Resodyn™
ACOUSTIC MIXERS
Innovative Mixing Technology

Advances in Pharmaceutical Processing Enabled By ResonantAcoustic® Mixing

Testimonials • Published Articles • Patents & Patent Applications

May 2022

This document is a portfolio of user testimonials, articles and patents/patents pending that reference Resodyn's ResonantAcoustic® Mixing (RAM) technology in a variety of pharmaceutical 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 development and processing of pharmaceuticals.

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Pharmaceutical Materials

Scientists, researchers and technical experts agree that ResonantAcoustic® Mixing (RAM) is exceptional in a wide variety of mixing and other processing functions for the pharmaceutical industry. The information in this Folio offers specific roadmaps to new discoveries, consistently higher quality, significant boosts in productivity, shorter time to market, and robust profitability.

RAM's breakthrough technology allows a single technology platform to process virtually any pharmaceutical material, including materials previously not possible or practical to manufacture. The contents herein is a rich assembly of information that describes experiments, methods and discoveries that demonstrate why nearly every major pharma company in the world is a Resodyn customer and RAM user for an exhaustive range of pharmaceutical processing applications.

Leading pharmaceutical companies all over the world rely upon RAM technology for drug development and production.

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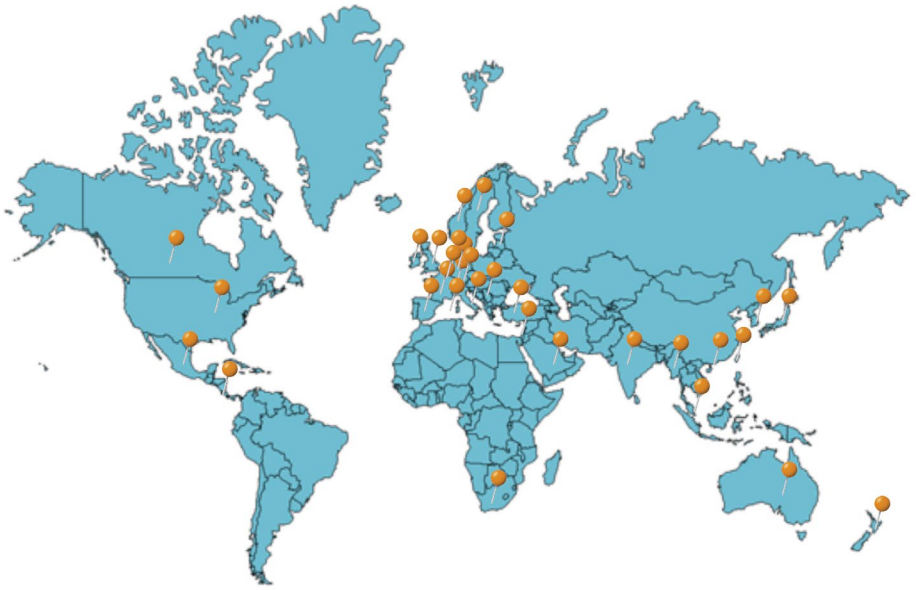

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= Pharma industry customers of RAM Technology

= Other customers of ResonantAcoustic® Mixers

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What pharmaceutical industry professionals are saying about RAM

"We use these LabRAMs day in and day out, 18-20 hours a day…we run the heck out of them. We're mixing several different powders in different quantities and no liquids. These [LabRAM] mixers do the trick."

- U.S.-based neutraceuticals company

"...having these LabRAM II units has changed our processes in a positive manner. Every process involved with these units has become more stream-lined, and yield better and more consistent results."

- Global pharmaceutical company

"Trace pharmaceutical powders were not mixed efficiently by the ordinary [V-mixer] method; however, these were mixed efficiently by the RAM method. The RAM method also addressed various problems associated with the ordinary method. The RAM technique can be applied to mixing processes with low drug content formulations, and it will be important in the future."

- RSC Advances article, 2013

"…[We had] challenges with mixing a viscous (~10,000cp) solids-loaded cream consisting of water, excipient, API, and a sticky acrylate adhesive. It used to take multiple material addition steps and up to 8 hours with an overhead stirrer to achieve desired uniformity. With a LabRAM we performed the mix in a little more than 2 min…"

- U.S. biopharmaceuticals company

RAM: The Pharmaceutical Mixer of Choice

Number of RAM systems sold for pharma materials mixing: **171**
Number of RAM pharma customers worldwide: **65**
Number of countries RAM has been sold into: **32**

PUBLISHED ARTICLES

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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
	Complete Cocrystal Formation during Resonant Acoustic Wet Granulation: Effect of Granulation Liquids	"Coprecipitated ASD powders (overhead mixing and resonant acoustic mixing) demonstrated superior tabletability and flow properties when compared to the spray drying powder. Careful choice of manufacturing process can be used to tune material properties of ASDs to make them more amenable for downstream operations like tableting."	2021
	A novel method for preparing stabilized amorphous solid dispersion drug formulations using acoustic fusion	"A diverse set of drug and polymer combinations have been effectively evaluated utilizing a newly developed method called acoustic fusion (which employs a LabRAM) to form amorphous solid dispersions (ASD) on the mg-scale, indicating that this approach is a general procedure that can be applied for ASD drug formulations."	2021
	Influence of guest and host particle sizes on dry coating effectiveness: When not to use high mixing intensity	"Examples from pharmaceutical applications include improving content uniformity of blends and powder flow...[using the] Resonant Acoustic Mixer (LabRAM) system..."	2020
	Impact of Method of Preparation of Amorphous Solid Dispersions on Mechanical Properties: Comparison of Coprecipitation and Spray Drying	"Coprecipitated ASD powders (overhead mixing and resonant acoustic mixing) demonstrated superior tabletability and flow properties when compared to the spray drying powder. Careful choice of manufacturing process can be used to tune material properties of ASDs to make them more amenable for downstream operations like tableting."	2019
	Ball-free mechanochemistry: in situ real-time monitoring of pharmaceutical co-crystal formation by resonant acoustic mixing	"The RAM technique...has been proposed as a method to perform mechanochemical processes under significantly more gentle conditions than those experienced during ball milling..."	2018

PUBLISHED ARTICLES

Icons	Publication Title (Live Links)*	RAM Application Summary	Year
	Influence of material properties on the effectiveness of glidants used to improve the flowability of cohesive pharmaceutical powders	"... [a Turbula mixer] and a highly efficient and effective mixer (LabRAM vibratory mixer) were used to further understand the effect of material properties on glidant effectiveness."	2018
	Mapping the dark space of chemical reactions with extended nanomole synthesis and MALDI-TOF MS	"The heterogeneous inorganic bases used in this study were made up as 0.5 M slurries in tert-amyl alcohol. When this mixture is irradiated on a PharmaRAM II Mixer at room temperature for 12 h at 18G in the presence of Norstone YTZ Grinding Media (0.5 mm), the resulting slurries do not significantly settle within 15 minutes on standing."	2017
	High-throughput screening and scale-up of cocrystals using resonant acoustic mixing	"RAM is...established as a scalable and environmentally friendly mechanochemical technique for the production of cocrystals."	2017
	Effect of resonant acoustic mixing on pharmaceutical powder blends and tablets	"Studies...carried out for several blends having various values of particle size, cohesion and concentration of the active pharmaceutical ingredient [showed] Resonant acoustic mixing is a good choice for blending low concentrations of cohesive APIs..."	2016
	Verification of the mixing processes of the active pharmaceutical ingredient, excipient and lubricant in a pharmaceutical formulation using a resonant acoustic mixing technology	"...RAM...efficiently contributes to powder flow and could produce an ideal mixing state with ease. The RAM method offers simple operation in comparison with ordinary method using a modified V-shape blender method, and it is expected to simplify pharmaceutical manufacturing facilities."	2016
	Characterization of resonant acoustic mixing using near-infrared chemical imaging	"Mixing in the RAM efficiently reduced the overall aggregate size of the cohesive API (semi-fine APAP, ~ 45 μm) used in a common blend of filler (microcrystalline cellulose, ~ 110 μm) and lubricant (magnesium stearate, ~ 10 μm)."	2016
	In-line and Real-time Monitoring of Resonant Acoustic Mixing by Near-infrared Spectroscopy Combined with Chemometric Technology for Process Analytical Technology Applications in Pharmaceutical Powder Blending Systems	This study examined the application of PAT with the combination of RAM, near-infrared spectroscopy, and chemometric technology as a set of PAT tools for introduction into actual pharmaceutical powder blending processes."	2016

PUBLISHED ARTICLES

Icons	Publication Title (Live Links)*	RAM Application Summary	Year
	Evaluation of resonant acoustic mixing performance	"The [LabRAM] resonant acoustic mixer reached minimum blend uniformity in as low as 30 seconds."	2015
	High-Throughput Tools for Optimizing Drug Nanosuspensions	"...To address this challenge, a procedure that screens and optimizes nanosuspensions in a high-throughput manner was developed using the Resonant Acoustic mixing system.18–21 In this technique, low-frequency, high-intensity acoustic energy is added to the container to homogeneously mix the contents in a low-shear gradient (Figure 3). Since the mixing process is applied homogeneously, consistent results can be observed for a wide range of different containers."	2015
	Development and Scale-Up of Cocrystals Using Resonant Acoustic Mixing	"...resonance acoustic mixing was applied to afford a practical and environmentally friendly approach to produce and scale up cocrystals."	2014
	A new and improved method for the preparation of drug nanosuspension formulations using acoustic mixing technology	"...this [resonant acoustic mixing] approach [is] highly suitable for the rapid evaluation of potential drug candidates in the discovery and development space."	2014
	Applying Dry Powder Coatings	"RAM was effective at applying dry powder coatings. The coated powders exhibited higher bulk density and superior powder flow performance compared with uncoated powders. This work demonstrated the following four main points: the RAM can effectively increase the bulk density of powders by applying dry powder coatings of silicon dioxide and magnesium stearate; a linear relationship exists between bulk density and the FFC for powders dry coated with hydrophobic silicon dioxide; bulk density measurements can be used as a screening method to determine the potential for flow property enhancements; and RAM could be used as a benchmarking tool for comil dry powder coating process optimization."	2011

PUBLISHED ARTICLES

Partial (edited) selection of searched technical articles using the following search terms (articles are live links):

- "Resonant Acoustic Mixing" AND/OR: "pharmaceutical," "RAM," "compound"

Complete Cocrystal Formation during Resonant Acoustic Wet Granulation: Effect of Granulation Liquids
R Tanaka, S Osotprasit, J Peerapattana, K Ashizawa…- Pharmaceutics, 2021- mdpi.com
….the current study was to achieve simultaneous completion of THPCIT cocrystallization and granulation during the resonant wet acoustic granulation (RAG … Our project team hypothesized that the RAG system would accomplish a powerful mixing of materials that would easily …
Related articles

A novel method for preparing stabilized amorphous solid dispersion drug formulations using acoustic fusion
Z Guo, C Boyce, T Rhodes, L Liu, GM Salituro…- International Journal of …, 2021- Elsevier
… As a general procedure, an acoustic heating block attached to a Labram resonant acoustic mixer was preheated … The vial was capped and then placed in the acoustic fusion heating block and lamped … While the heating/mixing time varied from 15 to 60 min, most drug samples …
Related articles

Influence of guest and host particle sizes on dry coating effectiveness: When not to use high mixing intensity
K Zheng, K Kunnath, Z Ling, L Chen, RN Davé- Powder Technology, 2020- Elsevier
… Examples from pharmaceutical applications include improving content uniformity of blends and powder flow, engineered … In what follows, the particle material properties, effects of particle sizes, and mixing intensity are … (9). The Resonant Acoustic® Mixer (LabRAM) system …
Related articles

Impact of method of preparation of amorphous solid dispersions on mechanical properties: Comparison of coprecipitation and spray drying
HH Hou, A Rajesh, KM Pandya, JW Lubach…- … of pharmaceutical …, 2019- Elsevier
… Precipitation by resonant acoustic mixing (RAM): GDC-0810 and HPMC-as MF (1:1 weight ratio) were dissolved in 30 … Figure 1. Experimental setup used to perform precipitation using acoustic mixing … for 1 H and 125.77 MHz for 13 C, along with a double resonance magic-angle …
Related articles

Ball-free mechanochemistry: in situ real-time monitoring of pharmaceutical co-crystal formation by resonant acoustic mixing
AAL Michalchuk, KS Hope, SR Kennedy…- Chemical …, 2018- pubs.rsc.org
… 1 Schematic representation of the resonant acoustic mixer (left), and photograph of experimental setup at … of approximately 61 Hz that corresponds to the mechanical resonance frequency of … Provided thorough mixing can be achieved, and new reactive interfaces can be formed …
Related articles

Influence of material properties on the effectiveness of glidants used to improve the flowability of cohesive pharmaceutical powders
D Sunkara, M Capece- AAPS PharmSciTech, 2018- Springer
… with the API or excipient using a low-intensity/low shear Turbula mixer (TURBULA® Basel, Switzerland) or a high-intensity vibratory mixer called the Laboratory Resonant Acoustic Mixer (LabRAM, Resodyn, USA) … In the case of vibratory mixing, 30 g of powder was mixed in a …
Related articles

PUBLISHED ARTICLES

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Mapping the dark space of chemical reactions with extended nanomole synthesis and MALDI-TOF MS
S Lin, S Dikler, WD Blincoe, RD Ferguson...- ..., 2018- science.sciencemag.org
... Research Article. Mapping the dark space of chemical reactions with extended nanomole synthesis and MALDI-TOF MS. View ORCID ProfileShishi Lin 1 ,; iew ORCID ProfileSergei Dikler 2 ,; View ORCID Profile ...
Related articles

High-throughput screening and scale-up of cocrystals using resonant acoustic mixing
Karthik Nagapudi, Evelyn Yanez Umanzor, Colin Masui
Small Molecule Pharmaceutical Sciences, One DNAway,South San Francisco, CAInternational Journal of Pharmaceutics www.elsevier.com/locate/ijpharm, Feb. 2017

Effect of resonant acoustic mixing on pharmaceutical powder blends and tablets
JG Osorio, K Sowrirajan, FJ Muzzio - Advanced Powder Technology, 2016 - Elsevier
Blending in a resonant acoustic mixer (RAM) was shown to be highly effective for low concentrations of cohesive active pharmaceutical ingredients (APIs) and lubricant (Osorio and Muzzio, 2015). However, changes in material properties of the final blend were ...
Related articles

Verification of the mixing processes of the active pharmaceutical ingredient, excipient and lubricant in a pharmaceutical formulation using a resonant acoustic mixing ...
R Tanaka, N Takahashi, Y Nakamura, Y Hattori... - RSC ..., 2016 - pubs.rsc.org
... processes of solid preparations, such as formulations consisting of pre-mixed excipients with a ... M. Otsuka, J. Gao and Y. Matsuda, Effects of mixer and mixing time on ... JG Osorio and FJ Muzzio, Evaluation of resonant acoustic mixing performance, Powder Technol., 2015, 278, 46 ...
Related articles

Characterization of resonant acoustic mixing using near-infrared chemical imaging
JG Osorio, E Hernández, RJ Romañach, FJ Muzzio - Powder Technology, 2016 - Elsevier
... to other techniques such as digital imaging (DI) [11], [12], [13], [14], magnetic resonance imaging (MRI ... 1. Laboratory scale resonant acoustic mixer with a 236-mL mixing vessel used in all experimental ... of blending parameters was 70g of acceleration and 4 min of mixing time for ...
Related articles

In-line and real-time monitoring of resonant acoustic mixing...for process analytical technology applications in pharmaceutical ...
R Tanaka, N Takahashi, Y Nakamura, Y Hattori... - Analytical ..., 2017 - jstage.jst.go.jp
Resonant acoustic® mixing (RAM) technology is a system that performs high-speed mixing by vibration through the control of acceleration and frequency. In recent years, real-time process monitoring and prediction has become of increasing interest, and process analytical ...
Related articles

Evaluation of resonant acoustic mixing performance
JG Osorio, FJ Muzzio - Powder Technology, 2015 - Elsevier ... 2).
The RAM is designed to operate at mechanical resonance, transferring almost all of the mechanical ... to the loose mass in the vessel by the propagation of an acoustic pressure wave. The RAM operates around 60 Hz, defined as the resonant frequency, at which the potential ...
Related articles

PUBLISHED ARTICLES

High-Throughput Tools for Optimizing Drug Nanosuspensions
DH Leung, T Rhodes, A Bak - wyattchina.com
… The high-throughput drug-sparing technology described in … tion of optimized nanosuspension
Related articles

Development and scale-up of cocrystals using resonant acoustic mixing
DJ am Ende, SR Anderson… - Organic Process Research …, 2014 - ACS Publications
… Development and Scale-Up of Cocrystals Using Resonant Acoustic Mixing … In the present work resonance acoustic mixing was applied to afford a practical and environmentally friendly approach to produce and scale up cocrystals …
Related articles

A new and improved method for the preparation of drug nanosuspension formulations using acoustic mixing technology
DH Leung, DJ Lamberto, L Liu, E Kwong… - International journal of …, 2014 - Elsevier
… In contrast to these methods, resonant acoustic mixing is a low shear approach which results in a … This drug slurry is then acoustically mixed in the presence of zirconia grinding media, resulting in … Herein we report this new acoustic milling process in detail as well as advantages …
Related articles

Applying Dry Powder Coatings | Pharmaceutical ... - PharmTech
https://pharmtech.com › view › applying-dry-powder-c... Oct 1, 2011
The authors experiment with a resonant acoustic mixer as a method for dry powder coating. Efficient handling and transport of fine-particle powders can be difficult because of the highly cohesive nature of the bulk powder mass.
Related articles

Relevant Patents

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

*Including patents with RAM as the preferred embodiment

Process for making agglomerates using acoustic mixing technology

WO EP US JP AU CA AU2013345062B2 Sai Prasanth Chamarthy Merck Sharp & Dohme Corp.
Priority 2012-11-16 • Filed 2013-11-12 • Granted 2018-02-08 • Published 2018-02-08
Described herein is a process for preparing agglomerates comprising: (i) providing a dry powder mixture of one, two, or three active pharmaceutical agent(s), and at least one excipient; and (ii) applying acoustic energy to said dry powder mixture to form agglomerates.

Method to Produce and Scale-Up Cocrystals and Salts Via Resonant Acoustic …

EP US US20150080567A1 Jerry Salan Nalas Engineering Services Inc.
Priority 2013-09-04 • Filed 2014-08-28 • Published 2015-03-19
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 …

Method and apparatus

WO EP US CN JP KR AU CA GB HK IL IN MX NZ RU SG MX2014011795A Matthew Green Vectura Ltd
Priority 2012-03-30 • Filed 2013-03-28 • Published 2015-01-12
A method is disclosed for making a pharmaceutical composition for pulmonary administration, the method comprising a step in which an inhalable pharmaceutically active material is acoustically blended in a resonant acoustic blender. The invention also relates to compositions for inhalation prepared …

Media milling process for the manufacture of active pharmaceutical ingredients …

WO EP US US20160317391A1 Balaji Bharatwaj Merck Sharp & Dohme Corp.
Priority 2013-12-17 • Filed 2014-12-12 • Published 2016-11-03
The invention disclosed herein is a novel media milling process performed in an atmosphere of propellants(s) utilizing a resonant acoustic mixing (RAM) device. The process is utilized to reduce the particle size of API (optionally including excipients) to a respirable size range while ensuring the …

Mechanical system that continuously processes a combination of materials

US US9808778B2 Lawrence C. Farrar Resodyn Corporation
Priority 2012-05-31 • Filed 2013-08-13 • Granted 2017-11-07 • Published 2017-11-07
The present application is directed towards systems and methods for continuously reacting a combination of materials by use of an acoustic agitator and a continuous process vessel. The system can react, fluidize, mix, coat, dry, combine or segregate materials. The continuous processing system can …

Patents, cont'd.

Method for producing dispersion and inkjet recording method

WO JP WO2018061989A1
Priority 2016-09-30 • Filed 2017-09-21 • Published 2018-04-05
Provided are: a method for producing a dispersion, comprising a step for obtaining a mixture by filling at least one type of particles selected from inorganic particles and organic particles, a dispersing agent, and a dispersion medium in a sealed container and mixing the substances filled in the …

Rapid allograft treatment systems and methods

WO EP US KR AU CA CL AU2016304809B2 Carolyn BARRETT RORICK Allosource
Priority 2015-08-07 • Filed 2016-08-08 • Granted 2020-09-24 • Published 2020-09-24
Provided are systems and methods for treating or processing tissue, and tissue products made using such systems and methods. The methods involve combining tissue with a processing solution in a processing vessel and applying resonant acoustic energy thereto. In some instances, the tissue is …

Solventless mixing process for coating pharmaceutical ingredients

WO EP US CN JP AR BR DK ES HR HU PL PT RS SI WO2014062444A1 Rajesh N. Dave New Jersey Institute Of Technology
Priority 2012-10-15 • Filed 2013-10-09 • Published 2014-04-24
SOLVENTLESS MIXING PROCESS FOR COATING PHARMACEUTICAL INGREDIENTS BACKGROUND OF THE INVENTION 1. Field of the Invention [0001] The present invention relates to coating active pharmaceutical ingredients for controlled release or applications associated with controlled release such as taste masking.

Method for producing dispersion and method for producing pigment dispersion for …

WO US JP JP6742426B2
Priority 2016-09-30 • Filed 2017-09-15 • Granted 2020-08-19 • Published 2020-08-19
Step A of preparing a mixture containing an edible pigment, an edible dispersant, and water, A step B of applying a hydrostatic pressure of 30 MPa or more to the mixture, A step C of performing a dispersion treatment on the mixture to which the hydrostatic pressure is applied, A method for …

Systems and methods for producing homogenous pharmaceutical compositions

US US20170281530A1 Michael Bennett The Compounders Depot, Inc.
Priority 2016-04-05 • Filed 2017-04-05 • Published 2017-10-05
Embodiments of the present disclosure generally relate to systems and methods for mixing pharmaceutical compositions, agents and/or ingredients together. In one embodiment, a method can include a shell and a flexible pouch disposed within the shell. The flexible pouch can include at least one …

High Throughput Methods for Screening Chemical Reactions Using Reagent-Coated …

US US20190033185A1 Amanda Dombrowski Abbvie Inc.
Priority 2017-07-31 • Filed 2018-07-23 • Published 2019-01-31
Systems, methods, and compositions for high throughput screening of micro-scale chemical reactions are disclosed. In particular, systems, methods, and compositions for handling small amounts of solid reagent are disclosed. For example, mechanical mixing is employed to obtain reagent-coated bulking …

Patents, cont'd.

Rapid acoustic tissue processing methods, systems, and devices

US US20180280575A1 Ryan Delaney Allosource
Priority 2015-08-07 • Filed 2018-06-01 • Published 2018-10-04
Provided are systems and methods for treating or processing tissue, and tissue products made using such systems and methods. Also provided are ball mill processing devices and systems useful for processing materials such as tissue. The methods involve combining tissue with or without a processing …

Methods of Producing Cellulose Nanocrystals

US US20190367704A1 Erik Dahl Uchicago Argonne, Llc
Priority 2018-06-05 • Filed 2018-06-05 • Published 2019-12-05
Presented herein for the first time are novel and highly efficient methods for producing CNCs. In exemplary embodiments, the method comprises mixing in a single reaction vessel a cellulose pulp, an acidic solution; and sodium chlorite, wherein the sodium chlorite reacts to form a bleaching agent, …

Solventless particle coating via acoustic mixing

US US20210009767A1 Christopher LAVALLEE International Flavors & Fragrances Inc.
Priority 2019-07-11 • Filed 2020-07-10 • Published 2021-01-14
A method for coating solid granules containing a carbohydrate, gum Arabic, or protein by combining the solid granules with at least one solid coating material, and applying acoustic energy to said combination is provided as are coated solid granules prepared by the method.

Methods and Devices for Producing Cellular Suspensions from Tissue Samples

WO US US20210096046A1 Ronald J. Pettis Becton, Dickinson And Company
Priority 2016-03-10 • Filed 2020-12-15 • Published 2021-04-01
Aspects of the present disclosure include methods of producing a cellular suspension from a tissue sample by applying resonant acoustic energy to a container comprising the tissue sample in a manner sufficient to produce a cellular suspension from the tissue sample. Resonant acoustic mixers and …

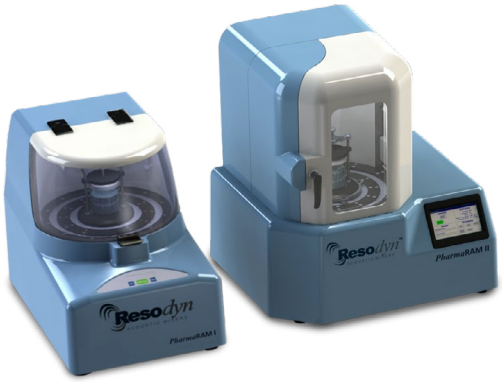
Pharmaceutical suspensions containing etoricoxib

WO WO2016036588A1 Michael HESLINGA Merck Sharp & Dohme Corp.
Priority 2014-09-03 • Filed 2015-08-28 • Published 2016-03-10
The present invention provides pharmaceutical suspensions containing etoricoxib particles having a median particle diameter of 0.2 to 14 µm, and an aqueous injection vehicle. The present invention also provides methods for administering and preparing such compositions.

Method of converting a crystalline compound to an amorphous compound, method of …

WO EP US AU CA US20160235677A1 Robert A. Hoerr Nanocopoeia, Llc.
Priority 2014-11-25 • Filed 2015-11-25 • Published 2016-08-18
A method of converting a poorly water soluble crystalline compound to an amorphous compound and a method of increasing the solubility of a poorly water soluble crystalline compound in biorelevant fluid at pH 6.5 is disclosed. The method includes dissolving the compound and a polymer in a solvent …

RAM 5



PharmaRAM I and II

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