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Harnessing the Therapeutical Value of *Curcuma longa* and *Curcumin* Nanoformulations: A Review

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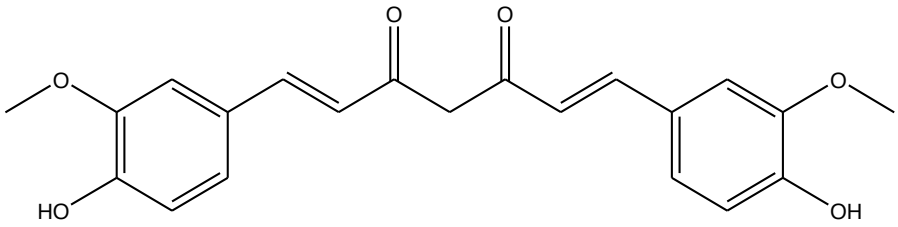
Abstract

Curcuma longa a member of the ginger family (Zingiberaceae), produces the rhizomes that are used to make turmeric. Rhizomes are subterranean horizontal stems that produce roots and shoots. It is becoming more difficult to control microbial infections and the healing of wounds due to the emergence and spread of antimicrobial medication resistance. The most potent and active ingredient in curcuma longa L., often known as turmeric, is curcumin, which has a long and proven history of use in medicine for skin care and human health. It has been suggested that curcumin possesses substantial antibacterial properties, and numerous efforts have been undertaken to ascertain its capacity to simultaneously regulate bacterial growth and facilitate wound healing. Curcumin formulations require addressing its limited water solubility, poor tissue absorption, and short plasma half-life due to its fast metabolism before they can be used as an effective wound healing treatment. To address the issue of curcumin's limited bioavailability, new curcumin nanoformulations have been developed. The medicinal uses of curcumin nanoformulations for antibacterial and wound-healing objectives are thus discussed in the current review.

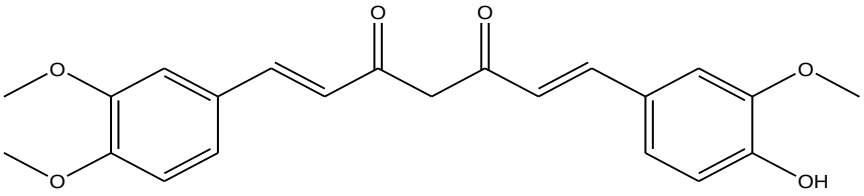
Keywords: Curcumin, Pharmacological activity, Nanoformulations and Wound healing.

Introduction

Turmeric is a well-known Indian spice that belongs to the ginger family (Zingiberaceae), contains curcumin as its main curcuminoids. The other two curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin. Turmeric gets its yellow color from compounds called curcuminoids, which are polyphenols **(Bush J.A. et al. 2001)**. At least two tautomeric forms of curcumin are known to exist: enol and keto and structure of exist form of curcumin was shown in **Figure 1**. Energy stability is higher for the enol form in both the solid phase and the solution **(Cheng A.L. et al. 2001)**. The "curcumin method" uses curcumin to quantify boron. When it combines with boric acid, a reddish-colored substance called rosocyanine is created. Curcumin can be used as a food coloring because of its vivid yellow color. Its E number as a food additive is E100.



CURCUMIN



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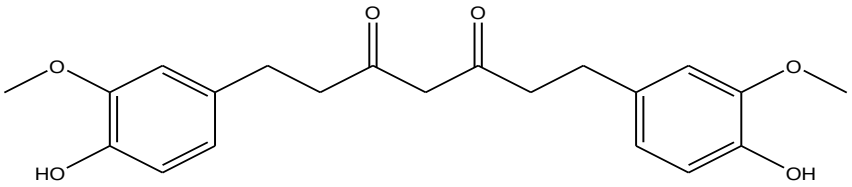

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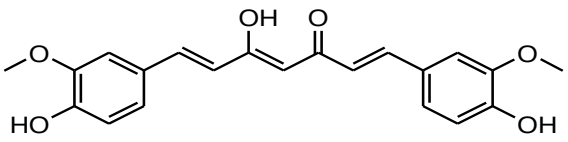
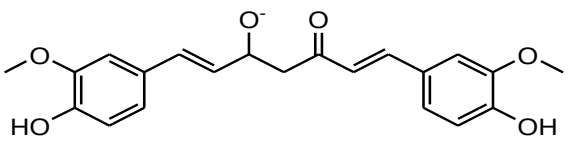


CURCUMIN ENOL FORM



CURCUMIN KETO FORM

Figure 1: Structure of curcumin and main curcuminoids

Properties of Curcumin

Curcumin exhibits antiviral, antifungal, anti-inflammatory, and antioxidant properties. Research has indicated that curcumin poses no toxicity to people. Curcumin works as an anti-inflammatory agent by inhibiting several compounds that are crucial to inflammation **(Hanif R. et al. 1997)**. Turmeric is a useful tool for decreasing post-surgical inflammation. Turmeric helps prevent atherosclerosis due to its ability to inhibit the production of blood clots. Curcumin inhibit the Helicobacter pylori the bacteria that causes stomach ulcers and has been connected to gastric malignancies. Curcumin has the ability to bind to heavy metals like lead and cadmium, lowering their toxicity. Curcumin's protective effect on the brain is explained by this characteristic. All the enzymes like Glutathione S-transferase, 5-lipoxygenase, and cyclooxygenase are all inhibited by curcumin **(Hour T.C. et al. 2002)**. It is a common spice shown in **Figure 2** that is most well-known for being an ingredient in curries and other Indian cuisines. Turmeric has also utilized for ancient Ayurvedic medicine, which combines the therapeutic benefits of plants with food **(Kawamori T. et al. 1999)**. Because of its several medical advantages, this remarkable herb has gained attention in the west. Turmeric shows the strong antioxidants activity.

Figure 2: Schematic representation of curcumin leaf and rhizome

The primary active ingredient in turmeric, curcumin, is an antioxidant that is just as potent as vitamins C, E, and beta-carotene. As such, consumers can use turmeric to prevent cancer, preserve their liver, and prevent premature aging. According to a number of published

researches turmeric also prevents the growth of certain cancer cell types. Turmeric is also a potent anti-inflammatory, which helps with ailments including bursitis, arthritis, and back pain **(Lal B. et al. 1999)**. The main three different characteristics of turmeric were reducing the inflammation.

First, turmeric reduces histamine synthesis, which causes inflammation. Finally, turmeric enhances circulation, which helps to wash toxins out of small joints where cellular wastes and inflammatory substances are usually trapped. Second, turmeric stimulates and prolongs the function of the body's natural anti-inflammatory adrenal hormone, cortisol **(Limtrakul P. et al.1997)**. The benefits of turmeric for digestion have also been proved by research. Due to its cholagogue properties, turmeric helps the body break down fats more easily, improves digestion, and flushes toxins out of the liver.

Active Constituents

Turmeric contains several volatile oils, such as tumerone, atlantone, and zingiberone, as well as the flavonoid curcumin (diferuloylmethane). Sugars, proteins, and resins are among the additional components **(Mukhopadhyay A. et al. 1982)**. Curcumin, which makes up 0.3-5.4% of raw turmeric, is the active ingredient with the most research behind it.

Pharmacokinetics

According to pharmacokinetic research conducted on animals, 40-85% of an oral dose of curcumin is absorbed intact and is processed in the liver and intestinal mucosa **(Mehta R.G. et al. 1991)**. Since curcumin absorbs slowly, bromelain is frequently added to formulations of curcumin to boost absorption and improve anti-inflammatory effects.

Curcumin Nanoformulations

Among the most promising techniques accessible today and in the near future is nanotechnology **(Gharpure K. et al. 2015)**. Typically, nanoformulations are developed to prevent enzymatic breakdown of integrated medications, control their release, modify their pharmacokinetics, and even lessen their toxicity **(Shakeri A. et al. 2016)**. Solid lipid nanoparticles (SLN), polymeric nanoparticles **(Gera M. et al. 2017)**, silver and gold nanoparticles, nanocapsules, liposomal and micellar delivery systems, cyclodextrins, dendrimers, and niosomes are among the primary Nanoformulations **(Naksuriya O. et al. 2014)**. Given curcumin's low bioavailability, fast metabolism, pharmacokinetic profile, photodegradation, and water solubility **(Naksuriya O. et al. 2014)**, these practical and effective methods can both support and improve the drug's biological activity **(Sharifi-Rad J.**

et al. 2020 & Tiyaboonchai W. et al. 2007). In the field of nanotherapeutics, the use of nanogels, nanocrystals, liposomes, and nanoparticles in the design and development of nanoformulations has significantly increased **(Feng J. et al. 2019 & Nguyen K. et al. 2020)**. This seems to be a smart way to boost the stability and bioavailability of curcumin in humans when taken orally **(Salehi B. et al. 2020, Salehi B. et al. 2020 & Sunagawa Y. et al. 2015)**. Many nanotherapeutic strategies have been put forth to boost the bio-dissemination of curcumin loaded with nanoparticles, also referred to as "nano-curcumin" or "nanoformulated curcumin," **(Flora G. et al. 2013)**. In curcumin nanoformulations, the molecule is encapsulated in a variety of substances, including collagen, polyethylene glycol (PEG) monoacrylate, gelatin-based nanofibers, and polylactic-co-glycolic acid (PLGA) **(Bisht S. et al. 2007)**. Numerous animal studies intended to evaluate the pharmacokinetics of nanoparticles and nanoformulations have shown improved plasma levels of curcumin administered by micro- and nanoformulations, indicating a high degree of efficacy for these modes of delivery **(Naksuriya O. et al. 2014)**. Certain formulations, including Meriva^{TM}, have gained significant traction in the functional food and nutraceutical markets because of their high levels of efficacy and safety **(Marczylo T.H. et al. 2007)**. For instance, testing on Theracurmin, a synthetically produced version of curcumin nanoparticles, indicated increased bioavailability **(Fadus M.C. et al. 2016 & Sunagawa Y. et al. 2015)**. Liposomes and micelles based on lecithin have also shown to be useful methods **(Gopinath D. et al. 2004)**. For curcumin formulation, liposomes, polymeric micelles, and polymeric nanoparticles have really proven to be beneficial methods because of their tiny particle size (10-100nm) and 15% to 20% high loading capacity **(Chereddy K.K. et al. 2013)**. For instance, PLGA and PLGA-PEG blend nanoparticles containing curcumin (1 h mean half-life) increased the curcumin mean half-life ($t_{1/2}$) in roughly 4 and 6 h, respectively **(Sunagawa Y. et al. 2015)**, and the C_{max} increased 2.9 and 7.4 times, respectively **(Khalil N.M. et al. 2013)**. Additionally, when using nanoparticles-carrier, in particular PLGA-PEG nanoparticles, there was a reduction in both curcumin distribution and metabolism. Moreover, the bioavailability of curcumin-loaded PLGA-PEG nanoparticles was 3.5 times higher than that of curcumin-loaded PLGA nanoparticles **(Khalil N.M. et al. 2013)**. The use of PLGA nanoformulations has also been associated with an increased curcumin bioavailability in several cancer cell lines; however, in the case of brain cancer, it is still unclear exactly how the form enters the brain **(Gera M. et al. 2017)**. The pharmacokinetics and biological distribution of curcumin-loaded PLGA-PEG-PLGA micelles, as well as an aqueous curcumin solution consisting of 45% PEG 400, 15% dimethylacetamide, and 40% dextrose **(Naksuriya O. et al. 2014)**, were evaluated using a

broadspectrum approach **(Sunagawa Y. et al. 2015)**. The results showed that, in comparison to the other curcumin form under study, PLGAePEGePLGA micelles significantly increased the clearance and distribution half-life ($t_{1/2}$), mean residence time, and AUC. More permeability was demonstrated by curcumin gelatine nanoparticles than in comparison of PLGA nanoparticles **(Nguyen K.T. et al. 2020)**.

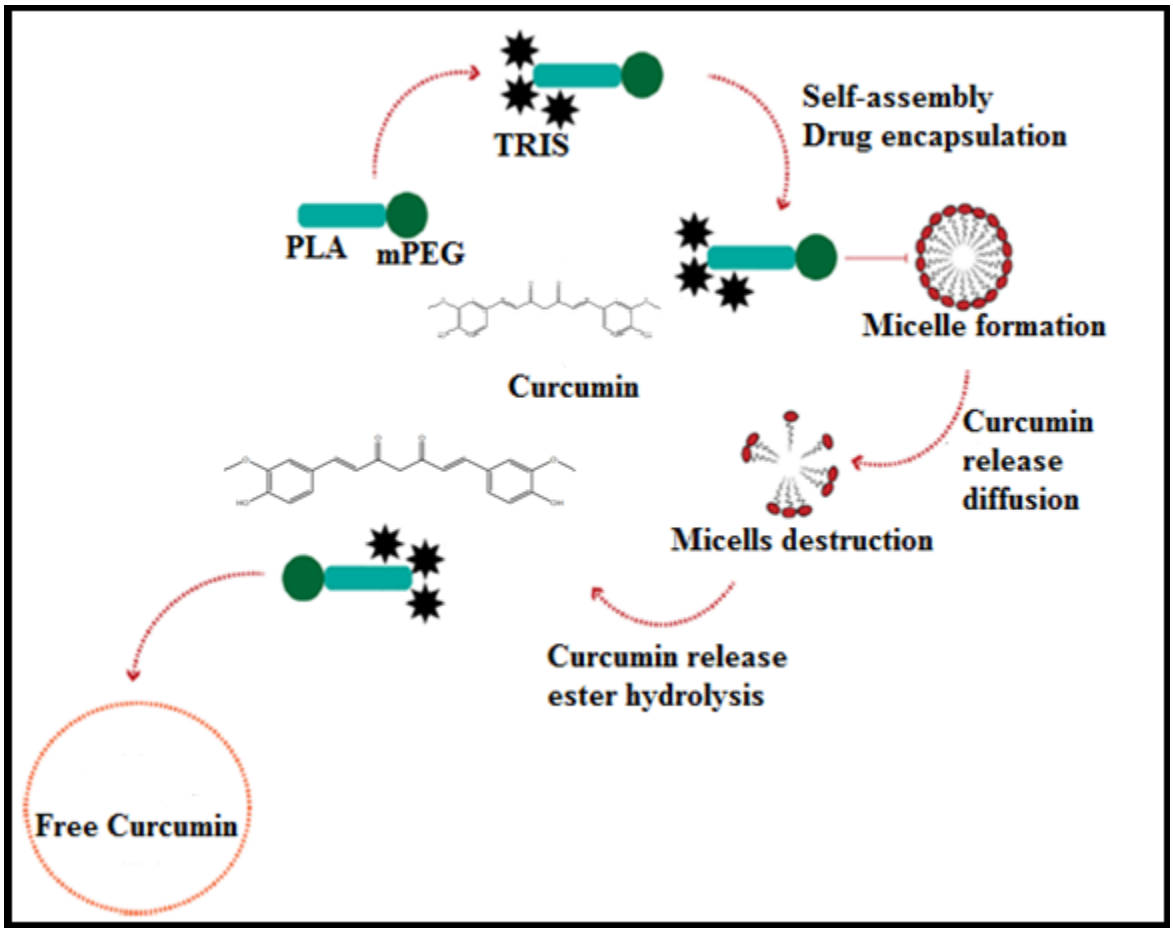
Curcuminoids stability in cream formulations increased as a result of the use of SLN as a drug delivery mechanism **(Tiyaboonchai W. et al. 2007)**. Curcuminoids loaded SLNs demonstrated chemical and physical stability using the micro-emulsion process at a moderate temperature, with a percentage of curcuminoids remaining >88% after six months **(Tiyaboonchai W. et al. 2007)**. In a similar vein, a recent study that used high-pressure homogenization in conjunction with a high-shear dispersion method describe curcumin loaded SLNs discovered that the pharmacokinetic profiles in rats as well as the chemical stability and dispersibility of curcumin in aqueous medium were improved (administered by jugular vein cannulation) **(Sun J. et al. 2013)**. Now recently, curcumin loaded SLNs combined with white wax and produced a long-lasting medication release that stopped the growth of Staphylococcus aureus **(Luan L. et al. 2019)**. Furthermore, these nanoformulations have demonstrated favorable safety profiles in both humans and animals; nevertheless, more research is required, particularly for prolonged or repeated doses. An unfavorable example is the documented occurrence of anti-PEG IgM (immunoglobulin M) production following repeated administration of PEG-coated nanoformulations **(Naksuriya O. et al. 2014)**. However, the tiny size and delayed release accelerated the rate of elimination, and the PEG shell on the surface of the nanoparticles shielded them from the host immune system's deterioration **(Cheng Y. et al. 2018 & Liu W. et al. 2016)**. These formulations based on nanotechnology have significantly increased the therapeutic efficacy of curcumin while simultaneously lowering toxicity **(Ghaemi-Jandabi M. et al. 2015)**. The goal of the work was to develop a topical curcumin loaded lipid carrier for treat skin conditions like psoriasis. *Ex-vivo* penetration experiments revealed that curcumin was more soluble in lipid so accumulated in the epidermal layer **(Kesharwani P. et al. 2020)**.

Curcumin's water solubility has also been increased and the likelihood of its systemic negative effects has been decreased through the use of various nanoformulation-based delivery systems, including liposomes **(Bisht S. et al. 2007)**, nanoparticles **(Kesharwani P. et al. 2020)**, polymeric micelles **(Krausz A.E. et al. 2015)**, phospholipid complexes **(Liu J. et al. 2013)**, cyclodextrin complexes **(Liu W. et al. 2016)**, nano-disks, nanofibers **(Naksuriya O. et al. 2014)**, solid lipids **(Shakeri A. et al. 2016)** and microemulsions

(Sharifi-Rad J. et al. 2020). Additionally, nanoformulation might show better heat stability **(Liu L.L. et al. 2019)**.

Pharmacological activities of curcumin and curcumin loaded nanoformulations

As previously said the major goal of creating curcumin nanoformulations is to improve its solubility in order to prevent its rapid metabolism in the intestine and, as a result, increase its bioavailability and cell uptake **(Dei Cas M. et al. 2019, Moorthi C. et al. 2013)**. Numerous investigations on animals have thoroughly examined the safety and accuracy of curcumin nanoformulations and have determined that this is related to its loading and release explained in **Figure 3 (Ravichandran R.J. et al. 2013)**.



mPEG: methoxy-poly (ethylene glycol), PLA: poly(lactic acid), TRIS: tris (hydroxymethyl) amino methane

Figure 3: Loading of curcumin and its release

Antimicrobial effects: In addition to becoming a major cause of public health problems and carrying a significant morbidity load, microorganisms that have developed resistance to

traditional medications have gradually reduced the effectiveness of treatment **(Anitha A. et al. 2011)**. Recent studies have shown promising results in suppressing microbial growth because of curcumin's significant antibacterial properties **(Moghadamtousi S.Z. et al. 2014)**. Curcumin has demonstrated encouraging antimicrobial properties against a variety of pathogens, including some fungi, viruses, and even parasites. Bacteria include S. aureus, Pseudomonas aeruginosa **(da Silva A.C. et al. 2018)**, Salmonella paratyphi, Escherichia coli, Penicillium notatum, Bacillus subtilis, Aspergillus niger, and Mycobacterium tuberculosis **(Gera M. et al. 2017)**. The growth of several bacteria, parasites, and harmful fungi is inhibited by curcuma longa essential oil and turmeric extract. Diets supplemented with 1% turmeric were shown to reduce small intestine lesion scores and improve weight gain in chicks infected with the caecal parasite Eimera maxima **(Krausz A.E. et al. 2015)**. Turmeric oil used topically inhibited dermatophytes and pathogenic fungus, however neither curcumin nor turmeric oil affected the yeast isolates in another animal investigation in which guinea pigs were infected with either pathogenic molds, dermatophytes, or yeast. The guinea pigs with dermatophyte and fungal infections showed improvements in their lesions, which vanished seven days after the use of turmeric. Curcumin exhibits a moderate level of action against main species of leishmania and plasmodium falciparum. To provide safe topical administration, an ideal formulation for curcumin-loaded nanostructured lipid carriers must have strong antibacterial activity and excellent curcumin penetration and retention in the skin layers **(Rapalli V.K. et al. 2020)**.

Wound healing effects: The process of healing a wound is quite intricate and involves multiple processes, which can be broadly classified as follows: development of fibrous tissues, collagen proliferation, aggregation and coagulation of radical chemicals, constriction of the wound, and finally granulation tissue and scar formation **(Tejada S. et al. 2016)**. Curcumin based nanoformulations' have been demonstrated many benefits in the treatment of burn wounds that are infected. They do this by lowering the load of bacteria in the afflicted area and promoting the heal **(Krausz A.E. et al. 2015)**. While improving wound healing in a mouse wound model, it has been shown to have a potent inhibitory effect on methicillin-resistant S. aureus (MRSA) **(Krausz A.E. et al. 2015)**. For example, MRSA-inoculated mice with burn injuries were given topical doses of 7.5mg/mL curcumin-encapsulated nanoparticles every day for seven days. When compared to the control mice, the wound bacterial load was much lower at the end of therapy, and the wound healing process was noticeably speed up by nanoformulated curcumin **(Krausz A.E. et al. 2015)**. Similarly,

according to **(Chereddy K.K. et al. 2013)** PLGA curcumin loaded nanoparticles have been shown ability to actively treat wounds while also improving the stability and solubility of curcumin. Similar results were reported by **(Ghaffari S. et al. 2018)** the use of curcumin formulated in SLNs (including cholesterol and tween 80) as a topical antibacterial agent in rats and to treat burn wounds produced similar outcomes when combined with ampicillin nanoformulated. After 14 days of topical application, this association was found to be effective in promoting wound healing and limiting the growth of P. aeruginosa, S. aureus, and E. coli **(Ghaffari S. et al. 2018)**. On female rats, curcumin-loaded gel-core hyalurosomes demonstrated the effectiveness of burn wound healing **(El-Refaie W.M. et al. 2015)**. Recently, **(Kalita S. et al. 2018)** a study was conducted on the effectiveness of lysozyme-capped gold nanoclusters (AUNC-L) with β-lactam antibiotic ampicillin (AUNC-LAmp) as an antibacterial hybrid surface functionalization for reversing MRSA resistance to ampicillin (and also to nonresistant strains). Notably, the study showed that applying the nano composite topically to diabetic rats lesions eliminated MRSA infection and accelerated the healing process. Finally, **(Kalita S. et al. 2018)** also demonstrated that this nanoformulation had any negative consequences at *in-vivo* locations. Additionally, new chloramphenicol loaded with poly (ε-caprolactone) (PCL)-pluronic composite nanoparticles (CAM-PCL-PNPs) is reported by the same scientists. Bioactivity for animal models of MRSA-infected burn wounds **(Kalita S. et al. 2015)**. In comparison to the free medication, this formulation reduced toxicity and showed noticeably increased anti-MRSA activity against 10 clinical isolates of MRSA strains. In addition, the in vivo tests displayed optimal MRSA clearance and increased the survival rate in comparison to the free chloramphenicol therapy. According to the findings, these nanoparticles might be employed in preclinical settings in the future **(S. Kalita S. et al. 2015)**.

The development of liposome nanocarriers as stable and effective dermal delivery vehicles of various compounds, such as curcumin, aims to prevent potential drug overdose and toxicity while simultaneously boosting drug efficiency **(Kianvash N. et al. 2017 & Zhao Y.Z. et al. 2013)**. After 8 days of treatment, propylene glycol nanoliposomes containing 0.3% curcumin significantly improved wound healing parameters in burned rats and shown antibacterial activity (comparable to silver sulfadiazine) **(Kianvash N. et al. 2017)**. Propylene glycol is widely utilized in topical formulations as an emulsifier and penetration enhancer **(Li W.Z. et al. 2016)**. When liposomes are modified with propylene glycol, deformable nanovesicles with enhanced skin layer penetration and retention capabilities are produced **(Zhao Y.Z. et al. 2013)**. As can be seen from the foregoing, curcumin bioavailability may be increased by

nanoformulations, allowing for the drug's long-term release at the dressing site and promoting wound healing **(Zhao Y.Z. et al. 2013)**.

Antioxidant effects: Turmeric and its curcumin component, both soluble in water and fat, have potent antioxidant properties similar to those of vitamins C and E. The effects of curcumin pretreatment on ischemia-induced cardiac alterations were found to be reduced in a feline heart research **(Munzenmaier A. et al. 1997)**. An *in-vitro* investigation was carried out using bovine aortic endothelial cells to assess the impact of curcumin on endothelial heme oxygenase-1, an inducible stress protein. Curcumin treatment for eighteen hours increased the cells' ability to withstand oxidative damage **(Park E.J. et al. 2000)**.

Hepatoprotective effects: Similar to silymarin, turmeric has been shown to have hepatoprotective properties. The hepatoprotective properties of turmeric have been proven in animal experiments against a range of hepatotoxic insults, such as Aspergillus aflatoxin, galactosamine, acetaminophen (paracetamol), and carbon tetrachloride (CCl_4) **(Park E.J. et al. 2000)**. Turmeric has antioxidant qualities and capacity to inhibit the production of pro-inflammatory cytokines which is primarily responsible for its hepatoprotective effects. After the treatment of curcumin reduces the liver toxicity in treated group in comparison of control group with acute and subacute carbon tetrachloride (CCl_4) induced toxicity **(Park E.J. et al. 2000)**. Turmeric extract reduced the generation of aflatoxin by 90% when administered to ducklings infected with Aspergillus parasiticus. Aflatoxin-induced necrosis, lipid alterations, and biliary hyperplasia were all restored by curcumin and turmeric. In addition to its choleretic effects, sodium curcuminate, a salt of curcumin, also increases biliary excretion of bile salts, cholesterol, and bilirubin. It also increases bile solubility, which may help prevent and treat cholelithiasis.

Anti-inflammatory effects: Curcuma longa's volatile oils and curcumin have strong anti-inflammatory properties. It was discovered that oral curcumin therapy was half as effective as cortisone or phenylbutazone in cases of acute inflammation and half as effective in cases of chronic inflammation **(Pendurthi U.R. et al. 1997)**. Oral injection of Curcuma longa dramatically reduced inflammatory swelling in rats with Freund's adjuvant-induced arthritis when compared to controls. Curcumin decreased the inflammatory neutrophil aggregation in monkeys because it can prevent the formation of pro-inflammatory prostaglandins from arachidonic acid and decrease neutrophil function in inflammatory conditions, curcuma. longa is thought to have anti-inflammatory effects **(Ramachandran C.**

et al. 2002). In order to reduce inflammation and irritation brought on by inflammatory skin disorders and allergies, curcumin can also be applied topically. However, caution must be taken to avoid staining clothing with the yellow color.

Anti-carcinogenic effects: Curcumin has been shown to reduce carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. These findings have been confirmed by *in-vitro* experiments using human cell lines and animal studies using rats and mice **(Reddy B.S. et al. 2002)**. Curcumin decreased the growth of tumors and the proliferation of cells in two investigations on prostate and colon cancer. Both *in-vitro* and *in-vivo* investigations have shown that curcumin and turmeric can decrease the action of a number of common carcinogens and mutagens in a range of cell types. Turmeric and curcumin have anticarcinogenic properties because they directly scavenge free radicals and act as direct antioxidants **(Shao Z.M. et al. 2002)**. They also indirectly raise glutathione levels, which helps the liver detoxify pollutants and carcinogens while also preventing the development of nitrosamines.

Cardiovascular effects: Turmeric reduces blood pressure and triglycerides, lessens the vulnerability of low-density lipoprotein (LDL) to lipid peroxidation, and prevents platelet aggregation, among other beneficial benefits on the cardiovascular system **(Sharma A. et al. 2000)**. Even at low doses of turmeric, these effects have been observed. In addition to decreasing plasma cholesterol and triglyceride levels, a trial of eighteen atherosclerotic rabbits given a low-dose (1.6–3.2 mg/kg body weight daily) of turmeric extract showed decreased susceptibility of LDL to lipid peroxidation **(Simon A. et al. 1998)**. Cholesterol and triglyceride levels were observed to decrease, albeit less than with the lower dose, but the greater dose did not prevent the lipid peroxidation of LDL. The impact of turmeric extract on cholesterol levels may be attributed to both an increase in the liver's conversion of cholesterol to bile acids and a decrease in the intestinal absorption of cholesterol **(Somasundaram S. et al. 2002)**. It is believed that the components of curcuma longa prevent platelet aggregation by potentiating prostacyclin synthesis and inhibiting thromboxane generation.

Gastrointestinal effects: Curcuma longa's constituents have a number of gastrointestinal tract-protective properties. The turmeric compound p-tolymethylcarbinol enhanced the secretion of pancreatic enzymes and raised the release of gastrin, secretin, bicarbonate, and prevented intestinal spasm **(Sreejayan, N. et al. 1994)**. Additionally, it has been demonstrated that turmeric prevents the formation of ulcers brought on by stress, alcohol,

indomethacin, pyloric ligation, and reserpine. In rats exposed to various gastrointestinal shocks, this resulted in a large increase in stomach wall mucus **(Sreejayan, N. et al. 1996)**.

Immunity booster effects: If certain cells manage to evade apoptosis, curcumin can potentially aid the body in fighting against cancer **(Srivastava R. et al. 1986)**. After consuming curcumin, researchers observed that there were more B type and CD_4^+ T-helper immune cells in the intestinal mucosa. Apart from its targeted activation of the immune system, curcumin also improves immunity overall **(Thaloor D. et al. 1998)**. Scientists in India have seen enhanced antibody production and heightened immunological response in mice administered curcumin.

Pregnancy and Lactation effects: While there is no proof that consuming turmeric as a spice during pregnancy or lactation has any negative effects, the safety of taking curcumin supplements during these times has not been determined **(Venkatesan N. et al. 2000)**.

Curcumin blocks NF-κB and the motogenic response in *Helicobacter pylori*-infected epithelial cells: Research shows that when the microbial pathogen Helicobacter pylori infects epithelial cells, it activates nuclear factor κB (NF-κB), induces genes that produce pro-inflammatory chemokines and cytokines, and causes a motogenic response (spreading of cells) **(Verma S.P. et al. 1997)**. It has been studied that curcumin (diferuloylmethane), the yellow pigment found in turmeric (Curcuma longa L.), inhibits H. pylori-induced NF-κB activation and the consequent production of interleukin 8 (IL-8). It has been shown that curcumin prevents NF-κB DNA binding, IκB kinases α and β (IKKα and β) from acting, and IκBα degradation **(Verma S.P. et al. 1998)**. Curcumin does not suppress the extracellular signal-regulated kinases 1/2 (ERK1/2), p38, or mitogen-activated protein kinases (MAPK), which are similarly triggered by H. pylori infection. Curcumin has been shown to inhibit the motogenic response caused by Helicobacter pylori **(Bush J.A. et al. 2001)**.. It has been determined that curcumin should be taken into consideration as a potential therapeutic drug that is effective against pathogenic processes triggered by H. pylori infection because it inhibits NF-κB activation and cell scattering **(Srivastava R. et al. 1986)**.

Conclusion

The information presented here suggests that curcumin nanoformulations hold great promise for the health of people and animals like, with a high degree of safety and little possibility for toxicity, even when used often. Topical curcumin nanoformulations enhance the antibacterial

and therapeutic benefits of curcumin by delivering it to the injured region. Clinical trials on human volunteers are yet absent, however preclinical evidence confirm the effectiveness of curcumin nanoformulations against various microorganisms and on the wound healing process, indicating a significant potential for novel medication development. Furthermore, it is unclear how to control the genetic, cellular wound environment and restore the chronic inflammatory process. Thus, in order to create unique, safe, and effective nanodrugs, more research is required to apply the knowledge gained from animal models to humans.

List of Abbreviations

SLNs: Solid lipid nanoparticles; mPEG: methoxy-poly (ethylene glycol); PLA: poly (lactic acid); TRIS: tris (hydroxymethyl) amino methane; CCl_4: Carbon tetrachloride; LDL: low-density lipoprotein; IgM: Immunoglobulin M; PEG: Poly ethylene glycol; AUC: Area under curve.

Ethics approval and consent to participate: Not applicable

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