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Short communication

Evaluation of 2D printing cartridges containing spray-dried drug-polymer particles

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Introduction

Since the discovery of the role of genes in individual variations in physiology and metabolism, the importance of personalized treatment of patients has been recognized and pursued. In this context, various types of 2D printing technologies have been identified to offer some potential solutions for personalized medication (Sterle Zorec & Dreu, 2023). These printing technologies offer several advantages over traditional bulk manufacturing of pharmaceuticals, including precise drug-on-demand deposition, the ability to combine multiple active ingredients into a single product, and the customization of individual drug assays. With the incorporation of micro/nanotechnology by printing particles from their suspensions, several other possibilities such as controlled and stimulation-dependent drug release or targeted dependent drug delivery have been demonstrated (Sterle Zorec & Dreu, 2023).

In this study, three different types of simvastatin-containing microparticles prepared by spray drying were redispersed in a medium consisting of different ratios of propylene glycol (PG) and water, which is a printable blank ink medium. Simvastatin (SIM) content in the medium was evaluated immediately after redispersion and after one month of storage. In addition, the antioxidant ascorbic acid (AA) was added to the original formulation to protect simvastatin from possible degradation during the storage period.

Materials and methods

SIM (Krka d.d., Slovenia), polycaprolactone of 14000 daltons (PCL, Sigma Aldrich, USA), Tween 20 (Sigma Aldrich, USA), lactose mesh 200 (Lek d.d., Slovenia), nanocelullose (NCC; Cellu Force, Canada) and Florite R calcium silicate (CaSi; Tomita Pharmaceutical, Japan), Ascorbic acid (AA; Sigma Aldrich, USA) were used in spray drying experiments. Chloroform (Merck KGaA, Germany), and purified water were used as O/W emulsion phases, while PG (Sigma Aldrich, ZDA) was used as redispersion medium.

Emulsions consisting of an organic (0.8 g SIM, 1.6 g PCL in 40 g chloroform) and an aqueous phase (4 g Tween 20, 120 g water) were prepared using the APV 2000 high-pressure homogenizer (SPX Flow, ZDA). Before spray drying, three different anti-adhesive agents were added to the emulsions (lactose, lactose/NCC and CaSi). Particles were prepared from these emulsions using Büchi Mini Spray-Dryer (B290, Büchi, Switzerland). The process parameters for spray drying were as follows: Drying gas flow rate of 38 m3/h, inlet temperature of 170 °C, spray rate of 18 ml/min and flow meter spray air (atomizing gas flow rate) of 8 mm (110 L/h).

The dry particles were then redispersed in a medium consisting of various ratios of PG and water (1:9, 1:1 in 9:1). 100 mg of the particles were redispersed in 20 ml of the medium and vortex mixed for 2 minutes. The drug content in the redispersed particles was analyzed by the UPLC method as previously described by Sterle Zorec et al., 2021.

Results and discussion

After redispersion of the dry particles, all formulations had a high SIM concentration, the highest being observed in the lactose/NCC particles (100%) dispersed in the most viscous medium (PG:water=9:1). The addition of AA generally increased the retention of the drug during redispersion, except for the particles with CaSi, where the

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drug content decreased significantly when AA was present in the formulation (Table I).

Table 1. SIM content in the redispersed formulations immediately after preparation (expressed in %, based on the SIM content in dry particles).

	Lactose		Lactose/NCC		CaSi	
PG:water	no AA	AA	no AA	AA	no AA	AA
1:9	92,4	82,03	81,42	82,09	99,50	79,03
1:1	93,34	90,23	87,24	96,81	75,87	44,97
9:1	89,68	84,58	86,98	104,47	89,59	47,61

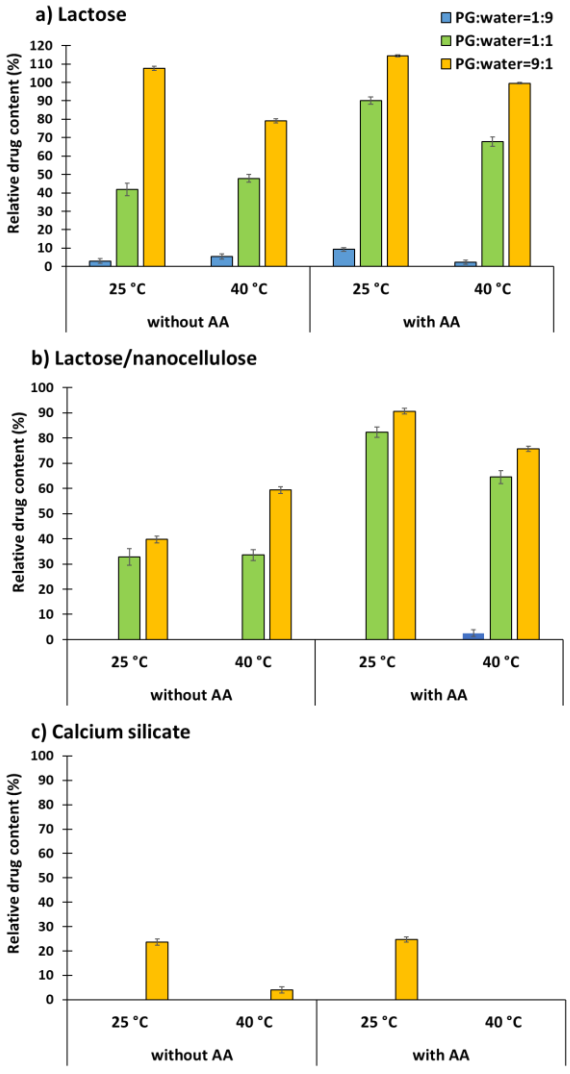

Fig. 1. The chemical stability of SIM in particles oflactose, lactose/NCC and CaSi (with and without AA) redispersed in three PG:water mixtures and stored at 25°C and 40°C for one month.

Figure 1 shows some differences in the chemical stability of SIM after one month of storage when particles with different antiadhesives are redispersed in different blank ink medium. Without AA in the formulation, the drug content in the dispersion was highest when lactose was used as an antiadhesive, regardless of the storage conditions and the medium used. The addition of AA to the formulation further increased the stability of the drug, but only in the case of lactose and lactose/NCC particles. The effect of AA addition varied depending on the dispersion medium used, with the greatest influence observed at a higher proportion of PG in the water (at ratios of 1:1 and 9:1). The lowest SIM content was found when CaSi antiadhesive was used, regardless of storage conditions and redispersion medium. Surprisingly, even the addition of AA did not increase the SIM content in CaSi dispersions over time, but on the contrary.

The most effective chemical preservation of SIM in the formulation under both storage conditions was achieved when lactose and lactose/NCC particles (both containing AA) were redispersed in a mixture of PG and water in a 9:1 ratio.

Conclusion

In the present study, it was shown that dry particles prepared by spray drying of emulsions can serve as a preformulation for the preparation of 2D printing cartridges by redispersing them in a suitable blank ink medium. Based on the chemical stability of the drug, the most promising formulations are PG:water=9:1 dispersions containing lactose or a combination of lactose and NCC particles.

References

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