

Hot Articles

“January|2017”

Health Science



Title: [Prolonged-release minitablets with carbamazepine – preliminary observations in vitro](#)

Author: Magdalena Dzajkowska, Kotlowska Hanna, Madanecka Anna, Szczepanska Maja, Doniza Dagmara, Sosnowicz Anna and Sznitowska Malgorzata

Journal: Journal of Pharmacy and Pharmacology

Early View: Version of Record online: 20 DEC 2016

Doi: 10.1111/jphp.12670

Abstract

Objective

The aim was to develop prolonged-release minitablets (MT) with carbamazepine (CBZ).

Methods

Matrix-type 3-mm MT (5 mg CBZ) were prepared by direct compression using hydrophilic (hypromellose) or hydrophobic polymers (ethylcellulose, Kollidon SR, glyceryl behenate). Coated prolonged-release MT (2.5 mm/3 mg of CBZ) were produced using ethylcellulose or Eudragit RL/RS. The release tests were performed in a basket apparatus with water or 1% sodium lauryl sulphate solution as dissolution media.

Key findings

High-viscosity hypromellose used as a matrix polymer resulted in slow release of CBZ (80% released during 12 h). Dissolution was slower from hydrophobic matrices. Non-swelling MT cores were successfully coated with Eudragit RL/RS, which resulted in the prolonged release of CBZ (80%/14 h), depending on the film thickness and Eudragit composition. Careful choice of pore formers in the coating film allowed to reduce lag time. Ethylcellulose was unsuitable as coating polymer due to low permeability to CBZ and unsatisfying mechanical resistance of the films modified with hypromellose.

Conclusion

Prolonged release of CBZ was obtained from both matrix-type and coated MT. Further development of MT as a single unit or multicompartement prolonged-release new dosage form especially suitable for children has been justified.

Database

Wiley Online Library

Title: [Efficacy of a novel iPod-based navigation system compared to traditional navigation system in total knee arthroplasty](#)

Author: Arun B. Mullaji FRCSed, MCh, MS Orth & Gautam M. Shetty MS Orth

Journal: Computer Assisted Surgery

Posted online: 26 Dec 2016 (Pages 1-13)

Doi: 10.1080/24699322.2016.1276630

Abstract

Background: This prospective study aimed to verify the efficacy of a novel, hand-held, iPod-based navigation system in comparison to traditional navigation system for total knee arthroplasty (TKA).

Methods: Limb alignment, tibial and distal femoral bone cut thickness and plane were recorded intraoperatively using both iPod-based and traditional navigation system in 36 knees undergoing primary TKAs.

Results: Intraoperatively, the iPod-based navigation system showed good to excellent correlation and reliability for tibial and distal femoral bone cut thickness, plane of the femoral cut and limb alignment when compared to the traditional navigation system.

Conclusions: Despite its quick registration feature, the iPod-based system has an efficacy similar to traditional navigation system and is a positive step towards making navigation systems for TKA more compact, user-friendly, time and cost-effective.

Database

Taylor & Francis Online

Title: [Microbiome, Growth Retardation, and Metabolism: Are they related?](#)
Author: Daniel J. Hoffman, Maiza Campos Ponce, Carla R. Taddei & Colleen M
Journal: Annals of Human Biology
Posted online: 07 Dec 2016 (Pages 1-19)
Doi: 10.1080/03014460.2016.1267261

Abstract

The prevalence of undernutrition has decreased in many parts of the developing world, but increased urbanization in many countries, combined with broad changes in diet, have provided a backdrop against which many challenges to human growth continue. Moreover, a number of studies now suggest that poor diet and growth in early childhood are risk factors for chronic diseases in adulthood. However, such problems appear to continue despite an improvement in food security or the delivery of nutritional supplements to children living in impoverished areas of urban centers. One area of research that has only recently begun to receive attention is the role of the microbiome as a critical factor in the transport and absorption of nutrients from food. Given that the microbiome has great potential to disrupt nutrient absorption, regardless of the amount or types of foods consumed, it very well may be central in limiting or modifying normal growth processes. Therefore, the focus of this review paper is to describe normal growth processes, the role of the microbiome in supporting or disrupting normal growth processes, and the potential impact on long-term health.

Database

Taylor & Francis Online

Title: [Inflammation and beyond: new directions and emerging drugs for treating atherosclerosis](#)
Author: Marie-Jeanne Bertrand & Jean-Claude Tardif
Journal: Expert Opinion on Emerging Drugs
Published online: 22 Dec 2016 (Pages 1-26)
Doi: 10.1080/14728214.2017.1269743

Abstract

Introduction: Cardiovascular (CV) atherosclerotic disease remains the leading cause of morbidity and mortality worldwide, despite the advances in contemporary therapies. Inflammation is an important process in atherosclerosis, leading to plaque rupture and acute coronary syndrome. Although statin therapy has substantially reduced CV events in primary and secondary prevention, many treated patients will have recurrent adverse CV events despite the standard of care. Thus, drug development aiming to target inflammatory pathways seems a promising avenue for novel therapies in atherosclerosis.

Areas covered: Statins have been extensively studied and are the most effective lipid-lowering drugs available for CV prevention. Novel anti-inflammatory drugs are being tested in Phase II and III trials, targeting pathways like interleukin-1, leukotrienes, TNF- α , P-selectin, CCL2-CCR2 and MAP Kinase.

Expert opinion: Novel anti-inflammatory therapies seem promising additions to address the residual CV risk present despite the current standard of care, but large clinical trials have not yet shown beneficial effects on clinical events. PCSK9 inhibitors have been shown to substantially reduce LDL-C, however their long-term safety and effects on CV risk are currently being investigated. Pharmacogenomics holds great potential in future lipid trials, enabling the identification of patients who will respond with greater benefits and smaller risk to therapies and to decrease failure rates in drug development, as genotype-dependent effects of the CETP inhibitor dalcetrapib were shown in the dal-OUTCOMES and dal-PLAQUE-2 trials.

Database

Taylor & Francis Online

Title: [Tanezumab in the treatment of chronic musculoskeletal conditions](#)

Author: Prakash Jayabalan & Thomas J Schnitzer

Journal: Expert Opinion on Biological Therapy

**Published
online:** 25 Dec 2016 (Pages 1-10)

Doi: 10.1080/14712598.2017.1271873

Abstract

Introduction: The management of pain associated with chronic musculoskeletal conditions represents a significant challenge for the clinician. There remains a need for novel medications that have a significant analgesic benefit and are also safe and well tolerated. Both pre-clinical and clinical data have provided evidence of the role of nerve growth factor (NGF) in a multitude of pain eliciting conditions. Therefore, the development of monoclonal antibodies to NGF for chronic painful musculoskeletal conditions has generated interest.

Areas covered: This manuscript is a review that examines both the pharmacological properties and clinical studies of tanezumab, the most widely studied antibody to NGF, for management of osteoarthritis (OA) and low back pain. In addition, the safety and tolerability profile and development history of tanezumab are also discussed.

Expert opinion: Most studies provide strong support for the ability of tanezumab to provide clinically meaningful pain relief in individuals with these conditions, with longer-term studies suggesting durability of effect. The adverse event profile appears favorable, assuming the risk mitigation strategies are effective at reducing the incidence of joint-related side effects. Further data are being collected to define the optimal dose and dosing strategy in both OA and chronic low back pain.

Database

Taylor & Francis Online

Title: [Post-marketing withdrawal of anti-obesity medicinal products because of adverse drug reactions: a systematic review](#)

Author: Igho J. Onakpoya, Carl J. Heneghan and Jeffrey K. Aronson

Journal: BMC Medicine 2016, 14:191

Volume: 14 **Issue:** 1 **Page:** 191 (Year 2016)

Doi: 10.1186/s12916-016-0735-y

Abstract

Background

We identified anti-obesity medications withdrawn since 1950 because of adverse drug reactions after regulatory approval, and examined the evidence used to support such withdrawals, investigated the mechanisms of the adverse reactions, and explored the trends over time.

Methods

We conducted searches in PubMed, the World Health Organization database of drugs, the websites of drug regulatory authorities, and selected full texts, and we hand searched references in retrieved documents. We included anti-obesity medications that were withdrawn between 1950 and December 2015 and assessed the levels of evidence used for making withdrawal decisions using the Oxford Centre for Evidence-Based Medicine criteria.

Results

We identified 25 anti-obesity medications withdrawn between 1964 and 2009; 23 of these were centrally acting, via monoamine neurotransmitters. Case reports were cited as evidence for withdrawal in 80% of instances. Psychiatric disturbances, cardiotoxicity (mainly attributable to re-uptake inhibitors), and drug abuse or dependence (mainly attributable to neurotransmitter releasing agents) together accounted for 83% of withdrawals. Deaths were reportedly associated with seven products (28%). In almost half of the cases, the withdrawals occurred within 2 years of the first report of an adverse reaction.

Conclusions

Most of the drugs that affect monoamine neurotransmitters licensed for the treatment of obesity over the past 65 years have been withdrawn because of adverse reactions. The reasons for withdrawal raise concerns about the wisdom of using pharmacological agents that target monoamine neurotransmitters in managing obesity. Greater transparency in the assessment of harms from anti-obesity medications is therefore warranted.

Database

Biomed Central

Title: [You have full text access to this contentCurcumin as a Potential Candidate for Treating Hyperlipidemia: A Review of Cellular and Metabolic Mechanisms](#)

Author: Yunes Panahi, Yasin Ahmadi, Manouchehr Teymouri, Thomas P. Johnston, Amirhossein Sahebkar

Journal: Journal of Cellular Physiology

Accepted online: 24 December 2016

Doi: 10.1002/jcp.25756

Abstract

Curcumin is an herbal polyphenol extensively investigated for antioxidant, anti-inflammatory and hypolipidaemic properties. In the present review, the efficacy of curcumin for improving a plasma lipid profile has been evaluated and compared with statins, a well-known class of medicines for treating hypercholesterolemia and hyperlipidaemia. Curcumin is presumably most effective in reducing triglyceride (TG), while statins are most efficient in lowering low-density lipoproteins-cholesterol (LDL-C). Additionally, various molecular and metabolic mediators of cholesterol and plasma lipid homeostasis are discussed in relation to how they are modulated by curcumin or statins. Overall, curcumin influences the same mediators of plasma lipid alteration as statins do. Almost all the pathways through which cholesterol trafficking takes place are affected by these agents. These include gastrointestinal absorption of dietary cholesterol, hepatocellular removal of plasma cholesterol, the mediators of reverse cholesterol transport and removal of cholesterol from peripheral tissues. Moreover, the reactive oxygen species (ROS) scavenging potential of curcumin limits the risk of lipid peroxidation that triggers inflammatory responses causing cardiovascular diseases (CVD) and atherosclerosis. Taken together, curcumin could be used as a safe and well-tolerated adjunct to statins to control hyperlipidaemia more effectively than statins alone. This article is protected by copyright. All rights reserved

Database

Wiley Online Library

Title: [Diverse Functions and Signal Transduction of the Exocyst Complex in Tumor Cells](#)
Author: Toshiaki Tanaka, Kaoru Goto and Mitsuyoshi Iino
Journal: Journal of Cellular Physiology
**Record
online:** 22 DEC 2016
Doi: 10.1002/jcp.25619

Abstract

The exocyst complex is a large conserved hetero-oligomeric complex that consists of Sec3, Sec5, Sec6, Sec8, Sec10, Sec15, Exo70, and Exo84 subunits. It has been implicated in the targeting of vesicles for regulated exocytosis in various cell types, and is also important for targeted exocytosis of post-Golgi transport vesicles to the plasma membrane. The exocyst complex is essential for membrane growth, secretion, and function during exocytosis and endocytosis. Moreover, the individual components of the complex are thought to act on specific biological processes, such as cytokinesis, ciliogenesis, apoptosis, autophagy, and epithelial-mesenchymal transition (EMT). As a result, recent studies suggest that the exocyst complex may be involved in several diseases such as kidney disease, neuropathogenesis, diabetes, and cancer. In this review, we focus on the diverse functions and cellular signaling pathways of the exocyst complex in various tumors.

Database

Wiley Online Library

Title: [Accuracy of tablet splitting and liquid measurements: an examination of who, what and how](#)
Author: Dana Abu-Geras, Dunja Hadziomerovic, Andrew Leau, Ramzan Nazim Khan, Sajni Gudka, Cornelia Locher, Maryam Razaghikashani and Lee Yong Lim
Journal: Journal of Pharmacy and Pharmacology
Record online: 28 DEC 2016
Doi: 10.1111/jphp.12671

Abstract

Objective

To examine factors that might affect the ability of patients to accurately halve tablets or measure a 5-ml liquid dose.

Methods

Eighty-eight participants split four different placebo tablets by hand and using a tablet splitter, while 85 participants measured 5 ml of water, 0.5% methylcellulose (MC) and 1% MC using a syringe and dosing cup. Accuracy of manipulation was determined by mass measurements.

Key findings

The general population was less able than pharmacy students to break tablets into equal parts, although age, gender and prior experience were insignificant factors. Greater accuracy of tablet halving was observed with tablet splitter, with scored tablets split more equally than unscored tablets. Tablet size did not affect the accuracy of splitting. However, >25% of small scored tablets failed to be split by hand, and 41% of large unscored tablets were split into >2 portions in the tablet splitter. In liquid measurement, the syringe provided more accurate volume measurements than the dosing cup, with higher accuracy observed for the more viscous MC solutions than water.

Conclusion

Formulation characteristics and manipulation technique have greater influences on the accuracy of medication modification and should be considered in off-label drug use in vulnerable populations.

Database

Wiley Online Library

Title: [The Value of MRI and Clinical Features in Differentiating Between Cellular and Fibrous Solitary Fibrous Tumors](#)
Author: Shuji Nagata, Hiroshi Nishimura, Kimberly K. Amrami, Jun Akiba, Tatsuyuki Tonan, Kiminori Fujimoto, Toshi Abe
Journal: American Journal of Roentgenology
Volume: 208 **Issue:** 1 **Page:** 10-17 (Year 2017)
Doi: 10.2214/AJR.16.16423

Abstract

OBJECTIVE. The purpose of this study is to evaluate the usefulness of MRI in differentiating between fibrous and cellular solitary fibrous tumors (SFTs).

MATERIALS AND METHODS. This retrospective study included 17 patients with histopathologically confirmed SFTs, including 10 patients with fibrous SFTs and seven patients with cellular SFTs. We evaluated the differences between fibrous and cellular SFTs with regard to clinical data and MRI findings, such as tumor margin definition, signal intensity, heterogeneity on T1- and T2-weighted images, presence of capsules, intratumoral cystic changes, flow signal void, perilesional edema, enhancement pattern on dynamic contrast-enhanced MRI (DCE-MRI), and mean apparent diffusion coefficient (ADC) values.

RESULTS. Statistically significant differences in fibrous and cellular SFTs were noted with respect to signal intensity on T2-weighted images ($p = 0.044$, by Fisher exact test) and enhancement patterns on DCE-MRI ($p = 0.005$, by Fisher exact test). Specifically, on T2-weighted images, five of the fibrous SFTs had high signal intensity, and the other five had signal isointensity, whereas all seven cellular SFTs had high signal intensity. On DCE-MRI, fibrous SFTs tended to show a gradual increase in enhancement, whereas cellular SFTs showed a rapid initial enhancement pattern. The mean (\pm SD) ADC value for cellular SFTs was $1.39 \pm 0.35 \times 10^{-3}$ mm²/s, whereas that for fibrous SFTs was $1.37 \pm 0.48 \times 10^{-3}$ mm²/s, with no statistically significant difference noted between the two ($p = 0.755$, by Fisher exact test).

CONCLUSION. Fibrous SFTs have nonspecific findings with regard to signal intensity on T2-weighted MR images and enhancement patterns on DCE-MRI, whereas cellular SFTs show high signal intensity on T2-weighted images and rapid initial enhancement on DCE-MRI.

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