Chitosan/Alpha-hydroxy acids hydrogel formulations with antibacterial efficacy against *Propionibacterium acnes* and *Staphylococcus aureus*: Effect of different cellulose polymers

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Introduction

Chitosan is a polysaccharide, naturally available and isolated of crustacean. It can be used for acne treatment because has potential antibacterial capability against *Propionibacterium acnes* and *Staphylococcus aureus*, which are the contributing pathogenic factors in the etiology of acne lesions.
Previous studies showed chitosan alfa-hydroxy acids (AHA) hydrogels formulated with 1.5% High Molecular Weight (HMW) chitosan, 10% AHA and pH ≥ 3.5 exhibited antimicrobial activity. Nevertheless, these products were not viscous enough to allow a suitable application onto the skin.
In order to optimize the viscosity of these hydrogels, the effect of two cellulose polymers, hydroxypropyl methylcellulose (HPMC) and hydroxyethylcellulose (HEC) on the antibacterial efficacy of chitosan AHA hydrogels was assessed.

Conclusions

The incorporation of two cellulose polymers (either HPMC or HEC) not interfere with antimicrobial activity of Chitosan alpha-hydroxy acids hydrogels with HMW chitosan against *Propionibacterium acnes* and *Staphylococcus aureus* in vitro.

The previously formulated hydrogels showed pseudoplastic behaviour while the hydrogels with cellulose polymers have viscoelastic properties, indicating good applicability onto the skin.

These data are in accordance with the FDA guidance (pH≥3.5 and 10% AHA) and can contribute to the development of a pharmaceutical formulation for the treatment of acne.

Aim

The aim of this study was to evaluate the effect of two cellulose polymers HPMC and HEC, on the antibacterial efficacy of Chitosan / Alpha-hydroxy acids hydrogels, for topical administration in acne treatment, against *Propionibacterium acnes* and *Staphylococcus aureus*.

Methods

Gels formulation and Characterisation

The hydrogels were prepared in deionised water containing lactic acid (5%), glycolic acid (5%), HMW chitosan (1,5%) and HEC or HPMC (1,5%).
Briefly, the polymers (chitosan and cellulose) were dispersed in an aqueous solution of acids. The resulting mixture was stirred without heating, at room temperature for 60 min until chitosan was dissolved and HPMC and HEC were hydratated.
For pH assessement was used a potenciometer (Metrohm, pH Meter 744) and the viscosity was evaluated by HAAKE model RHEOSTRESS RS-1, plate/plate, at 25°C.
A hydrogel with no polymers was used as control.

Antibacterial activity

The antibacterial activities of hydrogel formulations (at final concentration from 100 to 0.000097 mg/ml), were determined against *Propionibacterium acnes* ATCC 6919 (origin from Facial acne, London, UK, 1920) and *Staphylococcus aureus* ATCC 6538, by broth microdilution method, in Mueller-Hinton broth, recommended by the Clinical and Laboratory Standards Institute (n=3).
The Minimum Inhibitory Concentration (MIC) was calculated after absorbance lectures with an Absorbance Microplate Reader set to 630 nm (ELX808™ - BioteK).
Erytromycin solution (1mg/ml) and clindamycin solution (1mg/ml) were used as controls as well as a hydrogel without cellulose polymers.

Results

Apparent viscosity was higher for the HEC (733.1 Pa.s) and HPMC (998.7 Pa.s) gels, and lower for the control hydrogel (10 Pa.s).

Table 1 - Effect of cellulose polymers in antibacterial activity of hydrogel with 1.5% HMW chitosan, 10% AHA, pH= 3.5 (n=3, ± SD)

	Control	HPMC-Chitosan hydrogel	HEC-Chitosan hydrogel	Erytromycin solution	Clindamicin solution
P. acnes **MIC (mg/ml)**	6.25	6.25	6.25	0.0048	0.000097
S. aureus **MIC (mg/ml)**	0.625	0.625-0.781	0.625-0.781	0.0048	0.0039

The hydrogels formulated with cellulose polymers maintained the antibacterial activity and had similar MIC values for *S. aureus* and for *P. acnes* in a concentration ranging from 100 mg/ml to 0.000097 mg/ml (Table 1).

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