Anti-inflammatory bio-nanogels for improved wound healing and antibacterial effects

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INTRODUCTION

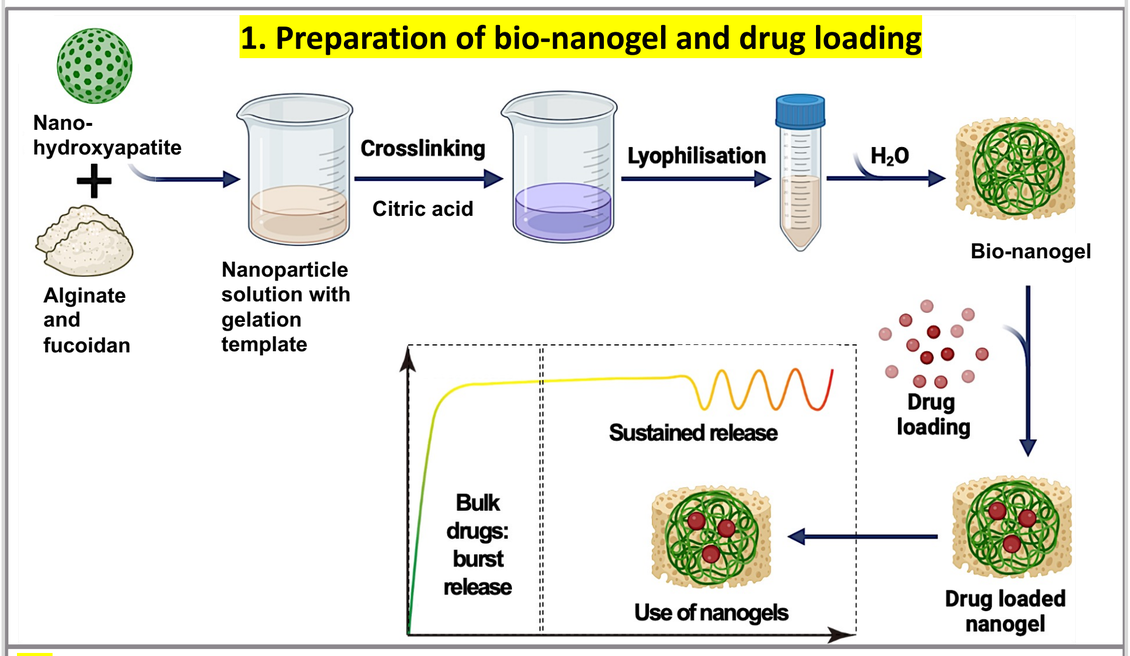
In everyday life, chronic infectious wounds are of immense concern due to long term patient discomfort and multiple hospital visits. Patients suffering from chronic wounds also tend to acquire secondary infections that makes the whole wound care management challenging. There is also evidence of increasing cases of chronic infectious wounds like Buruli ulcer in Australia, particularly in regions of Victoria[1]. Existing antibiotic therapies are long term due to the requirement of multiple dosing and are sometimes associated with side-effects that can affect vital organs such as liver and kidney. This opens a scope to strategize the application of antibiotic in such a manner that the amount and frequency of the dose can be reduced whilst wound healing accelerates. Use of hydrogels has been recommended to promote wound healing due to the moisture retaining properties of the gel and providing a platform for sustained release of antibiotics. We have recently developed and functionalised alginate-fucoidan based hydrogel where the polysaccharides has been isolated from seaweed waste. This hydrogel is multifunctional with antibacterial, anti-inflammatory, and sustained antibiotic delivery properties and is targeted for antibacterial wound healing.

OBJECTIVES

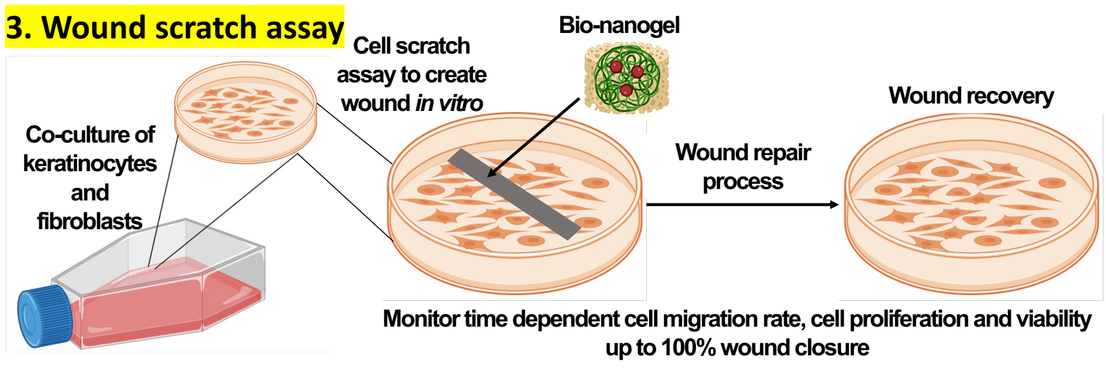
This study focuses on:

- Sustainable synthesis of bio-nanogels and their optimisation as carriers for existing antimicrobial drugs (e.g., rifampicin).
- Determining the drug delivery and wound healing efficacy of the drug-loaded nanohydrogels.
- Extend the findings for more complex infectious chronic wound management.

METHODS



2. a. Anti-inflammatory activities were assayed by monitoring inhibition of protein denaturation in the presence of gel[2].
b. Anti-oxidant activities were assayed by DPPH radical scavenging assay[2].
c. Antibacterial activities against *Escherichia coli* were assayed by microbroth dilution method[3].



RESULTS

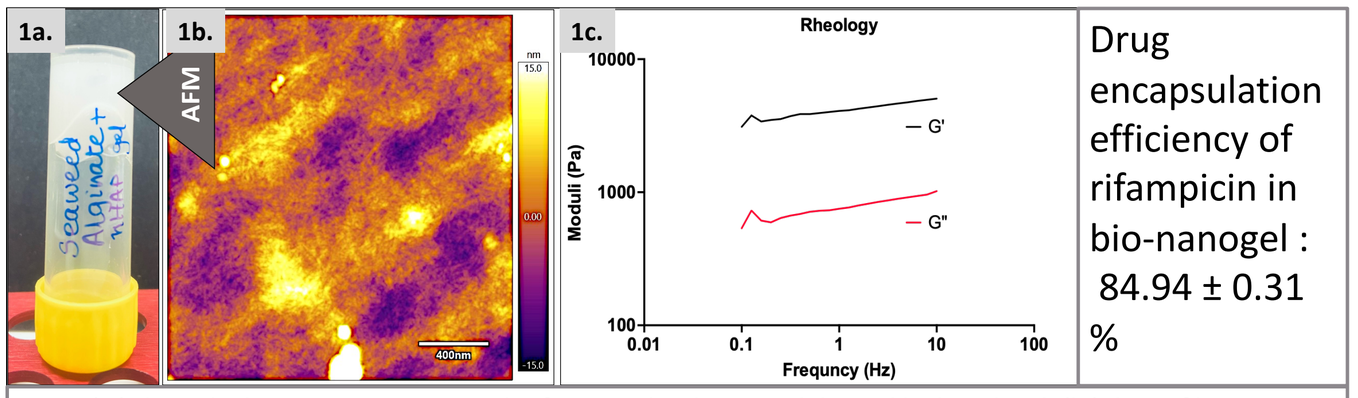


Fig. 1. (a.) shows hydroxyapatite nanoparticles functionalised seaweed derived hydrogel with (b.) dense fibrous network as observed via atomic force microscopy (AFM, scale 400 nm) and (c.) high moduli indicative of high elastic stability.

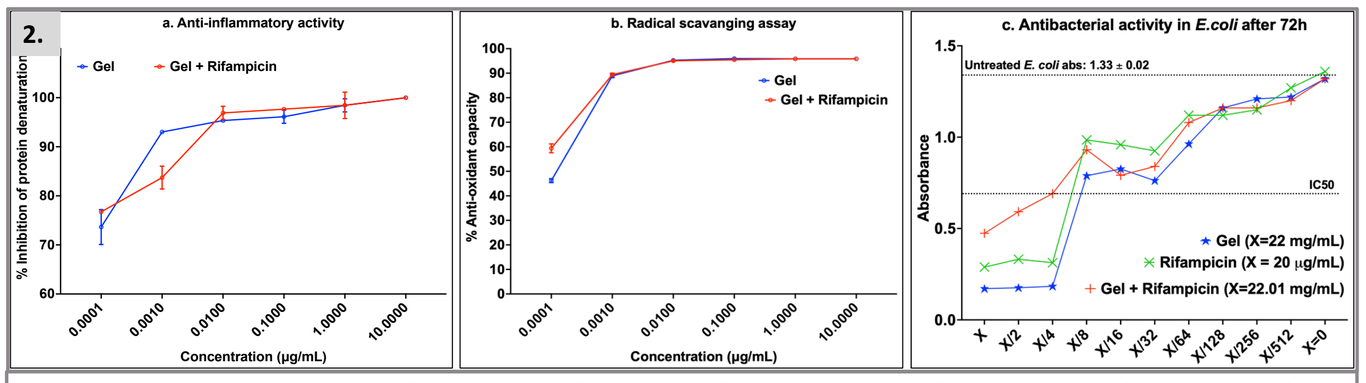


Fig. 2. shows concentration dependent (a.) anti-inflammatory, (b.) anti-oxidant and (c.) antibacterial (against *E. coli* up to 72 h of treatment) activities of bio-nanogel and rifampicin (4 µg/mL) loaded bio-nanogel.

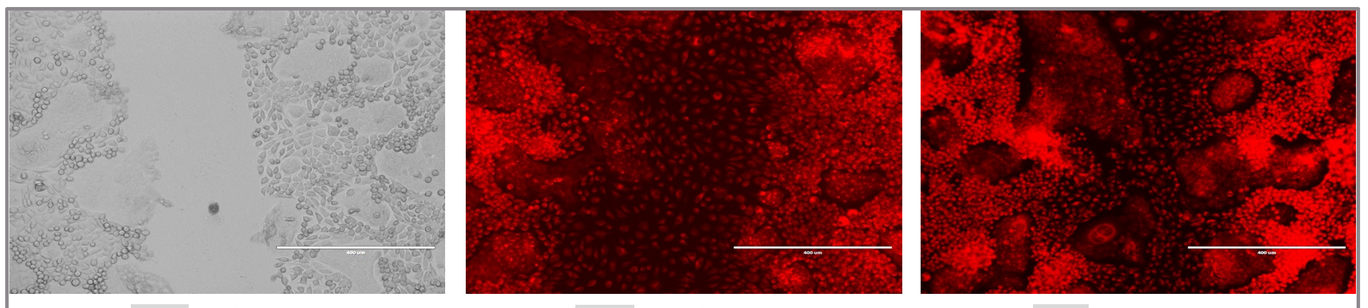


Fig. 3. (a.) shows *in vitro* scratch in keratinocyte and fibroblast co-culture at time 0 that on treatment with bio-nanogel undergoes rapid closure with (b.) 100% cell migration within 24 h and (c.) proliferation by 48 h. Scale: 400 µm.

DISCUSSION

- Seaweed waste was used to derive alginate and fucoidan fractions. Fucoidan – a sulphate polysaccharide is known for anti-inflammatory properties.
- A hydrogel was prepared by using hydroxyapatite nanoparticles that provided calcium ions to bind with guluronic residues of alginate in presence of citric acid.
- The hydrogel consisted of 3D networks of alginate, nanoparticles of hydroxyapatite and fucoidan molecules. Presence of a 3D network and nanoparticles enabled very high encapsulation efficiency for the rifampicin which is an approved antibiotic for treating chronic infectious wounds.
- Accelerated cell migration *in vitro* and antibacterial effects against *E. coli* were observed when the bio-nanogels were used as treatments.
- The drug loaded gel shows at par antibacterial efficacy even at 1/5th of the recommended dose of rifampicin suggesting sustained/slow release of antibiotic.
- For optimal management of infected wounds, this biodegradable drug loaded hydrogel is expected to provide a physical barrier to wound and moisturising effects and ensure slow release of rifampicin to prevent the need of multiple dosing.
- The whole concept assists in tying the circular economy with health impacts.

CONCLUSION

The bio-inspired functionalised hydrogel shows accelerated cell migration in simulated wound environment, efficient drug encapsulation, anti-inflammatory, anti-oxidant and antibacterial activities. This 3D hybrid system can be further explored for its wound healing ability with sustained antibiotic delivery and antibacterial effects against pathogenic bacteria including, MRSA and *Mycobacterium ulcerans* to provide sustainable solution against emerging chronic infectious wounds such as Buruli ulcer, endemic to regional Victoria.

REFERENCES & ACKNOWLEDGEMENTS

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