AN INVESTIGATION INTO TASTE MASKING OF A MICRONIZED PARACETAMOL USING AQUACOAT® ECD APPLIED VIA DIFFERENT GRANULATION PROCESSES

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INTRODUCTION AND PURPOSE

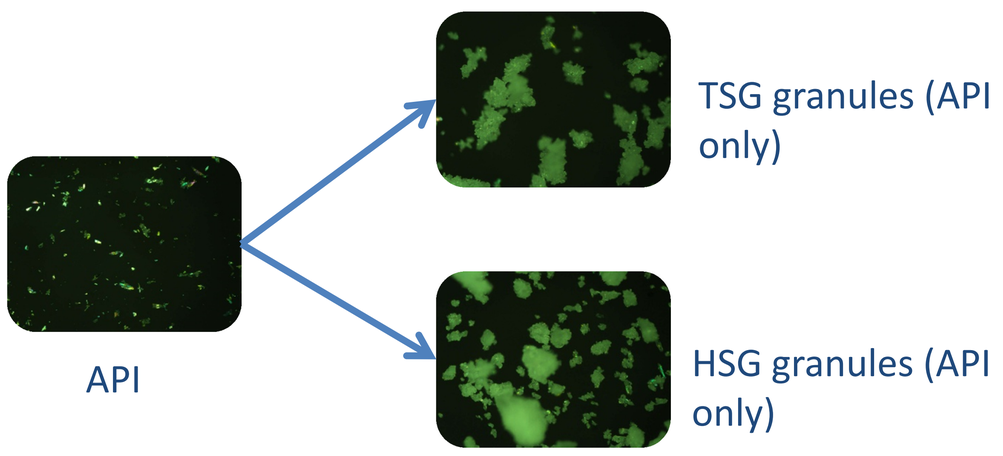
Taste masking is a very important step in the development of paediatric medications such as oral suspensions and tablets for products with APIs that are bitter or unpalatable. In this study, taste masking of a bitter, micronized API model (Paracetamol) was attempted using two different granulation methods. The influence of the type of granulation process and formulation on the properties of subsequent granules and taste masking effect was evaluated.

MATERIALS AND METHODS

- The aqueous ethylcellulose dispersion Aquacoat® ECD was used as the taste masking agent. Aquacoat® ECD was plasticized with Triethylcitrate (24%, based on ethylcellulose content).
- A micronized form of Paracetamol (d50 of 10 µm) was used as a model simulating a bitter, micronized API.
- The plasticized Aquacoat ECD was applied to the API via top spray granulation (TSG) in a fluid bed or via high shear granulation (HSG).
- API was granulated alone or with a pre-mix of MCC (Avicel® PH101) and lactose, since these are common excipients required to improve the granulation process and final granule properties.
- The particle size of the API and of the final granules was determined using sieve analysis and laser diffraction.
- Taste of the granules was assessed via a taste panel consisting of 4 adult males.
- The resultant granules were compacted into tablets using croscarmellose sodium (Ac-Di-Sol®) as a super disintegrant, mannitol as a filler/binder, and sodium stearyl fumarate (Alubra®) as a lubricant. Drug dissolution was measured in 0.1M HCl for 1h.

RESULTS AND DISCUSSION

- Robust granules could be produced using either granulation process, without the need for an additional wet binder. Photomicrographs of the API and granules are displayed below (5x magnification).



- Results are summarized on the following Table. HSG has better masked the taste when compared to TSG, especially when granulating the API only. If granulating only the API with TSG, a higher weight gain may help to further mask the taste.
- Granulation using a pre-mix showed better taste masking properties than granulation with API only. Furthermore, when a pre-mix was used, the type of process or weight gain did not dramatically change the taste rating.
- The size of the granules did not significantly influence the taste ratings. Granules of sizes varying from a smaller (~260 µm) to a much coarser (~525 µm) range showed similar and very acceptable taste ratings.
- No retardation of drug release was seen from any of the granulated samples, with 100% of the drug being released within 10 min. This was likely due to the micronized nature of the API, and the possibility that the EC worked as a matrix forming agent rather than as a sustained release coating of the API.

Type of process used	API only or Pre-mix	Weight gain after granulation	Particle size d50, by sieve analysis (µm)	Taste rating (0-5, 0 being the most bitter)
HSG	API only	11%	625	3
HSG	Pre-mix	17%	525	4
TSG	API only	26%	370	2
TSG	API only	40%	430	3
TSG	Pre-mix	24%	260	4
TSG	Pre-mix	39%	320	4

CONCLUSIONS

In conclusion, taste masking can be achieved via granulation of a micronized API, by using Aquacoat® ECD as the granulating liquid in fluid bed or high shear granulation processes. Granulation with high shear showed better taste masking potential with a lower weight gain requirement than granulation in a fluid bed. Furthermore, a pre-mix of the API with microcrystalline cellulose and lactose before granulation could further improve the taste of the final granules when compared to granulating the pure API. Both approaches provide efficient taste masking whilst maintaining immediate release profile of the drug.