British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1078

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 13th APS International PharmSci 2022

Antimicrobial cationic surfactant-loaded hydrogel coatings in preventing medical device-associated infections

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ARTICLE INFO

Received: 16/06/2022
Accepted: 07/07/2022
Published: 04/11/2022

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KEYWORDS: MDAIs, hydrogel, cationic surfactants, anti-adherence.

SUMMARY

Hydrogels described herein were developed as anti-microbial coating materials. Three different hydrogels, p(HEMA), p (85% HEMA-*co*-15% MMA) and p (85% HEMA-*co*-15% MAA) were loaded with two cationic surfactants, BAK and DDAB, respectively. DDAB owned better effectivity than BAK in killing *S. aureus* and *E. coli*. Compared to unmodified p(HEMA), all drug-loaded samples exhibited significant anti-adherence ability against *E. coli*, but on surfaces of all DDAB-loaded hydrogels, bacteria were below limit of detection, so DDAB was more effective than BAK in conferring anti-adherent properties.

INTRODUCTION

Medical device-associated infections (MDAIs) have become a challenge that can lead to medical and economic problems, causing increased morbidity, mortality of patients, and health care costs (Weinstein and Darouiche, 2001) (Venkatram, Rachmale and Kanna, 2010). Hydrogel is a widely used material in biomedical applications because its biocompatible and biodegradable properties. Meanwhile, hydrogel is capable to be loaded with drugs, acting as a sort of antimicrobial drug-loading coatings.

Cationic surfactants can be used as antimicrobial agents through their electrostatic and hydrophobic interaction with cellular structure of bacteria (Zhou and Wang, 2020). Therefore, benzalkonium chloride (BAK) and didecyldimethylammonium bromide (DDAB) herein were alternative candidates to conventional antibiotics, which were loaded into hydrogels to afford potential controlled release anti-microbial coatings for medical devices.

MATERIALS AND METHODS

Staphylococcus aureus (*S. aureus*) ATCC 29213, Escherichia coli (*E. coli*) ATCC 25922 were obtained from LGC Standards (Middlesex, UK). Benzalkonium chloride (BAK) was purchase from Sigma-Aldrich (Poole, Dorset, UK). Didecyldimethylammonium bromide (DDAB) was purchased from VWR international (Poole, UK).

MIC and MBC tests: The broth microdilution method recommended by Clinical and Laboratory Standards Institute (CLSI) was used to determine the MICs and MBCs of BAK and DDAB.

Bacteria adherence: Dry round discs of drug-unloaded hydrogel control and drug-loaded hydrogel samples were immersed in 10^6 CFU/mL inoculum for 4 hr or 24 hr, after which the amount of the adherent bacteria was counted.

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RESULTS AND DISCUSSION

1. MIC and MBC tests: From the **Table 1** below, MBC/MIC ratios of both BAK and DDAB were below 4 μg/mL, so they are bactericidal against *S. aureus* and *E. coli*. In addition, compared to BAK, MICs and MBCs of DDAB were all lower, so DDAB is more potent.

Table 1. *MICs and MBCs (μg/mL) of BAK and DDAB against S. aureus and E. coli at pH 7.3.*

Bacteria		BAK	DDAB
S. aureus	MIC (μg/mL)	2	1
	MBC (μg/mL)	4	2
	MBC/MIC ratio	2	2
E. coli	MIC (μg/mL)	8	2
	MBC (μg/mL)	16	2
	MBC/MIC ratio	2	1

2. Bacteria adherence:

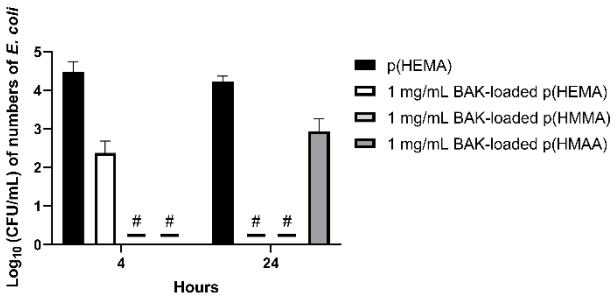

Fig. 1. *The log_{10} (CFU/mL) of numbers of E. coli to un modified p(HEMA), 1 mg/mL BAK loaded hydrogels after 4 hr and 24 hr in pH 7.3 inoculum. Columns and error bars represent means ± s. d (n=5). The hash symbol (#) means below limit of detection; limit of detection was 150 CFU/mL.*

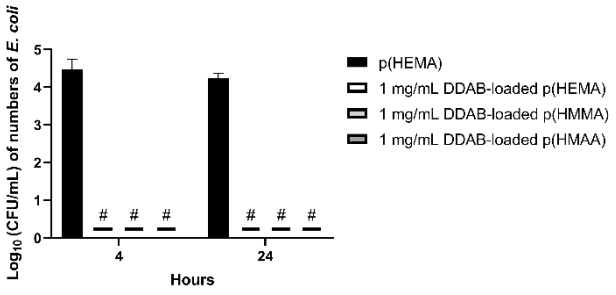

Fig. 2. *The log_{10} (CFU/mL) of numbers of E. coli to un modified p(HEMA), 1 mg/mL DDAB loaded hydrogels after 4 hr and 24 hr in pH 7.3 inoculum. Columns and error bars represent means ± s. d (n=5). The hash symbol (#) means below limit of detection; limit of detection was 150 CFU/mL.*

Significant reduction in bacteria adherence can be observed in both BAK and DDAB-loaded hydrogels when against *E. coli*, which can be seen in **Fig. 1** and **Fig. 2**, respectively.

From the **Fig. 1**, after 24 hr, except for BAK-loaded p(HMAA), the amount of the adherent *E. coli* on both BAK-loaded p(HEMA) and p(HMMA) was below limit of detection (LOD). From the **Fig.2**, after 4 hr and 24 hr, compared to unmodified p(HEMA) control, on surfaces of DDAB-loaded hydrogels, the amount of the adherent *E. coli* was all below LOD.

CONCLUSIONS

Both BAK and DDAB showed bactericidal effect when combating *S. aureus* and *E. coli*, but DDAB was stronger. From the results of bacteria adherence assay, significant reduction of adherent bacteria was observed in both BAK and DDAB loaded hydrogels compared to p(HEMA), but DDAB-loaded hydrogels showed stronger efficacy, shown as the amount of the adherent bacteria were below limit of detection (LOD, 150 CFU/mL) in all DDAB-loaded hydrogels. Therefore, compared to BAK, DDAB may be a more potent cationic surfactant.

ACKNOWLEDGEMENTS

Financial support from the School of Pharmacy, QUB, is gratefully acknowledged.

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