Mechanochemistry: A Growing Green Tool with Tremendous Potential

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Grinding equipment

Ball mills are the most commonly used equipment in **grinding mechanochemistry.**[3d]

Figure 1. Planetary ball mill

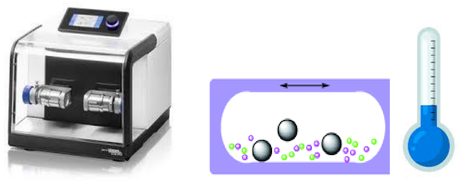

Figure 2. Shaker ball mill

- ✓ Enclosed, solvent-free reaction environment
- ✓ Well-defined operating parameters
- ✓ Balls and reaction jars of different kinds of materials (stainless steel, zirconia, Teflon®)

Mechanochemistry

Mechanochemistry studies the chemical and physicochemical transformations of substances in all states of aggregation produced by the effect of mechanical energy processes (*i.e.,* impact, compression, shearing, stretching, grinding, etc.). It was identified by **IUPAC** as one of **10 world-changing technologies** in 2019. There are **4 sub-branches** depending on the mechanical energy used for the process: **tribochemistry** (transformation induced by friction of surfaces), **macromolecular** (related to biological processes and soft condensed matter), **sonochemistry** (reactions induced by mechanical effects of sound) and **grinding,** which is **the most used method,** and involves reactions induced by grinding of the reactants with or without solvent.[1,3a]

Advantages vs. Disadvantages

- Avoid the use of solvents.
- Complies with most of the Green Chemistry Principles.
- Could produce products impossible to obtain by conventional solution methods.
- Better yields and shorter reaction times compared to solution reactions.
- Compatible with different kinds of reactions.

- Nomenclature and specific language are unclear and without a consensus.
- Limited understanding of mechanistic aspects.
- Limited development of *in situ* measurement devices.
- High cost of equipment.[3]

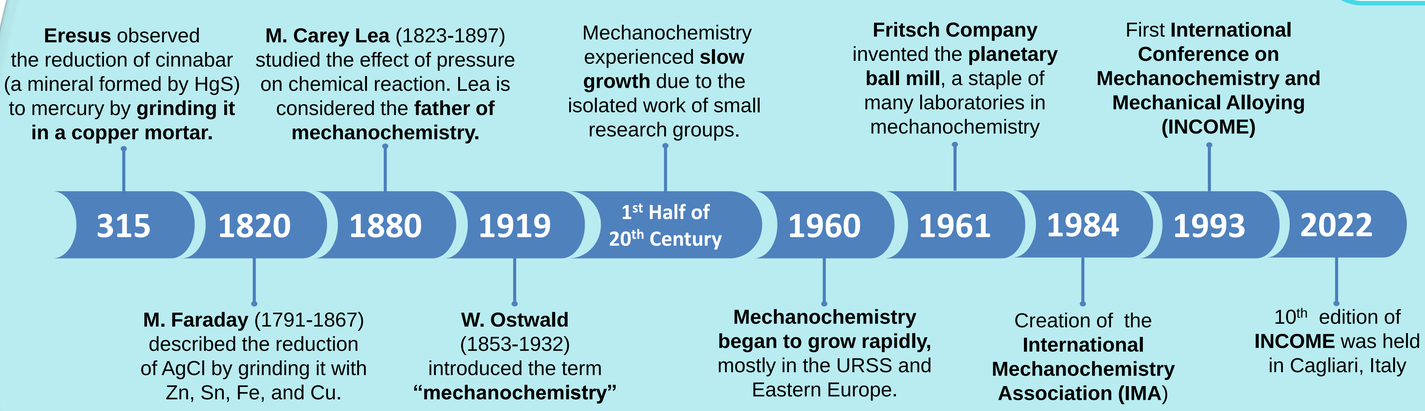

Figure 3. Brief historical summary of mechanochemistry.[2]

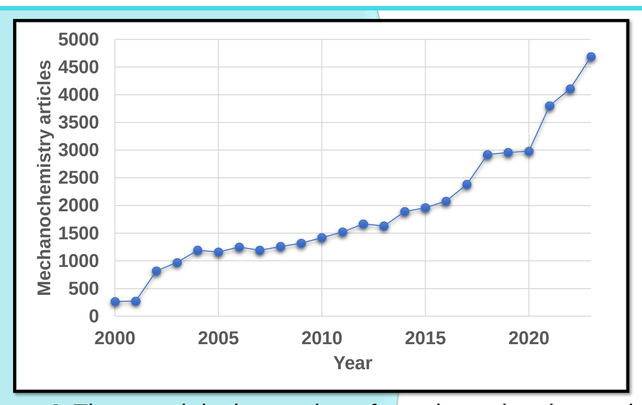

Figure 4. The growth in the number of mechanochemistry articles over the last 23 years.(**Source: Google Scholar**)

Synthesis of eco-friendly polyurethanes

Some **polyurethanes (PUs)** were synthesized by a mechanochemical method using a vibrational ball mill from biomass-derived reactants.

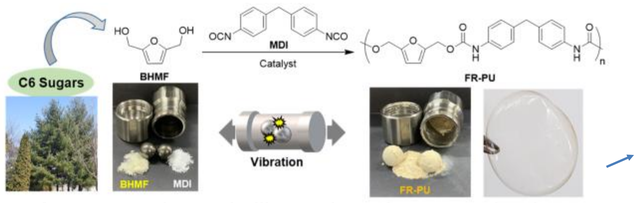

Figure 5. Schematic illustration of PUs synthesis using diols derived from biomass.

- ✓ Solvent-free
- ✓ Efficient
- ✓ Scalable

Parameters like frequency of grinding and time were optimized for the reaction to obtain the maximum conversion to the product, and avoid the degradation of it.[4]

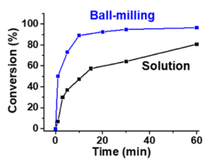

Figure 6. Ball milling and solution method comparison

Waste Prevention · Renewable raw materials · Easily degradable products · Atom Economy · Energetic efficient · Use of catalysts

Grinding operational conditions:

- **Neat grinding (NG):** friction between solids.
- **Liquid assisted grinding (LAG):** a solvent in catalytic amounts is added to the system to improve the process.
- **Ion Liquid assisted grinding (ILAG):** similar to LAG, but with the addition of a salt as an additive with the solvent.
- **Polymer assisted grinding (POLAG):** a polymer is added to enhance the reaction rate.[1]

Medicinal mechanochemistry

The aim of **Medicinal Mechanochemistry** is the study and application of mechanical force in the synthesis of pharmaceutical relevant active compounds. For example, a **very efficient and environmentally friendly** methodology based on **ILAG** for the synthesis of oligopeptides was developed.[5]

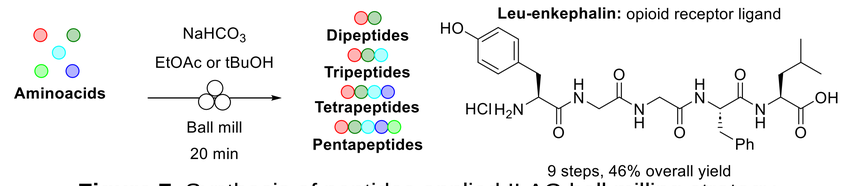

Figure 7. Synthesis of peptides applied ILAG ball milling strategy

- ✓ Catalytic amount of solvent
- ✓ Solvent-free Boc deprotection steps
- ✓ Gram scale
- ✓ Good and excellent yields (74-98%)

This tool could be useful for the synthesis of **therapeutic peptides** and others **APIs.**

Waste Prevention · Less dangerous chemical products · Energetic efficient · Less dangerous chemical synthesis · Safe reaction conditions · Reduce derivates

Conclusions and personal opinion

Mechanochemistry is a **highly potent and environmentally friendly synthetic tool** that undoubtedly merits further study. As shown in this poster, it reduces economic and environmental costs, enhances process efficiency, can be used for waste treatment and as a greener tool for the synthesis of **APIs** (Active Pharmaceutical Ingredients), among many other advantages. In my opinion, mechanochemistry should be seen as a **complement to solution synthesis**, not a replacement, and **it still needs to overcome certain challenges to fully expand its potential**. Undoubtedly, greener chemistry can be achieved with the use of mechanochemistry.

References:

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5) J. Bonnamour, T.-X. Métro, J. Martinez and F. Lamaty, *Green Chem*., **2013**, 15, 1116.