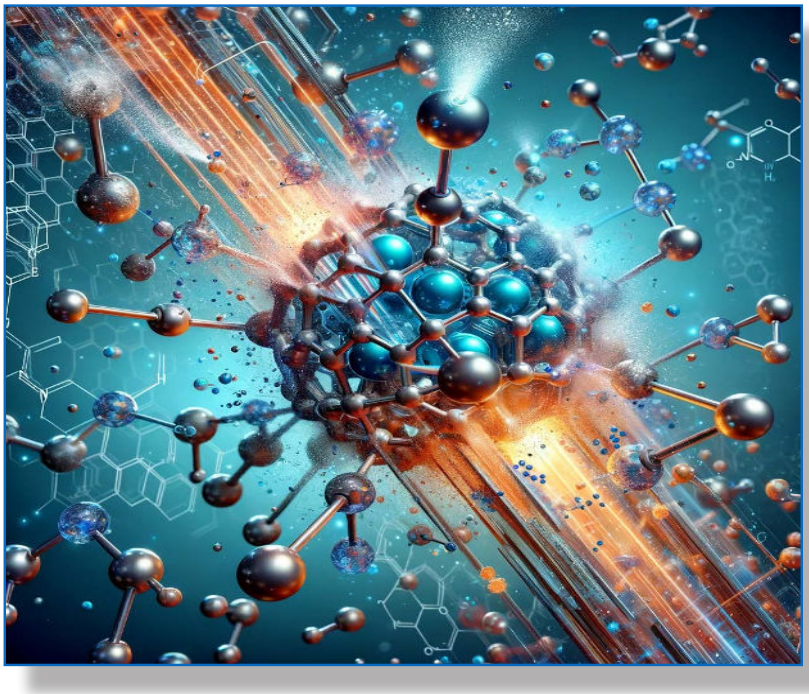
Advances in Mechanochemistry Processing Enabled by ResonantAcoustic® Mixing

Testimonials • Published Articles • Patents & Patent Applications



May 2024

This document is a portfolio of articles, patents/patents pending and user testimonials that reference Resodyn's ResonantAcoustic® Mixing (RAM) technology in a variety of mechanochemistry materials industry applications. This collection of abstracts and links to published articles is intended to provide insight into the value of RAM technology as a means of solving challenges, improving quality, and raising productivity in the development of "Green" Chemistry Processes.

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Mechanochemistry

Resodyn™ ACOUSTIC MIXERS

Mechanochemistry is the initiation of chemical reactions by mechanical forces such as grinding, shearing, milling, or mixing. Traditional mechanochemistry processing methodologies vary from hand grinding (i.e., mortar and pestle) to shaker and planetary mills for laboratory scale production. Previously, eccentric and horizontal high-energy ball mill devices were preferred for scaling up to batch production, while twin-screw and single-screw extrusion equipment were used for continuous mechanochemical processing.

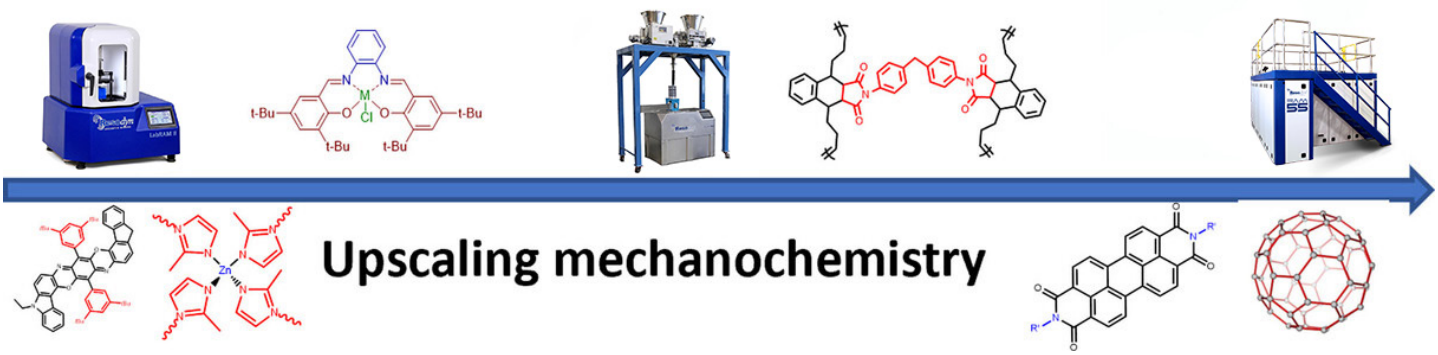
ResonantAcoustic® Mixing (RAM) demonstrates clear advantages over conventional mechanochemical processes, including reduced processing times, increased conversion efficiencies and eliminated contamination risks. **RAM** technology leverages acoustics to generate controlled mechanical force within a reaction vessel. **RAM** enables particle-to-particle collisions by promoting reaction kinetics, supplying the activation energy necessary to break and form chemical bonds. Acceleration and frequency are precisely controlled elements of **RAM** technology, allowing chemists to tailor the reaction. Temperature control and vacuum options are also available. The ability of **RAM** to fine-tune the reaction is invaluable toward managing specific product outcomes.

Mechanochemistry with **RAM** often eliminates, or substantially reduces, the use of solvents, heat, electricity and other external elements to complete chemical reactions. Furthermore, reactions requiring multiple intermediary products may also be simplified by employing **RAM** mechanochemistry.

System and process scale up is a pressing challenge for the further advancement of mechanochemistry production. **RAM** provides a consistent platform for scale-up of batch mechanochemical processing.

Companies all over the world rely upon RAM technology for mechanochemistry research and development

RAM technology is making Mechanochemistry a Global Reality.



Resodyn™ ACOUSTIC MIXERS

What "Green" Chemistry professionals are saying about RAM

"… RAM mechanosynthesis is shown to be faster, operationally simpler than conventional ball-milling, while also providing the first example of a mechanochemical strategy for ruthenium-catalyzed ene-yne metathesis. Reactions by RAM are readily and directly scaled-up …"

-Dr. Tomislav Friščić , et al
University of Birmingham, U.K.

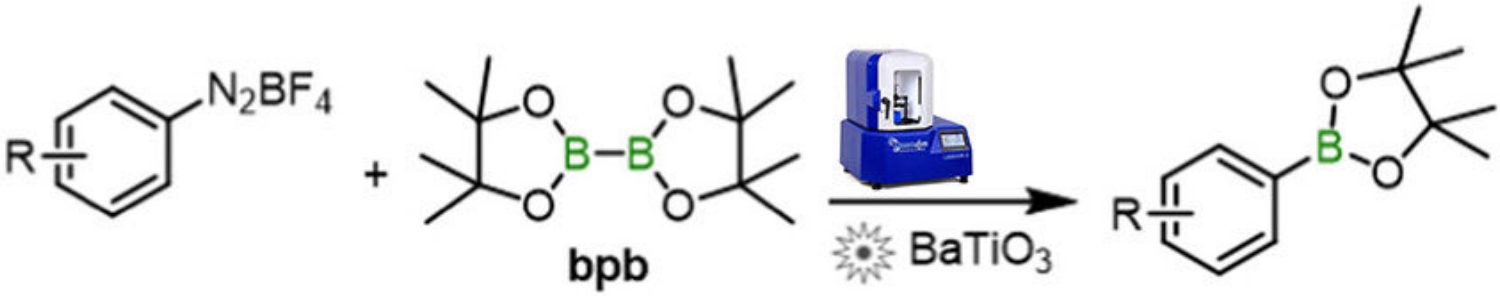
"The RAM exhibited remarkable performance in the Suzuki coupling reaction, achieving yields of approximately 90 % after 60 min and complete conversion after 90 min. The longevity of the milling vessel in the RAM was significantly extended compared to previous systems, thus offering increased durability for multiple reactions without deterioration …"

-Maxmilian Wohlgemoth, et al
Ruhr-Universität Bochum, Germany

" … it was shown that resonant acoustic mixing provides the mixing intensity required of lab-scale mechanochemical methods, such as liquid -assisted grinding, but now on a platform more amenable to larger-scale manufacture. Resonant acoustic mixing in general has been demonstrated to be scalable to volumes greater than 200 L and thus affords a potential new platform for co-crystallization processes."

-David J. am Ende, et al
Nalas Engineering Services, Essex, Conn., U.S.

RAM: The Future of Mechanochemistry



Icon Legend

- RAM testing, evaluation
- Material/chemical properties
- Powder/powder
- Liquid/powder
- Materials processing
- Materials/product quality

Icons	Publication Title (Live Links)*	RAM Application Summary	Year
	Mechanochemical Synthesis of Boroxine-linked Covalent Organic Frameworks	Real-time Raman spectroscopy permitted the first quantitative kinetic analysis of COF mechanosynthesis, while transferring the reaction design to **Resonant Acoustic Mixing** (**RAM**) enabled synthesis of multi-gram amounts of the target COFs.	2024
	Enhancement of Co2 Adsorption Kinetics Onto Carbon by Low-Frequency High Amplitude Resonant Vibrations	"In this work, a novel strategy is proposed to accelerate the CO2 uptake rate on carbon adsorbents by utilizing Low-Frequency High Amplitude (LFHA) r**esonant vibratory mixing** during the adsorption process to enhance adsorption kinetics."	2024
	Solvent-free surface modification of milled carbon fiber using resonant acoustic mixing	**"Resonant Acoustic Mixing** used as a green alternative for surface modification."	2023
	Halogen-bonded cocrystals via resonant acoustic mixing	"We report here on the production of eleven halogen-bonded (XB) cocrystalline architectures via neat and liquid-assisted **resonant acoustic mixing** (**RAM**)."	2024
	Resonant acoustic mixing (RAM) for efficient mechanoredox catalysis without grinding or impact media	**RAM** proceeds without formal grinding or impact media, is faster than the analogous ball-milling strategy, and is readily scalable.	2023
	Milling Media-Free Suzuki Coupling by Direct Mechanocatalysis- From Mixer Mills to Resonant Acoustic Mixers	"The **RAM** exhibits excellent performance in the Suzuki reaction, achieving yields of 90% after 60 minutes and complete conversion after 90 minutes. The longevity of the milling vessel is significantly improved in the **RAM**. . ."	2023
	Direct mechanocatalysis by resonant acoustic mixing (RAM)	"... **RAM**-based direct mechanocatalysis methodology is simple, enables the effective one-pot, two-step synthesis of triazoles via a combination of benzyl azide formation and CuAAC reactions on a wide scope of reagents, provides control over reaction stoichiometry that is herein shown to be superior ..."	2023

Icons	Publication Title (Live Links)*	RAM Application Summary	Year
	The "η-sweet-spot" (ηmax) in liquid-assisted mechanochemistry: polymorph control and the role of a liquid additive as either a catalyst or an inhibitor in resonant acoustic mixing (RAM)	"**Resonant acoustic mixing** (**RAM**) offers a simple, efficient route for mechanochemical synthesis in the absence of milling media or bulk solvents. Here, we show the use of **RAM** to conduct the copper-catalysed coupling of sulfonamides and carbodiimides."	2023
	Application of resonant acoustic mixing in the synthesis of vitamin C–nicotinamide variable stoichiometry cocrystals	"The use of **resonant acoustic mixing** (**RAM**) to synthesize variable stoichiometry cocrystals of nicotinamide and vitamin C was investigated...LA-RAM is demonstrated to be a scalable, environmentally friendly, ball-free method to make variable stoichiometry cocrystals."	2023
	Tinkering with Mechanochemical Tools for Scale Up	"... other mechanochemical syntheses.[37] Liquid-assisted **resonant acoustic mixing** (LARAM) ... rapid adoption at the R&D stage is evidenced by the increasing number of patents filed in the ..."	2023
	Metal-Catalyzed Organic Reactions by Resonant Acoustic Mixing	"...catalytic organic synthesis by **Resonant Acoustic Mixing** (**RAM**): a mechanochemical methodology that does not require bulk solvent or milling media... Reactions by **RAM** are readily and directly scaled-up without any significant changes in reaction conditions..."	2022
	Resonant acoustic-mixing technology as a novel method for production of negative-temperature coefficient thermistors	"...This study will be the lead to guide future studies into the cost-effective fast fabrication of negative-temperature coefficient thermistors by **resonant acoustic mixing** technology due to reduction of manufacturing costs by reducing processing time."	2022
	Time-resolved in situ monitoring of mechanochemical reactions	"... **resonant acoustic mixing** (**RAM**) cocrystallization of carbamazepine and nicotinamide by TRIS-XRD, the degree of bulk powder ..."	2022
	Application of mechanochemical activation in synthetic organic chemistry	" ... A recently emerged technique is **Resonant Acoustic Mixing** (**RAM**), which uses low-..."	2021
	Simple, scalable mechanosynthesis of metal–organic frameworks using liquid-assisted resonant acoustic mixing (LA-RAM)	"... mechanochemical syntheses. We demonstrate the use of liquid-assisted **resonant acoustic mixing** ... never been previously obtained in a mechanochemical environment ..."	2020
	Mechanochemistry for organic chemists: An update	"... A recently emerged technique is **Resonant Acoustic Mixing** (**RAM**), which uses low-frequency, high-amplitude acoustic resonance to agitate powder samples."	2018

Icons	Publication Title (Live Links)*	RAM Application Summary	Year
	Ball-free mechanochemistry: in situ real-time monitoring of pharmaceutical co-crystal formation by resonant acoustic mixing	"We present here the first in situ study of **RAM**-induced co-crystallisation monitored using synchrotron X-ray powder diffraction."	2018
	High-throughput screening and scale-up of cocrystals using resonant acoustic mixing	"This paper explores the effectiveness of resonant acoustic mixing **RAM** for screening and scale up of cocrystals. . . . Theophylline Oxalic acid cocrystals at an 80 gram scale with a net yield of 94%. **RAM** is thus established as an environmentally friendly mechanochemical technique for both high throughput screening and scaled up production of cocrystals."	2017

* Article links maybe limited by copyright restrictions. Detailed links on following pages
^ Results excerpted/paraphrased from articles.

Articles

Mechanochemical Synthesis of Boroxine-linked Covalent Organic Frameworks
Ehsan Hamzehpoo, Farshid Effaty, Tristan Borchers, Alexander Wahrhaftig-Lewis, Xavier Ottenwaelder, Tomislav Friščić & Dmytro F. Perepichka
Mechanochemistry enabled a >20-fold reduction in solvent use and ~100-fold reduction in reaction time compared with solvothermal methods, providing target COFs quantitatively with no additional work-up besides vacuum drying. Real-time Raman spectroscopy permitted the first quantitative kinetic analysis of COF mechanosynthesis, while transferring the reaction design to **Resonant Acoustic Mixing (RAM)** enabled synthesis of multi-gram amounts of the target COFs.

Enhancement of Co2 Adsorption Kinetics Onto Carbon by Low-Frequency High Amplitude Resonant Vibrations
Amirhosein Riahi, Ethan Heggem, Mario Caccia & Richard LaDouceur
In this work, a novel strategy is proposed to accelerate the CO2 uptake rate on carbon adsorbents by utilizing Low-Frequency High Amplitude (LFHA) **resonant vibratory mixing** during the adsorption process to enhance adsorption kinetics. With this approach, the rates of adsorption (characterized by the adsorption rate constant) exhibit increases of 115% and 50%, as calculated by two different kinetic models, Weber and Morris and the Pseudo-first-order model.

Solvent-free surface modification of milled carbon fiber using resonant acoustic mixing
Daniel J. Eyckens, David J. Hayne, Luke C. Henderson, Shaun C. Howard, Thomas J. Raeber, Ranya Simons, Andrea L. Wilde, Dilek Yalcin & Benjamin W. Muir
Resonant Acoustic Mixing (RAM) is used to rapidly modify the surface of milled carbon fiber using diazonium salts in solvent free conditions. This novel method allows tuning of the surface properties of this material and reduces the environmental footprint usually associated with surface modification of carbon fiber (discontinuous or otherwise)... Using **RAM** proved more efficient than positive controls produced under thermal conditions in solvent.

Halogen-bonded cocrystals via resonant acoustic mixing
Alireza Nari, Jeffrey S. Ovens & David L. Bryce
However, an eleventh stoichiomorphic cocrystal of p-DITFB and TMP is obtained exclusively via **RAM**, suggesting that the combination of RAM and milling approaches may afford a broader exploration of the polymorphic and stoichiomorphic landscape than the use of a single technique in isolation.

Resonant acoustic mixing (RAM) for efficient mechanoredox catalysis without grinding or impact media
Farshid Effaty, Lori Gonnet, Stefan G. Koenig, Karthik Nagapudi, Xavier Ottenwaelder & Tomislav Friščić
Resonant acoustic mixing (RAM) enables mechanoredox catalysis with BaTiO3 as the piezoelectric catalyst on model diazonium coupling reactions. RAM proceeds without formal grinding or impact media, is faster than the analogous ball-milling strategy, and is readily scalable. X-ray diffraction and spectroscopy indicate that reusability of BaTiO3 as a mechanoredox catalyst under ball-milling or RAM might be limited by boration.

Articles (cont.)

Milling Media-Free Suzuki Coupling by Direct Mechanocatalysis- From Mixer Mills to Resonant Acoustic Mixers
Maximilian Wohlgemuth, Sarah Schmidt, Maike Mayer, Dr. Wilm Pickhardt, Dr. Sven Grätz & Prof. Dr. Lars Borchardt
RAMs exhibit excellent performance in the Suzuki reaction, achieving yields of 90% after 60 min and complete conversion after 90 min. The longevity of the milling vessel is significantly improved in a RAM, allowing for at least 20 reactions without deterioration.

Direct Mechanocatalysis without Milling Media – From Mixer Mills to Resonant Accoustic Mixers
Maximilian Wohlgemuth, Sarah Schmidt, Maike Mayer, Wilm Pickhardt, Sven Graetz & Lars Borchardt
Here we describe the development of a sustainable and cost-effective approach for catalytic cross-coupling reactions in mechanochemistry. ... The **RAM** exhibits excellent performance in the Suzuki reaction, achieving yields of 90% after 60 minutes and complete conversion after 90 minutes. The longevity of the milling vessel is significantly improved in the **RAM**, allowing for at least 20 reactions without deterioration.

The "η-sweet-spot" (ηmax) in liquid-assisted mechanochemistry: polymorph control and the role of a liquid additive as either a catalyst or an inhibitor in resonant acoustic mixing (RAM)
Lori Gonnet, Tristan H. Borchers, Cameron B. Lennox, Jogirdas Vainauskas, Yong Teoh, Hatem M. Titi, Christopher J. Barrett, Stefan G. Koenig, Karthik Nagapudi & Tomislav Friščić
Resonant acoustic mixing (**RAM**) offers a simple, efficient route for mechanochemical synthesis in the absence of milling media or bulk solvents. Here, we show the use of **RAM** to conduct the copper-catalysed coupling of sulfonamides and carbodiimides. This coupling was previously reported to take place only by mechanochemical ball milling, while in conventional solution environments it is not efficient, or does not take place at all. The results demonstrate **RAM** as a suitable methodology to conduct reactions previously accessed only by ball milling and provide a detailed, systematic overview of how the amount of liquid additive, measured by the ratio of liquid volume to weight of reactants (η, in µL mg−1), can affect the course of a mechanochemical reaction and the polymorphic composition of its product.

Application of resonant acoustic mixing in the synthesis of vitamin C–nicotinamide variable stoichiometry cocrystals
Minhthi Bui, Paroma Chakravartya & Karthik Nagapudi
The use of **resonant acoustic mixing** (**RAM**) to synthesize variable stoichiometry cocrystals of nicotinamide and vitamin C was investigated. Liquid assisted **RAM** (LA-RAM) was used to generate two polymorphs, Form I and II, of the 1 : 1 cocrystal of nicotinamide and vitamin C at a 700 mg scale using ethanol and methanol respectively as the liquid additives. LA-RAM was used to scale up polymorphs I and II of the 1 : 1 cocrystal to 20 grams.

Tinkering with Mechanochemical Tools for Scale Up
Dr. Javier F. Reynes, Dr. Valerio Isoni & Dr. Felipe García
Besides the previous systems, **resonant acoustic mixing (RAM)**, which is based on rapid mechanical agitation... The absence of milling media that eventually leads to product contamination and the fact that the these reactors are simpler to control presents RAM as a prospective upscaling mechanochemical technology.

Articles (cont.)

Metal-Catalyzed Organic Reactions by Resonant Acoustic Mixing

Dr. Lori Gonnet, Cameron B. Lennox, Jean-Louis Do, Ivani Malvestiti, Dr. Stefan G. Koenig, Dr. Karthik Nagapudi & Prof. Tomislav Friščić

We demonstrate catalytic organic synthesis by **Resonant Acoustic Mixing** (**RAM**): a mechanochemical methodology that does not require bulk solvent or milling media. Using as model reactions ruthenium-catalyzed ring-closing metathesis and copper-catalyzed sulfonamide-isocyanate coupling, **RAM** mechanosynthesis is shown to be faster, operationally simpler than conventional ball-milling, while also providing the first example of a mechanochemical strategy for ruthenium-catalyzed ene-yne metathesis. Reactions by **RAM** are readily and directly scaled-up without any significant changes in reaction conditions, as shown by the straightforward 200-fold scaling-up of the synthesis of the antidiabetic drug Tolbutamide, from hundreds of milligrams directly to 30 grams.

Resonant acoustic-mixing technology as a novel method for production of negative-temperature coefficient thermistors

Berat Yüksel Price & Stuart R. Kennedy

The 0.1 mol% B2O3-added NiMn2O4, Ni0.5Co0.5Cu0.3Mn1.7O4 and 0.1 mol% B2O3-added Ni0.5Co0.5Cu0.3Mn1.7O4 negative-temperature coefficient thermistors (NTC) prepared by **Resonant Acoustic-Mixing** (**RAM**) technology were compared with samples produced by the traditional ball-milling technique. The metal oxide powders were weighed and mixed by a resonant acoustic mixer (**LabRAM 1, Resodyn Acoustic Mixers**) at 15 and 40 g acceleration for 20 min and 2 h... To the best of our knowledge, **RAM** was applied to produce NTC thermistors for the first time in this study.

Time-Resolved In Situ Monitoring of Mechanochemical Reactions

Dr. Adam A. L. Michalchuk & Franziska Emmerling

Mechanochemical transformations offer environmentally benign synthesis routes, whilst enhancing both the speed and selectivity of reactions. In this regard, mechanochemistry promises to transform the way in which chemistry is done in both academia and industry but is greatly hindered by a current lack of mechanistic understanding. The continued development and use of time-resolved in situ (TRIS) approaches to monitor mechanochemical reactions provides a new dimension to elucidate these fascinating transformations. We here discuss recent trends in method development that have pushed the boundaries of mechanochemical research.

Application of mechanochemical activation in synthetic organic chemistry

Gábor Varga, Pál Sipos & István Pálinkó

In recent years the use of mechanochemical activation in promoting synthetic reactions in organic chemistry became remarkably widespread. Indeed, mechanochemical treatment can be a very efficient form of energy transfer, and, often, it may provide with mild reaction conditions for otherwise difficult syntheses.

Simple, scalable mechanosynthesis of metal–organic frameworks using liquid-assisted resonant acoustic mixing (LA-RAM)

Hatem M. Titi, Jean-Louis Do, Ashlee J. Howarth, Karthik Nagapudi & Tomislav Friščić

We present a rapid and readily scalable methodology for the mechanosynthesis of diverse metal–organic frameworks (MOFs) in the absence of milling media typically required for other types of mechanochemical syntheses. We demonstrate the use of liquid-assisted **resonant acoustic mixing** (LA-RAM) methodology for the synthesis of three- and two-dimensional MOFs based on Zn(II), Co(II) and Cu(II), including a mixed ligand system. Impor-

tantly, the LA-RAM approach also allowed the synthesis of the ZIF-L framework that has never been previously obtained in a mechanochemical environment, as well as its Co(II) analogue.

Mechanochemistry for Organic Chemists: An Update

Davin Tan & Tomislav Friščić

We provide a brief overview of recent advances in the use of mechanochemical techniques for the synthesis of organic molecules and materials, highlighting selected examples of mechanochemical organic transformations and mechanistic studies, and especially those that illustrate chemical reactions or syntheses of molecular targets that have remained elusive to conventional solution techniques.

Ball-free mechanochemistry: in situ real-time monitoring of pharmaceutical co-crystal formation by resonant acoustic mixing

Adam A. L. Michalchuk, Karl S. Hope, Stuart R. Kennedy, Maria V. Blanco, Elena V. Boldyreva & Colin R. Pulham

Resonant acoustic mixing (**RAM**) is a new technology designed for intensive mixing of powders that offers the capability to process powders with minimal damage to particles. This feature is particularly important for mixing impact-sensitive materials such as explosives and propellants. While the **RAM** technique has been extensively employed for the mixing of powders and viscous polymers, comparatively little is known about its use for mechanosynthesis. We present here the first in situ study of **RAM**-induced co-crystallisation monitored using synchrotron X-ray powder diffraction.

High-throughput screening and scale-up of cocrystals using resonant acoustic mixing

Karthik Nagapudi, Evelyn Yanez Umanzor & Colin Masui

This paper explores the effectiveness of **resonant acoustic mixing RAM** for screening and scale up of cocrystals. 16 cocrystal systems were selected as test cases based on previous literature precedent. A 96 well plate set up in conjunction with zirconia beads was used for cocrystal screening using **RAM**. A success rate of 80% was obtained in the screen for plates containing solvent or solvent plus Zirconia beads. A proof of concept production of hydrated and anhydrous cocrystals of 1:1 Theophylline Citric acid system at a 400 mg scale was demonstrated using solvent and bead assisted **RAM**.

Relevant Patents

Approved and pending applications for work involving the use of ResonantAcoustic® mixing technology.*

*With RAM as the preferred embodiment

Powder Blend Processability Improvements Through Minimal Amounts Of Synergistically Selected Surface Coating Agents

US US20240024241A1 Rajesh N. Dave, Sangah Kim & Zhixing Lin New Jersey Institute Of Technology

Priority 2022-07-12 • Filed 2023-07-12 • Published 2024-01-25

High(greater than 30%) and/or low(less than 10%) loaded multiple API powdered/nanoparticle were tabulated with increased flowability and physical properties. Properties include blend flowability and uniformity, bulk packing density, compactability, tensile strength, and dissolution. Blending is done through solventless dry mechanical coating of at least one minority API component defined as the API component with the least weight per volume surface coated with nano-sized powders in lesser amounts by wt % of the blend, and preferably less than 10% dry coated of the minority API. An excipient may be dry coated in the lesser amount wherein the excipient is a minority component. Both minority excipient and minority API may be dry coated. Using dry coating instead of dry granulation and/or wet granulation techniques in producing tablets saves manufacturing steps, costs, and produces higher quality tablets with surprisingly higher properties than expected for low flowability solid powdered ingredients.

Highlighted Use: A LabRAM coated an API with Aerosil A200.

Composition, magnetic particle-containing film, and electronic component

WO EP US JP TW US20230238164A1 Tatsuo Ishikawa Fujifilm Corporation

Priority 2020-09-18 • Filed 2023-03-15 • Published 2023-07-27

An object of the present invention is to provide a composition that can form a magnetic particle-containing film having excellent magnetic permeability and excellent acid resistance, and has excellent sedimentation stability. Another object of the present invention is to provide a magnetic particle-containing film that relates to the composition, and an electronic component that includes the magnetic particle-containing film.The composition according to an embodiment of the present invention contains magnetic particles that contain 70% to 90% by mass of Fe atoms and have a crystal structure of Fe, an average particle diameter of 2 to 30 μm, and an aspect ratio less than 8, and a rheology control agent.

Highlighted Use: RAM technology created a stable material with excellent magnetic anisotropy.

Method for production of composite magnetic powders by autonomous grinding

SK SK132021A3, Bureš Radovan, Fáberová Mária

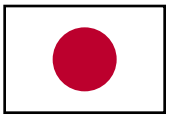
Priority 2021-2-25 • Filed 2021-2-25 • Published 2022-9-14

Ferromagnetism in the form of powdered magnetically soft metal or alloy is placed together with electro-insulating ceramic powder in a cylindrical container. The ratio of the height to the diameter of the container is 2:1. The container is filled with powder to a maximum of 1/3 of the volume. The powder mixture is autonomously ground by the action of **resonant acoustic energy** for 15 minutes to 360 hours. The particles of the powder mixture are given a gravitational acceleration of at least 20 g. Ferromagnetic particles are at least

Patents (cont.)

one order of magnitude larger than ceramic particles. Particles of the powder mixture are precipitated, ceramic particles are fragmented into smaller particles. Ferromagnetic particles act as a grinding medium. Fragmented ceramic particles are attached to the surface of ferromagnetic particles, the size of which does not change significantly during autonomous grinding. The powder composite material is further processed by pressing and sintering into magnetically soft components.
Highlighted Use: RAM combined ferromagnetic and ceramic particles.

Complexes Comprising Carbohydrate Polymers and Active Ingredients and Methods for Their Preparation



WO, EP, AU, JP, CA, US, JP2023510089A Felix Polyak, Dmitry Budovich
Priority 2019-12-13 • Filed 2020-12-11 • Published 2023-3-13
Disclosed herein are molecular complexes and compositions containing them. More specifically, carbohydrate polymers such as hyaluronic acid and its salts are bioactive selected from natural products and nutrients (amino acids, amino esters, hydroxy acids, hydroxy esters, vitamins, cannabinoids, etc.) and active pharmaceutical ingredients. Complexes with compounds to form stable molecular complexes. Complexation can be conveniently achieved using **resonant acoustic mixing** methods.
Highlighted Use: RAM technology combined carbohydrate polymers and biologically active compounds.

A method to produce and scale-up cocrystals and salts via resonant acoustic mixing

European Patent Office

US, EP EP2845852A1 Jerry Salan, Stephen R. Anderson, and David J. Am Ende, Nalas Engineering Services Inc.
Priority 2013-9-4 • Filed 2014-9-4 • Published 2015-3-11
A method to produce and manufacture cocrystals and salts is disclosed wherein crystalline solids and other components were combined in the desired proportions into a mixing chamber and mixed at high intensity to afford a cocrystalline product. No grinding media were required. The mixing system consists of a **resonant acoustic vibratory system** capable of supplying a large amount of energy to the mixture and is tunable to a desired resonance frequency and amplitude. The use of **resonant acoustic mixing** to assist cocrystallization is novel. This discovery enables the manufacture of cocrystals and salt forms, simplifying their manufacture and scale-up, and avoiding the use of grinding methods or grinding media. The present invention affords the manufacture of cocrystals and salts on kilogram to multi-ton scale and is adaptable to continuous manufacturing through the use of resonant mixing methods.
Highlighted Use: RAM technology can eliminate solvents and grinding material.

Resodyn™
ACOUSTIC MIXERS

RAM 5

RAM 5 Continuous

RAM 55

*Omni*RAM Continuous

*Omni*RAM H

RAM 5 H

RAM 55 H

*Omni*RAM

*Lab*RAM II *Lab*RAM I

*Lab*RAM II H

*Pharma*RAM I *Pharma*RAM II

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