

Nanomilling of poorly soluble drugs

About 90% of all newly developed active pharmaceutical ingredients (API) are poorly soluble which often reduces their bioavailability after oral application. One strategy to increase their solubility and thus to enable their therapeutic use is the reduction of API particle sizes down into the nanometer range. Successful nanomilling is an important part of pharmaceutical formulation development.

Finding the most suitable types as well as amounts of polymers and surfactants to efficiently grind the API's is a great challenge. The use of traditional means for such a screening approach like planetary ball mills is time consuming and requires rather large quantities of APIs, both limits the number of API/polymer/surfactant-combinations which can be tested. Furthermore, API particle sizes resulting from planetary ball milling frequently are not predictive to the particle sizes resulted from agitator bead mills used in large scale pharmaceutical drug production.

Nanomilling of poorly soluble APIs by the use of the ZentriMix 380R can overcome the limitations of the current milling procedures*.



ZentriMix 380R

Advantages of the ZentriMix-nanomilling method

- **Fast:** ZentriMix-milling takes place within 90 min.
- **Screening:** Up to 40 samples can be milled at the same time.
- **Very small batches:** Only 10 – 1000mg API is needed, API proportions up to 40%.
- **Safe:** Milling takes place in a tightly closed disposable 2 ml PP-vial. Sterile vials can be used if necessary. No cleaning of the milling chamber necessary.
- **Simple upscale:** The resulting particle sizes are identical to those resulted from agitator bead mills used in large scale pharmaceutical productions.
- **Gentle:** Despite very effective, the special milling process has no influence on the crystal structures of APIs.
- **Sample protection:** The cooled ZentriMix 380 R provides protection for thermosensitive APIs.

* Hagedorn, M., Bögershausen, A., Rischer, M., Schubert, R., Massing, U., 2017. Dual centrifugation - A new technique for nanomilling of poorly soluble drugs and formulation screening by an DoE-approach. *Int J Pharm.* 2017 Sep 15;530(1-2):79-88. doi: 10.1016/j.ijpharm.2017.07.047
Hagedorn M, Liebich L, Bögershausen A, Massing U, Hoffmann S, Mende S, Rischer M. Rapid development of API nano-formulations from screening to production combining dual centrifugation and wet agitator bead milling. *Int J Pharm.* 2019 Jun 30;565:187-198. doi: 10.1016/j.ijpharm.2019.04.082. Epub 2019 May 4. PMID: 31063837

ZentriMix-Nanomilling

1. Fill 2 ml vials* with -

- 0.1 - 1 g API/polymer/surfactant-suspension (containing 5 - 40% API)
- 1000 mg of milling beads (diameter 0.1-0.2 mm)**

2. ZentriMix-nanomilling:

- Rotation speed: 1,500 rpm
- Temperature: 0 °C
- Time: 90 minutes
- Samples: max. 40

3. Characterizing of the resulting nanoparticles: e.g. by LD, PCS, XRPD and / or

4. Use in biological test systems*** and / or

5. Production of pharmaceutical dosage forms like tablets, granulates etc.

*sterile Screw Cap Micro Tube, 2 ml, PP from Sarstedt, Germany, ordering no. 72.693.005 suitable for our adapter 3236

** Ceramic Beads made of Zirconium Oxide, Yttrium stabilised (Sigmund Lindner GmbH, Warmensteinach, Germany)

*** ZentriMix-milling can also easily be performed under sterile conditions using sterile starting materials and sterile ZentriMix-vials.



ZentriMix-Rotor carrying vial adapters for 2 ml Screw Cap Micro Tube. Each rotation unit carries two adapters which lie on each other. Only the adapters on top are visible.

Ordering informations

	Order no.
ZentriMix 380 R, Dual Centrifuge, refrigerated, without rotor, 200-240 V 1~, 50-60 Hz	3200
ZentriMix 380 R, Dual Centrifuge, refrigerated, without rotor, 110-127 V 1~, 60 Hz	3200-01
S-rotor, 2-place, 2500 RPM, without Adapter	3205
Adapter(Set), 20-place, for conical 2 ml Sarstedt PP micro tubes with screw cap (Cat.No. 72.693.005), for rotor 3206,3205 Set of 2 pcs.	3236
Removal aid for adapter 3236	3210

contact:

Andreas Hettich GmbH
Föhrenstr. 12
78532 Tuttlingen
Germany