1-Minute Nanocrystals: A fast, cost-effective and efficient technique to mill drugs using SpeedMixer®

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INTRODUCTION

Poor aqueous solubility remains one of the major challenges in drug development, affecting 70-90% of pipeline candidates. Nanocrystals (NCs) had emerge as a powerful solution, improving bioavailability by reducing particle size (**Fig. 1**).

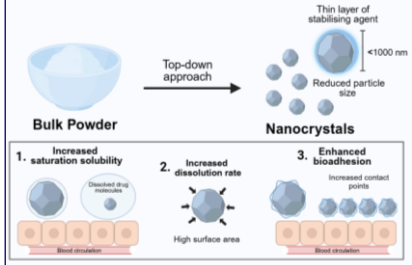

Fig. 1. NCs properties

While media milling is the most widely used approach for NCs production, it can be time-consuming and require significant amounts of active compound, limiting their applicability during early formulation screening. This study evaluates the feasibility of using dual asymmetric centrifugation (DAC) as a fast and efficient technique for NC formulation screening.

ACKNOWLEDGEDMENTS

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METHODS

NCs were produced using DAC with zirconia beads as the milling agent (**Fig. 2**). Ten drugs from the literature were tested for reproducibility, and three were selected to study the effects of process and formulation variables on particle size (PS) and polydispersity index (PDI). NCs were characterised for morphology, crystallinity, and stability. A Plackett-Burman design optimised the process for one drug, and a microhydrodynamic model quantified milling parameters, comparing DAC to conventional media milling.

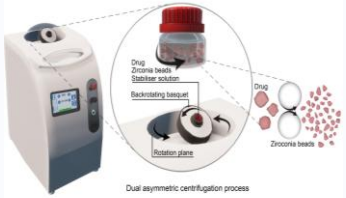

Fig. 2. NCs production process using DAC.

CONCLUSION

DAC is a **reproducible** and **efficient** method, delivering results in just 1-min, significantly reducing processing time, emerging as a game-changing tool for **high-throughput formulation screening** of drugs NCs.

RESULTS

1. Production of drug NCs using DAC

Table 1. PS and PDI obtained after 1 minute milling cycle (triplicates)

Drug	Mean PS (nm)	Mean PDI
ABZ	436 ± 13	0.225
IVM	574 ± 35	0.276
ACV	315 ± 39	0.265
ITZ	548 ± 15	0.231
CUR	272 ± 14	0.256
GCV	228 ± 22	0.211
SIM	504 ± 27	0.240
MTZ	175 ± 9	0.239
AmB	566 ± 30	0.254
MBZ	3787 ± 1426	0.323

2. Influence of different process variables on PS and PDI

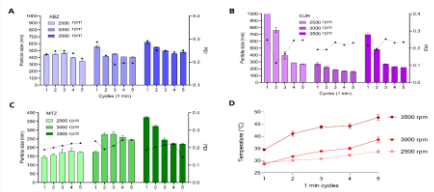

Fig. 3. Milling kinetics of ABZ (A), CUR (B), and MTZ (C) at 2500–3500 rpm. (D) Final temperatures. Bars: PS; dots: PDI.

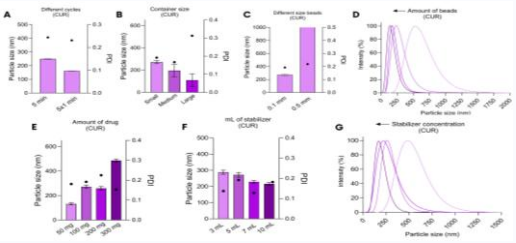

Fig. 4. A-D: Equipment-related variables; E-:G Formulation-related variables. Data shown for CUR. Bars: PS; dots: PDI.

3. NCs characterisation

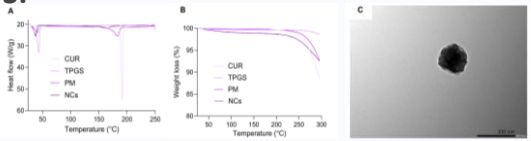

Fig. 5. DSC (A), TGA (B), and TEM (C) of CUR NCs

4. Optimisation of the milling process

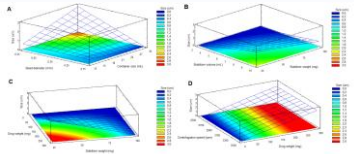

Fig. 6. Estimated response surfaces for PS of CUR NCs, as functions of different experimental factors

Table 2. Multiple response optimisation values

Response	Predicted	Obtained	
PS (nm)	318 ± 1	275 ± 3	Prediction error <15%
PDI	0.25 ± 0.01	0.23	
Temp (°C)	25.5 ± 0.7	26.2	

5. Microhydrodynamic analysis

θ in DAC (0.008–0.202 m^2/s^2) is superior to conventional milling devices (0.011-0.045 m^2/s^2), confirming superior milling efficiency.

θ: Granular temperature

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