INTRODUCTION
Polyvinyl acetate is a water insoluble polymer, which is frequently used as an excipient, for obtaining sustained release functionality of an oral pharmaceutical dosage form. The product is available as aqueous dispersion, and as a powder allowing its use in a huge variety of processes such as direct compression, granulation, film-coating or hot melt extrusion (HMES) [1, 2, 3]. In addition, the polymer is known to be used as base component of chewing gums. The aim of this study was the evaluation of Kollicoat® SR, a direct compression process, to gain tablets transferring into a gum when chewed.

MATERIALS AND METHODS
In the present case study, pre-agglomerated Paracetamol [acetaminophen] (Figure 1) was used as model active pharmaceutical ingredient (API). In a first processing step, the API was coated and agglomerated with an aqueous poly(vinyl acetate) dispersion (Kollicoat® SR 30 D). This procedure is known to allow a homogeneous embedding of the API into the chewing gum matrix. This was essential to delay drug liberation, thus providing sufficient taste masking features [4, 5].

The agglomeration process was done in a GPCG 3.1 (Glatt) fluid bed granulator with top-spray configuration and Granu 5 L product container. Kollicoat® SR 30 D (BASF) was sprayed with a solid matter content of 30%. A two-component nozzle with an orifice of 0.8 mm, applying an atomisation air pressure of 2.5 bar was used. The spraying dispersion contained 0.4% riboflavin (BASF) as additional component. The whole process was conducted with an airflow of 70 to 100 m3/h and an inlet air temperature of 60°C, which resulted in a product temperature of 35 to 38°C.

In order to gain a proper fluidisation of the particles and to prevent adhesion of the poorly flowing API powder onto the wall of the fluid bed granulator, 2.0% of fumed silica (Aeroxid® 200, Evonik) was added. The agglomeration process was stopped after gaining an increase in weight of 100%. The agglomerated paracetamol (57.0%) was blended (Turbulox® T2C tumble blander) with 40.0% Kollidon® SR (Karl, Figure 1), even though, some particles (Blind Kraft® 0.9% orange flavour (Symrise), 1.0% sucralose (New Trend Group) and 0.5% magnesium stearate (Bölscher).

Kollicoat® SR is a poly(vinyl acetate)/poly(vinyl pyrrolidone) based pharmaceutical excipient. It is a powdery and free flowing material that can be used in formulations processed via direct compression. Compression was performed with a Korsch XP 1 excenter single punch press using round shaped, flat faced, bevelled edge punches with a diameter of 25.0 mm. A compression force of 20 kN was applied at a tabletting speed of 10 tablets per minute. The tablets were compressed aiming for a tablet mass of 1220 mg, representing a paracetamol dose of 325 mg.

RESULTS AND DISCUSSION
To mask the poor taste of paracetamol and to allow its proper incorporation into the PVC chewing gum matrix, the API was initially coated with PVC dispersion. Adding 2.0% of fumed silica to the API resulted in a proper fluidisation of the powdery material during fluid bed coating/agglomeration and allowed an easy processing (Figure 1). Organoleptic testing indicated that a weight gain of about 25% was required to gain a sufficient taste masking property. However, to ensure an ideal incorporation of the API into the gum matrix and to slow down drug liberation, a final weight gain of about 100% was applied. As a result, the complete surface area of paracetamol was covered with polymer (Figure 2).

The coating process led to a distinct increase of the products particle size (Figure 3). Even though, some particles were larger than 300 – 400 µm, mouth sensation of these agglomerates was still very pleasant. This was most likely due to saliva acting as plasticiser and transforming the particle into a weak and supple mass. Because of this texture, the coated API can perfectly be embedded into a matrix of Kollidon® SR, which is based on the same polymers as Kollicoat® SR 30 D. The mixture could be tabletted easily, resulting in tablets of high tensile strength even at low compression pressures.

In order to allow chewing (crushing), tablets with a low band height of merely 3 mm. Furthermore, it was required to use punches with a diameter of 25 mm to enable a sufficient tablet mass carrying the required dose of 325 mg of Paracetamol (Figure 4).

Because of the low thickness, the tablet's appearance was very similar to a regular chewing gum and it was quite easy grind/crush the tablets with the teeth. After chewing for 2 to 5 seconds, the up-take of saliva allowed the crushed tablet fragments to form a supple, gum-like texture. Due to the contained flavour and sweetener, the initial taste of the chewing gum was very pleasant. However, Paracetamol got liberated over a long period, leading to a slightly bitter taste after some time. In order to improve the formulation, some sweetener and flavour should be incorporated in the sustained release agglomerates, produced in the fluid bed process. Alternatively, sustained release flavours could be added.

CONCLUSION
The aqueous poly(vinyl acetate) dispersion Kollicoat® SR 30 D can be employed to obtain taste masking of Paracetamol. Albeit the polymer is insoluble in water, paracetamol gets quickly liberated. The supple consistency of poly(vinyl acetate) in a wattle state provided a superior and non-sandy mouth sensation.

Because of this texture, the coated API can perfectly be embedded into a matrix of Kollidon® SR, which is based on the same polymers as Kollicoat® SR 30 D. The mixture could be tabletted easily, resulting in tablets of high tensile strength even at low compression pressures. Thus, height of the tablets needed to be low to allow the crushing of the tablet with the teeth. While taking up saliva, the tablet fragments instantly formed a supple, gum-like texture when chewed.

REFERENCES