

Paediatric-friendly chocolate-based dosage forms for the oral administration of both hydrophilic and lipophilic drugs fabricated with extrusion-based 3D printing

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Aim

Poor treatment adherence is a challenge commonly encountered within the paediatric population. Compliance with therapeutic regimen is a cornerstone for effective treatment and is highly dependent on the patient's acceptability of the dosage form. Organoleptic properties such as smell, taste and texture are key considerations for the development of paediatric dosage forms. The current study reports on a simple, cost- and time- efficient process for the development of a paediatric-friendly oral dosage form appropriate for the administration of both lipophilic and hydrophilic drugs, that is fabricated with extrusion-based 3DP.¹

Methods

Two active compounds, widely used within the paediatric population for pain relief and fever reduction, were used as model drugs, namely paracetamol (BCS class I) and ibuprofen (BCS class II). Bitter chocolate and corn syrup were used as excipients for the preparation of the ink formulations, which were amenable to 3D printing in different shapes. The chocolate inks were further characterized in terms of their thermal, textural and rheological properties, while drug crystallinity within the inks was assessed with X-Ray diffraction. In addition, drug dissolution from the printed dosage forms was evaluated in media simulating the oral and gastric phases.

Results

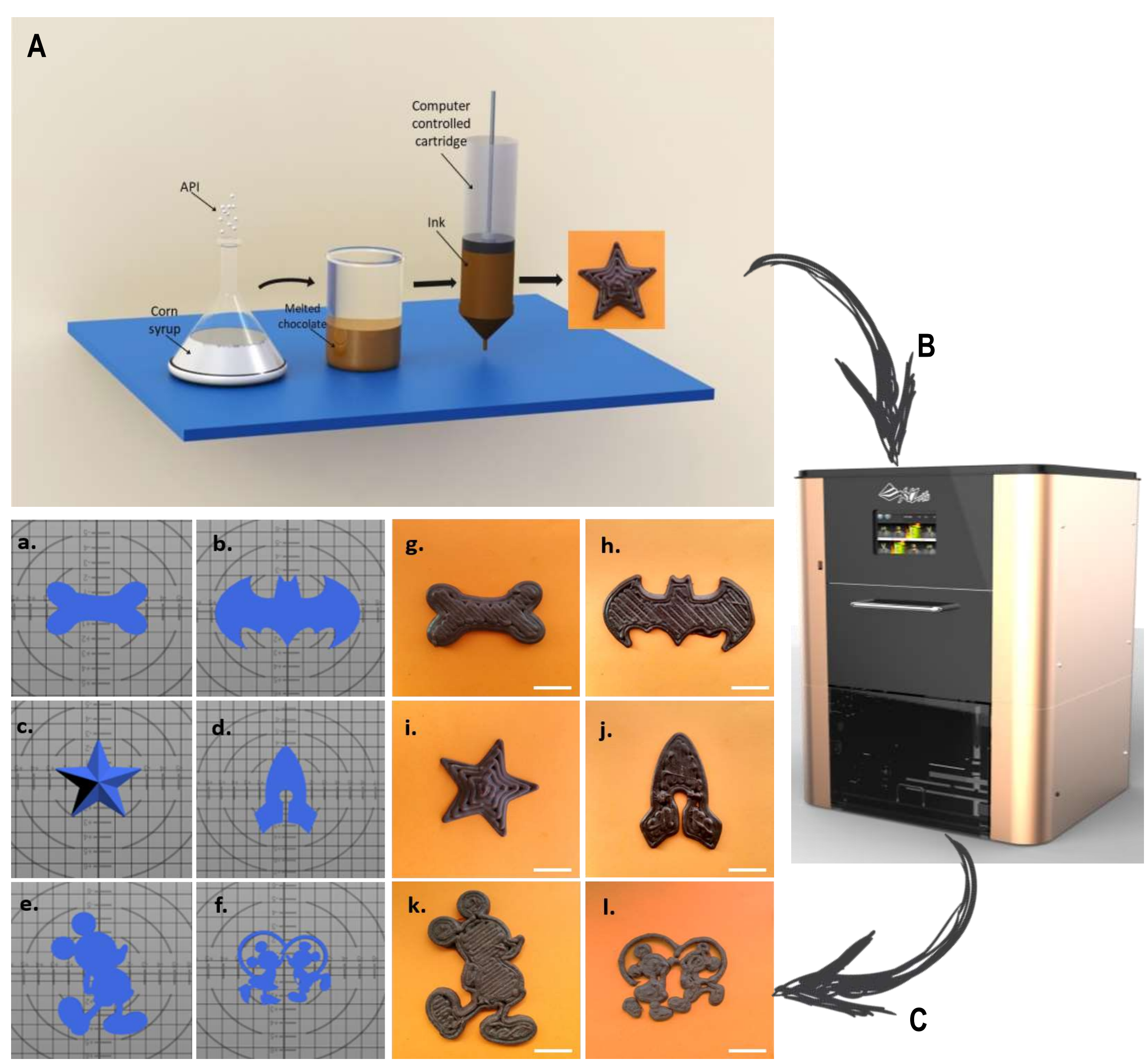


Figure 1. Schematic representation of **A.** the process for the development of paediatric-friendly chocolate-based dosage forms. The blank inks were prepared by first melting the bitter chocolate at 38 °C and adding the corn syrup preheated at the same temperature. The materials were then mixed gently with a rubber spatula until homogenization. For the drug-loaded printable chocolate inks, paracetamol was dissolved (PCT-ink) while ibuprofen was melted in the heated corn syrup at 79 °C (IBU-ink). The inks were 3D printed using **B.** extrusion-based 3D printing, based on **C.** the a-f. .stl files to obtain the g-l. 3D printed chocolate-based dosage forms. Scale bar: 20 mm.

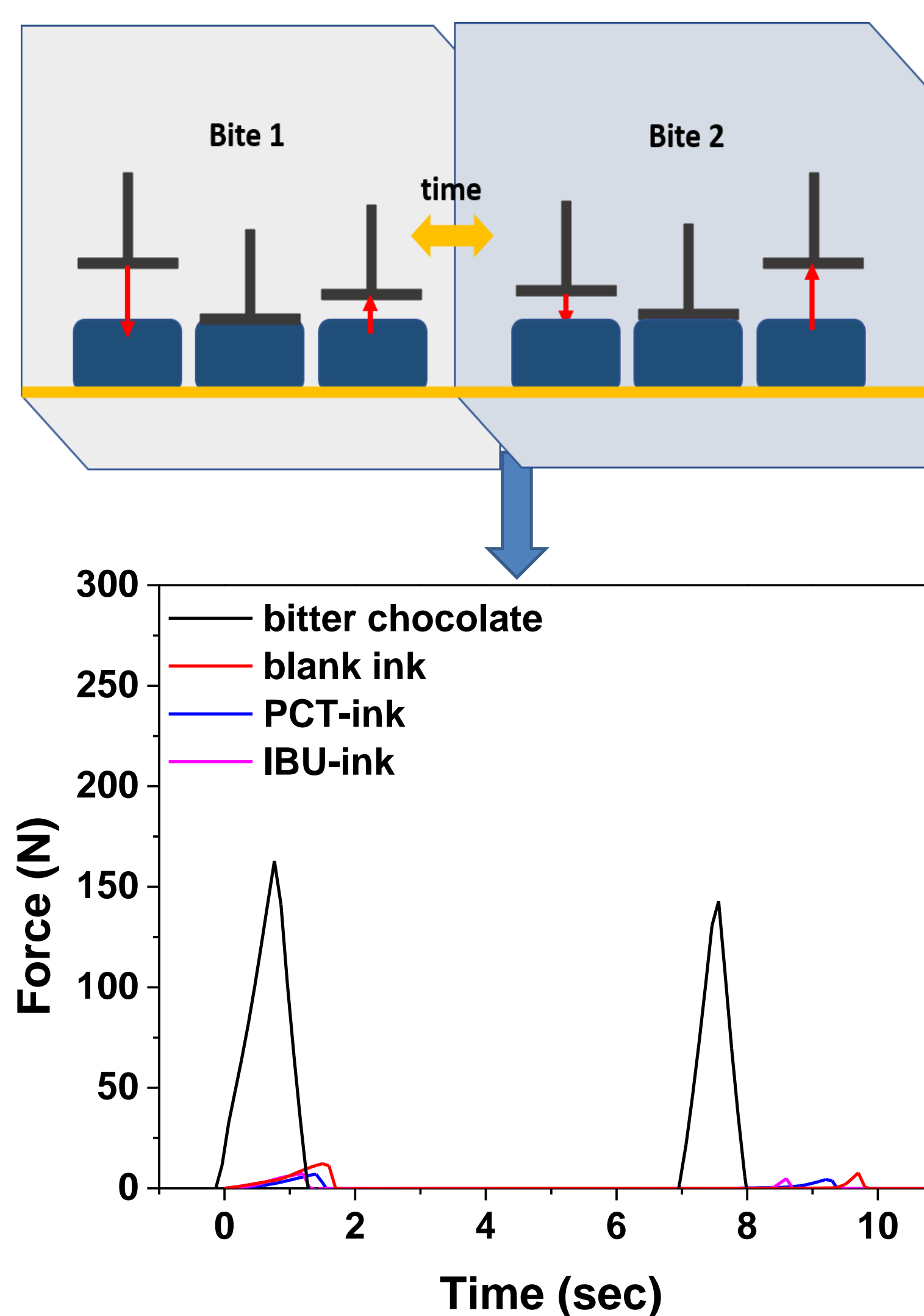


Figure 2. The bitter chocolate and the chocolate-based dosage forms were subjected to a double compression test. The texture profile analysis curves of the bitter chocolate and the chocolate-based dosage forms, showed that the chocolate-based dosage forms are a lot easier to process orally, compared to bitter chocolate.

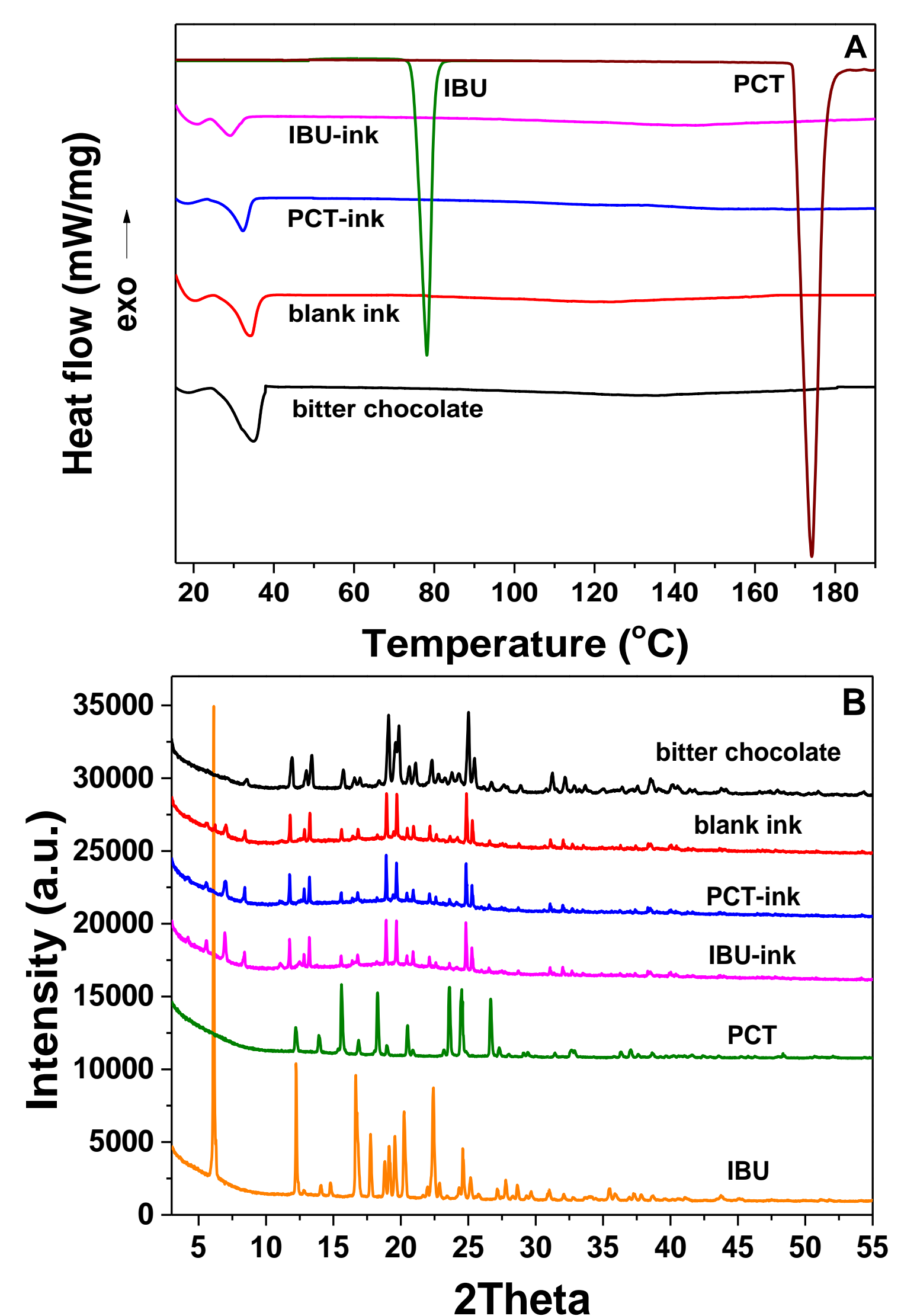


Figure 3. **A.** DSC thermograms and **B.** X-Ray diffractograms of the crystalline drugs, the bitter chocolate and the chocolate-based ink formulations. Thermal analysis showed that shorter oral processing is required for the prepared chocolate-based dosage forms, while X-ray diffractograms indicated possible drug amorphization.

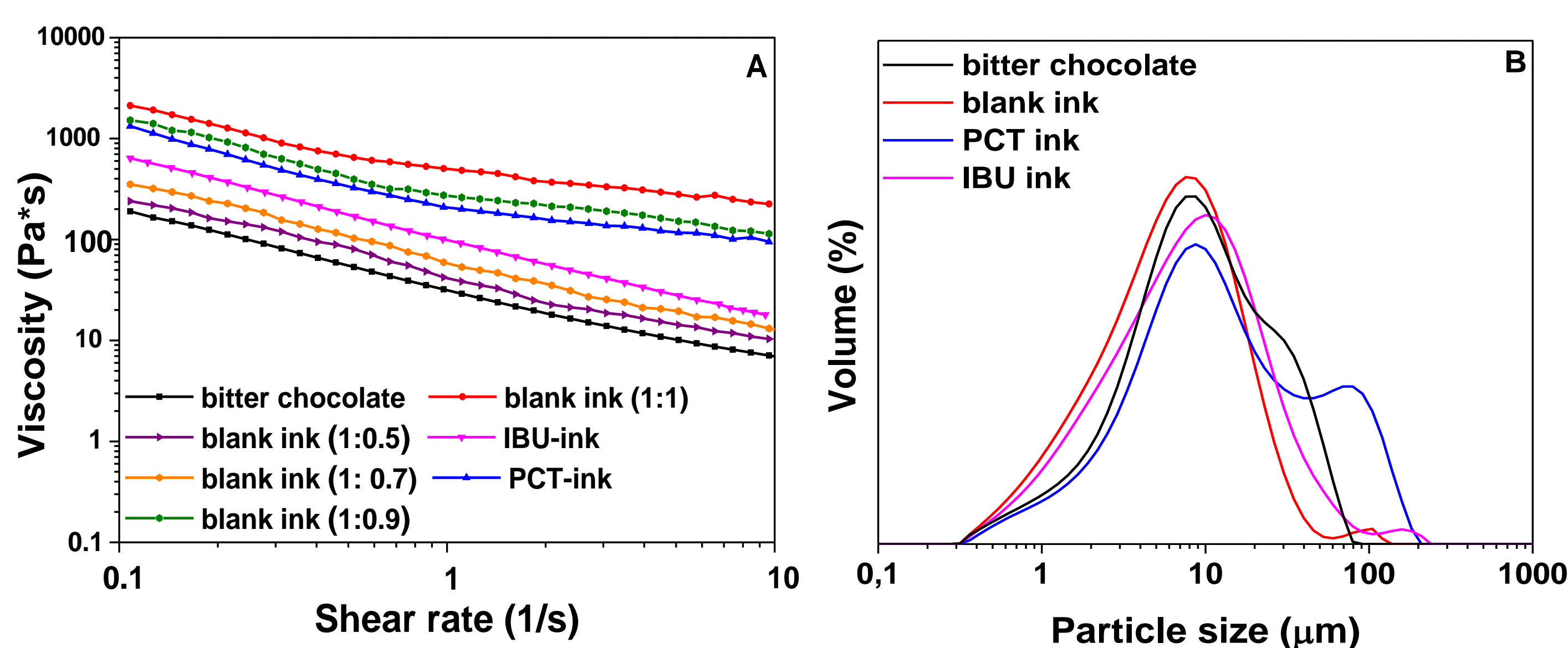


Figure 4. **A.** Flow curves of bitter chocolate and the chocolate ink formulations recorded at 45 °C and **B.** particle size distributions of the bitter chocolate and the chocolate ink formulations. The prepared chocolate ink formulations showed shear-thinning properties, while their mean particle size was within the micrometer range (<30 µm), indicative of acceptable quality for a chocolate-based product.

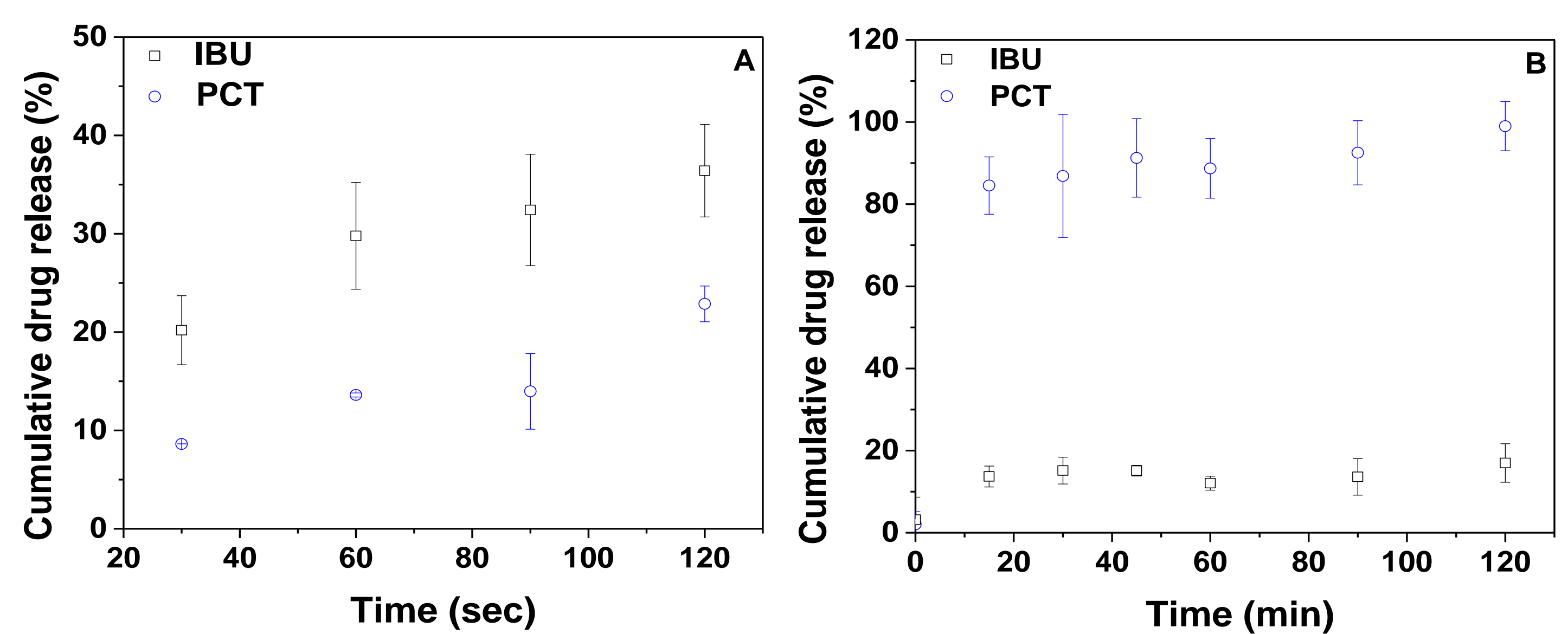


Figure 5. Release profiles of paracetamol and ibuprofen during *in vitro* digestion of the chocolate-based dosage forms in **A.** simulated saliva fluid pH 7.0 in the presence of α -amylase and **B.** in simulated gastric fluid pH 2.0 in the presence of pepsin at 37 °C, showing rapid and high dissolution of both drugs in SSF, constituting them readily available for absorption in the oral cavity and across the gastrointestinal tract during swallowing.

Conclusions

The current study reports on the development of a paediatric-friendly dosage form for oral drug administration employing extrusion-based 3D printing. The desirable mouth-feel properties were imparted through the formulation of a chewable chocolate-based dosage form, which could be 3D printed in customized designs upon patient's request. Adoption of 3D printing as the manufacturing process enabled flexibility in dose adjustment, while at the same time being cost-effective, convenient and potentially providing a more engaging role for the paediatric patient.

References

1. Karavasili C,* Gkaragkounis A, Moschakis T, Ritzoulis C, Fatouros DG. Pediatric-friendly chocolate-based dosage forms for the oral administration of both hydrophilic and lipophilic drugs fabricated with extrusion-based 3D printing. *European Journal of Pharmaceutical Sciences*, 2020, 147:105291