into two groups to research small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). Compared to patients receiving medicine without β-elemene injection, patients treated with β-elemene injection as an additional treatment for lung cancer showed accelerated improvements in survival and tumor response rate with minimal adverse effects.[62] A second, successful

study had 102 patients with esophageal squamous cell carcinoma who had surgery after receiving chemotherapy and radiation treatment. The standard chemotherapy treatment for esophageal squamous cell carcinoma resulted in a recurrence rate of around 60%, hence lowering the overall survival rate. As a result, this clinical study with β-elemene treatment reduced the amount of toxicity associated with synchronous chemoradiotherapy with cisplatin and 5-fluorouracil regimen and raised the survival (overall and progression-free) rate. If non-curcuminoids are encapsulated in distinct vesicles to assist target delivery, the effectiveness issues with several ongoing clinical trials – which stem from the absence of promised distribution at specified tissue sites – can be resolved. Phase solubility tests showed that the solubility of turmeric oleoresin was enhanced when it was combined with β-cyclodextrin through co-precipitation or kneading process. The inclusion complexes formed by this combination mostly included ar-turmerone and 1,8 cineole. These complexes have the ability to greatly enhance the biological activities of non-curcuminoids. Thus, a great deal of research has been done to enhance the real qualities of non-curcuminoids, particularly their solubility, bioavailability, and stability. This emphasis on developing such formulations may lead to significant advancements in clinical trials. Taking the lead, our research team at Aurea Biolabs developed a brand-new method called PNS technology, which uses a whole natural turmeric matrix made up of curcuminoids, essential oils, and water extract. A number of clinical studies were also carried out to demonstrate the matrix's effectiveness in delivering the most bioavailable form of curcumin to the intended location. A comparative investigation was carried out using two different formulations of curcumin in an open-labeled parallel arm design. In this trial, 45 male candidates in good health were given an oral 500 mg dosage as a single dose. This comparison analysis demonstrated the significant improvement in solubility and bioavailability that this formulation offers over the other two formulations. A pilot crossover research involving 12 healthy adult male participants was conducted to see whether the formulation's stated high bioavailability could be verified. The blood samples were examined for curcumin levels. The concentration maximum (Cmax) and area under the curve (AUC) measurements showed a tenfold improvement in bioavailability compared to curcumin (95% purity), which was indicative of encouraging results.[63] To support the licensing of non-curcuminoid drug delivery formulations for human use, large-scale experiments demonstrating their efficacy should be carried out.[64]

BIOLOGICAL ACTIVITIES OF NON-CURCUMENOIDS IN DIFFERENT DRUG DELIVERY FORMULATIONS

Research has demonstrated that non-curcuminoids have a primary implied potential to suppress cancer; yet, limited bioavailability and poor solubility in water have always been a significant cause for worry. To overcome these drawbacks and enable target delivery, researchers over the past few decades have been working on developing new delivery systems.

Cocrystals

Cocrystals are homogeneous crystalline formulations made up of two or more compounds joined by non-covalent and non-ionic bonds, such as hydrogen bonds, where one of the active moieties has a specific stoichiometric crystal structure. The physicochemical characteristics of these cocrystals can be advantageously altered, leading to an increase in hygroscopicity, solubility, dissolution, and stability. In addition, this formulation makes combination therapy – drug-herb, drug-drug, and herb-herb – possible. These combinations reduce side effects and increase patient compliance. There have been several attempts to successfully cocrystallize the component in turmeric and curcumin. A variety of benezenetriol and benezenediol coformers were used, including pyrogallol and resorcinol. These coformers successfully formed an O-H---O hydrogen bond between the hydroxyl phenol group and the keto functional groups of curcumin, enhancing the physicochemical properties of curcumin. Several techniques have also been established up to this point, namely, the formation of pure phase crystals containing curcumin by fast solvent evaporation. Furthermore, it was shown that curcumin significantly improved in terms of hygroscopicity, stability, and dissolution when compared to individual coformers.[65]

Solid lipid nanoparticles

Solid colloidal particles, known as solid lipid nanoparticles, are where medications or active substances are dissolved and entrapped. Studies revealed that β-elemene, produced in a solid lipid nanoparticulate (SLN) system using a variety of techniques, such as sonication, film ultrasonic wave, and extrusion, obtained a number of advantages: a sustained release pattern by strengthening the defenses against chemical degradation of labile compounds, and an increase in the drug's availability and efficacy. A comparative study between regular SLN and folate receptor-targeted SLN encapsulated β-elemene and turmeric oil was conducted.[66] The findings indicated that the latter circulates in the blood and various tissues for an extended duration, ultimately reaching a greater concentration. Therefore, it may be advantageous to increase the anticancer properties of solid lipid nanoparticles encapsulated in non-curcuminoid materials.

Nanocapsules

A non-toxic polymeric membrane forms the nanoscale shell of a nanocapsule, enclosing a liquid core inside. For

the encapsulation of ar-turmerone, Natrajan et al. created chitosan-alginate nanocarriers, which produced a clear supernatant and demonstrated their hemocompatibility using a hemolysis experiment. The carrier's high cell survival % suggests that it has a nanoscale shell and is harmless. In addition, using the MTT test, it was discovered that turmeric oil-loaded nanocapsules had antiproliferative action on A549 cell lines.[67] This implies that nanocapsules filled with non-curcuminoid agents might potentially enhance their anticancer effects.

CONCLUSION

The root of the turmeric plant, which contains a multitude of phytochemicals, vitamins, and minerals, is the most commonly utilized component of the plant in cooking and medicinal. Turmeric appears to be a generally secure medicinal plant. Its use in patients with hepatic and renal failure, as well as during pregnancy and breastfeeding, should be carefully considered. Turmeric is extracted to make a variety of goods. More investigation and experimental investigations are required for a better comprehension and well-informed assessment of its uses in therapeutic settings. In addition, creating contemporary models with relation to medicine administration methods and the bioavailability of its ingredients and evaluating their effectiveness are advised.

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