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Short communication

Pharmaceutical dosage forms by Vat Polymerization – from additive manufacturing to functional properties and formulation understanding

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Introduction

Current pharmaceutical production is not suitable for personalized medicines. Over the past few years, there has been a rapid increase in interest in 3D printing in pharmaceutical technology (Awad et al., 2018). The use of three-dimensional (3D) printing (additive manufacturing technology) in pharmacies could enable the production of patient-tailored batches of dosage forms with different dosing and release characteristics (Azad et al., 2020; Trenfield et al., 2018).

Understanding the physicochemical processes occurring during the printing process and drug release from the pharmaceutical products can help to design them consciously. The 3D Vat Polymerization technology seems to be one of the promising methods used in pharmacy (Stanojevic et al., 2021). On the other hand, one of the methods of spatiotemporal characterization of pharmaceutical matrices in situ are magnetic resonance methods including magnetic resonance imaging. These methods allow for the assessment of mass transport phenomena at the molecular and macro-level without disturbing the processes taking place inside this material (Baran et al., 2023; Kulinowski et al., 2015).

Materials and methods

Poly(ethylene glycol) diacrylate 700 (PEGDA 700), poly(ethylene glycol) 400 (PEG 400), D2O and diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide (DPPO) were purchased from Sigma-Aldrich Inc., St Louis, MO. Metronidazole was supplied by Hubei Hongyuan Pharmaceutical Technology Co., Ltd. Fengshan, China. All other chemicals and reagents used in the study were of analytical grade.

Pharmaceutical matrix templates was designed in 3D Builder software (Microsoft). Chitubox V1.9.4 software was used to sliced and to adjust printing parameters. All formulations were printed using a Sonik mini 8K printer (Phrozen,Taiwan). Printing conditions were established during the preliminary study and adapted to the type of matrix.

LF TD NMR relaxometry was performed using a 23 MHz NMR Rock Core Analyzer under PROSPA 4.26 software (Magritek, New Zealand and Germany). Three pulse sequences were used: FID, CPMG (Carr-Purcell-Meiboom-Gill) for obtaining 1D T2 relaxation times spectra Inversion-Recovery CPMG (IR-CPMG) for obtaining 2D T1-T2 relaxation time maps

Magnetic resonance imaging study was carried out at room temperature using 9.4 T Bruker Biospec MRI scanner (Bruker, Ettlingen, Germany) and multi-slice multi-echo (MSME) pulse sequence imaging was performed using 3D UltraShort Echo Time imaging technique.

Results and discussion

Fig. 1 presents exemplary results of images and T1/T2 maps obtained for a sample with a Pegda 30%/PEG 70% ratio. Printed pharmaceutical matrices in the form of oral tablets or wound dressings were tested by NMR methods. The results were compared with drug release studies. Measurements were carried out in appropriate setups in D2O or in vitro models of dressings on dry samples and

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hydrated samples up to 24h at different time intervals, respectively. Based on the analysis of MSME photos, components derived from water and propylene glycol were distinguished. The spatiotemporal evolution of these components was assessed. The Figure 1 show one-dimensional parametric images (profiles) in the form of calculated T2 relaxation times and related amplitudes (A) of individual signal components. The vanishing component indicates the hydration of the samples and the increase in the mobility of the polymer chains. After 24 h, stabilization of the samples was observed.

The more PEGDA in the composition, the harder the sample is and the less it releases the medicinal substance, and the relaxation times are lower. Only in the sample with 30% PEGDA content, two components from proton groups were observed, in the others only single exponents were matched. However, the results obtained from T1/T2 map measurements confirm the presence of at least two groups of protons with different mobility. Their mobility changes with the composition and hydration of the matrices. The peak around T2 = 0.1 ms indicates PEGDA-derived protons, while at T2 around 1000 ms, PEG-derived.

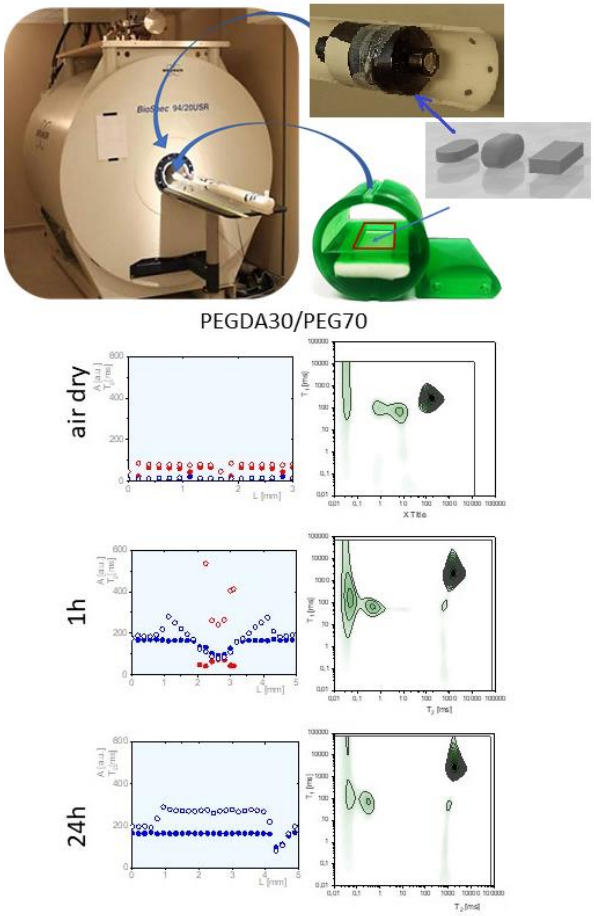

Fig. 1. Parametric profiles in terms of T2 relaxation time and signal amplitude (A) across the sample, T1/T2 maps.

Conclusion

3D printed tablets (printlets) could be characterized using NMR/MRI techniques including mass transport phenomena description, in particular for systems dealing with two mobile phases and how these phenomena could influence their functional properties.

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