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Exploring mechanochemistry in drug development: From laboratory to industrial applications.

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Introduction

The pharmaceutical industry is under growing pressure to innovate in ways that are not only effective but also environmentally sustainable. Mechanochemistry offers a powerful platform for achieving both goals by enabling chemical transformations using mechanical forces—such as grinding, shearing, or milling—without or with minimal use of solvents. What began as an academic curiosity has now evolved into a viable strategy for drug synthesis and formulation, with clear advantages in sustainability, efficiency, and scalability [1].

Mechanochemistry differs fundamentally from traditional chemistry by replacing thermal or solution-based activation with mechanical energy. Techniques such as ball milling, twin-screw extrusion, and resonant acoustic mixing allow for the initiation of chemical reactions in the solid state. This offers a cleaner, faster, and often more selective pathway for molecular transformations, reducing waste and bypassing complex purification processes [2].

One of the key challenges in pharmaceutical development is the synthesis of drug molecules that are poorly soluble or chemically unstable. Mechanochemistry enables the formation of pharmaceutical cocrystals and polymorphs, which can significantly enhance solubility, stability, and bioavailability. Moreover, it allows for solvent-free reactions, aligning well with green chemistry principles and reducing the environmental footprint of drug manufacturing [3].

Cocrystal formation via mechanochemistry has emerged as a valuable tool in optimizing the physicochemical properties of active pharmaceutical ingredients (APIs). By milling an API with a suitable co-former, new crystalline phases with improved solubility or mechanical properties can be obtained. Additionally, mechanochemical approaches are effective in discovering and isolating different polymorphs—distinct crystalline forms of the same drug—critical for regulatory approval and patent protection [4].

Solvents account for a significant portion of waste in pharmaceutical synthesis. Mechanochemical processes eliminate or drastically reduce solvent use, making them inherently cleaner and more sustainable. This is especially advantageous in synthesizing sensitive compounds that degrade in solution. Mechanochemistry also reduces energy consumption by operating at ambient temperatures and pressures, further enhancing its green credentials [5].

Conclusion

Mechanochemistry is revolutionizing drug development by offering cleaner, faster, and more efficient alternatives to traditional synthesis and formulation methods. From enhancing drug solubility through cocrystals to enabling scalable solvent-free synthesis, mechanochemistry aligns with the pharmaceutical industry's goals of innovation and sustainability. As technological and regulatory hurdles are addressed, mechanochemistry is poised to transition from

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niche laboratory technique to mainstream industrial tool in the near future.

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