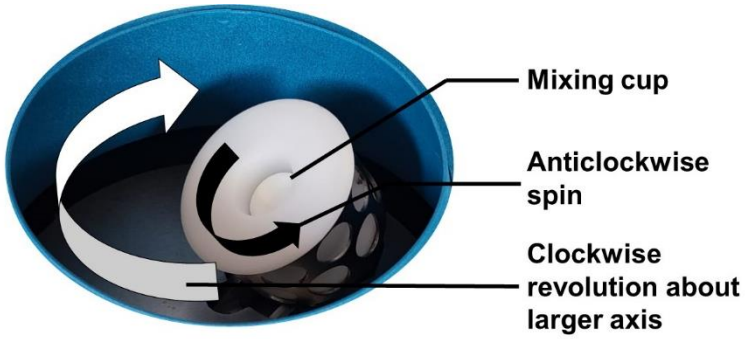
Exploring media-less mechanochemistry through SpeedMixing synthesis and discovery of pharmaceutical cocrystals

Yong Teoh, Ghada Ayoub, Igor Huskić, Hatem M. Titi, Christopher W. Nickels[c], Brad Herrmann[b], Tomislav Friščić[a]

a. Department of Chemistry, McGill University; b. FlackTek Speedmixer; c. Form-Tech Scientific.

Mechanochemistry is now a method of choice for the efficient discovery and synthesis of pharmaceutical solid forms, such as cocrystals. The solventless nature of mechanochemistry not only makes the manufacturing of cocrystals greener, but also bypasses solubility concerns, allowing highly soluble cocrystals to be discovered and synthesized from poorly soluble components.[1] This has attracted the attention of the pharmaceutical industry, which utilises cocrystals to alter the physicochemical performance of active pharmaceutical ingredients (APIs) in the solid state without altering their chemical structures (*e.g.* Entresto, Lexapro).[2] However, the contamination due to abrasion and/or chipping of milling media used in conventional mechanochemical techniques, such as grinding or milling, is a persistent cause of concern in pharmaceutical applications.

To address these challenges of mechanosynthesis in pharmaceutical materials science, we have recently explored the use of a FlackTek SpeedMixer, which employs SpeedMixing - a process based on rapid spinning to mix reactive components together. Here we disclose how the addition and control of minute quantities of liquid additives enables not only the rapid, scalable and polymorph-selective synthesis of various known pharmaceutical cocrystals, but also the discovery of previously overlooked solid API forms.



References: [1] Chadha *et al*. *Cryst. Growth Des.* **2017**, 17, 2386−240; [2] Tan, D.; Loots, L.; Friščić, T., *Chem. Commun*. **2016,** *52*, 7760-7781.