Evaluating poly(vinyl acetate) as taste masking agent for paracetamol formulated in chewable tablets

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INTRODUCTION

Orally disintegrating tablets (ODTs) have become a popular dosage form over the last years. In order to allow instant and fast disintegration, various formulation aspects need to be reflected (e.g. binder, disintegrant) [1, 2]. Nevertheless, total tablet mass as a result of an active pharmaceutical ingredient's (API) dose and potentially applied taste masking (e.g. coating) can lead to difficulties while obtaining the required tablet features. A single dose of paracetamol for instance can be as high as 500 mg. Hence, formulated paracetamol easily exceeds the U.S. Food and Drug Administration's recommendation for the maximum mass of an ODT [3].

In regard to their administration convenience, chewable tablets are comparable to ODTs and more suitable for high dose APIs, especially if they call for superior taste masking. The aim of this work was the evaluation of poly(vinyl acetate) as taste masking polymer for paracetamol and its subsequent formulation as a chewable tablet.

MATERIALS AND METHODS

Paracetamol (acetaminophene, APAP) fine powder (Fagron) was coated with an aqueous poly(vinyl acetate) dispersion (Kollicoat® SR 30 D, BASF) without plasticiser to apply the required taste masking features. In order to guarantee good flow characteristics of the fine powdery material, 2% fumed silica (Aerosil® 200, Evonik) was homogeneously incorporated into the bulk APAP. The coating process was conducted in a GPCG 3.1 fluid bed coater (Glatt) assembled with top-spray set-up and employing standard coating parameters (Table 1).

The coated API was tested in a standard USP Dissolution Apparatus 2 (ERWEKA), equipped with continuous on-line UV measuring (Agilent 8453), wave length: 243 nm. Hydrochloric acid (0.08 N) was employed as dissolution media (700 ml ±1%, 37°C ±0.5 K, n=3).

In order to obtain chewable tablets, the following excipients were added to the coated APAP: dextrose (C*PharmDex™, Cargill), sucralose (New Trend Group), super fine cross-linked poly(vinyl pyrrolidone) (Kollidon® CL-SF), milled menthol (BASF) and magnesium stearate (Bärlocher) (Table 2).

After mixing the components in a Turbula® T2C blender (Willy A. Bachofen) the compression was done using a lab-scale rotary press XL 100 (Korsch) equipped with round shaped, flat faced, faceted punches with a diameter of 10.0 mm. Compression forces of 6 to 17.5 kN were applied, aiming for a tablet mass of about 400 mg, and a crushing force of 50 N. The tablets were characterised (n=20) using a multi-tester (HT100, Sotax).

Table 1. Glatt GPCG 3.1 processing parameters and settings.

Parameter	Setting
Product bowl volume	5 l
Batch size (uncoated)	870 g
Nozzle orifice / position	1.0 mm / 1
Spray rate	20 g/min
Atomisation air pressure	2.5 bar
Inlet air temperature	60°C
Inlet air quantity	70–100 m^3/h
Product temperature	30–40°C

Table 2. Quantitative formulation of the chewable tablets.

Excipient	Quantity
APAP (coated)	42.1%
Dextrose	34.8%
Kollidon® CL-SF	20.0%
Sucralose	2.4%
Menthol	0.2%
Magnesium stearate	0.5%

RESULTS AND DISCUSSION

A fine powder grade of APAP was selected for this investigation (Figure 1) to ensure a smooth and pleasant mouth sensation of the final tablet after disintegration in the oral cavity. In order to allow a proper coating process (good flowability and fluidisation of APAP) some fumed silica needed to be added.

In organoleptic testing, it was found that a coating level of some 20% needed to be applied to gain a convenient taste. A combination of this product with suitable sweeteners and flavours ought to allow a compliant formulation. When exceeding a coating level of about 50%, the whole surface area was covered with poly(vinyl acetate) (Figure 2) and the bitter taste of APAP was fully masked.

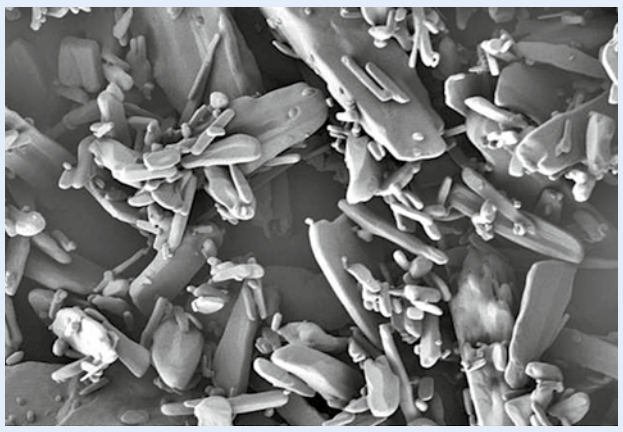

Figure 1. Scanning electron microscopy (SEM) image of uncoated APAP.

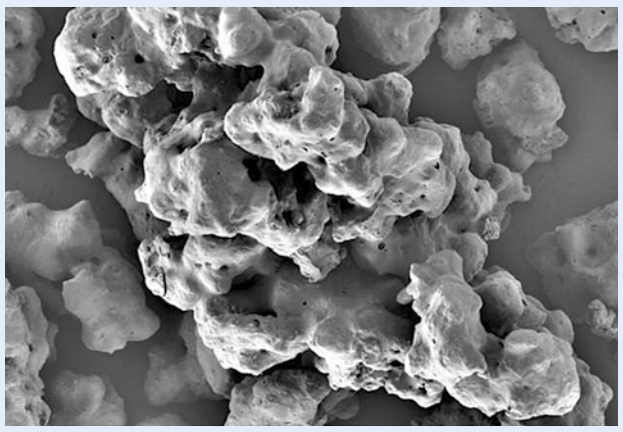

Figure 2. Scanning electron microscopy (SEM) image of coated APAP (coating level 52.5%).

The coating process led to a distinct increase in the APAP's particle size whereas no additional increase of particle size was found as soon as a coating level of 50% was exceeded (Figure 3). Interestingly, the mouth sensation of these samples was still pleasant, even though some particle were larger than 300–400 µm. This was most likely due to saliva acting as plasticiser and transforming the particle into a weak and gum-like mass.

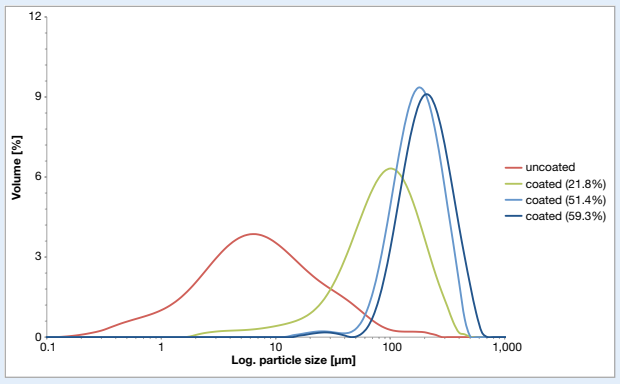

Figure 3. Particle size distribution (laser diffraction) of APAP coated with different amounts of poly(vinyl acetate) to obtain taste masking (coating level indicated).

Even though poly(vinyl acetate) is insoluble in water and is intended to be used for sustained release formulations, the large surface area of the aggregates still allows a fast liberation of APAP (Figure 4). It just needs to be considered that the coated material tends to agglomeration in the dissolution vessel hereby delaying drug release (blue curve, Figure 4). Hence, for dissolution testing the samples should be mixed with some additional fumed silica or talc to avoid wrong indications (violet curve, Figure 4).

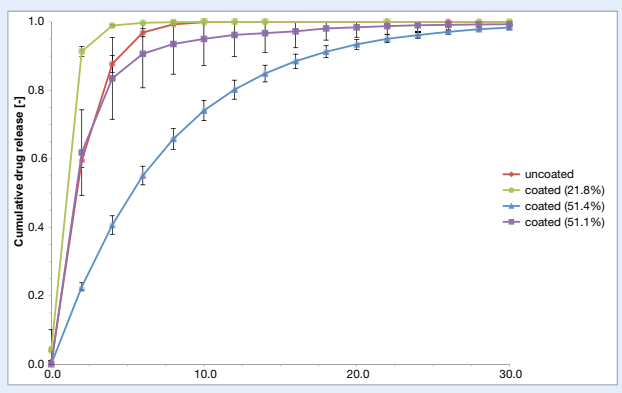

Figure 4. Dissolution profiles of uncoated and coated APAP.

The flow characteristic as well as the compressibility of the described tabletting formulation were excellent. The resulting tablets (crushing force 55 N) were convenient to chew. No bitter taste could be detected. Due to chewing, the tablets disintegrated rapidly and there was no unpleasant or sandy texture on the tongue worth noting.

CONCLUSION

Aqueous poly(vinyl acetate) dispersion can be employed to obtain taste masking of APAP. The coating level required ranges between 20–50%, depending on the final tabletting formulation. Albeit the polymer is insoluble in water, APAP gets quickly liberated due to the large surface area of the coated material. Considering the application (orally disintegrating dosage form), the coated aggregates were comparatively large in particle size. However, the chewing gum-like texture of poly(vinyl acetate) in a wetted state still provided a superior and non-sandy mouth sensation.

REFERENCES

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