
A Review: Development and Analysis of Curcumin-Based Herbal Tablets for Anticancer Application

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Abstract

This thesis looks at curcumin's ability to prevent breast cancer and makes a strong argument for its usefulness in this regard. Phytochemical examination of the selected plant indicates the presence of flavonoids, which have great antioxidant activity and are also known to be helpful in treating cancer. The effects of curcumin and its analogous compounds, including isoeugenol, eugenol orthodimer on cell toxicity. The ability to produce reactive oxygen species and the ability to scavenge radicals, were investigated. The characteristics of curcumin, a yellow pigment found in the rhizome of the Curcuma longa plant, are covered in this article. The review examines various formulation strategies, including the selection of excipients, methods of tablet preparation, and optimization techniques to enhance the bioavailability of curcumin. In vitro and in vivo research that evaluate the anticancer effectiveness of curcumin tablets against different cancer cell lines and animal models are also covered. Curcumin's involvement in preventing tumor growth, triggering apoptosis, and regulating inflammatory pathways is highlighted by an evaluation of its pharmacokinetics, safety profile, and mechanisms of action. According to the results, curcumin herbal tablets show promise as an adjuvant therapy for cancer treatment; nevertheless, more clinical research is required to develop standardized formulations and dosing schedules.

Keywords - Curcumin, Antioxidant, Anti-inflammatory, Curcuma Longa, ROS (reactive oxygen species), Anticancer, Herbal tablet, Phytochemical, Bioavailability, Dosage form, Pharmacodynamic.

INTRODUCTION

Curcumin, the primary component of turmeric, is extracted from the roots of the East Indian plant Curcuma longa. Curcuma longa is a perennial plant that is native to Southeast Asia and belongs to the Zingiberaceae family, which also includes gingers. Turmeric contains substances known as curcuminoids, which include curcumin, bisdemethoxy, and desmethoxy. One About 2–5% of turmeric is made up of the main curcuminoid, which is largely responsible for the spice's distinctive yellow hue and many of its medicinal properties. Ayurvedic medicine has traditionally used turmeric due to its well-known anti-inflammatory, anti-microbial, analgesic, and antioxidant qualities. These benefits extend beyond its use as a food enhancer and colorant. Since ancient times, curcumin has been used as a nutritional supplement.^[1]

Anti-cancer plants

Natural items, particularly plants, have long been used for medicinal purposes in many different cultures and civilizations. Many societies, including ancient Greece, Egypt, China, and India, have

utilized terrestrial plants as remedies for thousands of years. Many modern drugs are derived from plant-based compounds.⁴ (5) People have been employing plants for medical purposes since approximately 2600 BC. The use of herbal treatments in Ayurvedic medicine has a long history in India. Around 1000 BC, literature from the Susruta and Charaka eras describe the formulations and principles of Ayurveda. The significant contributions of the ancient Greeks have had a significant impact on herbal medicine.^[2]

Description

Plants in the *Curcuma longa* species synthesize curcumin, a vivid yellow chemical. This material is sold as a food coloring, food enhancer, herbal supplement, and cosmetic ingredient.

These are the phenolic pigments that give turmeric its distinctive yellow color. Despite its many uses, curcumin has not been shown to have any medicinal value in either clinical or laboratory study. The compound's intrinsic instability and low bioavailability make it difficult to research. It is therefore unlikely to produce insightful information for drug development.^[3]

SAR of Curcumin

The SAR is refers to the correlation between the chemical structure of these compounds and their biological activities. In the case of curcumin and its various derivatives, researchers study how specific modifications to the molecular structure affect their efficacy, potency, and interactions with biological targets.^[4]

Some key points in the SAR of curcumin and its derivatives include

Functional Groups

Modifications or substitutions of functional groups in curcumin's structure can lead to changes in its activity. For instance, altering the phenolic groups may affect antioxidant or anti-inflammatory properties.

Substituents

Adding or changing substituents on the curcumin molecule can influence its bioactivity. Different substitutions can enhance solubility, stability, and binding to target proteins.^[5]

Conjugation and Ring Modifications

Changing the conjugation pattern or modifying the aromatic rings can impact biological activity. These alterations might affect the compound's ability to interact with enzymes, receptors, or other biomolecules.

Stereochemistry

Isomeric forms of curcumin may have varying effects due to differences in spatial arrangement. Stereochemistry can influence how a molecule interacts with enzymes or receptors.^[6]

Bioavailability Enhancements

Many studies focus on modifying curcumin's structure to improve its bioavailability, as the native form has limited absorption. Derivatives might include delivery systems, nanoparticles, or prodrugs.^[7]

Target Specificity

Structural modifications can lead to derivatives with improved selectivity for specific molecular targets, potentially reducing off-target effects.^[8]

Toxicity and Safety

Altering the structure of curcumin can impact its toxicity profile. Some modifications might enhance safety or reduce potential adverse effects.^[9]

Pharmacokinetics

Changes in the structure can influence the compound's absorption, distribution, metabolism, and excretion, affecting its overall pharmacokinetic profile.^[10]

Synergistic Effects

Combining curcumin derivatives with other compounds might lead to synergistic effects, enhancing therapeutic outcomes.¹⁹ Research in this field aims to optimize curcumin derivatives for various applications, such as drug development, nutraceuticals, and medical treatments.^[11]

Uses

Curcumin, a natural antioxidant, possesses anti-inflammatory properties.

For patients with osteoarthritis, curcumin is a safe and effective long-term treatment option.

Curcumin has shown beneficial effects on multiple factors related to heart disease, exhibiting anti-inflammatory, antioxidant, and anti-thrombotic qualities.

Joint inflammation is a common characteristic of arthritis, and curcumin may be effective in alleviating its symptoms.

Turmeric is commonly used in cosmetics, dietary supplements, as a flavoring in food, and as a coloring agent in various South and Southeast Asian beverages.

The active ingredient in turmeric is often added to foods to give them an orange-yellow hue.^[12]

General information and History

It is a major global health concern and the second most common cause of death. In 2018, there were over 609,000 cancer-related fatalities and around 1.73 million new cases reported in the US. The last three decades have seen a steady incidence and fatality rate despite improvements in treatment. Despite advancements in treatment, the incidence and mortality rates have remained stable over the last three decades. Curcumin, a natural compound, exhibits anticancer properties mainly through two mechanisms: promoting cell death (apoptosis) and inhibiting tumor growth and spread by blocking various cellular signaling pathways.

Research has indicated that curcumin may be effective against a variety of cancers, including brain tumors, prostate cancer, head and neck squamous cell carcinoma, lung cancer, and breast cancer. Its efficacy is constrained, though. Originating from the subterranean stem of the East Indian plant *Curcuma longa* L., also known as turmeric, curcumin is a member of the diarylheptanoid group called curcuminoids. This curcuminoid complex also includes desmethoxycurcumin, bisdemethoxycurcumin, and cyclocurcumin. The dried plant material is commonly used in curry spices, which often contain various other ingredients. Additionally, turmeric and its derivatives have been used for many years as dietary supplements and herbal remedies, particularly for inflammation. While many studies focus on the biological effects of curcumin, some also investigate the underlying chemistry that contributes to its unique properties.²¹ Numerous companies market curcumin as a nutritional supplement, although in the United States, dietary supplements are regulated as foods rather than as pharmaceuticals.^[13]

Activity of Anti-cancer Effect

Human cancers such as melanoma, head and neck, breast, colon, pancreatic, prostate, and ovarian cancers have all been examined in relation to curcumin. According to epidemiological study, curcumin-rich foods' chemopreventive and antioxidant qualities may be responsible for India's low incidence of colon cancer. Curcumin's anticancer actions are multifaceted, impacting apoptosis and cellular development at several regulatory levels. It affects the development, growth, and spread of tumors as well as the early DNA abnormalities that lead to carcinogenesis. In addition to its direct effects on signaling proteins, oncogenes, and transcription factors, curcumin also affects when these carcinogenic processes occur. Given its diverse spectrum of effects on

cellular regulation, curcumin has potential as a chemotherapeutic treatment for a number of cancers.^[14]

Curcumin's effects on cancer

By preventing angiogenesis—the process by which new blood vessels are formed from preexisting ones—curcumin has been shown in numerous studies to possess potent anticancer effects. Endothelial cell activation, proliferation, invasion, and migration are some of the phases that make up angiogenesis. It has been demonstrated that curcumin inhibits several phases of this process, hence lowering angiogenesis in a variety of malignancies. Curcumin has also been shown to inhibit VEGF receptor signaling in vivo, which aids in halting lymphangiogenesis, the development of new lymphatic capillaries that are essential for the metastasis of cancer. Because cooking produces possibly carcinogenic or mutagenic

heterocyclic amines (HA), eating fried foods may increase the risk of gastrointestinal malignancies in Indian diets. According to one animal research, giving mice traditional Indian foods like deep-fried veggies increased their risk of developing stomach cancer by 20%. However, India has a moderate to low incidence of stomach cancer when compared to other nations. This is significant, as stomach tumors are often linked to the carcinogenic bacterium *Helicobacter pylori*. The widespread use of natural substances like turmeric may help explain their protective effects against cancer. The anticancer mechanisms of bioavailable curcumin are noteworthy, along with examples of tumors that have shown increased sensitivity to curcumin or its compounds.^[15]

Colon Cancer

Two phytochemicals, curcumin and luteolin, both present in foods, were examined in a study by Aromokeye and Si. They discovered that when combined, they had a stronger inhibitory effect on the growth of colon cancer. This study examined the molecular mechanisms underlying this anti-colon cancer effect. Lutein (LUT) at 30 μM (C15L30) and curcumin (Cur) at 15 μM together successfully inhibited the growth of human colon cancer CL-188 cells. This synergistic effect was also seen in DLD-1, another colon cancer cell line, proving that C15L30 works for a variety of colon cancer types. The combined treatment significantly decreased CL-188 cells' ability to heal wounds. Mice with tumors made from CL-188 cells continued to experience the synergistic effect because the combination.^[16]

Lung Cancer

Among the drawbacks of traditional chemotherapy for lung cancer include unfavorable side effects, irregular drug release, poor effectiveness, and the emergence of drug resistance. A unique absorption technique using modified nanoparticles (CBT) was created in order to overcome these difficulties. The goal of these carboxymethyl chitosan (CMCS)-based nanoparticles is to improve therapeutic efficacy and get around the problems associated with free medicines. By targeting the transferrin receptor (TfR) found on lung cancer cells, CMCS permits regulated medication release in response to pH and reactive oxygen species (ROS) levels. The study showed that curcumin and docetaxel (DTX) were effectively loaded into the nanoparticles, with corresponding drug-loading capabilities of 6.48% and 7.82%. Even at high concentrations of 500 $\mu\text{g/mL}$, these nanoparticles demonstrated good biosafety. Furthermore, CBT-DC helped to improve the immune-compromised.^[17]

Prostate Cancer

In the United States, prostate cancer is the most prevalent tumor kind. Particularly aggressive is its propensity to advance to a hormone-resistant stage. One of the most difficult aspects of treating prostate cancer (PC) is effectively halting tumor growth and halting the spread of other diseases. There have been encouraging advancements in the field of PC therapy due to a concentrated effort

in recent years to find novel chemicals. Nevertheless, resistance to several PC medications can culminate in metastatic castration-resistant prostate cancer (mCRPC), which is almost always fatal. Curcumin, a widely accessible dietary supplement, offers a compelling therapeutic option for those with mCRPC.^[18]

Pancreatic Cancer

One major issue in clinical practice is the increasing treatment resistance of pancreatic cancer. Because of its exceptionally high death rate, pancreatic cancer emphasizes the necessity for efficient treatment approaches. Sestrins are a class of stress-related proteins that function as antioxidants to control metabolism and cell division. Many studies have shown that turmeric, which contains the natural pigment curcumin, has a variety of pharmacological effects, such as anti-inflammatory, antioxidant, and perhaps anticancer qualities. Investigating the molecular processes underlying the combination anticancer effects of sestrin family members and curcumin on pancreatic cancer was the goal of the study.^[19]

Breast Cancer

The biggest killer of women, breast cancer, presents a serious problem. Recurrence rates are still high despite existing therapies such radiation therapy, chemotherapy, endocrine therapy, and lumpectomy, according to a meta-analysis of 21 retrospective studies. This demonstrates the continuous need for creative and successful therapy strategies. Curcumin therapy resulted in a concentration-dependent reduction in telomerase activity in a study including MCF10A normal mammary epithelial cells and MCF7 breast cancer cells. Although the c-Myc mRNA route was not involved, curcumin's downregulation of hTERT was linked to this impact. Another study examined curcumin's impact on cell cycle regulatory proteins, matrix metalloproteinases (MMPs), and NF- κ B using MDA-MB-231 and BT-483 breast cancer cell lines.^[20]

Pharmacological Effects of Curcumin

Antimicrobial and Antiviral Effects

Nanocurcumin, derived from *Penicillium notatum* and *Aspergillus niger*, showed significantly better aqueous dispersion compared to regular curcumin. By efficiently breaking down bacterial cell walls, nanocurcumin particles demonstrated a bactericidal effect, as demonstrated by transmission electron microscopy. Nanocurcumin had especially potent antibacterial activity. Curcumin demonstrated antibacterial activity by preventing the synthesis of matrix metalloproteinase-3 (MMP-3) and MMP-9 in mice infected with *Helicobacter pylori*. Curcumin also showed antifungal efficacy against 14 distinct strains of *Candida*. It blocked H⁺ extrusion from *Candida albicans* and *Candida glabrata*, severely decreased ergosterol levels in the fungal cell membrane, and decreased fungal cell release of proteinases.^[21]

Extraction of Curcumin from Turmeric

Turmeric's main bioactive ingredient, curcumin, has anti-inflammatory and antioxidant qualities. Extracting curcumin efficiently while preserving its integrity is essential for both research and commercial applications. Here's a comprehensive overview of the extraction techniques and their implications.^[22]

Extraction Techniques

Solvent Extraction:

Common Solvents

Ethanol, methanol, acetone, and water are frequently used. The choice of solvent affects yield and purity.^[23]

Process

Ground turmeric is mixed with the solvent and heated, allowing curcumin to dissolve. Afterward, the mixture is filtered to obtain the extract.^[24]

Enzyme-Assisted Extraction**Pretreatment with Enzymes**

Enzymes like cellulases can break down the plant matrix, enhancing curcumin release.

Benefits

This method can increase extraction efficiency and reduce the need for harsh solvents.^[25]

Ultrasonic Extraction**Ultrasound Waves**

Applying ultrasonic waves to the extraction mixture enhances solvent penetration and curcumin solubilization.^[26]

Efficiency

This method can significantly reduce extraction time and increase yield.

Microwave-Assisted Extraction**Microwave Energy**

Microwaves heat the solvent and turmeric mixture, accelerating the extraction process.^[27]

Outcome

Faster and often more efficient than conventional methods.

Steam Distillation**Process**

Involves passing steam through turmeric to vaporize volatile compounds, which are then condensed back to liquid.^[28]

Consideration

Primarily used for volatile oils but can also extract curcumin to some extent.

Detection and Quantification of Curcumin

Accurate detection and quantification of curcumin are vital for assessing quality and efficacy. Several analytical techniques are employed, each with its strengths.

Ultra-Performance Liquid Chromatography (UPLC)**Advancement over HPLC**

UPLC offers faster analysis times and higher sensitivity due to smaller particle sizes in the column.^[29]

Applications

Ideal for complex mixtures where resolution is crucial.

2. Mass Spectrometry (LC/MS)**Combination Technique**

Coupling HPLC with mass spectrometry allows for precise identification and quantification.^[30]

Benefits

Provides structural information and quantifies low concentrations effectively.

Capillary Electrophoresis**Separation Based on Charge**

Effective for separating curcumin based on its charge-to-size ratio.

Advantages

Requires less solvent and can analyze small sample volumes.^[31]

Fluorescence Detection

Sensitivity

Curcumin exhibits strong fluorescence when excited at 420 nm, making fluorescence detection highly sensitive for low concentrations.^[32]

Application

Particularly useful in biological samples where curcumin levels are often low.

Selection of the Plant

Curcuma longa was chosen for the analysis of its anticancer properties following a thorough review of existing literature and consultations with medical professionals, with guidance from Assistant Professor Mr. Bhupendra V. Madhavi.

Preparation of Crude Drug for Extraction

To prepare the extract, rhizomes and roots of *Curcuma longa* were selected. The plant material was dried in the shade to preserve its quality. After drying, the rhizomes and roots were mechanically crushed into a coarse powder. This powder was then sifted through a No. 16 mesh sieve, and the resulting fine powder was stored in an airtight container for further extraction.

Determination of Extractive Values

Soluble Extractive

To determine the soluble extractive values, 100 milliliters of various solvents—petroleum ether, ethanol, hydroalcohol, and distilled water—were utilized. Five grams of air-dried, coarsely ground medicinal material were macerated with these solvents for twenty hours in a safe flask. After this period, the mixture was allowed to sit undisturbed for an additional 15 hours following a 5-hour shaking process.

A shallow dish with a flat bottom was filled with 25 milliliters of the filtrate, which was then dried by evaporation. Following a 105°C heating process, the dried residue was weighed. The Ministry of Health and Family Welfare's recommendations were followed in calculating the percentage of soluble extractive by comparing this weight to that of the air-dried medicinal ingredient.^[33]

Process

An 80-mesh sieve was used to weigh, grind, and filter curcumin extract and other excipients.

All materials, except for talc and magnesium stearate, were combined and ground in a pestle and mortar, then sieved again through an 80-mesh sieve.

The extract was mixed with a starch/acacia solution, resulting in the formation of a lump.

This lump was screened through a sieve with an 18-mesh size to obtain granules, which were then dried in a Hoover dryer at 35°C.

Talc and granulated magnesium stearate were added to the dried granules.

The mixture was processed through an 18-mesh sieve again to remove larger granules before being placed in desiccators.

Finally, the granules were compressed using a tablet punching machine to achieve the desired shape and size.^[34]

Evaluation of Herbal Tablet

Uniformity of Weight

Twenty tablets from each formulation were selected randomly and weighed individually. To guarantee uniformity, the average weight of every tablet was determined and compared.

General Appearance

The overall appearance of the tablets was assessed, focusing on aspects such as color, odor, and texture.

Hardness Test

In order to guarantee that the tablets can endure mechanical strains while being handled, a certain degree of hardness is necessary. Using a Monsanto hardness tester, the hardness of 20 randomly chosen tablets from each formulation was assessed.

Percentage Friability Test

Using a Roche Friabilator, the friability of the tablets was assessed. Twenty randomly chosen tablets from each batch were dropped into the friability machine, which rotated at 25 revolutions per minute for four minutes. The weight loss from dust generation was then recorded, and the weight loss percentage was computed.

Disintegration Test

A digital microprocessor-based disintegration test apparatus (basket rack assembly, Lab India) was used to measure the tablets' disintegration time. A single tablet and its accompanying disk were placed into each tube, which was then immersed in a 1000 mL beaker of water. The wire mesh was kept at least 25 mm above and below the water's surface by adjusting the water level. The temperature was kept at 37°C throughout the test. Observations were made to ensure that all tablets disintegrated uniformly and passed through the wire mesh within the same time frame.^[35]

CONCLUSION

The formulation and evaluation of herbal tablets containing curcumin have shown promising results for potential anticancer activity. The tablets demonstrated compliance with established Pharmacopoeia standards, including consistent weight uniformity, adequate hardness, low friability, and a favorable dissolution time. These characteristics indicate that the tablets are stable and likely to ensure effective bioavailability. Curcumin, recognized for its significant anticancer properties, serves as a strong active ingredient in these formulations. This study not only supports the viability of curcumin-based herbal tablets but also sets the stage for future research into the isolation of other active compounds and the exploration of synergistic effects through polyherbal combinations.

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