Taste masking of Dexketoprofen trometamol granules with glyceryl distearate and High Shear Coating

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INTRODUCTION:

Orally Dispersible Granules (ODG)
- Easier administration and higher speed rate [1] (compared to tablet)
- Commonly used for anti-inflammatories drug

Dexketoprofen trometamol (DXKT)
- NSAID drug.
- It is the active S (+) enantiomer of ketoprofen
- Is characterized by a bitter and "burning" taste
- Not easy to perform an ODG formulation

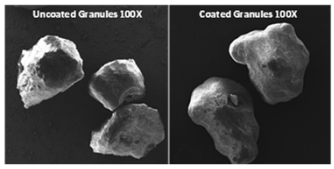
High Shear Coating (HSC)
- Innovative technique: employing interparticular frictional heating for melting the coating agent and no need of solvents.
- Optimization of the process reduced the amount of DXKT released in the mouth, maintaining unmodified the gastrointestinal one

High shear mixer

AIM OF THE WORK:

Taste masking of the active principle

Use of an innovative technique → **Improve PALATABILITY of the drug**



OPERATING PROCEDURE:

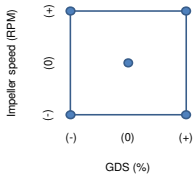
1) Preliminary evaluation: Literature data show the importance of size of the starting product [2]. A preliminary evaluation was made on different particle size fractions of DXKT and Granules with size 180-850 µm (M) were selected.
DSC and X-ray diffractometry analysis were performed on the granules, to confirm that granulation did not affect the solid-state characteristics of DXKT.

2) The work focused on the study of HSC process.
Desing of experiment (DoE) were applied, in order to identify and optimize the most significant process parameters. A Full Factorial Design, (2 factors at 2 levels), was performed. The M granules fraction was used.

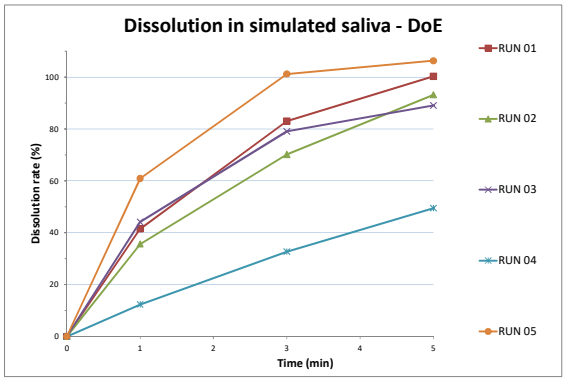
The responses evaluated are:
- time required to reach the temperature for partial melting of glyceryl distearate GDS (42°)
- dissolution in simulated saliva in 5 minutes (to evaluate the efficacy of coating)

Find out:
-Significant difference between high and low impeller speed
-A minimun % of GDS for a good coating is 20%
- Run 04 showed the best profile

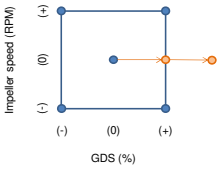
Variables	Level
Impeller speed	(+) 600 rpm (-) 300 rpm
% GDS	(+) 20 % (-) 10 %



RUN	Impeller (RPM)	Coating agent (%)
01	300	10
02	450	15
03	600	20
04	300	20
05	600	10

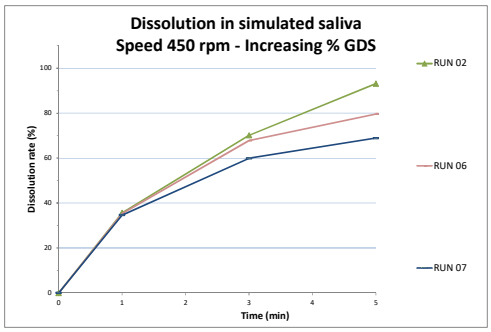


3) %GDS verification: The degree of coating achievable at 450rpm impeller speed were investigated on the edge and outside the DoE space. The M granules fraction were used and GDS % was increased up to 25% .



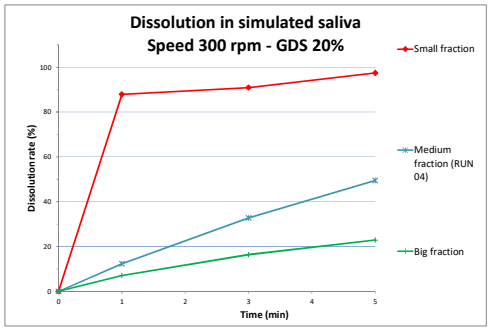
RUN	Impeller (RPM)	Coating agent (%)
06	450	20
07	450	25

No significant differences in dissolution rate of DXKT increasing % GDS.



4) DXKT fraction verification: The effect of particle size fraction on coating capacity was investigated on DXKT granulate fractions: > 850 µm (B) and < by 180 µm (S).
Speed was fixed at 300 rpm and GDS% at 20.

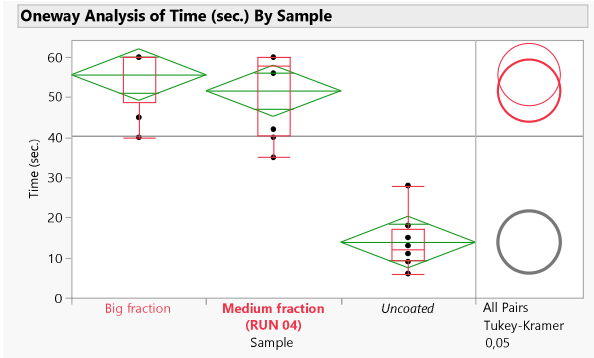
S fraction has too large a surface area to be adequately coated. With M and B fractions it's possible to obtain a good coating.



5) Taste Panel Test: was performed, to evaluate the effectiveness of the coating.
Parameter evaluated:
-time of onset of "burning effect"

Samples	Average time of onset of "burning effect" (sec)
Big fraction	55,6
Medium fraction (Run 04)	51,6
Uncoated	13,9

The difference between coated and uncoated granules is evident. Between the two covered granules, however, no significant difference appears.



CONCLUSION:

HSC technique performed at low impeller speed and with 20% coating excipient, is able to ensure effective taste masking, while maintaining the immediate gastrointestinal release profile.

References:
[1] Haack, Detlev, and Martin Koberle. "From Bitter to Sweet: Developing a User-friendly Painkiller: Hot-melt Coating Was Used to Develop Taste-masked Orally Disintegrating Granules of Acetaminophen and Caffeine." *Pharmaceutical Technology Europe* 28.12 (2016)
[2]Gattefossè, "High shear coating with Precirol ® ATO 5 for taste masking." pp. 1–4.