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EVIDENCE BASED VALIDATION OF CURCUMIN: FROM SCULLERY TO APOTHECARY

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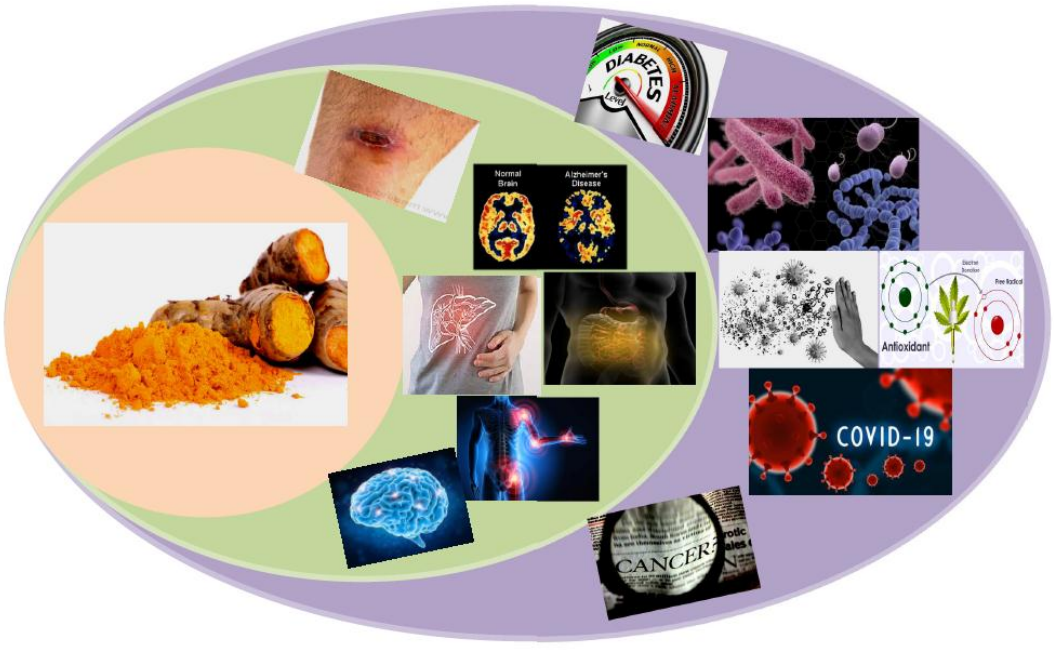
ABSTRACT

Turmeric (Curcuma longa L.) has been extensively studied in modern medicine while being an important part of Asian culture, owing to its use in various traditional medicine systems like Unani, Ayurveda and Siddha due to its array of medicinal properties since centuries. So far, 133 species of *Curcuma* have been identified throughout the world. The constituents of the plant have pharmacological or biological activity that have been exploited in pharmaceutical drug discovery and drug design. However, not much of the formulations have been employed due to its low bioavailability. Curcumin, the predominant curcumoid in turmeric, influences multiple signaling pathways and been found to possess anti-inflammatory, anti-oxidant, antimicrobial, hypoglycemic, wound healing, chemopreventive, chemosensitising and radio-sensitizing properties. Turmeric also has a latent role in the prevention and treatment of Alzheimer's disease. This paper discusses on evidence-based systematic review while evaluating the reported studies on various medicinal properties of the plant. Ways on which to improve its bioavailability have also been reported after rigorous research and summarized.

KEYWORDS: *Curcumin, Herbal, Antimicrobial, Bioavailabilty, Antioxidant.*

GRAPHICAL ABSTRACT



1.0 INTRODUCTION

Right at the beginning of time, humans have been using natural products for various purposes. With evolution, these natural products were used with more trust and notable results. Some used as secondary metabolites by higher animals in terms of defense against diseases and infections. Various chemical and medicinal products have been derived from these plants which plays an important and crucial role in our health care system, both in olden days and now.[1] Over 80% of individuals from the 3rd world country relies on natural products to meet their respective health care needs. According to recent findings, one in every three American uses natural

medicinal product and in every two-cancer patients, one uses natural products, this review limited to curcumin.

Historically, curcumin (diferuloylmethane), as shown in Fig. 1, which is a phenolic in nature has been used as a medicine for over 4000 years, to the root of Ayurveda (science of long life) to modern medicine. Its derived from the rhizome of *Curcuma longa* a perennial herb, which has been used most predominantly by the Indians as spices for food and other medical conditions.[2] Derived from the Arabic word *kurkum* which means "yellow", its name CURCUMIN was coined.[3]

It is golden yellow in color, and has a unique taste which provide the term called by its people as *"INDIAN SAFFRON"*. In India, its commonly known as *"HALDI"*. The country is the major exporter of turmeric world wide.

This article provides an in depth review based on the core values of curcumin through the angle of published evidence by various rated journals, pharmacological mechanism and validated ways to improve the bioavailability of curcumin.

Fig.1: Turmeric powder isolated from its rhizome.

The rhizome when uprooted has a golden yellow core with earthen brown skin, as evident from Fig. 1. Freshly cut rhizome has a typical odor that is distinguishable from a distance. The plant grows annually upto a height of 2.5 to 3 feet and almost every part of the plant has an organic compound, depicted in Fig. 2, exhibiting one or more pharmacologic activity. The figure also illustrates various sources of curcuminoids that are obtained from different species of the plant.

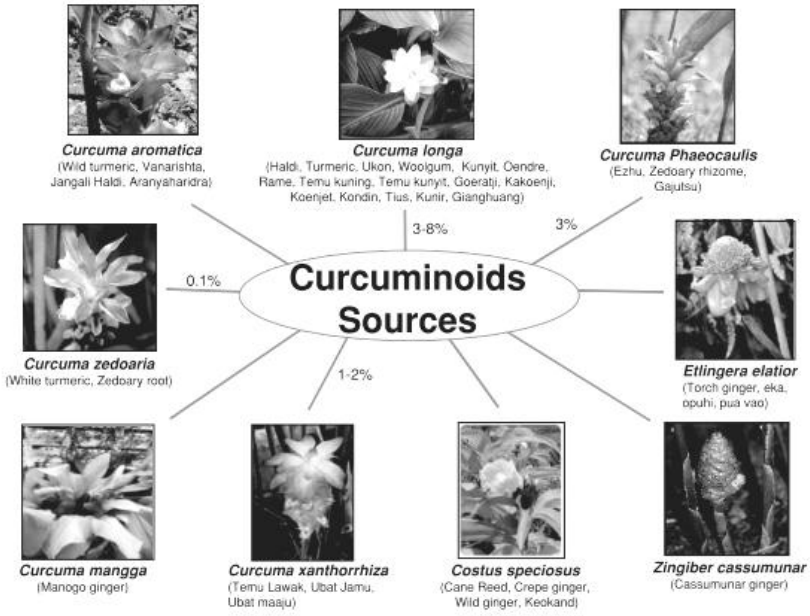


Fig.2: various sources of curcuminoids.

(Source: Mullaicharam A R, Maheswaran A. Pharmacological effects of curcumin. Int J Nutr Pharmacol Neurol Dis 2012;2:92-9)

2.0 CHEMICAL CONSTITUENTS

Turmeric contains a golden yellow-pigmented fraction known as curcuminoids, chemically related to the main ingredient, curcumin. Major curcuminoids present are curcumin I (77%), curcumin II also named as desmethoxycurcumin (17%), and curcumin III called as bismethoxycurcumin (3%) which overall form the 3 - 5% content of the curcumin from turmeric.[4]

Isolated first as a crystalline form in 1895, and identified as 1,6-hepta- diene-3,5-dione-1,7-bis(4-hydroxy-3-methoxyphenyl)-(1E,6E) or diferuloylmethane.

Synthesized by Lambe in 1910, the skeletal structure of curcumin was determined. Its insoluble in water and Ether but soluble in acetone, dimethylsulfoxide and phenol. It has a melting point of 183^0C, a molecular formula of $C_{21}H_{20}O_6$, and a molecular weight of 368.37 g/mol. Spectrophotometrically, the maximum absorption, λ_{max} of curcumin in methanol occurs at 430 nm and in acetone at 415– 420 nm.[5]

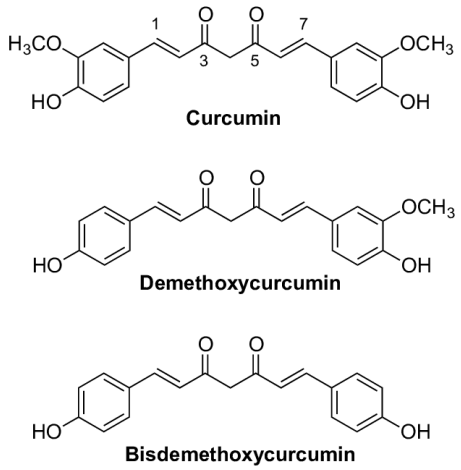


Fig.3: Structure of curcumin and its derivatives.

A member of the ginger family (*Zingiberaceae*), there are more than 113 species of curcumin are known worldwide, mostly distributed in Asia, Northern Europe and Africa.

More than 720 compounds were identified and isolated from different species of Curcuma. predominantly from the rhizome while some from the aerial parts or the fresh radix. They can be categorically grouped into phenylpropene, flavonoids, steroids, terpenoids, among others chemical.The chemical structure of the main constituent and its derivatives of this golden herb is shown in Fig. 3. Fig. 4 elaborates the newly isolated constituents in its chemical composition. Nevertheless, Curcumin still remains the most effective extract of this plant.

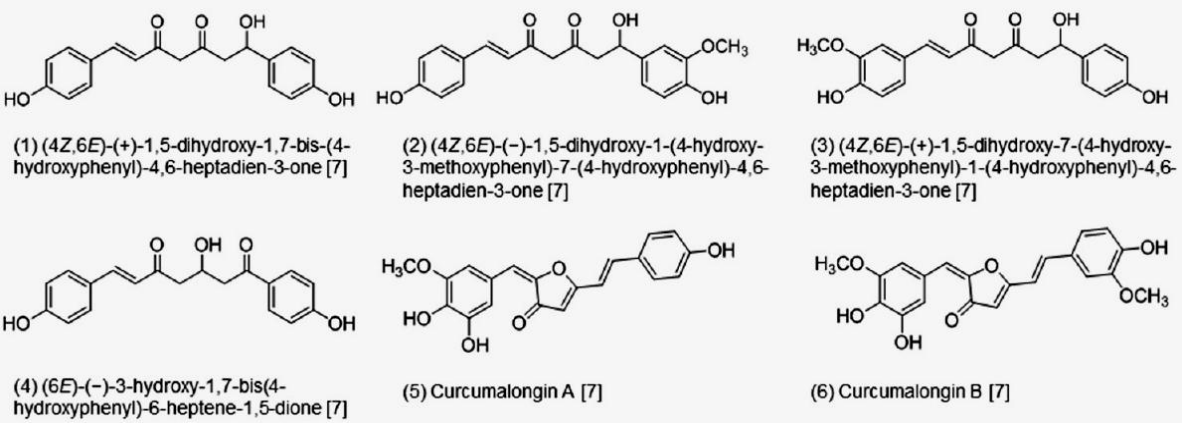


Fig. 4: The structures of newly isolated curcuminoids from Turmeric.

3.0 TRADITIONAL USES OF CURCUMIN

As easily accessible, inexpensive, traditional and non-toxic compound, curcumin have been used for a very long time for various kind of illnesses and diseases apart from its utilization as a beautifying agent. It has been used along history enhance digestion, protection of the skin against rays of sun, wound healing, as am immunity booster, an antioxidant with evidence that rolled on from one generation to another.

For diseases, it has been consumed around the world where it is popularly harvested for its antioxidant, antiulcer, cardiovascular and antidiabetic properties.

Since the ancient time, curcumin was also known as a food additive. This property is still exploited and the agent is used as an edible dye colouring agent and flavouring agent even today along with its usage as a stabilizer in jellies.

3.1 EVIDENCE BASED VALIDATION OF CURCUMIN

3.1.1 Potential Use In Covid-19

Used in the management of certain viral diseases, numerous curcumin derivatives such as tetramethylcurcumin have been shown to reduce swine flu (H1N1)-induced neuraminidase in the epithelial cells. It has also been useful in influenza virus infections. The hypothesis being COVID-19 of having such enzymes, shows that curcumin can exact similar effect to the virus. And as a natural ligand, it is a peroxisomal proliferator activated receptor (PPAR), helping in suppressing inflammatory responses by inducing cytokine production, can also play a vital role in COVID-19.

In an *in-silico* molecular docking, mitocurcumin which is a derivative of curcumin shows a potential to get blocked in an innate immune evasion mechanism of COV-19, and causes an enhancement in viral load clearance. It binds to NSP3 (largest protein encoded by the coronavirus genome) with high affinity and prevent the mediated suppression of viral cytokines.

Curcumin has been reported to inhibit the release and suppress numerous cytokines like Interleukins IL-1β, IL-6, IL8, TNFα, MCP-1, etc. Following the suggested interaction with these key components of the viral lifecycle and immune system, it is apparent that curcumin could prevent the COVID-19 infection. Moreover, in recent years, blood coagulation properties of curcumin (by inhibiting platelet aggregation, cyclooxygenase pathway, and blocking of calcium signaling) have been utilized in designing various materials and devices to handle influenza like illness.[6]

3.1.2 Anti-Inflammatory And Anti-Oxidant Activity Of Curcumin

Curcumin as reported By Hassan Zadeh *et el*,[7] possesses anti-inflammatory and anti-oxidant effect through various mechanism of which both includes the suppression of inflammasomes. These are important components that necessitate pathway that leads to inflammatory responses which activates caspase-1 leading to stimulation of maturation, proptosis as well as secretion of proinflammatory cytokines. Such cytokines like interleukin-18 (IL-18) interleukin-1β (IL-1β), and nuclear factor kappa-B (NF-κB) constitute the signaling pathway. Hence through such mechanism, curcumin provide its anti-inflammatory and anti-oxidant activity says H. Zadeh in his report. · A recent study also supports this theory as similar mechanism was established as the reason why there is an inflammatory suppression in an induced neurodegenerative disorder. The study shows that curcumin has an anti-oxidant effect, anti-convulsant and anti-inflammatory effects. According to their findings, after inducing febrile seizures in neonates' rate during a certain period of 11 days there is a decrease in IL-10, Tumor necrotic factor (TNF-α) and toll-like receptor (TLR4) protein expression after a succession administration of curcumin, which attenuates the inflammation cause by the seizures.[8]

On the contrary, Young Lee *et. al.*, reported that the anti-inflammatory effect of curcumin is limited to only few inflammatory diseases. However, a synergic effect of curcumin with *Allium hookri* (another herbal medicinal product with ancient history to reduce inflammation in rheumatic arthritis) inhibits inflammation via COX-2/iNOS pathway. This is done by measuring both the cytokines and immune cell count and comparing the morphological changes in inflamed skin tissue.[9]

3.1.3 Anti Depressant Activity

The antidepressant effects of curcumin have been evaluated through the forced swim test (FST) and tail suspension test (TST) in over a dozen studies on ??? in the past decade. These have consistently demonstrated that both acute and chronic administration of curcumin to rats and mice reduce immobility time.[10] For example, both in the acute models of FST and TST[11], and the chronic model of FST with a water wheel, curcumin had significant antidepressant-like activity compared with a vehicle control. The effects of curcumin were similar to those of fluoxetine and imipramine although when administered in combination, antidepressant effects were not enhanced.[12] Similar results have been found in other animal models for induced depression, with curcumin having similar antidepressant efficacy to fluoxetine.[12]

In an in-silico study, curcumin showed a strong binding affinity to monoamine oxidase-A (MAO-A) receptor. This demonstrated an evidence as a complementary component for anti-depressant pharmacotherapy.[13]

3.1.4 Anti-Microbial

The antimicrobial aspect of curcumin had been explored since time immemorial. Even to this day, various articles reported the antimicrobial effect of curcumin due to not known side effects and an overall harmless application. Different antimicrobial mechanisms have been demonstrated for turmeric, such as inhibition of bacterial cell membrane, inhibition on bacterial replication and gene expression, due to amphipathic properties of curcumin which allows it to penetrate the bacterial cell wall and make it more susceptible to other antibiotics.[14] In another report on the antibacterial effect of Curcumin, especially on S. aureus,[15] Teow *et.al.* Curcumin was found effective as antibacterial against both methicillin resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA) at a nominal concentration of as low as 25 µM (equivalent to 9.21 µg/ml), as it killed 50% of the bacteria after incubating for only 2 hours. In another study by Moghadamtousi and his group,[16] Curcumin, the chief ingredient of Turmeric was reported to exhibit anti bacterial, anti fungal and antiviral effect thereby confirming it as a natural antimicrobial agent. Shlar and his coworkers studied the efficacy of poorly soluble curcumin as nanoparticle delivery in two formulations against E.Coli.[17] Their findings suggested that depending on a delivery formulation, the antimicrobial properties of curcumin is exhibited which in-turn has practical connote on the applicability of curcumin nano-formulations. Table 1 gives an overall idea of the studies made on this particular herb.

Table: 1.

Bacteria	Aim of the Study	Result	Type	Reference
Streptococcus mutants	Prevention effect of Turmeric on adherence of *S.mutants* to extracellular surfaces	Bacteria is suppressed on the application turmeric extract	In-vitro	[18]
MRSA	To evaluate the synergistic effect of curcumin and antibiotic against methicillin resistance aureuous	Curcumin decreased the minimum inhibitory concentration to a greater extent compared to ampicillin	In-vitro	[19]
Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Treponema denticola	Study of anti-bacterial action of curcumin on periodontopathic bacteria, especially P. gingivalis.	Curcumin has anti-bacterial action against periodontopathic bacteria and may be an effective agent for preventing periodontal diseases	In-vitro	[20]
E.Coli	Study the novel anti-bacterial mechanism of curcumin that displays an apoptosis-like response in E. coli.	Curcumin stimulates an apoptosis-like response in E. coli	In-vitro	[21]

3.1.5 Antiviral Activity

Several studies[22][23] indicated that C. longa extracts have a wide spectrum of activity against viruses as well. When treated with curcumin, viral species like HIV-1, HIV-2, Parainfluenza Virus Type 3 (PIV-3), Feline Infectious Peritonitis Virus (FIPV), Vesicular Stomatitis Virus (VSV), Herpes Simplex Virus type 1 (HSV-1), Coxsackie Virus, Hepatitis B, Hepatitis C virus (HCV, HBV), Human Papillomavirus(HPV)[24], Japanese Encephalitis Virus (JEV), Dengue virus[25], (DENV), HCMV (Human cytomegalovirus), Epstein-Barr Virus, BHV 1 (Bovine Herpes Virus 1), Chikungunya virus, Ebola virus, Enterovirus 71 (EV71), RVFV (Rift Valley fever virus), HuNoV (Human Norovirus), RSV (Respiratory syncytial virus), VHSV (Fish viral hemorrhagic septicemia virus), IAV (Influenza A virus), SARS-Covid[26] have shown its sensitivity. However, the mode of action of the chemical constituent, curcuma, is different for different virus strains and is beyond the scope of discussion here.

3.1.6 Gastrointestinal Disorders

The anti-inflammatory effect of curcumin tends to ameliorate the inflammation cause by ulcers, reflux and in Zollinger Ellison syndrome. Reports reveal the activity of curcumin towards ulcer being mechanized by attenuating different ulcer causing effector like gastric acid hypersecretion, total peroxides, myeloperoxiase activity, IL-6, and apoptotic incidence, along with its inhibitory activity for pepsin.[27][28] As a matter of fact, curcumin plays a crucial key role in the inhibition of the activation of NF-κB pro-inflammatory cytokines and the IL-6/STAT3 signaling pathway. Therefore, it could be proposed as a novel therapeutic agent in several inflammatory diseases, such as Inflammatory Bowel Disease IBD.[29]

In treatment of crown disease, Hanai *et el*, used a randomized, double blind, multi centre trial while making a study with 89 patients with the disease. In a 6 months study, the patients were given 1000 mg of curcumin every morning and an equivalent amount after dinner, in combination sulfasalazine or mesalamine, which are all approved drugs for *Crohn* disease. The controlled set of patients were treated with sulfasalazine alone. The clinical activity index (CAI) and endoscopic index (EI) where all measured where the study concluded that curcumin had better clinical efficacy over placebo in relapse in addition to significantly improving CAI and EI.

3.1.7 Neuroprotective Activity

While vital neurons of the brain and synapses are lost in neuro-degenerative disorder, inflammation and oxidative damage play a role in aged related neurological disorders. Resourses and his coworker have shown that curcumin possess neuroprotective and cognitive-enhancing properties that help to prevent neuro-degenerative diseases like Alzheimer's disease and Parkinson's disease. Curcumin acts as a barrier against their degenerative ability when taken over the years.[30]

In an animal model with induced Parkinson disease, it was found that curcumin directly modulate the aggregation of α-synuclein, major constituent of Lewy bodies and a pathogenic hallmark of all synucleinopathathies, including multiple system atrophy (MSA), dementia with Lewy bodies (DLB) and Parkinson's disease (PD). Curcumin plays a proactive role here by preventing the aggregation in the dopaminergic neurons as its observed from gene as well as protein activity of a-synuclein. The outcome of this study assured that curcumin acted as a good candidate for targeted therapy for Parkinson disease and other related neurodegenerative disorder.[31] Curcumin was shown to improve the survival of cortical neurons deprived of oxygen and glucose and concomitant cell injury in an in vitro study. Moreover, the results of this study also suggested a decrease in the volume of infarct and oxidative stress following the focal cerebral ischemia in rat.

3.1.8 Alzheimer Disease

Curcumin serves to improve the cognitive function of the brain for Alzheimer disease, as well. The oxidative mechanism of curcumin also serves as added advantage to early improvement of the symptoms associated with Alzheimer's, exhibiting its antioxidant property.[32] As an anti-amyloidogenic agent in addition to anti-oxidant attribute, curcumin improves the quality of life in patients with Alzheimer's. Curcumin also served in delayed degradation of neurons affecting a decrease in β-amyloid plaques. It's activity as anti-inflammatory, antioxidant, metal-chelating properties, and decreased microglia formation, helped elevate the gross memory in patients with Alzheimer's Disease.[33] Following an *in vivo* retinal fluorescence imaging in a mouse model with curcumin, the result displayed that there is an immunoreactivity in the layer of the retina, due to interaction with β-amyloid. A characteristic of Alzheimer disease (AD) is amyloid beta. An intake of curcumin in requisite amount makes the retina a suitable surrogate tissue to assess amyloid beta in this disease.[34] In another study, Mishra and group deduced that curcumin has diverse results. It acts as antioxidant, metal chelator, has anti-inflammatory effects, helps in lowering β-amyloid plaques, delays degradation of neurons, and also decreases microglia formation. All these effects together improve the overall memory in patients with AD.[35] Another study done by Ishik *et. al.* revealed that there was effective reduction in cognitive impairment by STZ in rats while curcumin was administered and was recognized as a potential therapeutic agent for altering neurodegeneration in Sporadic Alzheimer's Disease. There was an appreciable decrease in the degree of neuronal loss after treating the rats with curcumin at a dose of 300 mg kg^{-1} day^{-1}.[36] Although there has been some work that gives evidence that curcumin can combat AD in animals, no such report is available to furnish this

effect in humans. Owing to limited bioavailability in human brain, scientists share a view that increase in the daily intake of curcumin-based curries is unlikely to alleviate Alzheimer's disease, as reported in Alzheimer's News Today.

3.1.9 Cardiovascular Disorder

In case of cardiac failure, curcumin have been established by several clinical trials to enhance the detoxifying enzymes such as glutathione s-transferase *in vivo*, and exert a cardioprotective activity by inhibiting free-radical specifically in myocardial ischemia. It has been shown that treatment with curcumin (50 mg/kg) with the addition of piperine (20 mg/kg) improves electrocardiographic and histopathological findings and level of lipids and antioxidant in an animal model in chemo induced cardio toxicity.[37] In an ongoing clinical trial of curcumin to improve vascular endothelial activity in middle aged patients, it has been found out after treating 84 patients with 2000 mg per day of curcumin and placebo, there was an increase in the forearm blood flow response of acetylcholine infusion up to 37%, enlarged the acute reduction in forearm blood flow induced by the nitric oxide synthase inhibitor NG monomethyl-L-arginine, and decreased the acute increase in blood flow to the antioxidant vitamin C whereas placebo had no effect. Also, this study enumerated that there is an increment of brachial artery blood flow of 36% as compared to those treated with the placebo. This report concluded that upon 3 months treatment with curcumin supplement there is an improvement in the vascular endothelial activity.[38]

Curcumin was found to be effective in the treatment of non-alcoholic fatty liver disease (NAFLD). It has shown to be vital against development of hepatic steatosis and its progression to steatohepatitis, though not explored in clinical trials until of recent. The effect of curcumin was investigated in a randomized double-blind placebo-controlled trial, patients with ultrasonographic (USG) evidence of NAFLD which were randomly assigned to receive an amorphous dispersion curcumin formulation (500 mg/day equivalent to 70 mg curcumin) or matched placebo for a period of 2 months. Various liver fat content, lipid profile, glycemic, transaminase levels, and anthropometric indices were evaluated at baseline and at the end of follow-up period. Compared with placebo, curcumin was associated with a significant reduction in liver fat content (78.9% improvement in the curcumin vs 27.5% improvement in the placebo group). There were also significant reductions in body mass index (BMI) and serum levels of total cholesterol, low-density lipoprotein cholesterol, triglycerides, aspartate aminotransferase, alanine aminotransferase, glucose, and glycated hemoglobin compared with the placebo group.[39]

3.1.10 Anti Cancer

Amongst the many ways used to combat cancer or malignant tumors like biological therapies, cryotherapy, targeted therapy, immune-therapy, radiation therapy and chemo therapy, herbal therapy or nature therapy is taking the centre stage these days, and more and more patients are opting the latter owing to serious side effects and or adverse effects of such therapies. More often combinations of one or more therapies are used. One of the major setbacks encountered with chemo therapy is the side effect associated with this treatment is most drugs not only affect the cancer cell but also the normal cell, hence there is a need for natural plant to be evaluated in order to lessen their side effects associated. A better way to combat a "golden age" disease with another "golden age" plant, namely the turmeric plant therapy. Diverse pharmacological effects of curcumin which includes apoptosis, anti-proliferative, anti-oxidant and anti-inflammatory attributes as discussed earlier have been proposed to be potential in cancer treatment. Recent studies show that, curcumin suppresses quite a number of key components in cellular transduction which includes, prostaglandin biosynthesis[40], phosphorylation catalyzed by kinases, c-jun-activated protein 1, inhibits cyclooxygenases and induces production of reactive oxygen species (ROS) which lead to apoptosis.[41] It is known that nuclear factor-kappa B (NF-ƙB), cytokines, and mitogen-activated protein kinase (MAPK) signal transduction play an important role in cell proliferation, transformation, and tumor promotion. Curcumin down-regulates the expression of various pro- inflammatory cytokines, tumor necrosis factor alpha (TNF- a), vascular endothelial growth factor (VEGF), interleukin-1, 2, 6, 8, 12 (IL-1, IL-2, IL-6, IL-8, IL-12) by inactivation of the NF- ƙB while it activates *p*38 mitogen-activated protein kinases (MAPK). Additionally, curcumin suppresses the matrix metalloproteinase family (MMPs), especially MMP-2 and MMP- 9, which are believed to be involved in tumor angiogenesis due to their matrix degrading capacity.[42]

In a randomized, double-blind, placebo-controlled trial to evaluate the role of curcumin on prostate cancer, it has been found out that, among the 82 patients which were evaluated for the analysis, there was an increment in the PSA level due to co-treatment with curcumin (39 and 43 patients in the curcumin and placebo groups).[43] In a study to find out the effect of curcumin supplementation during radiotherapy on oxidative status of prostate cancer, Hejazi et el reported that curcumin can increase the total anti-oxidant capacity (TAC) while decreases the activity of antioxidant enzymes; superoxide dismutase (SOD) in patients with prostate cancer after receiving radiotherapy. This serve as prove that curcumin improves the antioxidant activity without altering the therapeutic efficacy of the radiotherapy.[44]

3.1.11 Diabetes Mellitus

The effect of curcumin in glucose-lowering has been reported severally in animal models and clinical trials. The attribute is towards the properties of curcumin to exact its action on various targets in related to cell growth, lipid metabolism, apoptosis, oxidative stress and inflammation. Some studies related to the beneficial

effects of curcumin also reported that in diabetic nephropathy, curcumin have showed an induced stimulation of AMP-activated protein kinase (AMPK) which seems relevant to ameliorated the effect of hyperglycemia on kidneys.[45] An *in vivo* study, using a mice model showed that a reduction of glucose tolerance after an induced obesity and insulin resistance, post intraperitoneal administration of curcumin into the mouse.[46] The mechanism can be explained as the ability of curcumin to attenuate certain growth factors as study shown that according to El azab *et al*.

3.2 Pharmacokinetics Of Curcumin

In general, the bioavailability of nutraceuticals faces a setback due to their low absorption at the site of action. Curcumin also displays this poor solubility, chemical instability and very low pharmacokinetic profile. This low bioavailability is also exacerbated by the affinity of curcumin to bind to enterocyte proteins that can change its chemical structure.[47] Pharmacokinetic and bioavailability studies of curcumin have indicated its low intestinal absorption and rapid clearance from the body. Metabolism, absorption, biodistribution and excretion of curcumin in rodents have been reported in several studies. 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. In another research, absorption of curcumin was reported to be 60% after oral use in rat. A radio-tracing study with 3H-radiolabeled curcumin confirmed that curcumin is transformed during its intestinal absorption.[48] In a study to measure curcumin concentration in blood plasma of rat by chromatographic method after administering 90 mg/kg/day of curcumin combined in yoghurt, it was seen that a mere 0.47% of the total curcumin was available in the same.[49] In an attempt to study the availability of curcumin post 12 g of oral administration in ten healthy human male volunteers, D. Doberer and group reported that oral administration of the same has very low bioavailability in peripheral blood mononuclear cells.[50] Thus this study reports that though a single high oral dose of curcumin was delivered, plasma levels could not be detected, also no change in the HO-1 expression was detected owing to high metabolism rate in the liver. However, as an alternative to administration of curcumin alone to check the bioavailability and hence the related pharmacokinetic behaviour of the said herbal drug, curcumin was delivered in combination with a glucouronidation inhibitor, piperadine. As a result the availability of drug in the plasma was multiplied by twenty folds, raising the relative bioavailability value by 2000%.[51]

3.3 Conclusion and Future Perspective

Despite its major availability worldwide, and wide spread of action due to long term use, curcumin has suffered a major drawback due to its relatively less bioavailability. Various methods have been established over the years to tackle this problem and improve the therapeutic effect of this golden drug. In a study by Wei to improve the bioavailability of curcumin, using liposomes encapsulation, they constructed a long acting curcumin by coating bovine serum albumin (BSA). It was found out that its more spherical, homogenous in size and in conclusion tends to improve the bioavailability of curcumin by slow drug release, enhanced stability and low phagocytosis.[52] Mesoporous silica nanoparticles also prove its importance in improving the bioavailability according to a study conducted to evaluate its cardioprotective effect. it was undertaken to assess curcumin loaded mesoporous silica nanoparticles (MSNs) against doxorubicin induced myocardial toxicity in rats. The MSN based delivery was found to be of superior compared to curcumin delivered alone. And also indicates higher C_{max} and AUC values due to coated MSN.[53] In order to increase the solubility of curcumin and skin permeability, a nano emulsion of the drug was prepared using polymeric hydrogel. This curcumin was optimized by emulsification method and converting it into nano-emulgel using polyacrylic acid as a gelling agent. It was found out the release of curcumin follows Korsmeyer-Peppas kinetic release. This preparation exhibited quicker and early healing in the treatment of Psoriasis due to increase in the stability and skin permeability.[54]

In a method to study the inter-facial behavior of curcumin with respect of its stability, it was found out that the mixtures of curcumin and cetyl palmitate form Langmuir films, while none of the two pure components does. This effect was interpreted in terms of formation of a complex between curcumin and the hydrophobic, water insoluble cetyl palmitate. The hydrophilic-hydrophobic balance of the complex allows its penetration into the monolayer and mixing with the phospholipid phase.[55]

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