Curcumin Herbal Nano formulation for Diabetic Wound

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Abstract:

Diabetes wounds heal slowly and poorly, putting patients in a high-infection environment. This article provided a summary of recent developments in nanoparticles/gels and nanotechnology used to speed up the healing of diabetic wounds. The primary active and beneficial ingredient of Curcuma longa L., curcumin, has a long and illustrious history of medicinal benefits for human health care. It has been suggested that curcumin can heal wounds. However, issues like limited water solubility, poor tissue absorption, and a shortplasma half-life due to its quick metabolism must be resolved for curcumin formulations to be an effective treatment for wound healing. Curcumin nanoformulations, including nano emulgel, have addressed the problem of curcumin's low bioavailability. Thus, the formulation, characterization, and applications of curcumin nanoemulgel for diabetic wound healing are discussed in the current review.

Keywords*: Curcumin, diabetic wound, wound healing, nanoformulation, nanoemulsion.*

Introduction

Nano-formulations are tailored to the intended delivery site and improve the characteristics of conventional medications. The pharmaceutical industry is using Nano formulations such as liposomes, nanoemulsions, dendrimers, polymeric nanoparticles, and micelles to improve drug formulation[1,2]. Approximately 500 million people worldwide are thought to have diabetes mellitus (DM), and alarming growth is anticipated in the upcoming years. According to estimates, one in three to one in five diabetic individuals have chronic, non- healing wounds. throughout their lifetime is a diabetic foot ulcer (DFU)[2]. With its wide range of physicochemical features, nanotechnology is a dependable study field for wound- healing treatments. Their biochemical features, including hydrophobicity, interaction with organic molecules, and deeper degrees of tissue penetration, can be easily modified for practically any type of wound by modifying the material, size, and electrical charge of the nanoparticles[4].

The main curcuminoid present in turmeric, curcumin, is commonly recognized as its most active component. It has a history of using topical infection-like wounds to treat it, and it has shown better wound healing activity. The three most significant cur curcuminoids are curcumin, demethoxycurcumin, and bisdemethoxycurcumin. The difference between turmeric and curcumin solutions or extracts must be understood. One of the bioactive curcuminoid molecules that can be found in turmeric is curcumin. Curcumin makes up 75% of the active curcuminoids, even if turmeric only contains 29% of them. It is crucial to understand the difference between turmeric and curcumin supplements or an additional [6,7]. The ability of the curcumin molecule to target multiple pathological disorders makes it suitable for development as a therapeutic or nutraceutical agent. The Biopharmaceutics Classification System (BCS) classifies curcumin as a class II medication since it is both highly permeable and poorly water-soluble[8]. Anxiety, arthritis, metabolic syndrome, oxidative and inflammatory diseases, and hyperlipidemia have all been demonstrated to be stabilized by curcumin. Antioxidant, anti-amyloid, anti-microbial, anti-cancer, immune modulating, and neuroprotective characteristics are all possessed by curcumin. Low solubility, low stability, poor bioavailability, low penetration, quick metabolization, and a focus on efficacy are some of the known therapeutic curcumin barriers[10].

1. Hyperglycemia

Hyperglycemia can make a contribution to impaired wound closure, impaired functioning of more than a few skin cells, and peripheral neuropathy in diabetic patients. Hyperglycemia promotes atherosclerosis by blocking circulating nutritional vitamins from interacting with wounds, thereby impairing healing. Endothelial dysfunction, which is essential for wound healing via pressure-induced vasodilation, a reaction that is typically protective for the skin, can occur in diabetic patients due to hyperglycemia.

2. Pathophysiology

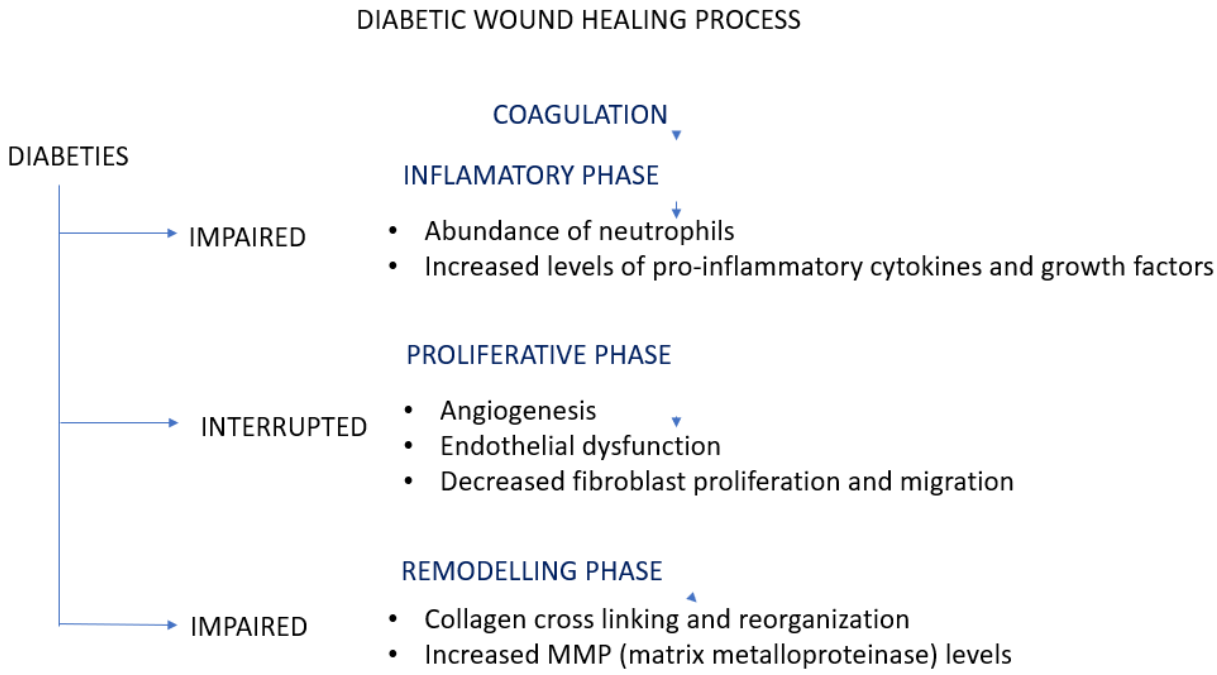

Figure 1: Diabetes wound healing process

3. How diabetes interferes with wound healing

The capabilities of the body to produce or respond to the hormone insulin, which works to help cells absorb and use blood glucose for energy, are influenced by diabetes. This insulin disturbance creates it difficult for the body to monitor and control blood glucose levels. Blood glucose levels that are persistently high impair white blood cell functionality. The immune system requires white blood cells to function properly. The body'sability to fight infections and repair wounds is compromised when white blood cells are widely distributed. Uncontrolled diabetes makes it harder for the body to heal wounds because it can affect circulation andreduce blood flow. As a result, the wounds might not heal or heal slowly[7].

4. Factors affecting wound healing

Typically, the stages of wound healing proceed in a sequential and time-dependent manner. Any interference with the healing process for wounds could result in pathological scarring or persistent wounds. Understanding the diverse variables that influence wound healing and their potential effectson it may be helpful in the development of therapeutic drugs for wound healing in diabetes and non-diabetic patients. Factors affecting wound healing are wound site, Immune state, Age, Disease state, Reactive oxygen species (ROS), Diet.

5. Nano formulation

Nano-formulations typically range in size from 10 to 100 nm. Organic and inorganic nanoparticles are twodifferent types. This group also includes compact and hybrid polymeric nanoparticles as well as micelles, dendrimers, and liposomes. Fullerenes, quantum dots, silica,

and metal nanoparticles are included in the second group.

5.1 Why Nano formulations are used

Traditional medicines have disadvantages like poor solubility, and low bioavailability that limits their clinical application." Nanoformulations" (NFs) are novel and advanced drug-delivery systems. They appear to have the potential for enhancing the solubility and bioavailability of medications. They can release loaded pharmaceuticals in response to specific internal and external stimuli in selected regions, allowing for controlled drug release within target tissues. Recent research has shown that NFs can target the release of active substances at illness sites, increasing their concentration in diseased tissues and minimizing side effects[1,2].

Advantages

- The opportunity for combining both hydrophilic and hydrophobic materials.
- Variable administration routes are feasible.
- Biodegradable, non-toxic, and able to be kept for longer durations in preservation.
- Can be used to deliver medicines under controlled conditions.
- Reduces the need for multiple doses.
- Greater stability and carrier capacity.

Disadvantages

- Its limited capacity for drug loading is a major downside.
- The biotransformation of polymeric carriers may lead to the formation of toxic metabolites afterrepeated administration.
- The polymeric nanoparticles deteriorate relatively slowly, resulting in toxic effects throughout the body

Different strategies of curcumin Nano formulation

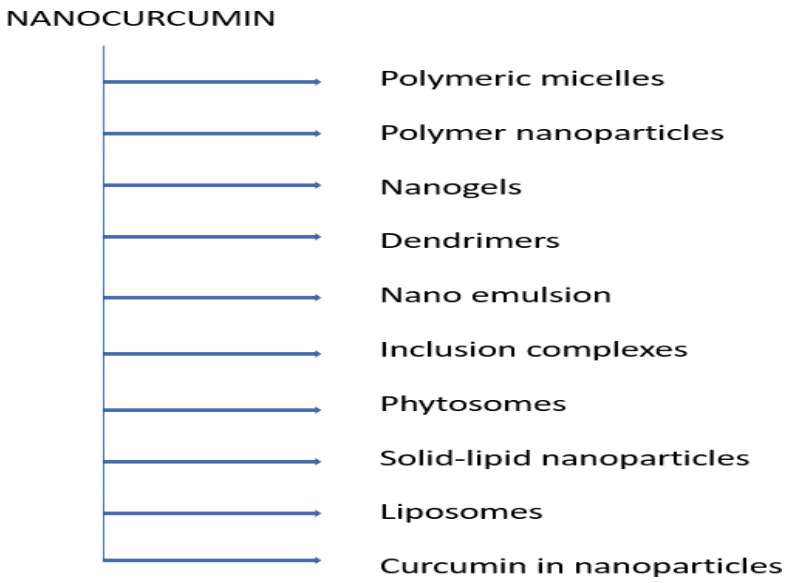

Figure 2 Different strategies of curcumin nanoformulation

6. Formulation of nanoemulsion by solvent evaporation technique

The single emulsion solvent evaporation technique has been used to develop curcumin-loaded nanoparticles.10 or 20 mg of curcumin powder was dissolved in the solvent mixture and mixed with such avortex for 30 min in a glass tube after 100-200 mg of PLGA polymer had been dissolved in 5 ml of dichloromethane. In a glass tube containing 10 ml of aqueous PVA solution, the drug/polymer mixture wasadded. After adding the drug/polymer mixture to the PVA solution, vortex for a further 1 minute at high speed. Using a probe sonicator, this polymer mixture was emulsified inside an ice water bath for 10 mins at40% amplitude. Under magnetic stirring, this emulsified mixture was poured into 30 ml of 0.5% aqueous solution. At 800 ° C dichloromethane was evaporated utilizing high magnetic stirring for about 3 hours.

Centrifugation was employed to separate the nanoparticles for 15 min at 20,000 rpm, and then three washes with distilled water. After accumulating the supernatants, pellets of the nanoparticles were reconstituted in 5ml of distilled water[8].

Expediency solvent evaporation technique

The basis of the solvent evaporation process is the agitation-based evaporation of an emulsion's internal phase. Solvent evaporation is one of the most popular, well-researched, simple, and available procedures among all the others. Thus, it is crucial to consider the fundamentals of how formulation factors affect the method to design and solvent evaporation. The key advantages of the method are its simplicity of use, swift handling for synthesizing nanoparticles, and lack of unreacted monomers or residual initiators in the createdpolymer dispersions based on prior purification of the pre-synthesized polymer. The drawbacks include the frequently wide (20–50%) size distribution of the generated particles and capsules, the frequently poor solidcontent of the dispersions, and the continual presence of surfactants. By concentrating the dispersions in vacuo and using dialysis, respectively, the last two issues can be resolved[8].

7. Characterization of nanoemulgel

7.1 Physical properties

The color, homogeneity, consistency, grittiness, and phase separation of the nanoemulsion gel compositionswere visually assessed.

7.2 pH Calculation

A digital pH meter was used to determine the formulations' pH levels. A 250 ml beaker containing nanoemulsion Gel was filled, the solution was tested using a pH meter, and the results were recorded. Two additional times, the same process and formulation were used. Three times, the pH of each produced combination was measured using asimilar method.

7.3 Viscosity Testing

On a viscometer with a spindle count of 64 installed, a container with up to 100 mL of gel was set down. After that, the spindle was lowered to the gel's predetermined limit. Using the viscosity value indicated on thetool, we then adjusted the speed to 0.6 rpm.

7.4 Spreadability

A glass plate assessing 20× 20 cm was placed over 0.5 g of gel to test the formulation's spreadability. A second glass plate was then placed on top of the first plate. 500 g of weight was placed on the top glass plate and left therefor five minutes. The gel spreading-related increase in diameter was noted

Spreadability = m ×l /t

m = weight tied to the upper

7.5 Extrudability

A hardness tester has been used to perform the extrudability test. The aluminum collapsible tubes were filled with 5 g of Nanoemulsion Gel. To properly hold the tube, the plunger is put to the test. Applying 1gm per cm2 for 30 seconds. Then, you repeated the procedure three times while observing the amount of Nanoemulsion gel that came from t[ube 6].

8. Formulation of curcumin nanoemulgel

To make curcumin nano gel, using a water carbomer gel matrix, the first hydrogel matrix was made by soaking the carbomer. And after that, the gel matrix was slowly and continuously stirred to incorporate thenanoemulsion. With the addition of a citric acid aqueous solution, the pH was adjusted to 6 to produce thedesired nano emulgel[15].

Conclusion

Based on the evidence available here, curcumin nanoformulations appear to have therapeutic potential in diabetic wound healing. Delivery of curcumin to diabetic wound sites is made possible by topical nanoemulsion gel, which also enhances therapeutic outcomes. Curcumin nano emulgel for wound healing has a significant potential for new pharmaceutical development, however, there haven't been any clinical studies yet. To create unique, efficient, and secure nano drugs, more study is required to apply the knowledge learned from human research[17].

Abbreviations

DW	diabetes Mellitus
DFU	Diabetic Foot Ulcer
BCS	Biopharmaceutics Classification System
ROS	Reactive Oxygen Species
NFs	Nanoformulations

Conflicts of interest:

The authors confirm that this article has no conflict of interest.

Credit author statement:

Dhanush R- conceptualization, validation, and writing the original draft. Deepan B- Review

and editing, formal analysis. Madeshwar M- drafting and editing. Murugappan M- supervision, draft review, analysis, and editing. Divakar-Draft writing and conceptual analysis.

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