

PEER-REVIEWED RESEARCH

APIs

Solubility, Polymorphism, Crystallinity, Crystal Habit, and Drying Scheme of (R, S)-(±)-Sodium Ibuprofen Dihydrate
By Tu Lee, Ying Hsiu Chen, Chyong Wen Zhang
(June 2007)

The racemic compound (R, S)-(±)-ibuprofen is a popular and well understood active pharmaceutical ingredient, but it has several disadvantageous formulation properties such as poor solubility, low melting point, and potential esterification with excipients containing an hydroxyl group. The authors investigate the use of an (R, S)-(±)-ibuprofen salt to evaluate these problems using various analytical methods to determine the polymorphism, crystallinity, and drying scheme.

ASEPTIC PROCESSING

The Application of Robotics to Aseptic Environmental Surface Monitoring
By Mayumi Maruyama, Tomoo Matsuoka, Motonari Deguchi, James E. Akers
(August 2007)

This article presents a study of an aseptic environmental monitoring system for surface contamination at critical areas using a robot.

BIOPHARMA

The Importance of Quality in Corrosion-Resistant Alloys
By Hira Ahluwalia, Brian J. Uhlenkamp
(March 2008)

In this topical review, the

authors discuss the rationale behind microstructural requirements for biopharmaceutical equipment and problems that may be encountered during the fabrication of high-performance corrosion-resistant equipment.

Mixed-Flow Fans Meet Biosafety Level Laboratory Requirements
By Charlie Gans
(November 2007)

Mixed-flow impeller systems exhaust laboratory workstation fume hoods, prevent reentrainment into the facility and adjacent facilities, and help companies comply with appropriate pollution-control standards.

CLEANING VALIDATION

Equipment Hold-Time for Cleaning Validation
By Richard J. Forsyth
(April 2008)

Regulatory agencies expect companies to establish and monitor clean equipment- and dirty equipment-hold times for manufacturing equipment as part of their cleaning validation program.

Setting Cleaning Validation Acceptance Limits for Topical Formulations
By M. Ovais, Lai Yeo Lian
(January 2008)

There is a need for current cleaning validation methods to be used for topical formulations. The authors highlight the issues and challenges encountered.

Materials of Construction Based on Recovery Data for Cleaning Validation
(October 2007)
By Richard J. Forsyth, Julia C.

O'Neill, Jeffrey L. Hartman

The material of construction is a factor in the recovery of residue in cleaning validation. An analysis of existing recovery data showed that recovery factors for drug products on various materials of construction may be categorized into several groupings.

CRYSTALLIZATION & POLYMORPHISM

Cocktail-Solvent Screening
By Tu Lee, Shi Ting Hung
(January 2008)

The authors propose extending initial solvent screening for a single-solvent system to the cocktail solvent screening of binary and ternary solvent mixtures.

DRUG DEVELOPMENT

Salt Selection in Drug Development
By Lokesh Kumar, Aeshna Amin, Arvind K. Bansal
(March 2008)

The selection of an appropriate salt form for a potential drug candidate is an opportunity to modulate its characteristics to improve bioavailability, stability, manufacturability, and patient compliance.

EXCIPIENTS

Technical Note: Influence of Common Excipients on the Crystalline Modification of Freeze-Dried Mannitol
By Stefan Schneid, Xenia Riegger, Henning Geiseler
(March 2008)

This technical note discusses the investigation of the influence of frequently used additives on the crystallization of mannitol.

Assessing *Hibiscus rosa-sinensis* Linn as an Excipient in Sustained-Release Tablets**By Giresh K. Jani, Dhiren P. Shah (January 2008)**

Natural gums and mucilage are biocompatible, cheap, readily available, and represent a potential source of excipients. The authors examine the functionality of mucilage extracted from the leaves of *Hibiscus rosa-sinensis* Linn as an excipient in a sustained-release tablet formulation.

Evaluating Mucilage from *Aloe Barbadensis* Miller as a Pharmaceutical Excipient for Sustained-Release Matrix Tablets**By Girish K. Jani, Dhiren P. Shah, Vineet C. Jain, Manish J. Patel, Disha A. Vithalan (November 2007)**

Natural gums and mucilage have been widely explored as pharmaceutical excipients. The goal of this study was to extract mucilage from the leaves of *Aloe barbadensis* Miller and to study its functionality as an excipient in pharmaceutical sustained-release tablet formulations.

Functionality-Related Characteristics of Excipients**By Henning G. Kristensen (October 2007)**

Amidst debate, the European Pharmacopoeia Commission is working to include physical or "functionality-related characteristics" of excipient materials in its monographs.

Joint Position Paper on Pharmaceutical Excipient Testing and Control Strategies**By Brian Carlin, Dale Carter, Moira Griffiths, Gregory****Larner, Kevin Moore, Barry Rothman, David Schoneker, Catherine Sheehan, Rajendra Upoor, Phyllis Walsh, Robert Wiens****(September 2007)**

This article presents collaborative positions among excipient manufacturers, drug product manufacturers, and members of the US Pharmacopeia on key issues pertaining to the control of pharmaceutical excipients stemming from a recent Pharmaceutical Quality Research Institute workshop.

FORMULATION**Dimethyl Sulfoxide USP, PhEur in Approved Pharmaceutical Products and Medical Devices****By A.S. McKim, Robert Strub (May 2008)**

The authors survey the approved applications of dimethyl sulfoxide USP, PhEur across the health-care industry and consider the suitability of DMSO from a regulatory and formulation compatibility standpoint.

The Disintegration and Dissolution of Nabumetone Dispersible Tablets**By H. N. Shivakumar, B.G. Desai, S. Narasimha Murthy, Ashish Sharma (December 2007)**

The authors analyzed the effects of complexation as well as the levels of ammonium bicarbonate and crospovidone on tablet wetting time (WT), disintegration time (DT), and percent dissolution efficiency at 60 min (%DE60).

Strategy for the Prediction and Selection of Drug Substance Salt Forms**By Harry G. Brittain (October 2007)**

Through consideration of the ionic equilibria of acids and bases, one may readily calculate the formation constant of a salt species solely on the basis of knowledge of the pK_a value of the acid and the pK_b value of the base.

Lubrication of Direct-Compressible Blends with Magnesium Stearate Monohydrate and Dihydrate**By Patrick Okoye, Stephen H. Wu (September 2007)**

The influence of magnesium stearate (MgSt) on powder lubrication and finished solid-dose properties presents big challenges to drug manufacturers.

PACKAGING**Packing-Line Improvement Based on a Fault-Tree Analysis Approach****By Arturo Toledo Rivero, Nelson Sierra Prado, Yohann Pérez Molina, Ian Toledo de Zayas (March 2008)**

This article focuses on upgrading and improving a packing process to comply with current good manufacturing practices. The authors sought to maintain proper quality assurance for finished products.

PARENTERAL FORMULATIONS**Converting Intravenous Dosing to Subcutaneous Dosing With Recombinant Human Hyaluronidase****By Michael F. Haller (October 2007)**

The preferred route of administration for an injected therapeutic agent is subcutaneous (SC), but SC injections are generally limited to no more than 1-2 mL in volume, representing a major challenge, especially for large protein biologics.

PROCESS CONTROL**EPCAM: A Strategy to Enable Manufacturing-Process Control Transformation****By James M. Prendergast, Michael Passow, Mike Ricci, Srinivas S. Dagalur, Dennis Bell, and Limuel Sagadraca (May 2008)**

The authors discuss how EPCAM can facilitate implementation of quality by design and process analytical technology.

QUALITY**Quality Systems for Drugs and Biologics****By Andrew G. Edwards (February 2008)**

FDA is modernizing and streamlining current good manufacturing practices. The author examines FDA's evolving approach to quality systems and how a manufacturer can implement a quality system framework.

The Application of Quality by Design to Analytical Methods**By Phil Borman, Phil Nethercote, Marion Chatfield, Duncan Thompson, Keith Truman (October 2007)**

To monitor and control processes or products, analytical methodology must be fit for purpose. An approach to apply quality by design principles to the de-

sign and evaluation of analytical methods has therefore been developed to meet these needs.

Acceptance Limits for the New ICH USP 29 Content-Uniformity Test

By James S. Bergum, Hua Li
(October 2007)

Revisions to the United States Pharmacopeia's (USP) uniformity test require manufacturers to establish new acceptance limits. The authors present their method for calculating acceptance limits consistent with USP's revised content-uniformity test requirements.

REGULATION

Biopharmaceutical Manufacturing: The Challenge of Global Regulatory Compliance

By Kelly Davis
(June 2008)

The author provides an overview of key regulatory issues for companies seeking to market their biopharmaceutical agents globally.

FDA's Direct Final Rule to Change the Pharmaceutical GMPs

By Barbara Immel
(June 2008)

This article discusses FDA's release of a direct final rule and a proposed rule to change the pharmaceutical current good manufacturing practices and proposes possible solutions.

Product Annual/Quality Review: US–EU Comparative Analysis and Interpretations

By John Y. Lee, John G. Grazal
(March 2008)

There are significant differences between the United States and European Union requirements for the annual review of records related to the manufacturing and control for pharmaceutical products and active pharmaceutical ingredients.

SOLUBILITY ENHANCEMENT

Preparation and Characterization of Meloxicam-Myrj-52 Granules Obtained by Melt Granulation

By Pramodkumar Sharma, Praveen Chaudhari, Hiren Bhagat, Nishant Varia
(December 2008)

Various manufacturing techniques can improve a drug's solubility, thus increasing its bioavailability. The authors examined whether melt granulation can enhance drug solubility using meloxicam as the drug substance and myrj-52 as the binder.

STERILIZATION

Innovation in Biological Indicator Evaluator Resistor Vessel Technology

By Kurt McCauley, John R. Gillis, James P. Agalloco
(August 2007)

The authors examine advances in the design and the application of biological indicator evaluator resistor vessels used to measure the resistance of bacterial spores in monitoring sterilization processes.

TESTING

Spectrophotometric Determination of Lead

By Lang Lang, Konghwa Chiu, Qingyong Lang
(April 2008)

The authors developed a reliable spectrophotometric method for determining and measuring trace amounts of lead in various samples.

Raw-Material Authentication Using a Handheld Raman Spectrometer

By Robert L. Green, Christopher D. Brown
(March 2008)

Using a handheld Raman spectrometer, the authors developed methods for 28 commonly used excipients and active ingredients.

Overcoming Disincentives to Process Understanding in the Pharmaceutical CMC Environment

By Laura Foust, Myron Diener, Mary Ann Gorko, Jeff Hofer, Gregory Larner, David LeBlond, Jerry Lewis, Dennis Sandell, Tim Schofield, Kim Vukovinsky, Ed Warner
(September 2007)

Larger and strategic sampling and testing plans can improve process understanding and characterization.

WATER SYSTEMS

Improving a Pharmaceutical Water System based on a Risk Analysis Approach

By Arturo Toledo Rivero, Nelson Sierra Prado, Anamarys González Alvarez, Danelys Cardoza Lobaina
(November 2007)

In this study, fault tree analysis applied to a water pretreatment and purification installation exposed cause-and-effect complex interrelations in possible fault events.

SPECIAL REPORTS

Small Wonder: Nanoparticle Strategies for Biological Drugs

By Erik Greb
(June 2008)

Nanoparticle-based systems present many advantages for the delivery of current and emerging biological drugs.

Cell Manufacturing on a Large Scale

By Michelle Hoffman
(June 2008)

Creating a kinder, gentler manufacturing process that doesn't kill the product is the goal of process developers doing large-scale cell culture for cell therapy.

Variability of USP Lot P Prednisone Reference Standard Tablets

By Walter W. Hauck, Gang Deng, Maria J. Glasgow, Mark R. Liddell, Pallavi Nithyanandan, and Roger L. Williams
(June 2008)

USP has conducted research on the performance of its prednisone RS tablets and dissolution procedure.

Unplugged: Developing Standards for Wireless Automation

By Maribel Rios
(May 2008)

ISA 100.11a and WirelessHART both seek to become the global standard for industrial wireless automation.

FDA's Pharmaceutical Quality Initiatives

By Representatives of the US Food and Drug Administration

**and Industry
(May 2008)**

A recent FDA–industry workshop discussed progress made to date and ways to further build upon FDA's *Pharmaceutical CGMPs for the 21st Century* initiative. This article reports on the outcome of that workshop and the action plan set forth.

**Inhalable Drugs on the
Launch Pad: Will They
Take Off?**

**By Erik Greb
(April 2008)**

Companies continue to develop inhaled insulin and other drugs, despite the problems that Pfizer's "Exubera" experienced.

**New Dimensions in Tablet
Imaging**

**By Maribel Rios
(March 2008)**

Chemical imaging of solid dosage forms has become a powerful analytical tool for the development of solid dosage forms.

**Pharmaceutical Technology's
Equipment and Machinery
Trends Survey**

**By Patricia Van Arnum
(March 2008)**

The pharmaceutical industry plans moderate increases in spending for equipment and machinery in 2008. Investments include equipment for solid-dosage manufacturing, active pharmaceutical ingredients, and parenteral manufacturing.

**Innovation in Equipment
and Machinery**

**By Patricia Van Arnum
(March 2008)**

Results from *Pharmaceuti-*

cal Technology's Equipment and Machinery Trends survey and industry members provide insight into product innovation.

**Clearing the Air
on Residual Solvents**

**By Maribel Rios
(February 2008)**

USP 467 Residual Solvents will take effect on July 1, 2008. But does the industry understand these specifications—and is it prepared?

**Outsourcing Clinical-Trial
Materials Heats Up**

**By Erik Greb
(January 2008)**

The outsourcing of clinical-trial materials grows as pharmaceutical companies adapt to a changing market.

**Manufacturing Investment
in Puerto Rico**

**By Patricia Van Arnum
(January 2008)**

Puerto Rico seeks to build its standing in biopharmaceutical manufacturing and research as it retains its role in bulk pharmaceutical and dosage manufacturing for small molecules.

**Pharmaceutical Technology's
Annual Employment Survey**

**By Maribel Rios
(December 2008)**

Nearly 1300 pharmaceutical employees provide insights into the issues most relevant to their jobs and the state of the industry workforce today.

**30 Years Hence: It Won't Be
Your Parents' Pharmaceutical
Industry**

**By Michelle Hoffman
(December 2008)**

What, we asked, will the

pharmaceutical industry look like in 2037 when *Pharmaceutical Technology* celebrates its 60th anniversary? Featuring industry experts' predictions in: Strategy and Regulation (Maribel Rios, Jill Wechsler), Outsourcing (Jim Miller), Solid-Dosage, (Robin Bogner), Ingredients (Richard Pederson), Formulation (Stuart Porter), Drug Delivery (Mansoor M. Amiji), Packaging (Hallie Forcinio), Analytical Testing (Maribel Rios), and Information Technology (Herschel Kenney).

**Programming a Seamless
Supply Chain**

**By Michelle Hoffman
(November 2007)**

Information technology is the glue that should unify a company while ironically, it enables further fragmentation. Experts talk about the successes and challenges for IT in helping a company function efficiently.

**Advances in
Transdermal Technologies**

**By Maribel Rios
(October 2007)**

Transdermal delivery takes up once-forbidden compounds, reviving markets and creating formulation opportunities.

**ICH Q10: A Recipe for
the Product Life Cycle**

**By Patricia Van Arnum
(September 2007)**

The draft guidance ICH Q10 for pharmaceutical quality systems is part of the ongoing move to a science- and risk-based approach in manufacturing.

**Preparing for FDA Inspections
in a Changing Regulatory
Environment**

**By Angie Drakulich,
Maribel Rios (August 2007)**

Industry and regulatory experts provide advice on inspection preparation and best practices.

**30 Years of Pharmaceutical
Technology & What Lies
Ahead (July 2007)**

A 30th-anniversary special edition, including a review of advancements in the following areas:

- Three Decades of Drug Regulation and Legislation (Jill Wechsler)
- The Evolution of FDA's Role in Ensuring Product Quality (Rakhi B. Shah, Mansoor A. Khan)
- A New Manufacturing Framework (Maribel Rios)
- Charting Process Improvement in Sterile Product Manufacturing (James E. Akers)
- A Look at 30 Years of Change in Pharmaceutical Automation (Bob Lenich, Christie Deitz)
- A Perspective on Computer Validation (Rory Budihandojo, Steve Coates, Ludwig Huber, Jose E. Matos, Siegfried Schmitt, David Stokes, Graham Tinsley, Maribel Rios)
- Contaminated LVPs and the Origins of Validation (William Garvey)
- Innovations Enable Packaging to Play Many Roles (Hallie Forcinio)
- Injectable Administration Systems (Frances DeGrazio)
- Statistical Implications of the CGMPs: A 30-Year Retrospective (Lynn D. Torbeck)

**Pharmaceutical Technology's
Manufacturers' Rankings**By Erik Greb,
Patricia Van Arnum
(June 2007)

Pharmaceutical Technology's Annual Manufacturers' Rankings provides perspectives on revenues, product positioning, R&D spending, pharmaceutical manufacturing activity, and capital projects of the major drug companies.

**Building Monoclonal
Antibody Production**By Patricia Van Arnum
(June 2007)

Pharma companies and CMOs build positions in mAbs.

**PHARMACEUTICAL
INGREDIENTS
REPORTS**

By Patricia Van Arnum

**Antibody Drug Conjugates: A
Marriage of Biologics and
Small Molecules**
(June 2008)

Antibody drug conjugates offer a niche opportunity for drug development and contract manufacturing.

**Unfolding Catalytic
Routes to APIs**
(May 2008)

Chemocatalytic and biocatalytic routes show promise for more efficient syntheses of select active ingredients.

**Measuring Excipient-Market
Growth (April 2008)**

Moderate growth is projected for the global excipients market. Excipient producers target blends and new grades for im-

proving functionality and performance.

**A Changing Path in Global
Sourcing**
(March 2008)

The European Union's REACH initiative has the potential to affect the flow of chemicals into the pharmaceutical supply chain.

**Charting Dosage-Form
Manufacturing**
(February 2008)

Contract manufacturers expand capabilities in aseptic processing, clinical-trial materials supply, and cytotoxic manufacturing.

Custom Synthesis of APIs
(January 2008)

Researchers and process chemists share approaches in synthesis of active ingredients and pharmaceutical intermediates.

**CMOs Expand Biologics
Manufacturing**
(December 2007)

A surge in capacity in contract microbial and mammalian cell-culture is underway to meet rising production needs for biopharmaceuticals.

**Investing in High-Potency
Manufacturing**
(November 2007)

Market demand for cytotoxic drugs is leading CMOs to expand their API manufacturing and formulation services.

Advancing ODT Technology
(October 2007)

Orally disintegrating tablets (ODTs) continue to attract attention as an alternative to conventional oral dosage forms.

**Advances in Asymmetric
Synthesis**
(September 2007)

Researchers forward approaches for catalytic hydroformylation, asymmetric hydrogenation, and biocatalysis to achieve enantioselectivity.

**Favorable Outlook for
Generic APIs**
(August 2007)

A spate of drugs are scheduled to come off patent, offering vast potential and competition.

**Improving Routes in
API Manufacturing**
(July 2007)

Catalytic routes to producing atorvastatin and sitagliptin are recent advancements.

**Nanotechnology Advances in
Drug Delivery**
(June 2007)

Nanotechnology is emerging as a tool for resolving challenges in delivering poorly water soluble and highly potent drugs.

SUPPLEMENTS

To view *Pharmaceutical Technology's* supplements, please visit pharmtech.com and click on "The Magazine."

- Tableting and Granulation (May 2008)
- Drug-Delivery (April 2008)
- Information Technology (November 2007)
- Pharmaceutical Chromatography (October 2007)
- Pharmaceutical Ingredients (September 2007)

COLUMNS

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