International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2023-2035 www.ijprajournal.com ISSN: 2456-4494

"Review on: Different approach of curcuminn bioavailability."

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Date of Submission: 05-06-2024 Date of Acceptance: 15-06-2024

ABSTRACTS
Curcumin, a compound found in turmeric, has been utilised for centuries in traditional Indian and Chinese medicine to address a multitude of ailments. It is also recognized for its wound healing properties. Curcumin constitutes approximately two to five percent of turmeric, which is responsible for its vibrant yellow hue. This polyphenolic pigment and fat-soluble substance, known as curcuminoids, are predominantly employed in the Indian subcontinent. Numerous clinical trials have been undertaken to explore the extensive therapeutic applications of curcumin.The forefront of nanoformulation research has seen a significant focus on the creation and advancement of herbal nanoparticles. Curcumin, the vital bioactive component found in curcuma longa, a plant with a long history in traditional medicine, possesses therapeutic properties that can effectively prevent and treat various ailments. Despite its proven efficacy in treating human ailments, curcumin faces challenges in terms of limited bioavailability, primarily due to poor absorption, rapid metabolism, and rapid systemic clearance. To address these issues, the revolutionary concept of nanotechnology can be employed to enhance curcumin's solubility, stability, and bioavailability.
Keywords: curcuminn, bioavailability

I. INTRODUCTION

An organic anti-inflammatory substance is curcumin. Curcumin is a bioactive compound that has anti-inflammatory properties, but it takes very high doses to be therapeutically effective. Nevertheless, this indicates that it may be able to combat inflammation, which is a factor in a number of illnesses and ailments.

Since ancient times, curcumin, a yellow polyphenolic pigment derived from the rhizomes of the Curcuma longa L. plant (also known as turmeric), has been used in Chinese and Ayurvedic medicine, as well as in cooking and food coloring.

The ginger family flowering plant Curcuma longa is the source of turmeric.Often, it is offered in spice jars. When purchased fresh, though, it resembles ginger root but has a richer yellow to golden hue.Turmeric is used to treat aches and pains, digestive problems, and skin conditions in India. In actuality, it's a mainstay of traditional healing practices like Ayurvedic medicine.

Although turmeric contains a wide variety of plant compounds, curcuminoids are the group with the strongest health benefits. Curcumin, demethoxycurcumin, and bisdemethoxycurcumin are three prominent curcuminoids. Curcumin is the most potent and health-promoting of these. Turmeric gets its unique color and flavor from curcumin, which makes up 2-8% of most preparations.Curcumin has anti-inflammatory, anti-tumor, and antioxidant properties on its own.

Biological Source: Rhizomes of Curcumin Longa
Family: Zingiberaceae.
Formula: $C_{21}H_{20}O_6$

Geographical source: It is not a wild plant; it is only known to be domesticated. Turmeric is most widely produced, consumed, and exported from India. Bangladesh, China, Thailand, Cambodia, Malaysia, Indonesia, and the Philippines are among the countries that cultivate a lot of turmeric. erect, evergreen herb that can grow up to one meter tall.

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Chemical Constituents: The three curcuminoids that make up turmeric are curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin. Other components of turmeric include sugars, proteins, resins, volatile oils (tumerone, atlantone, and zingiberone), and curcumin.

Curcumin makes up two to five percent of turmeric. Approximately 77% diferuloylmethane, 18% demethoxycurcumin, and 5% bisdemethoxycurcumin make up curcumin preparations. With an absorption maxima of 420 nm, curcumin is hydrophobic by nature and dissolves in oils, acetone, ethanol, and indimethylsulfoxide. Acids cause curcumin's color to shift from yellow to a deep red, and this form is utilized in religious rituals.

In 1815, curcumin was separated from turmeric, and diferuloylmethane was recognized as the structure in 1910. Turmeric is a versatile spice that grows naturally in tropical regions like Southeast Asia.

Turmeric was restricted to Asia until the 12th and 13th centuries AD, but it is now used as a pigment, spice, food coloring, additive, and medicinal herb.

Turmeric has been used since 19,00 BCE in Indian Ayurvedic medicine. Turmeric has therefore only recently—in the past 12 to 15 years—reached clinical phases I and II.

Curcumin is used as an alternative to medication in Southeast Asia for a variety of conditions, including skin infections, wounds, sprains, jaundice, and allergies.A multitude of clinical trials are carried out in an effort to comprehend the diverse therapeutic applications of curcumin.

It was noted in studies on curcumin's antioxidant properties over the past few decades, and the compound's possible uses were identified.

Following oral administration, curcumin metabolizes to produce curcumin glucuronide and curcuminsulfonate. Nevertheless, curcumin is broken down into tetrahydrocurcumin, hexhyrdrocurcumin, and hexhydrocurcuminol when it is given intraperitoneally or systemically.

Traditional Chinese and Indian medicine uses curcumin as a wound-healing agent in addition to treating a variety of illnesses.

Curcumin has recently been the subject of a great deal of research, which has demonstrated that it inhibits the growth of cancer cells and induces cell death through a variety of signaling pathways.

Consequently, curcumin has gained popularity as an anti-cancer and chemopreventive drug since it causes cell death. Preclinical research on animal models and a variety of in vitro experiments can be used to demonstrate this.

Physical Property

- The compound curcumin, also known as diferruloylmethane, is hydrophobic and polyphenolic. Its structural scaffold is diarylheptanoid, and its molecular weight is 368.39. Its molecular formula is C21H20O6, and its logP range is 2.56-3.29.
- Curcumin is stable in the pH range of 1-6; its color in the solution is primarily due to its protonated-neutral-deprotonated form (giving rise to a distinct red-yellow-red color).
- Curcumin is easily soluble in dichloromethane, methanol, ethyl acetate, and other solvents but insoluble in water.
- It can pass through the blood-brain barrier and demonstrates exceptional physicochemical characteristics, including affinity for lipid membranes and interactions with protein hydrophobic domains.

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- A qualitative analytical method for detecting boric acid and borates—which turn orange-red in acidic solutions and greenish-black in alkaline solutions—is the use of turmeric paper infused with alcoholic extract of turmeric.
- Curcumin can be extracted from turmeric using a variety of methods, including Soxhlet, ultrasonic, microwave, supercritical CO2, enzyme-assisted extraction, high-efficiency column chromatographic techniques, and HPLC-MS detection in clinical samples.
- Curcumin has been used as a flexible and multipurpose matrix for MALDI-mass spectroscopy imaging applications.

Chemical Property

- Curcumin pharmacophore demonstrates a few special characteristics: Michael's addition to the peptides' sulfhydryl group; the creation of various metal chelates with both bivalent and charged metal species.
- The best way to characterize the curcumin's structure is as two aryl vinyl scaffolds with a keto (or enol) extension, depending on the pH, overlapping with each other via a methylene spacer. Because of this structure's usefulness as an electron donor, the pharmacophore also demonstrates antioxidant activity.
- As a typical Bronsted-Lowry acid, curcumin is protonated and deprotonated in response to pH variations.
- Visible spectroscopy is the most effective method for studying ion alteration because this process is accompanied by significant changes in light absorption in the visible region. Multiple hydroxyl anions become less stable at pH values greater than 7, which makes curcumin unstable.
- Moreover, carbon-carbon bond fission also breaks conjugate bonds. • The main breakdown products are ferulic acid and feruloyl methane; further breakdown results in the production of vanillin and acetone.
- Curcumin interacts with free radicals and, like polyphenols, experiences chemical changes (through substitution and condensation reactions).
- Curcumin demonstrates reversibility, a characteristic of α, β-unsaturated ketone, or ester, as well as nucleophilic addition reaction via its conjugated π-electron systems. Because curcumin can chelate with metal, certain users may be at risk for iron chelation and anemia.

Medicinal use of curcumin:

- Curcumin possesses antiviral, antifungal, anti-inflammatory, and antioxidant properties.
- Curcumin inhibits molecules, which are crucial in the event of inflammation, to produce anti-inflammatory effects.
- Turmeric works well to lessen inflammation following surgery.
- Curcumin also lowers low-density lipoprotein (LDL) and raises high-density lipoprotein (HDL), inhibits platelet aggregation, and lowers inflammation, all of which lower the risk of myocardial infarction and cardiovascular disorders.
- Curcumin exhibits activity against inflammatory bowel disease, arthritis, colitis, gastritis, and fever by suppressing the inflammatory markers.
- Curcumin has antifungal, antiviral, anti-inflammatory, antioxidant, neuroprotective, and anti-rheumatoid arthritis and anti-osteoarthritis activity.
- Turmeric inhibits the growth of H. pylori, the primary cause of gastric ulcers and a risk factor for gastric cancer.
- Curcumin is regarded as an antifibrotic substance that prevents liver fibrosis by acting as a hepatoprotective agent.
- Curcumin causes individuals with diabetes mellitus II to become resistant to insulin.
- It is possible to prevent the toxicity of heavy metals by binding lead and cadmium with curcumin, which has a protective effect on the brain.
- Curcumin's anti-psoriatic action can be seen when applied topically.
- Curcuma longa improves digestion by increasing the amount of bile from the gall bladder. It also inhibits glutathione S-transferase, cyclooxygenase, and 5-lipoxygenase.

Chemistry

- The polyphenols called curcumins are what give yellow color. Curcumin belongs to multiple functional groups.
- Two alpha and beta unsaturated carbonyl groups bind polyphenols together to form an aromatic ring.
- A diketone is created by the two carbonyl groups. While the alpha, beta-unsaturated carbonyl is added nucleophilically, the diketone forms stable enols or is readily deprotonated to form enolates.(11)

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- Curcumin breaks down into Trans-6-(40-hydroxy-30-methoxyphenyl)-2, 4-dioxo-5-hexanal, ferulic acid, feruloylmethane, and vanillin in 30 minutes at a basic pH.
- The degradation in culture media or phosphate buffer above pH 7 is completely blocked by the addition of antioxidants like ascorbic acid, glutathione, or nacetylcysteine, or by the presence of human blood or foetal calf serum.
- Curcumin degrades much more slowly in acidic environments; after one hour, less than 20% of the total curcumin had broken down.

PHARMACOLOGICAL ACTIVITIES

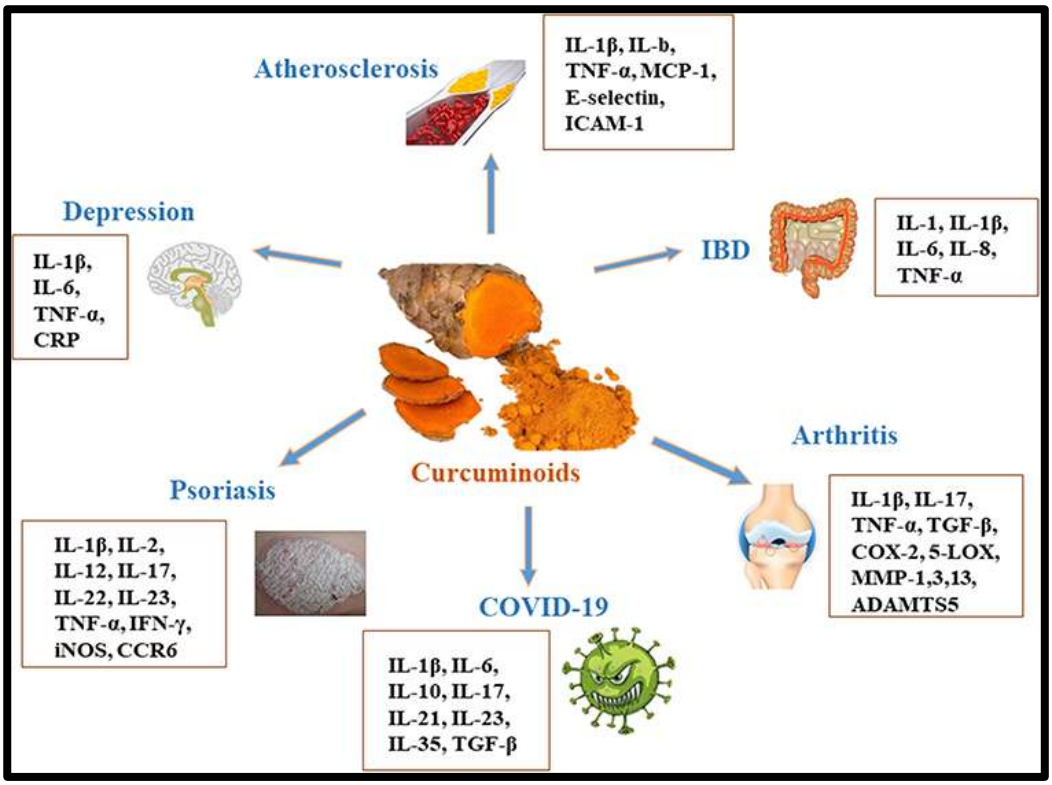

Fig . 2 Pharmacological activity

Inflammation

The enzyme linked to the activation of inflammatory substances is inhibited by curcumin. Curcumin exhibits a natural anti-inflammatory effect comparable to that of certain steroidal medications. It works similarly well to phenylbutazone, which is prescribed to treat arthritis and post-operative inflammation.

A complicated physiological and pathological process is inflammation. Usually, inflammation is the body's adaptive reaction to maintain homeostasis in the face of harmful stimuli and conditions (like infection and tissue damage). There are two types of inflammation: acute inflammation and chronic inflammation. Acute inflammation is transient and typically advantageous to the host. Chronic inflammation is defined as inflammation that lasts longer than six months or more. It can be a contributing factor in many chronic conditions, including pancreatitis, diabetes, obesity, arthritis, cardiovascular, neurological, metabolic, and some types of cancer.

Anti-inflammatory Activity Mechanisms of Curcumin

The four components of the inflammatory pathway are effectors, mediators, sensors, and inducers. There are differences and unclear physiological and pathological mechanisms underlying inflammation brought on by various inflammatory triggers.Anti-inflammatory effects of drugs generally involve one or more of the following mechanisms: they act on receptors and signaling pathways; they control how target tissues respond to inflammatory mediators; they reverse the effect of the medium on the target tissue;they

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generate anti-inflammatory mediators, and so forth.By controlling inflammatory signaling pathways and preventing the synthesis of inflammatory mediators, curcumin has anti-inflammatory properties.

Curcumin binds to Toll-like receptors (TLRs) and modulates downstream signaling pathways such as Activator Protein 1 (AP-1), Mitogen-activated protein kinases (MAPK), and nuclear factor kappa-B (NF-κB), controlling inflammatory mediators and treating inflammatory diseases.

Curcumin acts on Peroxisome proliferator-activated receptor gamma (PPARγ) to down-regulate NF-κB.By controlling the Janus kinase/Signal transducer and activator of transcription (JAK/STAT) inflammatory signaling pathway, curcumin can also have anti-inflammatory effects. Furthermore, cytosolic multiprotein complexes known as the NOD-like receptor pyrin domain-containing 3 (NLRP3) inflammasome are implicated in the etiology of numerous inflammatory diseases.

Three proteins make up the NLRP3 complex: a protease called caspase-1, an apoptosis-associated speck-like protein with a caspase recruitment domain, and a sensor protein. One possible mechanism of action for curcumin in the treatment of inflammatory diseases is the direct inhibition of NLRP3 inflammasome assembly or the inhibition of NLRP3 inflammasome activation through NF-κB pathway inhibition.

Curcumin reduced pro-inflammatory mediator levels in inflammatory cell and animal studies. These mediators included IL-1, IL-1β, IL-6, IL-8, IL-17, IL-27, TNF-α, NO, Regulated upon activation normal T cell expressed and secreted factor (RANTES), Granulocyte colony-stimulating factor (G-CSF), and Monocyte chemotactic protein-1 (MCP-1).

Curcumin has also been demonstrated in clinical trials to lower inflammatory mediators.A double-blind, randomized, placebo-controlled clinical trial found that 80 mg of curcumin nanomicelle daily significantly reduced plasma levels of TNF and CRP.

Curcumin's ability to regulate immune cells is advantageous for the treatment of inflammatory illnesses.Curcumin primarily affects T helper 17 cells, T regulatory cells, and dendritic cells. Th17 is a significant pro-inflammatory cell that stimulates the inflammatory response by producing IL-17, IL-22, and IL-23. Treg cells stop the body from becoming inflamed.

Th17 and Treg numbers and functions can fluctuate, which can result in an aberrant immune response and inflammation. As a result, preserving the balance between Th17 and Treg is beneficial for both treating inflammatory illnesses and immune homeostasis.By blocking the IL 23/Th17 pathway, curcumin inhibits Th17 differentiation and controls the Treg/Th17 rebalance.

Inflammatory processes have a close relationship with oxidative stress. Oxidative stress, which is brought on by the buildup of reactive oxygen species (ROS), intensifies inflammation by activating transcription factors linked to inflammation. Because curcumin inhibits nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and increases the activity of antioxidant enzymes, it lowers the production of reactive oxygen species (ROS). Curcumin is associated with the Nrf2-Keap1 pathway. Curcumin's antioxidant properties help to reduce inflammation.

Effect of Curcumin on Inflammatory Bowel Disease

IBD, which primarily consists of Crohn's disease (CD) and ulcerative colitis (UC), is a recurrent, chronic inflammatory disease. The distinction between the two is that although UC primarily affects the colonic epithelium, CD can affect the gastrointestinal tract anywhere from the mouth to the anus and is usually characterized by transmural inflammation. IBD is now a widespread illness. The prevalence of inflammatory bowel disease (IBD) is rising everywhere, whether in developed or developing nations, putting a financial strain on the world economy. IBD's etiology is still unclear, although it may have something to do with immunity, environment, or genetics.

UC Individuals with recurrent and chronic colon inflammation produce too many pro-inflammatory factors, which eventually destroy the intestinal barrier. Impaired gut mucosal barrier subsequently makes the inflammatory symptoms worse. There are three main ways that dextran sulfate sodium salt (DSS) induces NLRP3 inflammasome activation in colitis-induced mouse models: by producing ROS, releasing cathepsin B, or excreting K+. Many inflammatory diseases, including IBD, are influenced by the pro-inflammatory cytokine IL-1β, whose maturation and secretion are facilitated by stimulated NLRP3.

By preventing the activation of NLRP3 inflammasomes and the production of IL-1β, curcumin significantly protects against severe DSS-

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induced colitis. This leads to improved weight loss, a lower disease activity index, and an extended colon. By controlling the TLR4/NF-κB/AP-1 signaling pathway, curcumin can reduce the synthesis of pro-inflammatory factors like IL-1, IL-6, IL-8, and TNF-α, which helps to reduce intestinal inflammation in IBD patients. Curcumin has the ability to lower inflammatory markers, improve quality of life, and successfully induce and maintain symptom relief in UC patients. Patients with active mild to moderate Crohn's disease have shown good safety and significant clinical and endoscopic efficacy when using theracurmin.

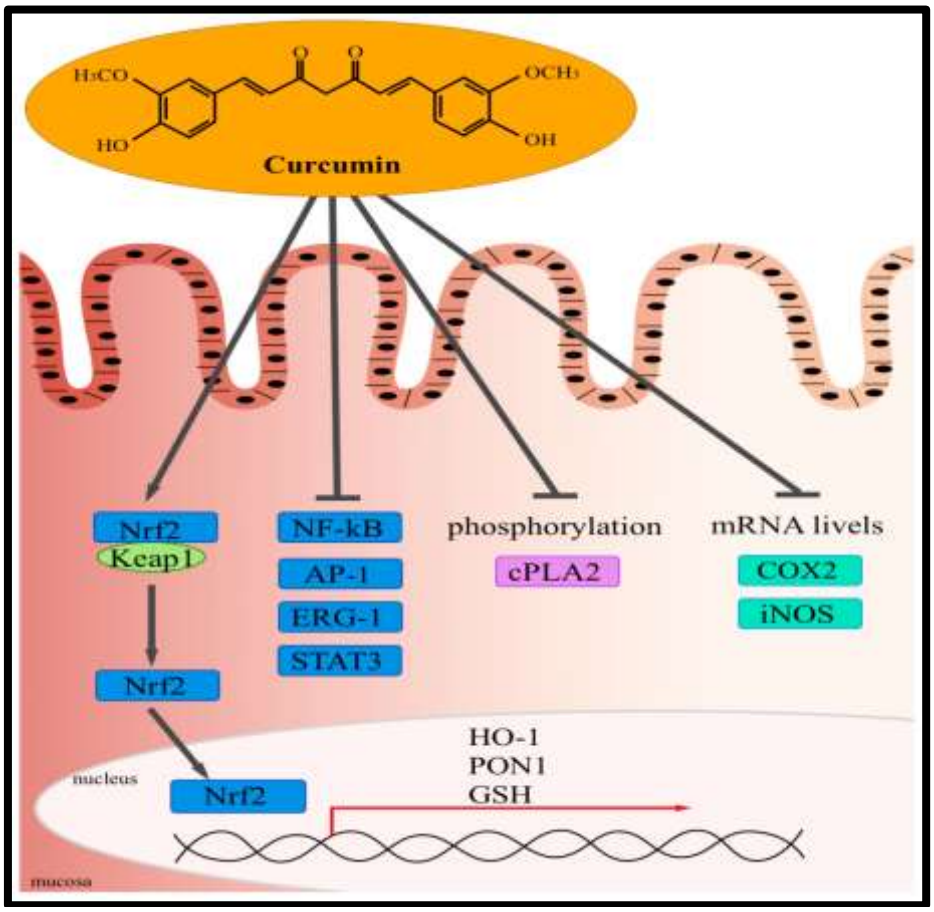

Fig 4 Effect of Curcumin on Inflammatory Bowel Disease

One significant intracellular catabolic process that helps to prevent and mitigate the onset and progression of UC is autophagy. According to recent research, autophagy, inflammation, and gut microbiota all have an impact on how IBD develops. Owing to its natural product origins and high level of safety, curcumin possesses anti-inflammatory and antioxidant properties as well as the ability to regulate autophagy and gut microbiota. The interaction of gut microbiota, inflammation, and autophagy and their roles in the onset and progression of IBD constitute a novel avenue for elucidating the pathophysiological mechanism of IBD and identifying promising targets for therapeutic interventions.

When treating IBD, curcumin is a safe and useful adjuvant medication. Curcumin helps patients with inflammatory bowel disease (IBD) by reducing oxidative stress, inflammatory markers, and endoscopic symptoms. Nevertheless, there is still insufficient clinical evidence to support curcumin's use as a therapeutic agent for IBD because there are no agreed-upon guidelines for curcumin administration form, administration method, dosage, and model selection indexes. According to certain research, oral curcumin did not significantly improve over a placebo in terms of reducing UC's clinical symptoms. These days, most researchers concur that curcumin is used as adjuvant therapy, and that adding the right amount

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of curcumin to mesalazine can enhance the therapeutic

On the other hand, curcumin may also be advantageous in treating a more prevalent intestinal illness. Irritable bowel syndrome, also known as IBS, is a functional bowel disorder that typically manifests as bloating, diarrhea, or constipation in addition to abdominal pain. Patients with Irritable Bowel Syndrome were assessed using the IBS-SSS to determine the impact of curcumin. Abdominal pain, other symptoms, and IBS-SSS can all be effectively treated with curcumin, which also enhances patient quality of life. Studies indicate that curcumin's anti-inflammatory properties may contribute to its beneficial effects on IBS.

Effect of Curcumin on Arthritis

Osteoarthritis (OA), rheumatoid arthritis (RA), and gouty arthritis are the three primary forms of arthritis. The most prevalent type of joint disease, osteoarthritis, is a degenerative condition that is accompanied by inflammation. Osteoarthritis is more prevalent in women and those over 50. Subchondral bone, synovial inflammation, and cartilage could all be important factors in the etiology of osteoarthritis. Inflammatory cytokines like TNF-α, IL-1β, IL-6, and matrix-degrading enzymes are produced in response to stimulation of osteoblasts, chondrocytes, and synovial cells. This results in the destruction of joints and clinical symptoms like pain and swelling. The main matrix-degrading enzymes in osteoarthritis are matrix metalloproteinase (MMP)1, 3.13, a disintegrin, and metalloproteinase with thrombospondin-like motifs (ADAMTS)-5.

Because of its anti-inflammatory and cartilaginous protective properties, curcumin has the ability to decrease joint inflammation and relieve pain symptoms. Curcumin increased the chondroprotective transcriptional regulator Cbp/p300 interacting transactivator with ED-rich tail 2 (CITED2) and suppressed the mRNA expression of pro-inflammatory mediators IL-1β and TNF-α, MMPs 1.3 and 13, and ADAMTS5. These effects were observed in primary cultured chondrocytes.

In rat models of arthritis induced by lipopolysaccharide (LPS), collagen II, and monoiodoacetic acid, curcumin reduces the synthesis of inflammatory mediators such as TNF-α, IL-17, IL-1β, transforming growth factor-β (TGF-β), and cyclooxygenase-2 (COX-2). It also reduces cartilage and synovial inflammation. By blocking the TLR4 pathway and the NF-κB signaling pathway that it leads to, curcumin reduces inflammation. In addition to downregulating pro-inflammatory factors, activation of the NF-κB pathway prevents matrix-degrading enzyme expression. Curcumin prevented the production of MMP-1 and MMP-3 induced by IL-1β by blocking the activation of the AP-1 and NF-κB signaling pathways. Furthermore, tetrahydrocurcumin, a metabolite of curcumin, demonstrated comparable effectiveness in halting the worsening of osteoarthritis by reducing cytokine and MMP3–MMP13 expression in the articular cartilage. (32)

An inflammatory autoimmune disease called RA is characterized by persistent synovial joint inflammation, which can cause serious joint damage. A significant factor in the onset of rheumatoid arthritis is IL-10. Curcumin can control the TLR-4 receptor and its downstream pathway in addition to having an anti-inflammatory effect. In macrophages, curcumin can up-regulate the level of IL-10 while down-regulating TNF-α, IL-1β, IL-6, IL-12, IL-15, and IL-8. FM0807, a derivative of curcumin, is a curcumin salicylate monoester that preserves the β-dike tone structure while incorporating a salicylate. It is possible that FM0807 works as an anti-arthritic agent by preventing the expression of factors that cause inflammation.

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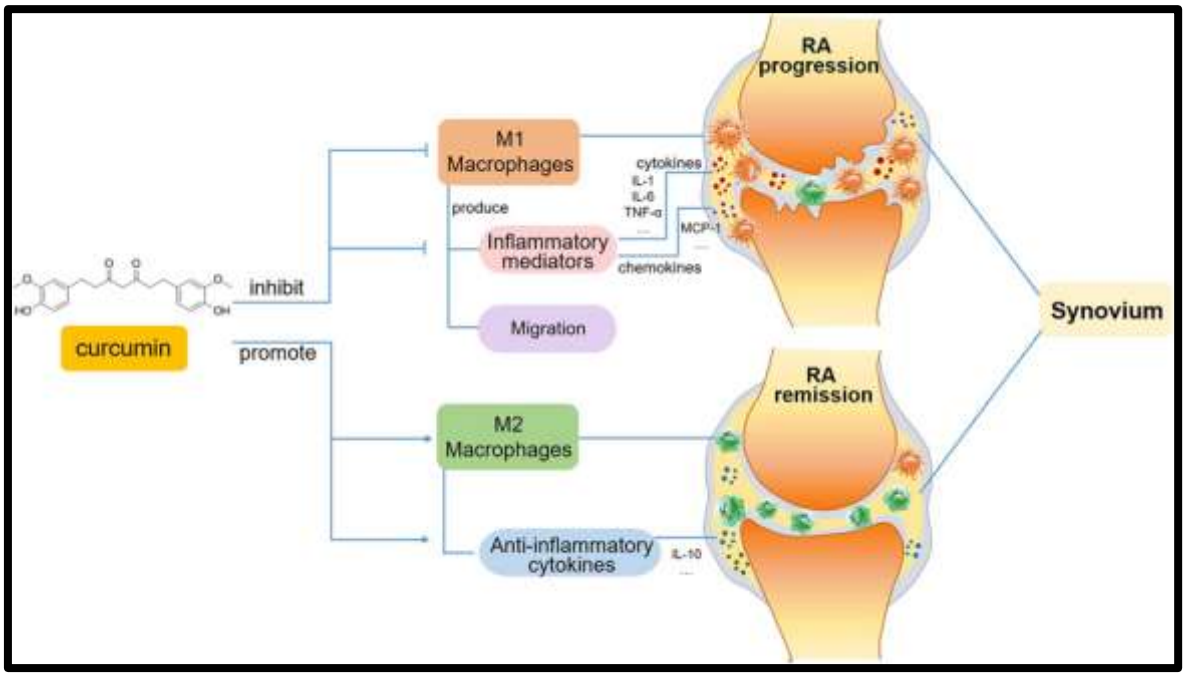

Fig 5 Effect of Curcumin on Arthritis

Recurrent inflammatory arthritis brought on by hyperuricemia and the buildup of inflammatory monosodium urate (MSU) crystals in the synovium and joints is the hallmark of gouty arthritis, also known as gout. It frequently affects adults over 40 years of age. Curcumin inhibits the NLRP3 inflammasome activity and the TLR4/NF-κB signaling pathway, thereby effectively mitigating the inflammatory response induced by MSU.

One natural anti-inflammatory medication is curcumin. Its beneficial effect on arthritis has been demonstrated by numerous preclinical studies. Treatment for osteoarthritis in the knee was the main focus of clinical trials. Turmeric extract decreased oxidative stress and IL-1β, enhanced clinical symptoms, and inhibited inflammation in a clinical trial treating osteoarthritis in the knee. When it came to treating knee pain, turmeric extract outperformed a placebo; however, it had no effect on the composition of cartilage or knee effusion, or synovitis. Turmeric extract, ginger, and black pepper make up a herbal formulation.

This substance, like naproxen, increases prostaglandin E2 (PGE2) levels in patients with osteoarthritis of the knee. In a randomized pilot study, 45 RA patients were divided into three groups and given either the combination of 50 mg of diclofenac sodium and 500 mg of curcumin or neither medication alone. The administration of curcumin, as compared to diclofenac sodium, demonstrated a significant improvement in both the American College of Rheumatology and the overall Disease Activity Score. Curcumin's efficaciousness in treating arthritis has been demonstrated in clinical trials. However, due to a lack of evidence, curcumin is not currently recommended as a treatment for arthritis. Currently, dietary supplements containing curcumin are commonly used to support joint health. In the future, more extensive research involving patients with arthritis is required.

Effect of Curcumin on Psoriasis

Inflammatory skin disease psoriasis is a chronic condition that affects one million or more people worldwide. Psoriasis is caused by autoimmune, genetic, and environmental factors. Comorbid conditions like psoriatic arthritis, depression, metabolic syndrome, obesity, liver disease, kidney disease, and cardiovascular disease are frequently present in people with psoriasis. Inflammation is thought to play a role in their pathogenesis. It is well recognized that dendritic cells are crucial to the early stages of psoriasis.

Myeloid dendritic cells secrete IL-23 and IL-12, which stimulate Th22 and Th1 cells, IL-17-producing T cells, and the production of inflammatory cytokines like IL-17, IFN-γ, TNF, and IL-22. This, in turn, triggers the inflammatory cascade linked to psoriasis. Psoriasis develops as a result, which is typified by local tissue infiltration,

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erythema from skin thickening, and keratinocyte proliferation. Curcumin acts on MAPKs, AP-1, and NF-κB pathways to inhibit T cell activation, proliferation, and the production of pro-inflammatory factors. It also has anti-inflammatory, anti-oxidative, and immunomodulatory properties.

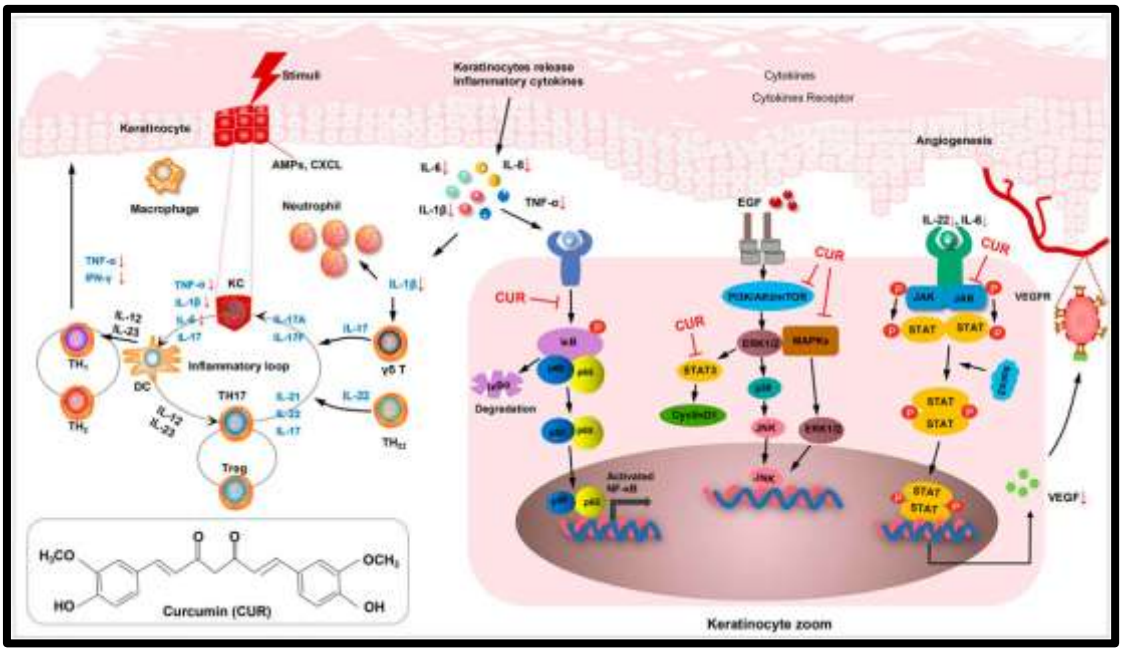

Fig 6 Effect of Curcumin on Psoriasis

DC can be kept immature by curcumin, which has an effect on the presentation of antigens, the synthesis of cytokines, and the activation of adaptive T cell responses. Curcumin inhibits CD4(+) T cell production of IL-17. Curcumin can effectively inhibit T cell proliferation, proinflammatory cytokines, and multifunction in peripheral blood mononuclear cells of psoriasis stimulated in vitro. It can also inhibit T cell production of IFN-γ, IL-17, granulocyte-macrophage colony stimulating factor (GM-CSF), and IL-22. Curcumin suppresses pro-inflammatory cytokines, such as IL-17, TNF-α, IFN-γ, and IL-6, which in turn prevents imiquimod-induced differentiated HaCaT cells from proliferating.

Psoriasis research can be conducted using transgenic mice that express the VEGF protein. Because the inflammatory skin condition in the transgenic rat model of keratin (K) 14-VEGF shares cellular and molecular features with psoriasis, such as distinct vascular and epidermal alterations. Following curcumin treatment, cytokine levels of TNF-α, IFN-γ, IL-2, IL-12, IL-22, and IL-23 decreased to normal levels.

This could be because curcumin inhibits Kv1.3 channel currents, which in turn prevents T cell proliferation, or curcumin affects the NF-κB, AP-1, and MAPK signaling pathways in psoriasis-affected mice. Moreover, studies demonstrate that curcumin directly inhibits the production of IFN-γ, thereby mitigating TPA-induced inflammation. Curcumin nanohydrogel decreased the expression of TNF-α and iNOS while restoring the normal distribution of ZO1 and occludin, two TJs proteins, in an imiquimod-induced psoriasis model. Following topical application to mice, curcumin was able to reduce CC Chemokine receptor 6 (CCR6) protein expression, IL-17A, IL-17F, TNF-α, and IL-22 mRNA levels, as well as inflammation symptoms.

Curcumin has been the subject of a few clinical trials for psoriasis, but the sample size and quality of the evidence are small. a Phase II, open-label, two-stage Simon trial giving patients with plaque psoriasis 4.5g/d of oral Curcuminoid C3 Complex. Although oral curcumin was well tolerated, it was unclear if the improvements were the result of a placebo effect or a spontaneous remission of the illness.

There are many different ways that curcumin works to treat psoriasis. It can prevent dendritic cells from maturing, speed up the polarization of anti-inflammatory macrophages, inhibit pro-inflammatory factors and T cells, limit the growth of vascular endothelial cells, affect genes that make psoriasis more likely, and more.

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Since curcumin is made from natural plant materials, it is safe to use and won't have any negative side effects after a long period of use. Topical curcumin has a promising future in the treatment of psoriasis, and nanogels prepared with suitable substrates can improve transdermal absorption.

Effect of Curcumin on Depression

Depression is a severe psychological illness that affects 4% of people worldwide. Although the exact pathophysiological mechanism underlying depression is still unknown, inflammation, monoaminergic neurotransmitters, neurotrophic factors, and the hypothalamic-pituitary-adrenal axis are thought to play a significant role. Depression is known to be significantly induced by psychological and social stress.

According to studies, stress can trigger an inflammatory response by activating NF-κB and other pathways. The cytokines that are released can impact synaptic plasticity, neurotransmitter metabolism, and other processes, ultimately resulting in depression. There is strong evidence now that depression and inflammation are closely related. Proinflammatory cytokines TNF-α and IL-1 were used to elicit depressive-like behavior in animal models of depression. Consequently, medication therapy that reduces inflammation and cytokines may be a useful tool for treating and improving depression.

Jieyu-wan and Xiaoyao-san, two traditional Chinese medicines used to treat stress and mood disorders, contain curcumin. Due to its neurotrophic, antioxidant, and anti-inflammatory qualities, curcumin may be a very effective treatment for depression. Rats exposed to chronic unpredictable mild stress exhibited depressive-like behaviors and elevated levels of cytokines linked to depression, which is a classic model of depression research.

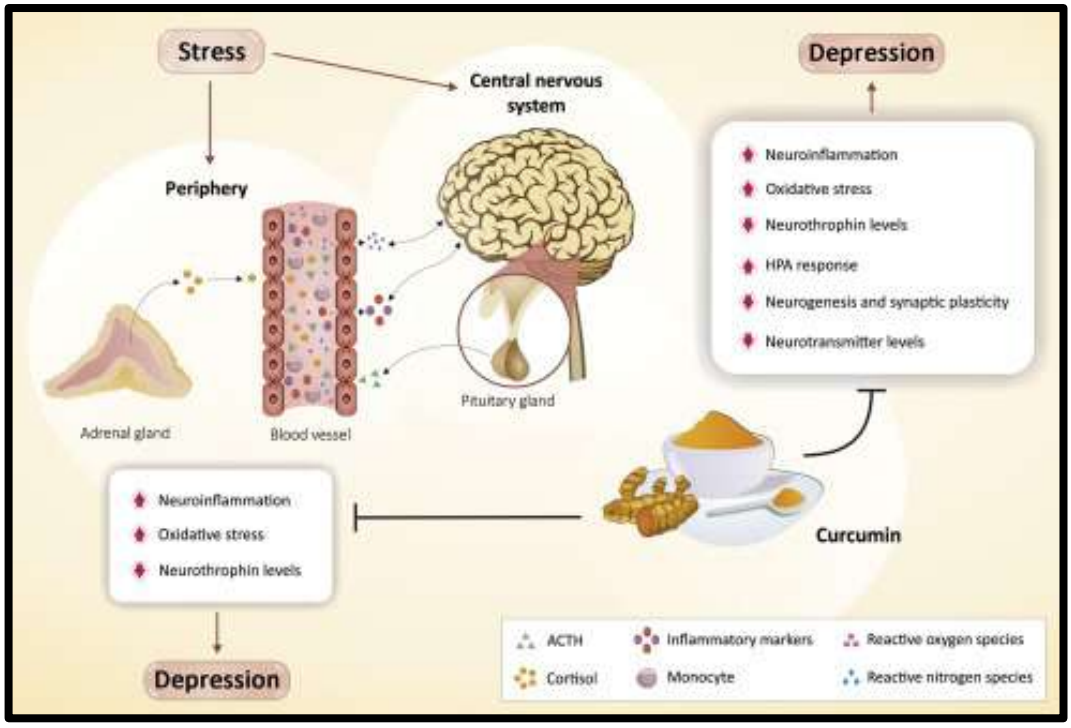

Fig 7 Effect of Curcumin on Depression

Curcumin treatment effectively corrected the depression-like behavior of stressed rats, as evidenced by the relevant test results from the Open Field, Sucrose Preference, Forced Swimming, Social Interaction, and High Level Maze tests. By inhibiting NLRP3 inflammasome activation through down-regulating IL-1β/NF-κB signaling, curcumin administration also reduces the mRNA expression of proinflammatory cytokines, such as IL-1β, IL-6, and TNF-α. In chronic unpredictable mild stress-induced rats, curcumin improves IL-1β-induced neuronal apoptosis by inhibiting the P38 pathway.

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Although not entirely conclusive, curcumin's anti-inflammatory effect is one reason for its improvement in depression. Curcumin has anti-inflammatory qualities as well as the ability to block the release of monoamine oxidase, serotonin, and dopamine. It also controls neurotrophic factors, the hypothalamus pituitary adrenal axis, hippocampal neurogenesis, and neuroplasticity. Like fluoxetine and estradiol, curcumin also has a similar efficaciousness to oestradiol in improving the depressive behavior of ovariectomized rats.

Although curcumin has demonstrated promising antidepressant effects in animal models of depression, consistent, encouraging outcomes from clinical trials have not been observed. Curcumin has been shown in a meta-analysis of nine clinical trials to potentially alleviate anxiety and depressive symptoms in depressed patients. After 5–8 weeks of monotherapy or antidepressant enhancement therapy, there was no compelling evidence in randomized controlled trials or other clinical trial designs that patients with major depression would benefit from different curcumin extracts (doses of 500–1000 mg/d) compared to placebo (or no treatment)

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Problems of Curcumin Bioavailability

Any agent's bioavailability is influenced by a number of factors, including high absorption rates, quick bodily excretion and clearance of intrinsic activity, low serum levels, brief half-lives, apparent rapid metabolism, and restricted tissue distribution. As per the findings of a study primarily focused on the pharmacokinetics, metabolites, and systemic bioavailability of curcumin in cancer patients.

A phase I clinical trial involving 25 patients with multiple precancerous lesions was carried out. Oral doses of 4g, 6g, and 8g of curcumin were administered daily for three months. The identification of serum curcumin concentrations indicates low absorption and limited systemic bioavailability of curcumin. Following a dose of curcumin, serum levels rise for one to two hours before sharply declining. Despite this, the study did not identify curcumin's metabolites or excretion.

A high dose of 12g/day of curcumin has been shown in phase I clinical trials to be safe for use in humans, although the demonstrated bioavailability is not good. The low levels of curcumin in the tissue and plasma are caused by rapid metabolism, rapid systemic elimination, and poor absorption. A number of strategies have been used to increase curcumin's bioavailability.

Serum concentration –

A significant discovery in curcumin research is the identification of extremely low levels of curcumin in the bloodstream. In a study conducted in 1978 by Wahlstrom and Blennow, Sprague-Dawley rats were used to examine how curcumin is absorbed, distributed, and excreted in the body. The results showed that curcumin is poorly absorbed through the gut, as indicated by the minimal amount of curcumin found in the rats' blood plasma after they were orally given 1 g/kg of curcumin.

Tissue distribution

The biological effects of curcumin rely on how it is absorbed and distributed in the body's tissues. These findings suggest that the way curcumin is processed in tissues after intraperitoneal treatment cannot be directly compared to the observations made after oral administration or consuming it with food.

Metabolites

Research has examined the metabolism of curcumin in both rodents and humans through various methods. Curcumin undergoes conjugation processes like sulfation and glucuronidation at various tissue locations following absorption. An initial biodistribution analysis revealed that the liver plays a key role in metabolizing the majority of orally administered curcumin in rats.

Half-Life The systemic elimination of curcumin from the body is an additional factor that greatly impacts its biological effects.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2023-2035 www.ijprajournal.com ISSN: 2456-4494

Different approach of curcuminn bioavailability

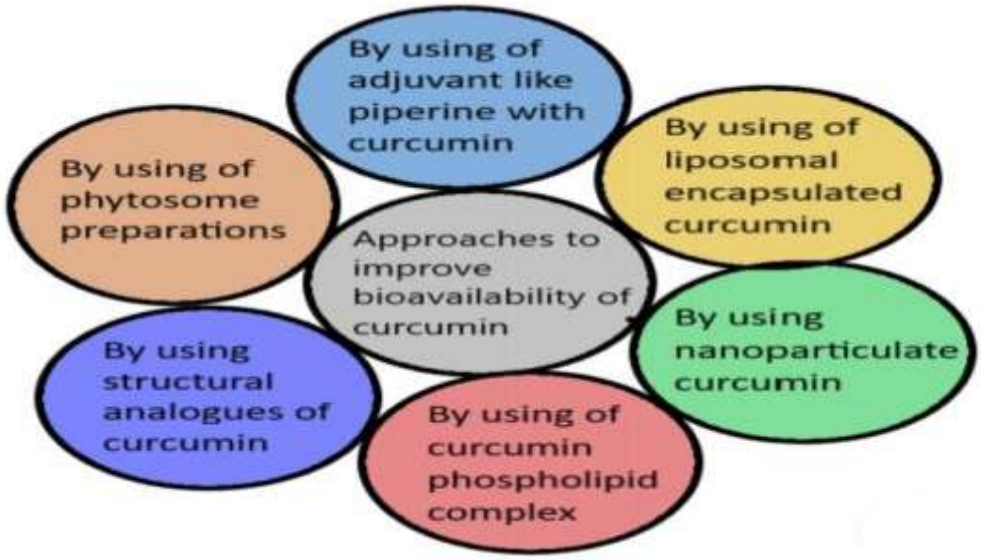

Fig . Different approach of curcuminn bioavailability

It has been reported that the approaches used for curcumin have resulted in rapid absorption and a peak plasma half-life. Despite its low bioavailability, curcumin has shown therapeutic activity in treating various diseases such as cancer, cardiovascular diseases, diabetes, arthritis, neurological diseases, and Crohn's disease. However, in order to enhance the bioavailability of curcumin for future treatments, further research is required.

II. CONCLUSION

The yellow polyphenolic compound curcumin is extracted from the rhizome of Curcuma longa, a member of the Zingiberaceae family of ginger plants. The main sources of turmeric's yellow color are polyphenolic pigment and a fat-soluble substance known as curcuminoids. There are a number of factors that affect curcumin's bioavailability, so different approaches have been used to increase it. These include encapsulating curcumin in liposomes, preparing nanoparticles, using solvent evaporation method, preparing phytosome and non-phytosome curcumin, etc. The choice of nanoparticles as a drug delivery vehicle led to the development of several formulations. An in vivo study involving healthy volunteers revealed that when a cream containing SLNs loaded with curcumin was topically applied over a cream containing free curcumin, the efficacy of the former improved. The novel curcumin nanoparticle system (CURN), the novel and effective drug delivery system (DDS) of guanidine-functionalized PEGylated mesoporous silica nanoparticles, the formulation of loading CUR into the functionalized surface of the nanocarrier pores, and the nanoCurcTM - Predistilled monomers of VP, AA, and NIPAAM are prepared and assessed; these are useful for a variety of uses. The following curcumin nanoparticle formulations have been evaluated in vitro and in vivo: TPGS-Stabilized Curcumin Nanoparticle strategies, which exhibit good pharmacokinetic and pharmacodynamic properties after intravenous administration; and Biodegradable nanoparticle formulation of bis-demethoxycurcumin analogue.

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