

Pharmacological Review on *Curcuma longa*

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Abstract: Cancer is that the second leading reason for death within the world and one in every of the most important public health problems. Despite the good advances in cancer therapy, the incidence and mortality rates of cancer remain high. Therefore, the hunt for more efficient and fewer toxic cancer treatment strategies remains at the forefront of current research. Curcumin, the active ingredient of the herbaceous plant, has received great attention over the past twenty years as an antioxidant, anti-inflammatory, and anticancer agent. During this review, a summary of the medicinal chemistry and pharmacology of curcumin and its derivatives in relevancy anticancer activity, their main mechanisms of action, and cellular targets has been provided supported the literature data from the experimental and clinical evaluation of curcumin in neoplastic cell lines, animal models, and human subjects. Additionally, the recent advances within the drug delivery systems for curcumin delivery to cancer cells are highlighted. In this review also presents work is to formulate and evaluate the gel of Turmeric extract. The extracts was prepared by maceration method the medicinal property of haridra effectively and simply. The gel formulations was designed by using aqueous extract in varied concentration and also evaluated by various physicochemical parameter. The physicochemical parameter of the formulation are dole out by different parameter I, e PH, viscosity, spreadability, etc.

Keywords: Curcumin; anticancer; structure activity relationship; cellular pathway; mechanism of action; delivery system, Maceration

I. INTRODUCTION

- The use of turmeric dates back nearly 4000 years to the Vedic culture in India, where it had been used as a culinary spice and had some religious significance.
- It probably reached China by 700 ad, geographical area by 800 ad, geographical area by 1200 ad, and Jamaica within the eighteenth century.
- India being one in all the foremost producers of turmeric, contributes 80% to global production. Scientists still look at the heart-protective possibilities of turmeric.
- One small study found that turmeric can help push back heart attacks in folks that have had bypass surgery.(1)
- Major turmeric producing states in India are the southern states of province, province and Karnataka, the eastern states of Orissa and province, and therefore the western state of Maharashtra.
- September 2019 was reported as 48,119 hectares.

1.1 Benefits

- Turmeric Gradually Increases Antioxidants in our body
- Turmeric Might Prevent Cancer.
- Turmeric Helps Lower Cholesterol.
- Turmeric Can Help Prevent and Treat Alzheimer's disease.
- Turmeric Can Treat Skin Conditions.
- Turmeric Can Benefit People with Depression.

People who mustn't take turmeric include those with gallbladder problems, bleeding disorders, diabetes, oesophageal reflux disease (GERD), infertility, iron deficiency, disease, hormone-sensitive conditions and arrhythmia. Pregnant women and people who are visiting undergo surgery mustn't use turmeric. Drink Warm Turmeric Water Every Morning For 7 Days On Empty Stomach, this may Change Your Life Forever. This spice is great and has many health benefits for our bodies. It helps with cardiovascular health, inflammation, brain health, arthritis, liver protection, prevents aging, digestion, fighting cancer then on. It can cause nausea and diarrhea, especially in high doses or after long-term use. It may additionally pose a risk of ulcers in high doses. As a topical treatment, it can cause skin irritation. Caution is suggested when turmeric is taken by people known to possess gallstones; consult your health care provider first. It improves liver function. The antioxidant effect of turmeric appears to be so powerful that it's going to stop your liver from being damaged by toxins. This can be excellent news for those that take strong drugs for diabetes or other health conditions which may hurt their liver with long-term use.⁽²⁾ Turmeric has been traditionally used as an antiseptic, antibacterial, anti-inflammatory, choleric, and carminative agent within the treatment of wounds and burns, gastrointestinal and liver disorders, system diseases (e.g., asthma, cough, runny nose, sinusitis), anorexia, and rheumatism

II. PLANT PROFILE

The natural ingredients utilized in this study was collected I, turmeric. the small print of the fabric employed in the anti cancer are give below :



Biological Source

Its obtained from a rhizomatous perennial plant of *Curcuma longa* belonging to the Zingiberaceae. Synonyms : Indian Saffron; haldi ; Curcuma ; Rhizoma cur-cumae

Geographical Source

The plant could be a native to southern Asia and is cultivated extensively in temperate region. It is grown on a bigger scale in India, China, Malay Archipelago, and Malaya .

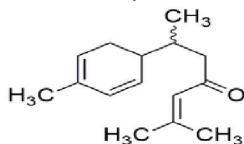
Cultivation

Pits are crammed with well decomposed cattle manure or compost, seed rhizomes are placed over it then covered with soil. The optimum spacing in furrows and ridges is 45-60 cm between the rows and 25 cm between the plants. A seed rate of two,500 kg of rhizomes is required for planting one hectare of turmeric. Turmeric plant could be a perennial herb 60 – 90 cm high with a brief stem and tufted leaves ; the rhizomes, which are short and thick, constitute the turmeric of commerce. The crop required a hot and moist climate, a liberal installation and a well drained soil. It thrives on any soil alluvial but the soil should be loose and friable. The field should be prepared by ploughing and turning over to a depth of about 30 cm and liberally measured with farmyard and green manures. The crop is prepared for harvesting in about 9-10 months when the lower leaves turn yellow. Harvesting. Depending upon the range, the crop becomes

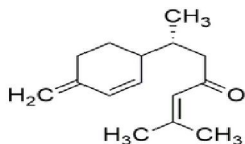
ready for harvest in 7-9 months after planting during January-March. Early varieties mature in 7-8 months, medium varieties in 8-9 months and late varieties after 9 months.

Chemical Constituents

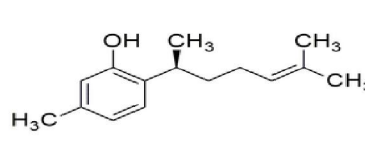
- Turmeric contains yellow colouring matter called as curcuminoids (5%) and essential oils (6%).
- The chief constituents of the colouring matter is curcumin I (60%) additionally with small quantities of curcumin III, Curcumin II and dihydrocurcumin.
- The volatile oils contain mono and sesquiterpenes like zinziberene (25%) alpha – phellandrene, sabinene, turmerone, borneol and cineole.



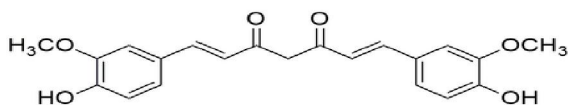
Turmerone



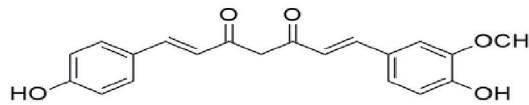
Curlone



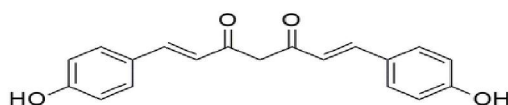
Curcuphenol



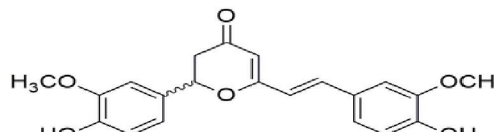
Curcumin (CUR)



Demethoxycurcumin (DMC)



Bisdemethoxycurcumin (BDMC)



Cyclocurcumin (CC)

Uses

1. In India, it had been traditionally used for disorders of the skin, upper tract, joints, and systemaalimentarium.
2. Today, turmeric is promoted as a dietary supplement for a range of conditions, including arthritis, digestive disorders, respiratory infections, allergies, disease, depression, and lots of others.
3. Turmeric is employed as an herbal medicine for autoimmune disease, chronic anterior uveitis, conjunctivitis, carcinoma, small pox, chicken pox, wound healing, tract infections, and liver ailments
4. Turmeric is often utilized in Thai curries and other savory dishes.
5. Yellow curries get their color from turmeric.
6. Thai yellow curry paste is created with turmeric and utilized in recipes for meat, seafood, vegetables, noodles, and soups.

Turmeric used as Anticancer Agent

Cancer

Cancer may be a disease within which a number of the body's cells grow uncontrollably and spread to other parts of body .A disease within which abnormal cells divide uncontrollably and destroy body tissue .

Treatment

Turmeric reduces inflammation, which is at the foundation of the many diseases, including cancer.

Animal and lab studies show that turmeric can help prevent cancer growth and kill certain cancer cells, but we do not know if it's the identical effect in humans. The main mechanisms of action by which curcumin exhibits its unique anticancer activity include inducing apoptosis and inhibiting proliferation and invasion of tumors by suppressing a spread of cellular signaling pathways. Several studies reported curcumin's antitumor activity on carcinoma, carcinoma,

head and neck epithelial cell carcinoma, prostatic adenocarcinoma, and brain tumors, showing its capability to focus on multiple neoplastic cell lines. In spite of all the above mentioned advantages, curcumin's applications are limited because of its low solubility which ends in poor oral bioavailability and also low chemical stability.

One of the most causes of cancer is that the loss of balance between cell proliferation and necrobiosis. When the cells skip death thanks to the absence of the apoptotic signals, uncontrolled cell proliferation occurs, resulting in differing types of cancer. Curcumin disturbs the balance within the mitochondrial membrane potential, resulting in enhanced suppression of the Bcl-xl. protein^[3]. The extrinsic apoptotic pathway works through increasing the death receptors (DRs) on cells and triggering the tumor necrosis factor (TNF)-related apoptosis. Curcumin also contributes to the present pathway by upregulating the expression of death receptors DR4 and DR5^[4-6].

In vitro studies showed a noteworthy ability of curcumin and its derivatives to induce apoptosis in numerous cell lines by inhibiting or downregulating intracellular transcription factors. These factors include NF- κ B, activator protein 1 (AP-1), cyclooxygenase II (COX-2), gas synthase, matrix metalloproteinase-9 (MMP-9), and STAT3. A recent work has found a replacement anticancer mechanism for curcumin by decreasing the glucose uptake and lactate production (Warburg effect) in cancer cells via downregulation of pyruvate kinase M2 (PKM2). The inhibition of PKM2 was achieved by suppressing the mammalian target of rapamycin-hypoxia-inducible factor 1 α (TOR-HIF1 α)^[7]. Several studies have investigated the flexibility of curcumin and its derivatives to suppress multiple different carcinomas by interacting with different molecular targets.

In Vitro and in Vivo Studies

Curcumin has shown very promising ends up in suppressing neoplastic cell growth and proliferation in several differing kinds of cancer, like prostate, colorectal, breast, pancreatic, brain, head, and neck cancers.

What comes next may be a summary of the anticancer activity of curcumin and its derivatives in several varieties of cancer supported the information from in vitro studies in several neoplastic cell lines and animal studies.

III. PHARMACOLOGICAL ACTIVITIES OF CURCUMIN

3.1 Prostate Cancer

Researchers have found that turmeric and its extract, curcumin, may help prevent or treat prostatic adenocarcinoma. The warm, bitter spice contains anticancerous properties that will stop the spread and growth of cancerous cells.^[8] If you're curious about using turmeric medicinally, see your doctor about it. They'll work with you to see whether this is often the simplest addition to your current regimen. Prostate cancer occurs when malignant cells form within the prostate. The prostate may be a small, walnut-sized gland between a man's bladder and rectum.^[9] About 1 in 5 Trusted Source American men are diagnosed with glandular carcinoma in his lifetime. Researchers have found that turmeric and its extract, curcumin, may help prevent or treat adenocarcinoma. The warm, bitter spice contains anticancerous properties that will stop the spread and growth of cancerous cells.^[10,11] If you're curious about using turmeric medicinally, sit down with your doctor about it. They can work with you to see whether this is often the simplest addition to your current regimen.^[12]

3.2 Colorectal Cancer

Colorectal cancer comes third behind prostatic adenocarcinoma and carcinoma because the commonest kind of malignant cancer^[15]. Although patients diagnosed with colorectal carcinoma undertake surgical removal of the tumor tissue together with chemotherapy, quite 1/2 the patients suffer from relapses^[16]. Administration of curcumin was found to cut back M (1) G levels within the malignant Colorectal cells without changing COX-2 protein levels.^[17] Additionally, curcumin treatment was able to down regulate miR-21 gene, which is over expressed in colorectal cancer cells, by inhibiting AP-1 (activator protein) binding to miR-21 promoter. Treating HCT 116 colorectal cancer cells with curcumin resulted in an exceedingly cell cycle arrest within the G2/M phase via miR-212 gene regulation and inhibited the tumor tissue growth. However, an in vivo study in mice with colorectal cancer demonstrated an improved response to irradiation when combined with curcumin thanks to its ability to focus on nuclear factor (NF- κ B)^[18]. Another study has managed to boost curcumin inhibition activity against carcinoma cells by combining it with ERRP, a pan-erb B inhibitor.^[19]

3.3 Head and Neck epithelial cell Carcinoma

Head and neck epithelial cell carcinoma (HNSCC) is that the sixth commonest sort of cancer worldwide, with over 30,000 diagnosed cases each year.^[20] HNSCC generally arises within the mouth, paranasal cavities, larynx, and pharynx. In vitro studies of curcumin in several head and neck neoplastic cell lines have proven its ability to inhibit cell growth because of its effects on variety of cellular pathways involved in cell proliferation, most notably NF-kB and STAT3, which are found to be overexpressed in several head and neck carcinomas^[21-22]. Curcumin was shown to downregulate NF-kB and inhibit the interleukin-6 (11-6)-mediated phosphorylation of STAT3, thus inhibiting the proliferation of the cancer cells^[22-23].

3.4 Breast Cancer

Breast cancer has shown an alarming record as a number one explanation for death in women^[24]. Despite lumpectomy, therapy, chemotherapy, and endocrine therapy, the recurrence rate of carcinoma has been reported to be still high supported a meta-analysis of 21 retrospective studies^[25]

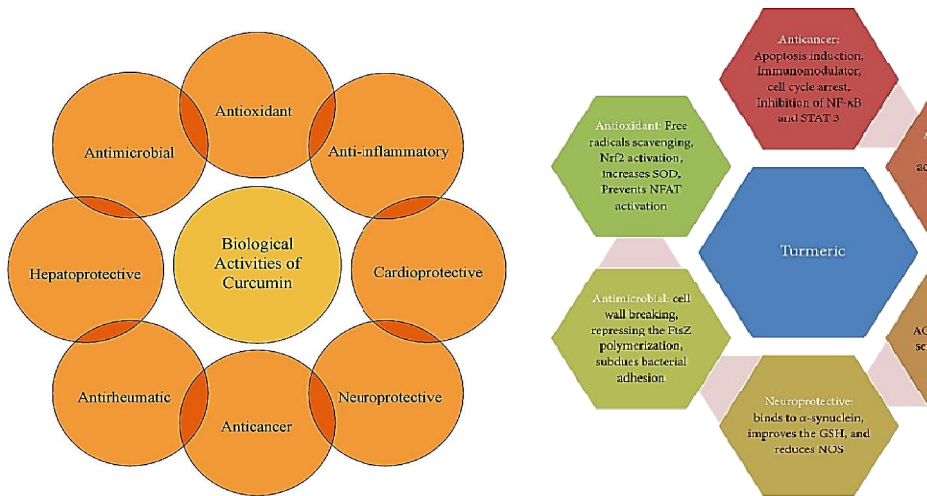
Therefore, there's still a requirement for more efficient therapeutic strategies. during a study on MCF-10A human mammary epithelial cells and MCF-7 carcinoma cells a tangible call telomerase activity was observed as a results of treatment with curcumin in an exceedingly concentration-dependent manner which was correlated to downregulation of hTERT by curcumin but not through the c-Myc mRNA pathway.^[26] The effect of curcumin on cell-cycle regulatory proteins, matrix metalloproteinases (MMPs), and NF-kB was evaluated in MDA-MB-231 and BT-483 carcinoma cell lines^[27]. In agreement with the previous studies on other carcinoma cell lines, this study also confirmed the flexibility of curcumin to downregulate NF-B, resulting in an antiproliferative effect [28-29]. However, a decrease in cyclic Dt in MDA-MB-231 cells and a decrease in CDK4 BT-483 were observed after treatment with curcumin. Combining arabinogalactan and curcumin enhanced apoptosis induction by increasing ROS levels, disturbing the mitochondrial membrane and decreasing glutathione in MDA-MB-231 cell line^[30]. Moreover, curcumin led to the inhibition of breast tumor via overexpression of the p53 gene and reduction of antigen ki-67 levels. Another study on MDA-MB-231 cells has shown that curcumin also inhibits inflammatory cytokines CXCL1/2. Inhibiting CXCL1 and a pair of by curcumin ends up in inhibiting the expression of a series of metastasis-promoting genes like chemotactic receptor CXCR4^[31-32]. Dimethyl curcumin (ASC-19) has also been reported to be effective against estrogen-dependent carcinoma via inhibiting several kinds of steroid receptors.^[33]

3.5 Brain Cancer and Glioblastoma

The incidence rate of central systemanervosum (CNS) tumors, including brain tumors, are predicted to extend by 6% within the UK between 2014 and 2035^[34]. Glioblastoma (GBM), which is that the commonest malignant brain cancer in humans, accounts for about 15% of all CNS tumors^[34-35]. Within the treatment of brain tumors and GBM, surgical intervention and therapy are limited because of infiltration of cancer cells into the healthy brain, resulting in damaging effects after treatment^[36]. Therefore, alternative therapies using naturally derived compounds like curcumin with less side effects than the standard treatments are receiving more attention. Curcumin has multiple molecular targets, therefore, combating brain tumors may take different cellular pathways, including apoptosis, autophagy, angiogenesis, invasion, and metastasis^[35]. Although penetrating the barrier (BBB) is taken into account the rate-limiting step for Several anticancer agents, curcumin was ready to cross the BBB in high levels^[37]. Moreover, an in vivo study using human glioma U-87 cells xenografted into athymic mice showed that curcumin is ready to suppress glioma angiogenesis through inhibiting MMP-9 and downregulating endothelial cell markers (CD31 and CD105 mRNA)^[37]. Curcumin was also ready to induce G2/M cell cycle arrest by increasing protein kinase 1 (DAPKI) in U-251 malignant glioblastoma cells, which indicates that suppressing DAPKI by curcumin doesn't only induce cell arrest but also inhibits STAT3 and NF-B and activates caspase-3 scella.

3.6 Other pharmacological activity:

Turmeric possesses several biological activities including anti-inflammatory, antioxidant, anticancer, antimutagenic, antimicrobial, antiobesity, hypolipidemic, cardioprotective, and neuroprotective effects.



IV. CONCLUSION

Turmeric plant in main active ingredient is turmeric extract .*Curcuma longa* is help to stop many pathological state .like anti-inflammatory, antioxidant ,anticancer , antiandrogenic effects .The main ingredient of turmeric plant is turmeric shown many effect against several differing types of cancer , including adenocarcinoma ,breast cancer, colorectal cancer ,pancreatic cancer .Curcumin and other derivatives is low potency there for higher dose are required to urge more therapeutic response and that they increases the adverse effects and reduces the patient problem . Curcumin has one drawback of structural modification is difficult to induce achieve a balance between efficacy likewise as solubility and in most cases.

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