บทความที่น่าสนใจประจำเดือน พฤษภาคม 2557

Title :	Characterization of New Specific Copper Chelators as Potential Drugs for the Treatment of Alzheimer's Disease
Author :	Dr. Michel Nguyen, Dr. Anne Robert, Dr. Alix Sournia-Saquet, Dr. Laure Vendier and Dr. Bernard Meunier
Journal :	Chemistry - A European Journal: Article first published online: 5 MAY 2014 DOI: 10.1002/chem.201402143
Abstract :	The non-controlled redox-active metal ions, especially copper, in the brain of patients with Alzheimer disease (AD) should be considered at the origin of the intense oxidative damage in the AD brain. Several bis(8-aminoquinoline) ligands, such as 1 and PA1637, are able to chelate Cu2+ with high affinity, and are specific chelators of copper with respect to iron and zinc. They are able to efficiently extract Cu2+ from a metal-loaded amyloid. In addition, these tetradentate ligands are specific for the chelation of Cu2+ compared with Cu+. Consequently, the copper ion is easily released from the bis(8-aminoquinoline) ligand under reductive conditions, and can be trapped again by a protein having some affinity for copper such as human serum albumin (HSA) proteins. In addition, the copper is not efficiently released from [Cu(CQ)2] in reductive conditions. The catalytic production of H2O2 by [Cu2+-Aβ1−28]/ascorbate is inhibited in vitro by the bis(8-aminoquinoline) 1, suggesting that 1 should be able to play a protective role against oxidative damages induced by copper-loaded amyloids.
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Title :	Effect of Different "States" of Sorbed Water on Amorphous Celecoxib
Author :	Ganesh Shete, Swathi Kuncham, Vibha Puri, Rahul P. Gangwal, Abhay T. Sangamwar and Arvind Kumar Bansal
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 6 MAY 2014 DOI: 10.1002/jps.23999
Abstract :	Glass transition temperature (Tg) of an amorphous drug is a vital physical phenomenon that influences its visco-elastic properties, physical, and chemical stability. Water acts as a plasticizer for amorphous drugs thus increasing their recrystallization kinetics. This reduces the solubility advantage of an amorphous drug. Hence, there is an interest in understanding the relationship between water content and Tg of amorphous drug. We have studied the effect of "state" of sorbed water on Tg of amorphous celecoxib (ACLB). ACLB was allowed to sorb water at relative humidity of 33%, 53%, 75%, and 93%. ALCB showed biphasic sorption of water designated as "bound" and "solvent-like" state of water associated with ACLB. Molecular modeling studies provided deeper insights into the interaction of water with ACLB. A distinct co-relationship between the state of water and its plasticization capacity was observed. Bound state of water had a very profound effect on the fall in experimentally observed Tg (Tg-exp) value. Solvent-like state of water had little impact on Tg-exp value. Tg of ACLB–water mixture was predicted by Gordon–Taylor equation (Tg-pre). The deviations in Tg-exp and Tg-pre were correlated to volume non-additivity and non-ideal mixing. This study has implications on the development of formulations based on amorphous forms.
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Title :	Can CAM treatments be evidence-based?
Author :	Pekka Louhiala and Harri Hemil
Journal :	Focus on Alternative and Complementary Therapies : Article first published online: 2 MAY 2014 DOI: 10.1111/fct.12110
Abstract :	In this article, we first take a critical look at the definitions of evidence-based medicine (EBM) and complementary and alternative medicine (CAM). We then explore the question of whether there can be evidence-based forms of CAM. With the help of three examples, we show that EBM and CAM are not opposites, but rather concepts pointing at different dimensions. Each of the three examples is an evidence-based treatment according to three to five randomised, double-blind placebo controlled trials with consistent findings and narrow pooled confidence intervals. The most reasonable interpretation for the existence of evidence-based CAM treatments seems to be that the opposite of CAM is 'mainstream medicine', and the demarcation line between CAM and mainstream medicine is not simply defined by the question of whether a treatment works or not. Some effective treatments may belong to the CAM domain for historical reasons and because of preconceptions within mainstream medicine. Therefore, some treatments that currently lie outside mainstream medicine can be evidence-based.
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Title :	Dual-Frequency Calcium-Responsive MRI Agents
Author :	Dr. Pascal Kadjane, Prof. Dr. Carlos Platas-Iglesias, Dr. Philipp Boehm-Sturm, Dr. Vincent Truffault, Dr. Gisela E. Hagberg, Prof. Dr. Mathias Hoehn, Prof. Dr. Nikos K. Logothetis and Priv.-Doz. Dr. Goran Angelovski
Journal :	Chemistry - A European Journal: Article first published online: 5 MAY 2014 DOI: 10.1002/chem.201400159
Abstract :	Responsive or smart magnetic resonance imaging (MRI) contrast agents are molecular sensors that alter the MRI signal upon changes in a particular parameter in their microenvironment. Consequently, they could be exploited for visualization of various biochemical events that take place at molecular and cellular levels. In this study, a set of dual-frequency calcium-responsive MRI agents are reported. These are paramagnetic, fluorine-containing complexes that produce remarkably high MRI signal changes at the 1H and 19F frequencies at varying Ca2+ concentrations. The nature of the processes triggered by Ca2+ was revealed, allowing a better understanding of these complex systems and their further improvement. The findings indicate that these double-frequency tracers hold great promise for development of novel functional MRI methods.
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Title :	The Role of Payload Hydrophobicity in Nanotherapeutic Pharmacokinetics
Author :	Povilas Norvaisas and Arturas Ziemys
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 6 MAY 2014 DOI: 10.1002/jps.23996
Abstract :	Although drug delivery with nanovectors is regarded as one of the paradigm-

	shifting advances in modern medicine, the compatibility and performance of drug–vector formulations have not been systematically studied in terms of their physicochemistry and pharmacokinetics (PKs). The drug delivery systems (DDSs), currently available in clinics or trials, were analyzed based on hydrophobicity and anatomical therapeutic chemical (ATC) classification of drug payloads. Four major types of DDSs differentiated based on DDS structure and drug hydrophobicity, where payload hydrophobicity decreased: micelles, serum albumin, liposome membrane, and liposome interior. A strong relationship between the increase in half-life in DDS formulation and drug hydrophobicity was found with up to 200-fold greater increase for hydrophilic drugs. The analysis results seemingly integrated PKs, ATC, and hydrophobicity to reinforce the development or optimization of drug delivery vectors and their formulations.
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Title :	What Is the Mechanism Behind Increased Permeation Rate of a Poorly Soluble Drug from Aqueous Dispersions of an Amorphous Solid Dispersion?
Author :	Kerstin J. Frank, Ulrich Westedt, Karin M. Rosenblatt, Peter Hölig, Jörg Rosenberg, Markus Magerlein, Gert Fricker and Martin Brandl
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 24 APR 2014 DOI: 10.1002/jps.23979
Abstract :	Our aim was to explore the influence of micelles and microparticles emerging in aqueous dispersions of amorphous solid dispersions (ASDs) on molecular/apparent solubility and Caco-2 permeation. The ASD, prepared by hot-melt extrusion, contained the poorly soluble model drug ABT-102, a hydrophilic polymer, and three surfactants. Aqueous dispersions of the ASD were investigated at two concentrations, one above and one close to the critical micelle concentration of the surfactants blend in the extrudate. Micelles were detected at the higher concentration and no micelles at the lower concentration. Apparent solubility of ABT-102 was 20-fold higher in concentrated than in diluted dispersions, because of micelles. In contrast, Caco-2 permeation of ABT-102 was independent of the ASD concentration, but three times faster than that of crystalline suspensions. Molecular solubility of ABT-102 (equilibrium dialysis) was also independent of the ASD concentration, but by a factor 2 higher than crystalline ABT-102. The total amount of ABT-102 accumulated in the acceptor during Caco-2 experiments exceeded the initial amount of molecularly dissolved drug in the donor. This may indicate that dissolution of amorphous microparticles present in aqueous dispersions induces lasting supersaturation maintaining enhanced permeation. The hypothesis is supported by a slower drug permeation when the microparticles were removed.
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Title :	An exploration of Australian hospital pharmacists' attitudes to patient safety
Author :	Daniel J. Lalor, Timothy F. Chen, Ramesh Walpola, Rachel A. George, Darren M. Ashcroft3 and Romano A. Fois
Journal :	International Journal of Pharmacy Practice: Article first published online: 28 APR 2014 DOI: 10.1111/ijpp.12115
Abstract :	Objectives

	To explore the attitudes of Australian hospital pharmacists towards patient safety in their work settings. Methods A safety climate questionnaire was administered to all 2347 active members of the Society of Hospital Pharmacists of Australia in 2010. Part of the survey elicited free-text comments about patient safety, error and incident reporting. The comments were subjected to thematic analysis to determine the attitudes held by respondents in relation to patient safety and its quality management in their work settings. Key findings Two hundred and ten (210) of 643 survey respondents provided comments on safety and quality issues related to their work settings. The responses contained a number of dominant themes including issues of workforce and working conditions, incident reporting systems, the response when errors occur, the presence or absence of a blame culture, hospital management support for safety initiatives, openness about errors and the value of teamwork. A number of pharmacists described the development of a mature patient-safety culture – one that is open about reporting errors and active in reducing their occurrence. Others described work settings in which a culture of blame persists, stifling error reporting and ultimately compromising patient safety. Conclusion Australian hospital pharmacists hold a variety of attitudes that reflect diverse workplace cultures towards patient safety, error and incident reporting. This study has provided an insight into these attitudes and the actions that are needed to improve the patient-safety culture within Australian hospital pharmacy work settings.
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Title :	In-vitro/in-vivo characterization of trans-resveratrol-loaded nanoparticulate drug delivery system for oral administration
Author :	Gurinder Singh and Roopa S. Pai
Journal :	Journal of Pharmacy and Pharmacology : Article first published online: 30 APR 2014 | DOI: 10.1111/jphp.12232
Abstract :	Objectives The current studies entail successful formulation of systematically optimized (OPT) nanoparticulate drug delivery system to increase the oral bioavailability using Eudragit RL 100 of trans-resveratrol (t-RVT), and evaluate their in-vitro/in-vivo performance. Methods t-RVT-loaded Eudragit RL 100 nanoparticles (t-RVT NPs) were prepared by nanoprecipitation method. The nanoparticles (NPs) were systematically optimized using 32 central composite design and the OPT formulation located using overlay plot. The pharmacokinetic and in-vivo biodistribution of t-RVT NPs were investigated in rats, and various levels of in-vitro/in-vivo correlation (IVIVC) were established. Key findings The OPT formulation (mean particle size: 180 nm) indicated marked improvement

	in drug release profile vis-à-vis pure drug and marketed formulation (MKT). Augmentation in the values of Ka (5.64-fold) and AUC0–24 (7.25-fold) indicated significant enhancement in the rate and extent of bioavailability by the optimized trans-resveratrol-loaded Eudragit RL 100 nanoparticles (OPT-t-RVT NPs) compared with pure drug. Level A of IVIVC was successfully established. OPT-t-RVT NPs showed 4.11-fold rose in the values of t-RVT concentrations in liver. In-situ single pass intestinal perfusion studies construed remarkable enhancement in the absorptivity and permeability parameters of OPT-t-RVT NPs. Conclusions The results, therefore, insight into the role of solubility enhancement and trounce enterohepatic recirculation for improving the oral bioavailability of t-RVT.
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Title :	Big Data Bioinformatics
Author :	Casey S. Greene, Jie Tan, Matthew Ung, Jason H. Moore and Chao Cheng
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 6 MAY 2014 05:18 AM EST | DOI: 10.1002/jcp.24662
Abstract :	Recent technological advances allow for high throughput profiling of biological systems in a cost-efficient manner. The low cost of data generation is leading us to the "big data" era. The availability of big data provides unprecedented opportunities, but it also brings out challenges in data mining and analysis. In this review, we introduce key concepts in the analysis of big data, including both "machine learning" algorithms as well as "unsupervised" and "supervised" examples of each. We note packages for the R programming language that are available perform machine learning analyses. In addition to programming based solutions, we review webservers that allow users with limited or no programming background to perform these analyses on large data compendia.
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Title :	S-allylcysteine prevents cisplatin-induced nephrotoxicity and oxidative stress
Author :	Tania Gómez-Sierra, Eduardo Molina-Jijón, Edilia Tapia, Rogelio Hernández-Pando, Wylly Ramsés García-Niño, Perla D. Maldonado, José Luis Reyes, Diana Barrera-Oviedo, Ismael Torres and José Pedraza-Chaverri
Journal :	Journal of Pharmacy and Pharmacology: Article first published online: 29 APR 2014 | DOI: 10.1111/jphp.12263
Abstract :	Objectives Cisplatin (CP) is an antineoplastic agent that induces nephrotoxicity and oxidative stress. S-allylcysteine (SAC) is a garlic-derived antioxidant. This study aims to explore whether SAC protects against CP-induced nephrotoxicity in rats. Methods In the first stage, the SAC protective dose was determined by measuring renal damage and the oxidative stress markers malondialdehyde, oxidized proteins and glutathione in rats injected with CP. In the second stage, the effect of a single dose of SAC on the expression of nuclear factor-erythroid 2-related factor-2 (Nrf2), protein kinase C beta 2 (PKCβ2) and nicotinamide adenine dinucleotide phosphate oxidase subunits (p47phox and gp91phox) was studied. In addition,

	the effect of SAC on oxidative stress markers and on the activity of catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) in isolated proximal and distal tubules were evaluated. Key findings SAC (25 mg/kg) prevented the CP-induced renal damage and attenuated CP-induced decrease in Nrf2 levels and increase in PKCβ2, p47phox and gp91phox expression in renal cortex and oxidative stress and decrease in the activity of CAT, GPx and GR in proximal and distal tubules. Conclusions These data suggest that SAC provides renoprotection by attenuating CP-induced oxidative stress and decrease in the activity of CAT, GPx and GR.
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