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Short communication

Development of spray-dried Paracetamol microparticles for taste masking

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Introduction

Taste masking constitutes a critical challenge in the design of oral pharmaceutical dosage forms, particularly for pediatric and geriatric populations, in whom patient compliance is highly dependent on palatability (Walsh et al., 2014). A considerable number of active pharmaceutical ingredients (APIs), including paracetamol (PA), are characterized by an intrinsically bitter taste, which can significantly compromise adherence to therapy.

Paracetamol (PA), a BCS Class I analgesic, presents a significant formulation challenge due to its pronounced bitterness in direct oral dosage forms. Polymer-based approaches, particularly using Eudragit® EPO, effectively address this limitation by preventing drug release at salivary pH while enabling rapid release under acidic conditions (Evonik, 2020).

Spray-drying is a scalable technique for producing microparticles with controlled properties. A single-nozzle system enables rapid solvent evaporation and uniform API distribution within a polymer matrix (Tontul and Topuz, 2017; Vehring, 2008).

The present study aimed to develop spray-dried PA microparticles using Eudragit® EPO and copovidone as functional excipients, with the objective of achieving efficient taste masking while preserving appropriate physicochemical and performance attributes for oral administration.

Materials and methods

Paracetamol (PA), Eudragit® EPO and copovidone VA 64 were kindly donated from Alkaloid AD, Skopje, N. Macedonia.

The formulations consisted of a total of 5 g of solid components, comprising PA, Eudragit® EPO, and copovidone, dissolved in 50 mL of 70% (v/v) ethanol. The compositions were systematically varied with respect to the mass ratio of PA and Eudragit® EPO, while the proportion of copovidone was maintained constant at 15% in all three formulations. Specifically, the PA content ranged from 45% to 60%, with a corresponding decrease in the Eudragit® EPO fraction from 40% to 25%, enabling evaluation of the influence of polymer-to-drug ratio on the properties of the resulting microparticles. Initially, an accurately weighed quantity of Eudragit® EPO was dissolved in 70% (v/v) ethanol under magnetic stirring at a constant speed of 300 rpm. Upon complete dissolution of the polymer, copovidone was added and allowed to dissolve fully, resulting in a clear and homogeneous solution. Subsequently, the accurately weighed amount of PA was gradually incorporated into the system under continuous stirring until a uniform

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dispersion/solution was obtained, suitable for subsequent spray-drying processing. Spray-drying was performed using a BUCHI Mini Spray Dryer B-290 (Swiss) under the following conditions: inlet temp. 105 °C, outlet temp. ~70 °C, feed rate 5 mL/min. and 100% aspiration.

Spray-dried microparticles were characterized in terms of particle size (Mastersizer 2000, Malvern Instruments, UK), moisture content (Karl Fischer titration (Ph. Eur. 2.5.12) using a Mettler Toledo EVA V3), FTIR spectroscopy (Agilent Cary 630, ATR mode) and PA content (UV–Vis spectrophotometry (Agilent Cary 60) at 243 nm). Taste-masking efficiency was evaluated by measuring drug release in simulated saliva pH 6.75. Microparticles (~50 mg) were dispersed in 5 mL of medium, stirred for 30 s, filtered (0.45 µm) and PA concentration was determined. Taste masking was expressed as % drug released.

Results and discussion

The results indicate that the drug-to-polymer ratio plays a key role in determining both the technological performance and taste-masking efficiency of the spray-dried PA microparticles. The production yield ranged from ~ 28-49%, with lower values observed for formulation with higher polymer content (P1, 45%), likely due to increased adhesion of particles within the spray-drying system (Vehring, 2008). Organoleptic evaluation showed that P1 provided the most effective taste masking, followed by P2, whereas P3 exhibited noticeable bitterness and was excluded from further investigation. The reduced performance of P3 can be attributed to its lower Eudragit® EPO content (25%), which was insufficient to adequately suppress PA release in the oral cavity (Evonik, 2020).

Particle size analysis revealed D50 of approximately 204 µm (P1) and 188 µm (P2), with slightly larger particles observed at higher polymer content, consistent with spray-drying behavior (Vehring, 2008). The residual moisture content was around 2% for both formulations, which is within acceptable limits and favorable for stability and flow properties.

FTIR analysis confirmed the absence of chemical interactions between PA and excipients, indicating physical incorporation of the drug into the polymer matrix, most likely as a coprecipitate system (Huang and Dai, 2014).

Taste-masking efficiency, evaluated in simulated saliva (pH 6.75), showed drug release values of approximately 19.5% for P1 and 28.3% for P2 after 30 seconds, confirming effective masking within the commonly accepted threshold (<20–30%) (Walsh et al., 2014). In contrast, rapid drug release in acidic medium (0.1 M HCl) confirmed prompt dissolution under gastric conditions, in line with the pH-dependent solubility of Eudragit® EPO (Bodmeier, 1997).

Conclusion

The results demonstrate that the drug-to-polymer ratio is a key factor for effective taste masking of PA, and that spray-drying is a suitable and scalable approach for the development of taste-masked PA microparticles.

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