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## Review Article

## Wound-healing effects of curcumin and its nano formulation

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## ABSTRACT

Wound healing is a method of tissue repair or regeneration. Section Damages. Plants and plant-derived bioactive substances have been found effective in the treatment of many diseases. Types of wounds. Curcumin is a natural polyphenol that has been used since ancient times. Ayurveda is used times for its healing properties to relieve pain and aid in many healing processes. Plates. Various studies of curcumin administration to the site of pain have reported the following effects: Curcumin eliminates reactive oxygen species and increases the ability to improve collagen deposition, Chapter: Granulation data finally makes the wound contract. Curcumin is widely available and has been studied for its ability to relieve pain, but in addition it has low solubility and rapid metabolism. The short plasma half-life limits its application in wound healing. Since nanotechnology existed Chapter Proven to be a good method for wound healing with proper support Chapter injury sites. This review highlights the potential of curcumin and its Nano formulations; Preparation of liposomes, nanoparticles, nano emulsions, etc. usage This article is about Curcumin's many biomedical applications underlie its anti-biofilm properties Chapter and its wound healing effect.

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## 1. Introduction

To show Skin is the largest organ of the mortal body and makes up 15 of the mortal body. Weight with an area of roughly 20 square measures (about twice the area of an apartment bedroom).<sup>1</sup> Protects the internal structure All physical, natural, chemical and stresses coming from outside a. It also includes thermoregulation, immunomodulatory analysis, Prevention of dehydration, perceptivity and cohesion with vitamin cholecalciferol (D3).<sup>2-4</sup> Composition Damage or disturbance of the healthy structure of the skin is defined as a crack. The crack is fine Section is classified according to position, depth, etiology, type of injury, and appearance.<sup>5</sup> Clinically, injuries are

classified as habitual or acute injuries. robotic pain mending time is roughly 8- 12 weeks (about 3 months), with habitual injuries taking longer mending (sometimes Section), indeed for a numerous months due to habitual illness. Age, obesity, injury and habitual complaint Diabetes, cancer, etc. conditions can beget habitual pain.<sup>6,7</sup> Article Healing is a physiological process involving common action hemostatic, inflammatory, proliferative and kerchief redoing stages.<sup>8</sup> Stop the bleeding is the first and most important response in the first numerous beats after injury. Thewoundedlb., 22882/ 24 layoff accompanying pain Chapter Hemostasis stage. The addition stage is actuated when the fibrin coagulates Section is created by allowing neutrophils to move to the crack point to remove and organize bacteria. Chapter Correct phagocytes cache converting growth factor  $\beta$  (TGF-  $\beta$ ), transferring out a life signal, allowing the crack

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**Figure 1:** Curcumin

to begin healing. Blood monocytes Chapter Lymphocytes separate into kerchief macrophages, which causes growth release. Chapter importunity Chapter fibroblasts regenerate damaged blood vessels. Growth is the third stage. Chapter Dermal kerchief conformation. Angiogenesis, epithelialization and collagen product Chapter TGF-  $\beta$  initiated by fibroblasts, platelets, and macrophages induces collagen product Chapter in Fibroblasts The final stage of this process is modification during treatment; IT Chapter New caste formed by dermal fibroblasts of the crack. The original type III collagen in the injured area is replaced by type I collagen forcross- linking. And rearranged along the voltage line.<sup>9,10</sup> multitudinous are heritable and acquired Factors analogous as diabetes can intrude with the crack mending process. Diabetic ulcer cases had increased inflammation and abnormal cellular infiltration, Chapter scars in cytokine product, neuritis, and shy neovascularization. meliorate health Medical Costs, Aging, Biofilm conformation, and Diabetes trouble Factors Chapter With obesity, habitual injuries come a major medical, social and profitable problem Chapter Competition. Medicare heirs at law linked according to the 2018 tale said about 8.2 million people (about half the population of New York) were injured. The periodic crack of the request, conforming of products, is anticipated to reach 15–22 billion bones (about 68 per person in the US) by 2024. In the united countries' Only 4,444 people, roughly 5.7

million cases (about twice the population of Arkansas), are injured each time The treatment cost of is roughly 20 billion US bones.<sup>11</sup> It all boils down to this There are multitudinous extensive and challenging crack mending studies. Shops are always their Chapter form medium.<sup>12</sup> As the disquisition progressed, interest completely changed. Active chemical constituents of shops. Curcumin is at the top of the crack mending process. Curcumin is a naturally being low molecular weight polyphenol conflation set up in the turmeric and sweet rhizome of *Curcuma longa*.<sup>13</sup> Curcumin(77) is the most Substance Main bioactive element of turmeric rhizome, followed by desmethoxycurcumin bisdemethoxycurcumin(3) and cyclocurcumin.<sup>3</sup> It took multitudinous times. Traditional medicine is used to treat pain and heal injuries. This Topical operation of curcumin has been shown to be effective in crack mending movement. Curcumin works in multitudinous stages, including inflammation, development, and development. Chapter Proliferative phase, thus perfecting the overall process of crack healing. But Part Certain limitations analogous as poor bioavailability, lack of water solubility, and rapid-fire- fire dissolution Metabolism affects the remedial effect of curcumin. toxic at high attention Cosmetics is another strike of curcumin.<sup>13–15</sup> So come together Section Limiting factors for replacing curcumin with different nano delivery systems are interesting places to explore to unlock all compounding possibilities District Medical. This review highlights the part and significance of curcumin and its nano expression for crack healing. Various pharmacological exertion are interrelated. Composition also mentions this in the judgment.

### 1.1. Chemistry and use of curcumin

The molecular formula of curcumin is  $C_{21}H_{20}O_6$ . Its structure consists of three corridor. The conflation is shown in Figure 1 two sweet rings with methoxy and hydroxyl groups. There are groups at the ortho position attached to the seven- carbon relation with  $\alpha$ ,  $\beta$ - unsaturation Nominal  $\beta$ - diketone half.<sup>16</sup> Due to the presence of the diketone group, curcumin expands Chapter occasion- Enol tautomerism. Ketone form predominates in slightly acidic and neutral conditions,<sup>17</sup> whereas the enol form predominates under certain conditions. The result shows this Chapter- Trans- isomerism. This conversion rate is more stable Chapter Difference between two types of phenolic formaldehyde- Methoxy group of the curcumin backbone. The measured ground state dipole moment of curcumin is 10.77D.<sup>18</sup> one. quotidian value Octanol/ Water Dispenser Chapter Curcumin has a log P) value of 3.2, making it effective Insoluble in water but answerable in lipids.<sup>16–19</sup> one. It has sufficient transmembrane permeability due to its lipophilic point. Composition Curcumin can be incorporated into arid results with the help of lipids, surfactants and albumin Chapter Included in advanced

attention Curcumin micelles of showed good results. still, surfactants Chapter It has been proved that curcumin is effective against multitudinous conditions. Alzheimer's complaint, multiple sclerosis, rheumatoid arthritis, atherosclerosis, etc. Chapter poison, fibrosis and impaired crack healing, inhibition of thrombosis and inhibition of platelets were collected<sup>20</sup> It has also been described as anti-bacterial. Anti-cancer, anti-inflammatory, anti-mutagenic, anti-inflammatory, anti-proliferative, anti-aging, anti-amyloid, anti-hypercholesterolemia substance. one. Prevents the activation of the transformation of rudiments and products produced by free revolutionaries Chapter  $\kappa$ B),<sup>15</sup> product of cytokines and other cellular processes important for cells Chapter Survival. It also inhibits signal transducer and activator of recap (STAT) proteins. Curcumin- induced inhibition of NF $\kappa$ B- DNA list suppresses the pro- seditious response Molecular Matrix Metalloproteinase 9 (MMP-9) and Matrix Metalloproteinase 3 (MMP-3) and also reduces pro-seditious cytokines analogous as excrescence necrosis factor 1 (TNF-1), interleukin 1 (IL- 1), and interleukin 8 (IL- 8). Curcumin also reduces the expression of COX- 2, prostaglandins and prostaglandins by binding to the COX- 2 (prostaglandin endoperoxide synthase 2) protein. Thromboxane emulsion. also, curcumin is a versatile antioxidant patch. Part Fights free revolutionaries allowed to reduce reactive oxygen species (ROS) Chapter Injury caused by muscle pain due to crushing. It has been noted that curcumin is also effective.

### 1.2. Effect of curcumin on fibroblast proliferation

Granulation serviette and collagen product and deposit. also, Chapter Fibroblasts in the crack terrain are really the most important treatment system. Fast and beautiful crack check. Fibroblasts develop commonly Composition Curcumin treatment against bullying Chapter many studies have proven that it will beget fibroblasts to enter the painful area. Ravan far et al. Curcumin has been shown to accelerate cell proliferation and dock the incendiary process, which indicates an increase in fibroblasts. Distribution/ 1mm<sup>2</sup> crack area and rapid-fire- fire epithelialization 3.4a. Effect of curcumin on granulation kerchief conformation Chapter Four days after skin injury, granulation kerchief or new matrix begins to form, Chapter Section Extracellular matrix. Curcumin improves the conformation of granulation kerchief, provides a stable base for epithelial cell migration, and promotes the regeneration of epithelial cells. Chapter Differences that heal injuries. Aslam et al. Studies show granulation kerchief with little collagen, neovascularization, an moderate inflammatory cells ( D- F) were set up in the curcumin- treated group. They were also tutored Curcumin Zano nanocomplex treated groups were set up features, including large collagen packets, heavy collagen packets in the dermis, are nearly normal. Fibrosis, angiogenesis and

collagen matrix changes ( G- I).

### 1.3. Effect of curcumin on collagen deposition

The extracellular matrix must be rearranged and reshaped to heal wounds Chapter Make a comeback. Extracellular matrix, including granulation tissue and collagen, provides support to cells and contains various proteins and polysaccharides. Collagen is the most abundant protein in the skin extracellular matrix, accounting for 70-80%. Is good. The tissue consists only of established collagen fibers. Article Final result of wound healing. Therefore, adequate collagen production and accumulation is ideal for wound healing. Curcumin stimulated Accelerates this process by improving collagen and extracellular matrix synthesis. Treatment. Curcumin has been shown to tend to improve wound healing. Treatment, because it can begin to produce and release collagen for three days after use related to wound as reported by Mahmoud et al., 2022. Qian et al. show curcumin can cause wound exudate by causing the gradual release of curcumin, thereby accelerating it. The healing process promotes both collagen deposition and vascularization.

### 1.4. The role of curcumin in the treatment of diabetic foot ulcers (DFU)

Serious complications of diabetes, called diabetic bottom ulcers ( DFU), are frequently caused by Section Ischemia, complaint, original pain, diabetic neuropathy, supplemental vascular complaint (PVD) and diabetic neuropathy. Diabetic ulcers are a habitual condition. Good detainments pain. Amputation compared to severe pain ( control hemostasis) Section If DFU isn't treated in its early stages, the outgrowth is generally, [55] DFU status Chapter moment DFU uses different types of treatments Chapter Hyperbaric relief Studies show that diabetic cases with bottom ulcers Section Strict diabetes control reduces the liability of treatment termination. also, Chapter factors contribute DFU to metabolic changes and crack mending. A well-known condiment called curcumin was studied for its mending capacities Diabetic bottom ulcer. Curcumin helps heal injuries by reducing oxidative stress Section seditious Conditioning promote growth and form phases Section over. also, PPAR-  $\gamma$  ( PPAR-  $\gamma$ ), spark lipoprotein lipase. ( LPL ( LPL), and low- viscosity lipoprotein receptor (LDLR) may increase insulin perceptivity, glucose immersion in muscle and adipose towel and ameliorate lipid homeostasis, contributing to curcumin's anti-diabetic goods. According to exploration by Kamar et al., the mending process was enhanced by a curcumin- nanoparticle- loaded hydrogel with completere-epithelialization an unbroken dermo-epidermal junction, and dermal junction reconfiguration with much further collagen deposit and VEGF and AQP3 product. These findings demonstrated that the operation of

dastard- NP/ HG significantly altered the kinetics of crack mending in diabetic skin injuries compared to those that entered dastard/ HG.[63] In a Sprague Dawley diabetic rat model, Li et al.(2019) created curcumin- loaded chitosan nanoparticles to ameliorate diabetic crack mending by reducing inflammation. also, they discovered that Cur-CS- Nsight significantly enhances angiogenesis in vivo and in vitro while reducing macrophage intermediated inflammation. likewise, Mahmood et al.(2022) developed a curcumin loaded tone- emulsifying medicine delivery system and set up that it dramatically accelerated crack mending andre-epithelialization compared to the undressed and purely medicine- treated groups in an in vivo diabetic crack model.

## 2. Scale Up Process and Toxicity Associated with Curcumin

Nanotechnology is a vastly explored field in the 21st century. It has piqued public attention because of the demands and operations of NanoSystems in numerous fields of pharmaceutical lore's. NanoSystems, because of their size, shape and structure, retain an array of advantages over the traditional systems. still, at the same time, it suffers from some truly sensitive enterprises. Exposure of NanoSystems in the terrain is necessary and hence, nanotoxicity disquisition is gathering the interest of experimenters encyclopedically(127,128). Their unique physicochemical parcels enable NanoSystems to interact with the natural systems and may lead to changeable and undesirable consequences. Hence, a comprehensive disquisition into nano- memoir relations must be conducted to insure the proper and safe use of nano- paraphernalia. The maturity of curcumin Nano phrasings reported in the literature mooted sweats to enhance curcumin delivery to address the problems of low solubility, poor immersion, quick metabolism, and confined bioavailability. These were primarily attained using targeted delivery, controlled release Muc adhesion, enhance stability, lower cellular absorption(129,130). therefore, adding curcumin bioavailability would be fulfilled by using nanotechnology.

## 3. Patent Technology

The number of cases detected with habitual injuries is rising encyclopedically, obliging the ubiquitous development of crack mending inventions developed for colorful crack settings. Patent data is the primary source of knowledge; results pulled from patents are vital in determining ultramodern technological patterns.(Table 2 gives a description of patents). Patent interpretation is constantly used to assess the competitive request in specialized variations at an advanced manufacturing or public position, to determine positive technological aspects,

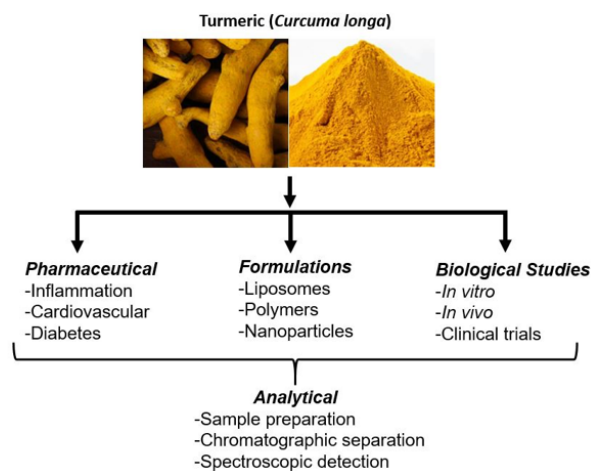


Figure 2:

and to examine transnational request eventuality. likewise, Patent analysis makes it simple to prognosticate unborn advancements of a specific assiduity. Because of the large number of people being diagnosed with diabetes as well as rotundity, the demand for the rapid-fire- fire- fire mending process has increased mainly. Besides that, innumerable crack- mending inventions are being enhanced to manage this high demand(138). In patent WO2014147638A1, the formulators claimed that curcumin patches and Tulsu excerpts are employed in the expression matrix to further increase the rates of the herbal medicinal values and to give a synergistic effect, whereby all the constituents cooperate to produce better mending issues(139). also, the invention is described in US20190060253A1 which represents an expression of curcuminoid and turmeric essential oil painting oil oil painting. likewise, this patent describes that this expression increases the bioavailability of curcumin and its natural exertion(140). It describes how to apply curcuminoid with turmeric essential oil painting oil oil painting to increase the bioavailability of curcumin for oral supplementation against colorful conditions and for the operation of crack mending. also, the use of turmeric to speed up the mending of injuries is the focus of the current invention. USOOS40504A(141). It's presupposed that turmeric factory to cure habitual ulcers by enhancing microcirculation, promoting angiogenesis, encouraging the creation of granulation kerchief, and speeding up the process of- epithelialization. Any kind of injury to the body that causes the skin or other kerchief to be broken, cut, pierced, or ripped,etc., can be treated, including surgical injuries( analogous as incisions), ulcers, and other types of external injuries. This patent also describes a fashion for encouraging the healing of a crack in a case that primarily involves giving the case a crack-mending conflation made of a sufficient volume of turmeric cream. US20050181036A1 describes the development of an

aerosol containing lipids and curcumin patches(142). In this, curcumin is circulated in a lipid vehicle and an arid soap in the pharmaceutical compositions of the present invention, making them suitable for aerosol delivery to a subject. Small arid aerosol patches with lipids, lipid complexes, liposomes, and interacting curcumin- lipid or curcumin- liposomes are the subject of the present invention. various combinations of patches are propelled or transported by air or air with added oxygen. It's noted that curcumin, one or further lipids, and an arid soap can be combined to produce pharmaceutical lipid vehicle compositions of curcumin that are suitable for aerosol delivery to a subject, handed that the transition temperature of the lipid if only one lipid is present, or the mean transition temperature of the lipids, if further than one lipid is incorporated, is lower than about 15° C and the composition can be nebulized. The styles of the present invention can be used to speed up the healing of injuries and stop wrinkle conformation.

#### 4. Curcumin Encapsulated Nano Delivery Systems

For Targeting Wound Healing Curcumin belongs to class IV of the biopharmaceutical type system, i.e. Low solubility and low permeability(66,67). These parcels affect in reduced absorption, bioavailability, and stability. also, it shows a truly fast metabolism at specific intervals in the body. To overcome t Nanoparticles these limitations, multitudinous phrasings have been tried and tested, including nanoparticles, liposomes, nanogels, nano-emulsion, and the use of an adjuvant and nanocrystals(68 – 71). Nanotechnology has proven to be an effective fashion to accelerate crack healing by stimulating applicable mobility through various healing phases. Nanotechnology-predicated paraphernalia, analogous as nanomaterials, nano balconies, nanofibers, and biomaterials are also popular for the enhanced original delivery of the active element.

#### 5. Curcumin: A Promising Solution for Wound Healing

Curcumin, a compound widely available, has garnered attention for its potential to alleviate pain. However, its application in wound healing has been limited due to its low solubility and rapid metabolism, which results in a short plasma half-life. Nevertheless, recent advancements in nanotechnology have paved the way for innovative approaches to wound healing, offering promising solutions to address these challenges. In this review, we will explore the potential of curcumin and its Nano formulations in wound healing, shedding light on their biomedical applications including their anti-biofilm properties and wound healing effects.

#### 6. Nanotechnology for Wound Healing

Nanotechnology has revolutionized the field of wound healing, providing effective methods to enhance the

therapeutic potential of curcumin. Scientists have successfully utilized nanoscale formulations such as liposomes, nanoparticles, and Nano emulsions to overcome the limitations of curcumin, resulting in improved drug delivery, increased stability, and prolonged release at injury sites. These novel techniques allow curcumin to exert its healing properties more efficiently, promising a brighter future for wound care.

#### 7. Liposomes: Unlocking Curcumin's Potential

One noteworthy Nano formulation technique is the use of liposomes. These artificial vesicles composed of lipids have demonstrated great potential in enhancing curcumin's bioavailability and stability. By encapsulating curcumin within liposomes, its solubility is improved, ensuring efficient drug distribution and promoting optimal wound healing. Furthermore, liposomes protect curcumin from degradation, increasing its therapeutic impact.

#### 8. Embracing Small-Scale Excellence

Nanoparticles represent another groundbreaking approach to curcumin delivery. These tiny particles possess unique properties that enable sustained release, ensuring a steady supply of curcumin at the wound site. Their high surface area to volume ratio allows for enhanced interaction with the wound, promoting accelerated healing. Moreover, nanoparticles can be tailored to specifically target wound sites, optimizing curcumin's therapeutic potential.

#### 9. Nano emulsions: Unleashing Curcumin's Healing Power

Nano emulsions have emerged as a promising tool for delivering curcumin due to their improved solubility and stability. These finely dispersed oil-in-water emulsions offer enhanced bioavailability and increased chances of curcumin interacting with skin cells effectively. By encapsulating curcumin within Nano emulsions, its wound healing properties are unleashed, fostering a conducive environment for tissue regeneration.

#### 10. Biomedical Applications and Beyond

Curcumin Harnessing 's vast biomedical applications go beyond its wound healing effects. Its inherent antioxidant properties make it an excellent candidate for combating biofilm-related issues, shedding light on its potential as an antimicrobial film. Moreover, studies have indicated its usefulness in diabetic foot management, offering hope for individuals grappling with this condition.

#### 11. Navigating FDA Regulations and Patents

While the potential of curcumin and its Nano formulations in wound healing is promising, it's important to navigate

the regulatory landscape. Ensuring compliance with FDA regulations guarantees the safety and efficacy of these novel approaches. Additionally, patent protection plays a crucial role in fostering innovation and incentivizing further research in this field

The utilization of curcumin and its Nano formulations presents an exciting frontier in wound healing. Nanotechnology has proven to be a transformative ally, enabling the delivery of curcumin with enhanced efficiency and stability. From liposomes to nanoparticles and nano emulsions, these innovative techniques hold great promise in revolutionizing wound care. As we continue to explore new horizons, it's clear that curcumin's remarkable potential extends beyond wound healing, making it a versatile compound in biomedical applications. With careful consideration of regulatory frameworks and patent protection, we can unlock the full potential of curcumin and pave the way for round breaking advancement breaking advancements in wound healing and beyond.

### 11.1. Wound Healing potential of curcumin: mechanism of healing

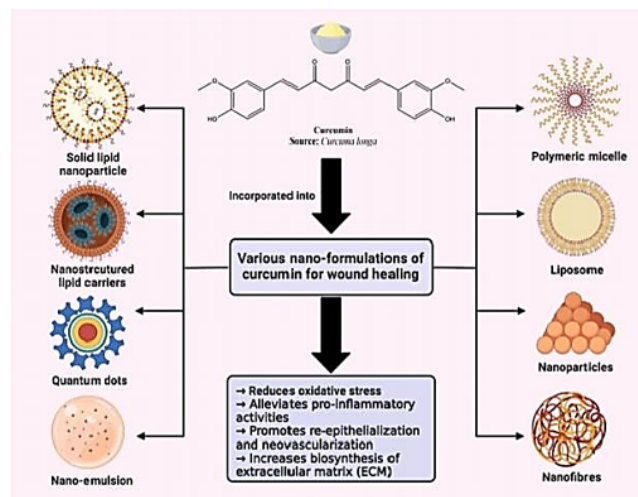


Figure 3:

Recent biomedical applications have provided strong evidence of wound healing. Article All functions of curcumin play an important role in wound healing (Figure 2). Curcumin is a natural polyphenol antioxidant component that has been studied in detail. Its potential as a wound healing agent has been discovered in recent years. one. First Article The purpose of wound healing is to restore tissue integrity and maintain homeostasis. one. Curcumin increases wound healing by increasing the rate of wound shrinkage. Up to 20% healing of the wound area has been reported. one. Eroglu et al. Substance Curcumin inhibits the inflammatory response and accelerates wound healing edited. Haidari et al. Curcumin has been shown

to improve collagen deposition Supports angiogenesis in chronic wounds one. Pharmacies 2022, 14, x for review 5/25 a Chapter The structure and the phenolic hydroxyl (-OH) group provide the ROS scavenging ability. It also supports the production and activity of antioxidants such as glutathione (GSH) and their products. Stimulation of cytoprotective signaling pathways, e.g. Chapter Molecular mechanisms leading to oxidative stress and increased ROS species in wound healing. This regulation of Nrf2 is important for cell protection Oxidative damage. Reactive cysteine in response to electrophilic and oxidative stress Woodpecker remains.

## 12. Conclusion and Future Expectations

Curcumin is a powerful anti-inflammatory and antioxidant compound. despite the benefits mentioned above but also has limitations such as poor stability and lack of bioavailability. Combinations and the use of Nano formulations have been used to overcome these limitations. This review includes references to studies that provide insight. Article Curcumin transforms into wound healing. Topical formulations and nanostructures of curcumin have been developed and evaluated for many years to increase the effectiveness of curcumin. Therapeutic potential. The main reason why external nanoparticles are preferred is the advantage of Curcumin is that it provides optimal solubility, improved bioavailability and control. Releases the active ingredient curcumin; this can help deliver the drug over an extended period to accelerate wound healing. These molecular mechanisms regulate the genetic and cellular wound environment and heal Chapter Undetermined chronic disease. Therefore, more research is needed for translation. New, effective, Chapter: Doubters decide the best dosage Article Curcumin is important for many purposes, especially Chapter Section Additional drug testing. Although modern science of various medicinal preparations Curcumin appears to be safe, with most research data collected in vitro Section and in vivo studies available, clinical studies are still needed. Medical procedures in recent years, trial design, patient populations, risk assessment, Part and precision instruments. Results of clinical trials may inspire professionals Further research into the development of curcumin-based formulations. Moreover, Article Development of a cost-effective and scalable nanoencapsulation system for curcumin Rapid business needs to reduce production costs and increase competitiveness with other industries drugs. Therefore, curcumin Nano formulations may be useful in the future Article Many biological, but more research is needed, especially in the medical field. Provides researchers with a deeper understanding. More research is needed overall Determination of the effectiveness of curcumin-based formulations for mechanical use from bench to bed.

### 13. Source of Funding

None.

### 14. Conflict of Interest

None.

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