Antimicrobial photodynamic and wound healing activity of curcumin encapsulated in silica nanoparticles

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Highlights

- •
  Curcumin-silica nanoparticle shows photodynamic inactivation effect against planktonic form of P. aeruginosa and S. aureus.
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  Curcumin-silica nanoparticle shows photodynamic inactivation effect against biofilm form of P. aeruginosa and S. aureus.
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  Curcumin-silica nanoparticle represents wound healing activity and does not show significant toxicity against human normal fibroblast cells.

Abstract

The multidrug resistance of pathogenic bacteria has become a serious problem to public health. Therefore finding novel approaches to combat multidrug resistant bacteria have therefore become increasingly important. One promising approach is antimicrobial photodynamic therapy (aPDT) which involves the use of photosensitizer (nontoxic dyes) that are excited by visible light and produce oxygen free radicals in the presence of oxygen. In this study, we investigated the antimicrobial photodynamic effect of free curcumin and curcumin silica nanoparticle as photosensitizer on planktonic and biofilm forms of *Pseudomonas aeruginosa, Staphylococcus aureus*. After performing MTT assay (to evaluate curcumin nano complex toxicity on human fibroblast cells), the effect of aPDT at 465 nm on bacteria in the planktonic and biofilm forms were investigated. The results showed that by using curcumin in the form of curcumin-silica nanoparticle as photosensitizer, there is a reduction in the number of bacteria in planktonic condition and bacterial biofilm production. Curcumin-silica nanoparticle not only did not show any significant cytotoxic effect against human normal fibroblast but also showed wound healing properties as confirmed with in vitro scratch assay. Therefore, aPDT based curcumin-silica nanoparticle could be suggested as novel approach in the treatment of multi drug resistant bacteria in chronic wound infection condition.

Introduction

Chronic wounds represent an important challenge for wound care and are universally colonized by bacteria. Bacteria are as two forms of planktonic (free-floating) and biofilm in nature. Microbes in biofilm form can tolerate 10–1000 times higher levels of antibiotics than their planktonic form [1]. Biofilm is implicated in numerous bacterial infections including those associated with the urinary tract, ear, cystic fibrosis, periodontal disease and chronic wounds [2]. The bacteria can form biofilm as a survival mechanism that confers the ability to resist environmental stress and antimicrobials due to a variety of reasons, including low metabolic activity. Additionally, the exopolymeric substance (EPS) contained in biofilm acts as a mechanical barrier to immune system cells, leading to collateral damage in the surrounding tissue as well as chronic inflammation, which eventually will delay healing of the wound [[2], [3], [4]]. Therefore, it is important to improve new approaches to combat against biofilm infections. Biofilm is associated with impaired epithelialization and granulation tissue formation, and promotes a low-grade inflammatory response that interferes with wound healing. It is reported that at least half of all chronic wounds contain

biofilm [5]. Biofilms could act by contributing to bacterial infection, inflammation, inhibiting antibiotic penetration into the wound. The two most common nosocomial pathogens responsible for biofilm-associated infections are *Staphylococcus aureus* (Gram-positive pathogen) and *Pseudomonas aeruginosa* (Gram-negative pathogen) [6]. Disabling biofilm resistance may enhance the ability of existing antibiotics to combat barrier against drug penetration enter in biofilm structure [4]. Therefore novel antibiofilm approaches needed to be developed. Antimicrobial photodynamic therapy (aPDT) has confirmed effective against a wide range of pathogens. It can be an appropriate method to conflict with biofilm and antimicrobial-related resistance [7]. The aPDT used photoactivatable compounds known as photosensitizers which is successively stimulated by light at specific wavelength lead to production of reactive oxygen species (ROS). ROS produced during illumination can show lethal effects on microbial pathogens [8]. Recently it is reported that curcumin can acts as photosensitizer [[9], [10], [11], [12], [13]]. Curcumin, a yellow colored polyphenol is the most dynamic component of turmeric, a botanic agent consequent from the dried rhizome of the turmeric plant (*Curcuma longa*). The studies recommended that curcumin has antitumor, antioxidant, and anti-inflammatory properties [14,15]. The antibacterial activity of curcumin against various bacteria such as *Staphylococcus aureus*, *Trichophyton gypseum, Salmonella paratyphi*, and *Mycobacterium tuberculosis* was also reported as first paper in this field [16]. Many studies report that curcumin inhibits the growth of both Gram-positive and Gram-negative bacteria [[17], [18], [19]]. Formulations of curcumin in nanoparticles, liposome, micelles and phospholipids complexes are being prospected to decline its hydrophobicity, increase solubility to increase blood flow time, and its permeability through membrane barriers [20]. Among these options nano formulations of curcumin such as nanocrystals, nano emulsions and polymeric nanoparticle encapsulated curcumin got enormous interest and advance in the recent years [[21], [22], [23], [24], [25]]. To the best of our knowledge, there is no report in the literature on the aPDT with curcumin intercalated in silica nanoparticle. The main objective of this study was to determine the effect of curcumin silica nanoparticle on planktonic and biofilm of two bacterial also the effect of the curcumin –silica nanoparticle on wound healing.

Section snippets

Synthesis and characterization curcumin–silica nanoparticle

Curcumin was obtained from Sigma (Sigma-Aldrich Co. LLC, St. Louis, MO, USA). The loading of curcumin was performed according to batch method [26], employing an $m(SiO_2)$:m(Cur) = 10:1. In brief, SiO_2 (200 mg) and curcumin (20 mg) was dissolved in PEG-400(1 %) (5 mL distilled water), and then stirred for another 24 h. The solution was centrifuged (12,000 r/min) for 10 min. At the end, the curcumin-loaded material was repeatedly washed with distilled water and dried at 50 °C for overnight giving

Characterization of curcumin–silica nano particle

TEM (Fig. 1A) and SEM (Fig. 1B) images show that the sample of curcumin–Si nano particle has uniform morphology with particle sizes ranging from 36 to 40 nm. FTIR analysis is one of the important tools for the efficient identification of encapsulated chemical molecules. As it can be seen in Fig. 1C, in

FTIR spectrum, free curcumin displayed the characteristic intensities of O H str at 3450 cm^{-1}, the

aromatic CC str at 1580 and 1480 cm^{-1}, CO str at 1600 cm $^{-1}$, aromatic CO str at 1250 cm^{-1},

Discussion

Antimicrobial photodynamic therapy is a novel strategy that uses light at specific wavelength and a photosensitizing agent to eliminate bacteria [29]. The ROS generated during the aPDT process will react

with almost all the biomolecules and cellular components of bacteria lead to the death of bacteria. *S. aureus* and *P. aeruginosa* are major causes of wound infections [30]. The development biofilms is a way for these microorganisms that helps them to resistance against most of antibiotics [31].

Conclusion

The present study confirmed the enhanced antimicrobial and anti-biofilm activities of curcumin-silica nanoparticle against *P. aeruginosa* and *S. aureus* cultures using aPDT. The antibacterial activity was significant against both the test bacteria, but the Gram positive bacteria, S. aureus, was found to be more susceptible than Gram negative, P. aeruginosa. Antibiofilm efficacy of the curcumin-silica nanoparticle was also studied and confirmed through different assays (inhibition of biofilm by

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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