Journal for Re Attach Therapy and Developmental Diversities
eISSN: 2589-7799
2023 December; 6 (9s) (2): 2011-2015

Mucoadhesive Hydrogel Patch Loaded With Dox To Treat Chronic Wounds

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ABSTRACT

Chronic wounds represent a significant clinical burden due to their persistent inflammatory state, susceptibility to infection, and impaired healing response. This study aimed to develop and characterize a mucoadhesive hydrogel patch loaded with doxycycline (DOX) as a localized therapeutic strategy for chronic wound management. The patch was formulated using a composite of 3% cellulose and 5% chitosan, incorporating 100 mg of doxycycline into the hydrogel matrix. The developed system was subjected to comprehensive characterization including scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), contact angle measurement, hemocompatibility, and in vitro cytotoxicity assays. Results demonstrated that the patch exhibited a porous and interconnected morphology, favorable hydrophilic surface properties, excellent blood compatibility, and high cell viability. The incorporation of doxycycline was confirmed without significant chemical alteration of the polymer network. The findings suggest that this mucoadhesive hydrogel patch can provide sustained drug release, adhere effectively to moist wound surfaces, and create a conducive healing microenvironment. In conclusion, the doxycycline-loaded cellulose-chitosan hydrogel patch shows promising potential as an advanced wound dressing for the treatment of chronic wounds, combining controlled drug delivery with biocompatible and mucoadhesive properties.

Keywords: Mucoadhesive hydrogel, doxycycline, chronic wounds, chitosan, cellulose, wound healing, drug delivery

1. INTRODUCTION

Chronic wounds, including diabetic foot ulcers, venous leg ulcers, and pressure injuries, are a major healthcare challenge characterized by delayed healing, recurrent infection, and prolonged inflammation. These wounds often fail to progress through the normal phases of healing, leading to significant patient morbidity and increased treatment costs. Traditional wound dressings frequently lack the ability to modulate the wound microenvironment or provide controlled therapeutic delivery, highlighting the need for advanced biomaterial-based solutions.

Over the past decade, hydrogels have gained considerable attention as ideal wound dressing materials due to their unique physicochemical properties. Hydrogels are three-dimensional networks of hydrophilic polymers capable of absorbing large amounts of water or biological fluids while maintaining structural integrity. Their high water content provides a moist wound environment, which is widely recognized as conducive to epithelialization, angiogenesis, and autolytic debridement. Furthermore, hydrogels are permeable to oxygen and water vapor, non-adherent to wound beds, and can be engineered to possess mucoadhesive properties, thereby extending residence time at the application site and enhancing localized drug bioavailability.

The selection of polymer components is critical in designing hydrogels for specific applications. Natural polymers such as chitosan and cellulose offer inherent biocompatibility, biodegradability, and bioactivity. Chitosan, a derivative of chitin, possesses intrinsic antimicrobial and hemostatic properties, while cellulose provides mechanical strength and stability. Their combination can yield a synergistic system suitable for sustained drug delivery and wound management.

Doxycycline, a broad-spectrum tetracycline antibiotic, has emerged as a multifunctional agent in wound healing beyond its antimicrobial effects. At sub-antimicrobial doses, doxycycline acts as a potent inhibitor of matrix metalloproteinases (MMPs), enzymes that are often overexpressed in chronic wounds and contribute to excessive tissue degradation and impaired healing. Additionally, doxycycline modulates inflammatory responses, reduces oxidative stress, and has been shown to improve collagen organization and minimize scar formation. These pleiotropic actions make doxycycline an attractive therapeutic candidate for incorporation into a localized delivery system aimed at chronic wound therapy.

This study therefore aims to develop, characterize, and evaluate a novel mucoadhesive hydrogel patch composed of cellulose and chitosan, loaded with doxycycline, for the potential treatment of chronic wounds. The patch is designed to combine the wound-friendly properties of hydrogels with the sustained, localized delivery of doxycycline to address infection, inflammation, and dysfunctional healing simultaneously.

2. MATERIALS AND METHODS

The mucoadhesive hydrogel patch was formulated using cellulose and chitosan as the polymeric base, with doxycycline incorporated as the active therapeutic agent. Cellulose at a concentration of 3% (w/v) was used to provide structural

integrity, while 5% (w/v) chitosan was included to impart mucoadhesive and antimicrobial properties. Doxycycline hyclate (100 mg) was uniformly dispersed into the polymer blend. The hydrogel was prepared by first dissolving chitosan in a 1% acetic acid solution under continuous stirring. Cellulose was separately dissolved in distilled water and then combined with the chitosan solution under gentle agitation. Doxycycline was subsequently added to the polymer mixture and thoroughly blended to ensure homogeneous distribution. The final solution was cast into petri dishes and allowed to dry at ambient temperature to form flexible, film-like hydrogel patches.

The fabricated patches were characterized using a suite of analytical techniques. Surface and cross-sectional morphology were examined using scanning electron microscopy (SEM) to assess pore structure and uniformity. Chemical compatibility and molecular interactions between the polymers and doxycycline were investigated using Fourier-transform infrared spectroscopy (FTIR). Surface wettability and mucoadhesive potential were evaluated through contact angle measurements. Hemocompatibility was determined via a hemolysis assay using human red blood cells to ensure blood safety. In vitro cytotoxicity was assessed using the MTT assay on L929 fibroblast cells to confirm biocompatibility. Additionally, an in vitro drug release study was conducted in phosphate-buffered saline (PBS, pH 7.4) to profile the release kinetics of doxycycline from the hydrogel matrix.

3. RESULTS

The scanning electron microscopy (SEM) analysis revealed that the hydrogel patch possessed a highly porous and interconnected network structure, which is advantageous for exudate absorption, oxygen permeability, and cell migration. The FTIR spectroscopy confirmed successful incorporation of doxycycline into the cellulose-chitosan matrix without significant chemical degradation or undesirable interactions, indicating good compatibility among the components.

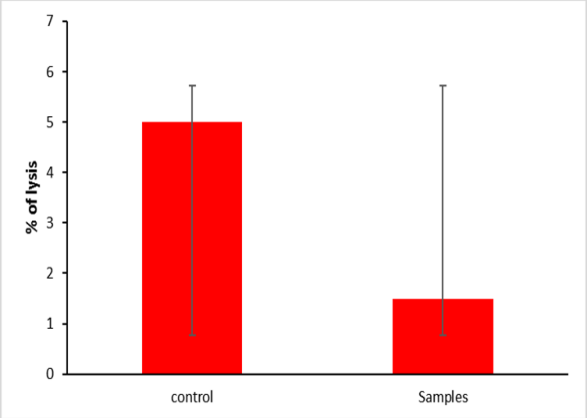

Fig 1- Hemocompatabiility test for mucoadhesive hydrogel patch loaded with dox

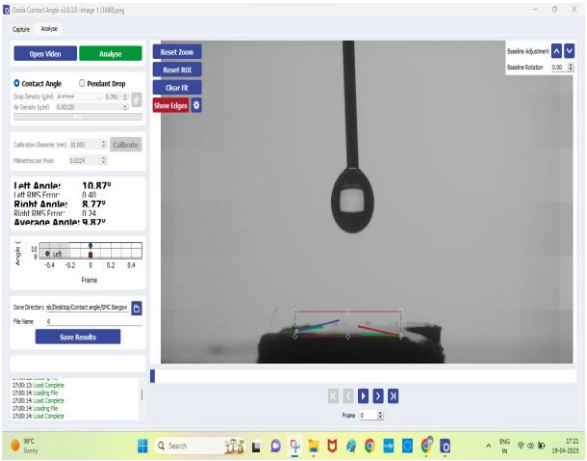

Fig 2- Contact angle of mucoadhesive patch loaded with dox

The contact angle measurements demonstrated the hydrophilic nature of the patch surface, with low contact angles suggesting favorable wetting and mucoadhesive properties suitable for adherence to moist wound beds. Hemocompatibility testing showed negligible hemolytic activity (less than 2%), confirming that the patch is non-hemolytic and safe for contact with blood components.

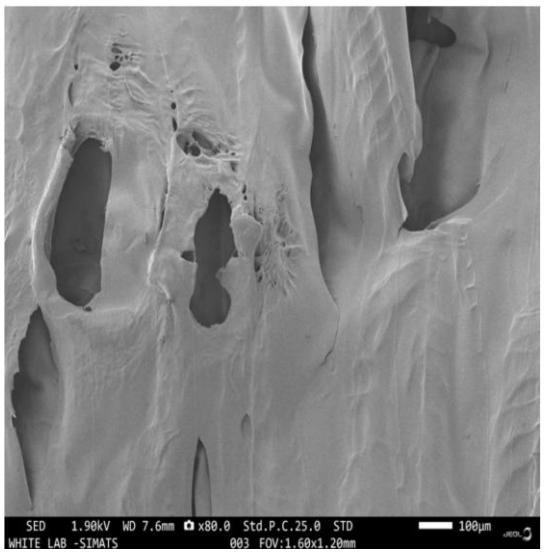

Fig 3- SEM Morphology of mucoadhesive hydrogel patch loaded with dox

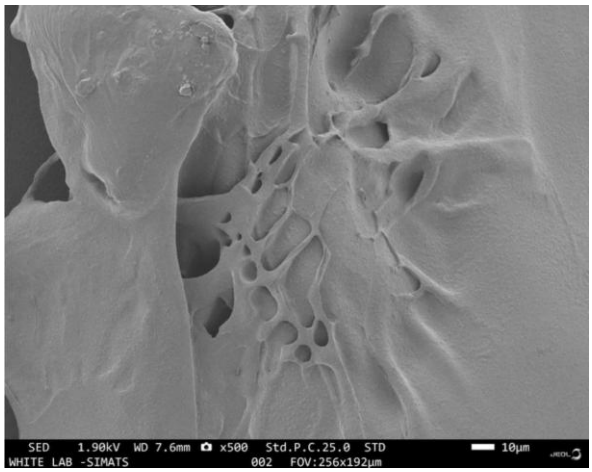

Fig 4- SEM Morphology of mucoadhesive hydrogel patch loaded with dox

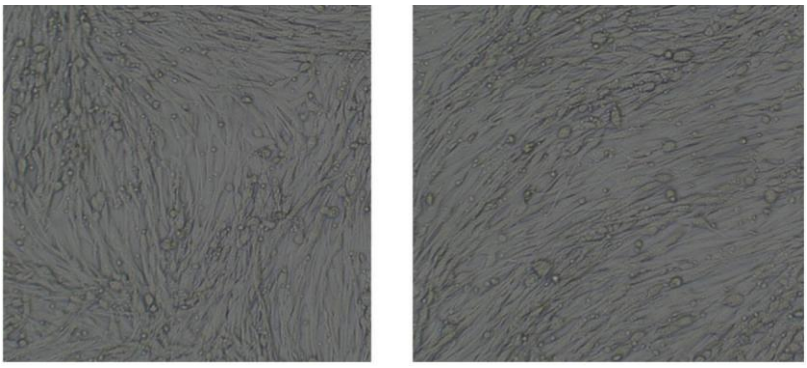

Fig 5- Cells of mucoadhesive hydrogel patch loaded with dox

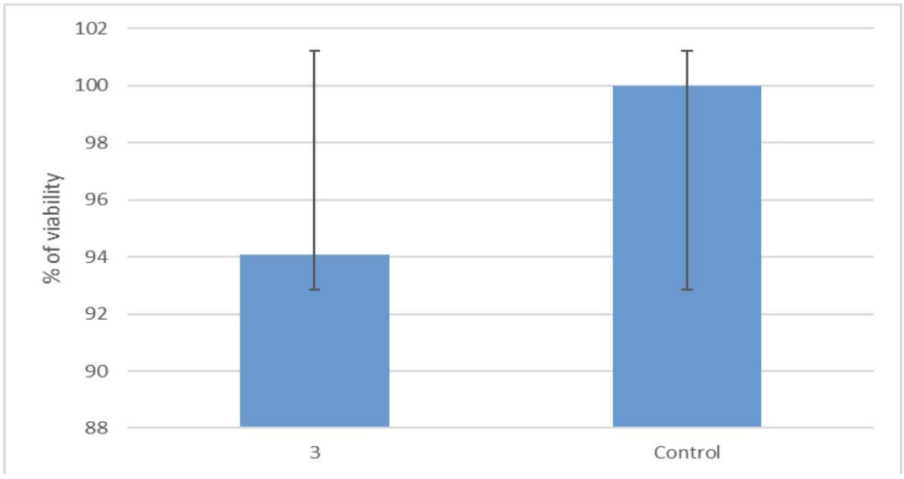

Fig 6- Cell viability of mucoadhesive hydrogel patch loaded with dox

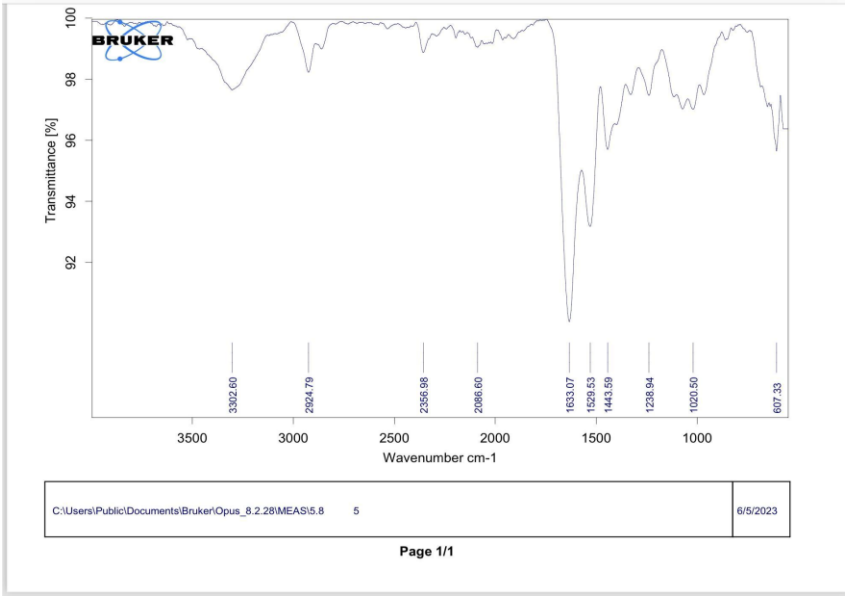

Fig 7- FTIR spectometry of mucoadhesive hydrogel patch loaded with dox

Cytotoxicity evaluation using the MTT assay indicated high cell viability (over 90%) after exposure to the patch extract, confirming its biocompatibility and non-toxic nature toward mammalian fibroblasts. The drug release profile indicated a sustained and controlled release of doxycycline over an extended period, which is desirable for maintaining therapeutic concentrations at the wound site while minimizing frequent dressing changes.

4. DISCUSSION

The developed cellulose-chitosan-doxycycline hydrogel patch integrates several desirable features for an advanced wound dressing. The combination of cellulose and chitosan leverages the mechanical robustness of cellulose and the bioadhesive, antimicrobial, and healing-promoting properties of chitosan. This polymeric synergy creates a stable yet flexible matrix that can maintain a moist wound environment, absorb excess exudate, and facilitate gaseous exchange.

The inclusion of doxycycline adds a critical therapeutic dimension. By providing localized and sustained release, the patch can deliver doxycycline directly to the wound site, where it can exert antimicrobial effects against common wound pathogens while simultaneously inhibiting MMP activity and modulating inflammation. This multifunctional approach addresses several pathological aspects of chronic wounds simultaneously.

The observed porous microstructure supports cell infiltration and nutrient diffusion, which are vital for tissue regeneration. The hydrophilic surface enhances intimate contact with the wound bed, improving adhesion and retention. Excellent hemocompatibility and high cell viability underscore the patch's safety profile, suggesting good tolerability in clinical settings.

These findings are consistent with existing literature that highlights the role of hydrogel-based dressings in promoting moist wound healing and the therapeutic benefits of topical doxycycline in reducing scarring and enhancing collagen organization. The controlled release mechanism further aligns with modern wound care strategies that emphasize sustained drug delivery to improve efficacy and patient compliance.

5. CONCLUSION

In conclusion, a mucoadhesive hydrogel patch composed of cellulose and chitosan and loaded with doxycycline was successfully developed and characterized. The patch exhibited favorable structural, mechanical, and biological properties, including porosity, surface wettability, blood compatibility, and low cytotoxicity. Its ability to provide controlled release of doxycycline, coupled with its mucoadhesive and moist wound-healing capabilities, positions it as a promising therapeutic dressing for chronic wound management. Future research should focus on in vivo validation of wound healing efficacy, long-term stability studies, and clinical translation to assess its full therapeutic potential.

6. ACKNOWLEDGEMENTS

The authors extend their sincere gratitude to Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, and Saveetha University for providing the necessary infrastructure, resources, and support to conduct this research successfully.

7. CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this work.

8. SOURCE OF FUNDING

This research was funded by Saveetha Institute of Medical and Technical Sciences, Saveetha Dental College and Hospitals, and Saveetha University.

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