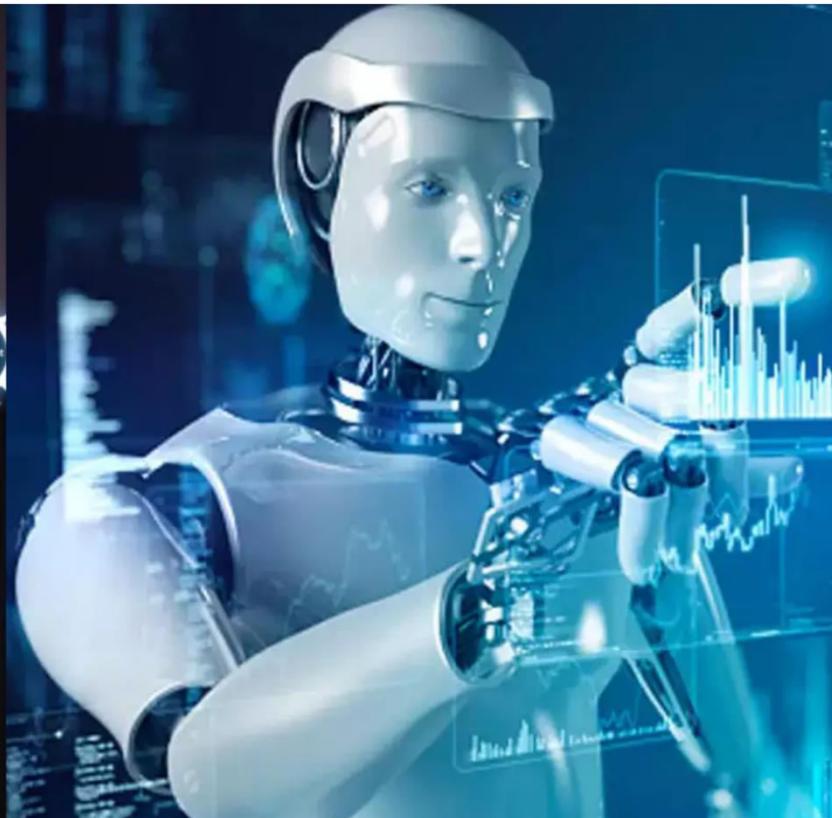




International Journal of Innovative Research in Science Engineering and Technology (IJIRSET)

(A Monthly, Peer Reviewed, Refereed, Scholarly Indexed, Open Access Journal)



Impact Factor: 8.699

Volume 15, Special Issue 1, January 2026

Synthesis of Drug Molecules by Grinding Method: An Environmentally Friendly Green Chemistry Approach

Pratiksha Somarde, Soji Mathew, Anshika Gupta, Poonam Khandagale, Tejas Yadav

U.G. Student, Department of Pharmaceutical Chemistry, Indala Institute of Pharmacy, Kalyan, Maharashtra, India

U.G. Student, Department of Pharmaceutical Chemistry, Indala Institute of Pharmacy, Kalyan, Maharashtra, India

U.G. Student, Department of Pharmaceutical Chemistry, Indala Institute of Pharmacy, Kalyan, Maharashtra, India

U.G. Student, Department of Pharmaceutical Chemistry, Indala Institute of Pharmacy, Kalyan, Maharashtra, India

U.G. Student, Department of Pharmaceutical Chemistry, Indala Institute of Pharmacy, Kalyan, Maharashtra, India

ABSTRACT: Green chemistry focuses on the design of chemical processes and products that reduce or eliminate the use and generation of hazardous substances. Conventional pharmaceutical synthesis often relies on toxic organic solvents, high temperatures, and long reaction times, leading to environmental pollution and safety concerns. The grinding method, also referred to as solvent-free or mechanochemical synthesis, represents an environmentally friendly strategy for the synthesis of drug molecules by avoiding hazardous solvents and significantly reducing reaction time and energy consumption. In the present study, a drug molecule was synthesized using a simple mortar and pestle grinding technique under mild and natural conditions. The progress of the reaction was monitored using thin-layer chromatography (TLC), while purification and characterization of the synthesized compound were carried out using standard analytical techniques such as UV spectroscopy, IR spectroscopy, and melting point determination. The results revealed that the yield and purity obtained through the grinding method were comparable to or even higher than those achieved using conventional solvent-based techniques. By promoting atom economy, reducing waste generation, and improving overall sustainability, this approach provides a greener alternative for pharmaceutical synthesis. Therefore, the grinding method can be considered an effective, economical, and environmentally benign approach that strongly adheres to the principles of green chemistry.

KEYWORDS: Green chemistry; Solvent-free (grinding) method; Mechanochemistry; Sustainable synthesis; Reaction monitoring; Spectral characterization

I. INTRODUCTION

The pharmaceutical industry is one of the most important sectors contributing to global healthcare; however, it is also a major consumer of chemicals, solvents, and energy. Traditional synthetic routes employed for the preparation of drug molecules often involve the use of hazardous organic solvents, prolonged heating, and multi-step reaction pathways. These conventional methods not only increase the overall cost of drug production but also generate a significant amount of chemical waste, posing serious threats to human health and the environment.

In recent years, increasing awareness of environmental protection, sustainability, and regulatory pressure has driven the pharmaceutical industry toward the adoption of greener synthetic methodologies. Green chemistry provides a scientific framework for the design of chemical processes that minimize environmental impact while maintaining high efficiency and product quality. Within this framework, mechanochemistry has emerged as a powerful and innovative approach.

The grinding method, a simple form of mechanochemical synthesis, involves the application of mechanical energy through

manual or mechanical grinding to promote chemical reactions. This method eliminates or significantly reduces the need for organic solvents and external heating, making it particularly attractive for sustainable pharmaceutical synthesis.

II. GREEN CHEMISTRY: CONCEPT AND PRINCIPLES

Green chemistry is defined as the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. The concept was formalized through the twelve principles of green chemistry, which serve as guidelines for developing environmentally benign chemical processes.

Key principles relevant to grinding-based synthesis include waste prevention, atom economy, safer solvents and auxiliaries, energy efficiency, and inherently safer chemistry. The grinding method satisfies these principles by eliminating toxic solvents, reducing the number of synthetic steps, and lowering energy consumption.

In pharmaceutical chemistry, the implementation of green chemistry is particularly important due to large-scale manufacturing and strict environmental regulations. Grinding-based synthesis provides an excellent platform for translating green chemistry principles into practical pharmaceutical applications.

III. MECHANOCHEMISTRY IN PHARMACEUTICAL SCIENCE

Mechanochemistry refers to chemical reactions that are induced by mechanical force rather than thermal or photochemical

energy. In mechanochemical processes, mechanical stress leads to the breaking and formation of chemical bonds, enabling reactions to occur under mild conditions.

In pharmaceutical science, mechanochemistry has gained importance due to its ability to facilitate solvent-free reactions, improve reaction rates, and enhance product selectivity. Mechanochemical techniques such as grinding and ball milling have been successfully applied to the synthesis of active pharmaceutical ingredients, intermediates, and pharmaceutical cocrystals.

The growing interest in mechanochemistry is driven by its compatibility with green chemistry principles and its potential for sustainable drug development.

IV. GRINDING METHOD: PRINCIPLE AND TECHNIQUE

The grinding method is one of the simplest and most widely used mechanochemical techniques. It involves triturating solid reactants together using a mortar and pestle or mechanical grinding equipment. The mechanical energy generated during grinding promotes intimate contact between reactants, facilitating chemical transformations.

Reactions carried out using the grinding method generally occur under ambient temperature and pressure, eliminating the need for external heating or cooling. This not only reduces energy consumption but also simplifies experimental procedures.

The grinding method is particularly suitable for laboratory-scale synthesis, educational experiments, and early-stage pharmaceutical research.

V. SOLVENT-FREE AND LIQUID-ASSISTED GRINDING

Solvent-free grinding involves carrying out reactions without the addition of any solvent. This approach maximizes the environmental benefits of green chemistry by completely eliminating solvent-related hazards.

Liquid-assisted grinding (LAG) uses a very small quantity of solvent to enhance reaction kinetics and improve product formation. The solvent does not act as a reaction medium but facilitates better mixing and molecular interaction.

Both approaches significantly reduce solvent consumption compared to conventional synthesis and are widely used in pharmaceutical mechanochemistry.

VI. EXPERIMENTAL METHODOLOGY IN GRINDING-BASED SYNTHESIS

In a typical grinding-based synthesis, reactants are accurately weighed and transferred to a mortar. The reactants are then ground continuously using a pestle for a specific duration. The mechanical energy generated during grinding initiates and sustains the chemical reaction.

The simplicity of this methodology makes it suitable for small-scale drug synthesis and academic research. The absence of solvents simplifies product isolation and purification, further reducing waste generation.

VII. REACTION MONITORING USING THIN-LAYER CHROMATOGRAPHY

Thin-layer chromatography (TLC) is widely used to monitor the progress of grinding-based reactions. TLC allows rapid detection of reactants, intermediates, and products, providing valuable information about reaction completion.

In solvent-free synthesis, TLC is particularly useful because it requires only a minimal amount of solvent and provides quick results. The use of TLC enhances the efficiency and reliability of grinding-based pharmaceutical synthesis.

VIII. ANALYTICAL CHARACTERIZATION OF SYNTHESIZED DRUG MOLECULES

Characterization of synthesized drug molecules is essential to confirm their identity, purity, and structural features. UV spectroscopy is used to study electronic transitions and conjugated systems present in the molecule.

IR spectroscopy provides information about functional groups and confirms the formation of desired chemical bonds. Melting point determination serves as a simple yet effective method for assessing purity and crystalline nature.

Together, these analytical techniques ensure the reliability and quality of grinding-synthesized drug molecules.

IX. YIELD, PURITY, AND COMPARATIVE EVALUATION

Grinding-based synthesis often results in high yields and purities due to efficient molecular interactions in the solid state. Comparative studies have demonstrated that grinding methods can achieve yields comparable to or higher than conventional solvent-based techniques.

The reduction in side reactions and simplified purification contribute to improved overall efficiency, making the grinding method a valuable green alternative.

X. ADVANTAGES OF GRINDING METHOD

The grinding method offers numerous advantages, including elimination of hazardous solvents, reduced reaction time, lower energy requirements, operational simplicity, cost-effectiveness, and environmental sustainability.

These advantages make the grinding method particularly attractive for green pharmaceutical synthesis and academic research.

XI. LIMITATIONS AND CHALLENGES

Despite its benefits, the grinding method has certain limitations. Not all chemical reactions are suitable for mechanochemical synthesis. Scale-up remains challenging due to equipment limitations and difficulty in controlling reaction parameters.

Addressing these challenges through technological advancements is essential for broader industrial adoption.

XII. PHARMACEUTICAL APPLICATIONS

Grinding-based mechanochemistry is widely applied in the synthesis of drug intermediates, active pharmaceutical ingredients, pharmaceutical cocrystals, and polymorph screening. These applications highlight the versatility of the grinding method in pharmaceutical research.

XIII. FUTURE PERSPECTIVES

Future developments in mechanochemical synthesis are expected to focus on improving scalability, automation, and process control. Integration with catalysis and continuous manufacturing may further enhance sustainability. The growing emphasis on green chemistry will continue to drive interest in grinding-based pharmaceutical synthesis.

XIV. CONCLUSION

The grinding method represents a powerful green chemistry approach for the synthesis of drug molecules. By eliminating hazardous solvents, reducing energy consumption, and minimizing waste generation, it offers a sustainable alternative to conventional pharmaceutical synthesis. Continued research and technological innovation will further expand its applicability and industrial relevance.

REFERENCES

1. Anastas PT, Warner JC. Green Chemistry: Theory and Practice. Oxford University Press.
2. James SL et al. Mechanochemistry: opportunities for new and cleaner synthesis. Chemical Society Reviews.
3. Friščić T et al. Mechanochemistry for synthesis. Angewandte Chemie International Edition.
4. Sheldon RA. Green and sustainable manufacture of pharmaceuticals. Green Chemistry.
5. Baláž P. Mechanochemistry in Nanoscience and Pharmaceuticals. Springer.
6. Haneef, J. & Ali, S. *Medicinal mechanochemistry: Sustainable and efficient route towards synthesis of active pharmaceutical ingredients*, Sustain. Chem. Pharm. **45**, 102044 (2025).
7. Tan, D. et al. *Chem. Commun.* **52**, 7760–7781 (2016) — mechanochemical synthetic protocols and green metrics evaluation.
8. Ying, P., Yu, J. & Su, W. *Liquid-assisted grinding mechanochemistry in the synthesis of pharmaceuticals*, Adv. Synth. Catal. **363**, 1246–1271 (2021).
9. *Sustainable and solvent-free synthesis of molecules of pharmaceutical importance by ball milling*, Chem. Commun. (2025).
10. Solares-Briones, M. et al. *Mechanochemistry: A green approach in the preparation of pharmaceutical cocrystals*, Pharmaceutics **13(6)**, 790 (2021).
11. Jug, M. & Mura, P. A. *Grinding as solvent-free green chemistry approach for cyclodextrin inclusion complex preparation*, Pharmaceutics **10(4)**, 189 (2018).
12. Wahan, S. K. et al. *A facile mechanochemical solvent- and catalyst-free synthesis of functionalized 4-thiazolidinones*, SynOpen **07(04)**, 615–618 (2023).



INTERNATIONAL
STANDARD
SERIAL
NUMBER
INDIA



INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN SCIENCE | ENGINEERING | TECHNOLOGY

 9940 572 462  6381 907 438  ijirset@gmail.com



www.ijirset.com

Scan to save the contact details