Macedonian pharmaceutical bulletin, 69 (Suppl 1) 219 - 220 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.107
Short communication

Hydrophilic polymer based oral formulations studied by NMR relaxometry and UTE MRI - towards polymer mobilization and erosion assessment

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Introduction

Hydrophilic polymers are widely used as drug carriers for modified/controlled release. But the hydration-related phenomena still need to be studied in depth. Various approaches exist to elucidate hydration-related phenomena in hydrophilic matrices (Caccavo et al., 2016). Most of them give a simplified picture of these phenomena. Nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) techniques are also used for this purpose. But the vast majority of the studies are performed using ^{1}H NMR/MRI during incubation in H_2O. In this case, the signal from the hydration medium dominates the results, i.e., images and relaxation time distributions/maps (Baran et al., 2023). Only some research uses D_2O as a hydration medium, but they present one-dimensional profiles in spatially restricted conditions (Dahlberg et al., 2007, Dahlberg et al., 2011). Sodium alginate based matrices containing sodium salicylate (ALG/SA), salicylic acid (ALG/SNA), and alginate placebo matrix have been studied recently in H_2O. The results reflect the mobility of water molecules (Juszczyk et al. 2021a, Juszczyk et al. 2021b). However, an unexplored and interesting issue is to acquire images and T_1-T_2 relaxation time distributions of protons included originally in polymer and water bound to polymer chains in the unhydrated (air-dry) sample.

The goal of the study was to approach the assessment of polymer mobilization and subsequent erosion using D_2O as hydration media and a combination of imaging and relaxometric magnetic resonance techniques.

Materials and methods

Sodium alginate (Protanal LF 240 D) compressed matrices of oblong shape were prepared: placebo (ALG), alginate with sodium salicylate (ALG/SNA), and alginate with salicylic acid (ALG/SA). The matrices were incubated in 30 mL of D_2O up to 4 h. NMR and MRI measurements were performed for air-dry samples, immediately after immersion and at 1, 2, 3 and 4 h after immersion.

^{1}H LF TD NMR relaxometry was performed using a 23 MHz NMR Rock Core Analyzer (Magritek, New Zealand and Germany) using Inversion-Recovery CPMG (IR-CPMG) for obtaining 2D T_1-T_2 relaxation time maps. Echo-time used in CPMG sequence was 60 microseconds.

Magnetic resonance imaging was performed using 9.4 T MRI research scanner (Bruker BioSpin GmbH, Ettlingen, Germany) with 3D UltraShort Echo Time imaging technique at echo-times 20-1200 microsecond.

Results and discussion

Fig. 1 presents exemplary results of UTE MR images and T_1-T_2 maps obtained at 4 h of incubation. The samples were incubated in D_2O, which is not detected in ^{1}H MMR/MRI. Therefore the source of the MR signal to build images and T_1-T_2 maps are protons in polymeric chains and attached bound water included in the solid air-dry matrix tablet (before incubation).

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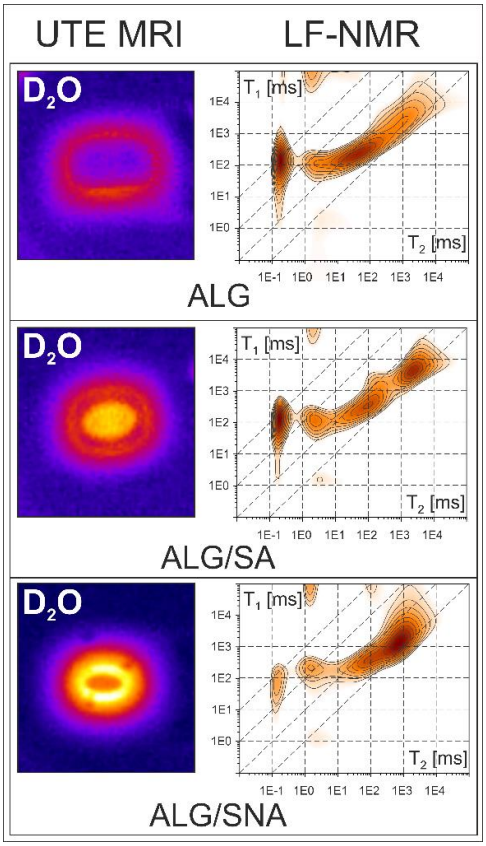

Fig. 1. Axial UTE images at echo time of 20 microseconds (left column) and T_1-T_2 maps (right column) of the sodium alginate based matrices after 4 h of incubation in D_2O.

UTE images show that the spatial distribution of polymer and water bound to polymer chains undergo changes depending on the solubility of the drug substance. T_1-T_2 maps show modes representing various states of polymer matrix from solid (T_1/T_2~1000), and semi-solid (T_1/T_2~100) to a viscous solution. The intensity of the modes also depends on the solubility of the drug incorporated in the matrices. Additionally, proton fraction, which has exchanged to bulk, originally proton-free, medium manifested as a mode at T_2>1s (T_1/T_2 close to 1).

UTE images and T_1-T_2 maps show the complexity of the processes and different "hydration patterns" depending on the particular formulation. Further data analysis is performed towards calculating T_2^* relaxation time maps. These maps will reflect polymer mobilization.

Conclusion

Combined, LF TD NMR relaxometry and UTE MRI of alginate based matrices during hydration in D_2O allow new, complementary to previous studies, views on hydration processes of hydrophilic polymer-based matrices. We suppose, that the combination of these two techniques will enable the assessment of polymer mobilization and subsequent erosion of hydrophilic, polymer based formulations.

Acknowledgements: Funding: This work was supported by the Polish National Centre for Research and Development (NCBR), grant number POIR.04.01.04-00-0142/17 “Innovative testing methodology for drug products under development”.

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