

บทความที่น่าสนใจประจำเดือน กรกฎาคม 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	Intranasal Piperine-Loaded Chitosan Nanoparticles as Brain-Targeted Therapy in Alzheimer's Disease: Optimization, Biological Efficacy, and Potential Toxicity
Author :	Yosra S. R. Elnaggar, Samar M. Etman, Doaa A. Abdelmonsif and Ossama Y. Abdallah
Journal :	Journal of Pharmaceutical Sciences: Article first published online, 3 JUL 2015 DOI: 10.1002/jps.24557
Abstract :	<p>Piperine (PIP) is a phytopharmaceutical with reported neuroprotective potential in Alzheimer's disease (AD). Oral PIP delivery suffers from its hydrophobicity and pre-systemic metabolism. In this article, mono-disperse intranasal chitosan nanoparticles (CS-NPs) were elaborated for brain targeting of PIP. Formula optimization was based on particle size (PS), zeta potential (ZP), polydispersity index (PDI), % entrapment efficiency (% EE), release studies, and transmission electron microscopy. AD was induced in 48 male Wistar rats on which full behavioral and biochemical testing was conducted. Brain toxicity was assessed based on Caspase-3 assay for apoptosis and tumor necrosis factor for inflammation. Spherical NPs with optimum % EE (81.70), PS (248.50 nm), PDI (0.24), and ZP (+56.30 mV) were elaborated. PIP-NPs could significantly improve cognitive functions as efficient as standard drug (donepezil injection) with additional advantages of dual mechanism (ACh esterase inhibition and antioxidant effect). CS-NPs could significantly alleviate PIP nasal irritation and showed no brain toxicity. This work was the first to report additional mechanism of PIP in AD via anti-apoptosis and anti-inflammatory effects. To conclude, mucoadhesive CS-NPs were successfully tailored for effective, safe, and non-invasive PIP delivery with 20-folds decrease in oral dose, opening a gate for a future with lower AD morbidity.</p>
Database :	Wiley Online Library

Title :	Reducing unacceptable missed doses: pharmacy assistant-supported medicine administration
Author :	Wasim Baqir, Kate Jones, William Horsley, Scott Barrett, David Fisher, Richard Copeland, David Campbell and Rosemary Stephenson
Journal :	International Journal of Pharmacy Practice: Article first published online, 28 JAN 2015 DOI: 10.1111/ijpp.12172
Abstract :	<p>Objectives</p> <p>The potential harm from omitted and delayed medicines for hospital inpatients was highlighted by the National Patient Safety Agency (NPSA). Despite evidence of omitted doses, few interventional studies have been reported on preventing the problem. This study aimed to assess the impact on omitted doses when medicine administration was supported by pharmacy assistants (PAs).</p> <p>Methods</p> <p>PAs were trained to support nurses on medicine administration rounds. Using stratified random sampling, two intervention and control wards were selected. Three study groups were defined: (A) intervention group (PA-supported medicine administration); (B) intra-ward control group; and (C) inter-ward control group. Primary outcome measure was number of patients with unacceptable omitted doses (UODs) in group A versus C. Secondary outcome measures were patients with critical UOD (cUOD), as defined by the NPSA, in groups A, B and C and UODs in group B versus A and C. Data were collected over 2 weeks (December 2011 and February 2012).</p> <p>Key findings</p> <p>Using aggregated data over 2 weeks, 778 patients were assessed; 308 were male (40%). The overall proportion of patients with ≥ 1 UOD was 12.4% (n = 96). The proportion of patients with ≥ 1 UOD was 1.1% (n = 2) in group A (intervention) and 18.5% (n = 68) in group C (control). There were significantly fewer patients with cUOD in group A (1.1%; n = 2) compared with group C (7.4%; n = 27).</p> <p>Conclusion</p>

	PA-supported medication rounds can significantly reduce the rate of omitted doses. This study provides evidence for a potential solution to the problem of omitted doses for hospital inpatients.
Database :	Wiley Online Library

Title :	The studies of N-Octyl-N-Arginine-Chitosan coated liposome as an oral delivery system of Cyclosporine A
Author :	Jin Deng, Zhenhai Zhang, Chunyan Liu, Lifang Yin, Jianping Zhou and Huixia Lv
Journal :	Journal of Pharmacy and Pharmacology: Article first published online, 23 JUN 2015 DOI: 10.1111/jphp.12448
Abstract :	<p>Objectives</p> <p>An amphiphilic polymer N-Octyl-N-Arginine-Chitosan (OACS) was synthesized to coat the Cyclosporine A (CsA) liposomes (CL) to decrease the destruction of liposomes in gastrointestinal tract (GI) tract and improve its oral absorption.</p> <p>Methods</p> <p>CL and OACS-CsA liposomes (OACS-CL) were prepared by rotary-film evaporation method, and characterized by dynamic light scattering, transmission electron microscopy, atomic force microscope and releasing properties. In-situ single pass perfusion experiment and in-vivo studies in rats were carried out to verify its absorption enhancement.</p> <p>Key findings</p> <p>The characterization results showed that its particle size, zeta potential and morphology changed before and after polymer coating. Release experiment indicated that OACS could slow down drug release and protect its degradation in the stomach. In-situ single pass perfusion proved that the absorption of OACS-CL at the jejunum was enhanced about 3 and 22 times compared with commercial preparation of microemulsions (Tianke) and CsA suspensions, respectively. In vivo, $AUC_0 \rightarrow \infty$ of three different OACS-CL groups (93.48 ± 2.54, 100.98 ± 13.08 and 99.01 ± 19.02 h·μg/ml, respectively) were higher than those of</p>

	<p>Tianke ($69.34 \pm 7.93 \text{ h} \cdot \mu\text{g/ml}$), CL group ($54.31 \pm 6.70 \text{ h} \cdot \mu\text{g/ml}$) and suspensions ($31.14 \pm 1.30 \text{ h} \cdot \mu\text{g/ml}$).</p> <p>Conclusions</p> <p>Therefore, OACS coated liposomes can be an effective strategy to promote drug's absorption and further reduce the anaphylactic reaction of abundant surfactants in commercial preparations.</p>
Database :	Wiley Online Library

Title :	When Should Genome Researchers Disclose Misattributed Parentage?
Author :	Amulya Mandava, Joseph Millum and Benjamin E. Berkman
Journal :	Hastings Center Report: Volume 45, Issue 4, pages 28–36, July/August 2015
Abstract :	<p>As analytic tools for genomic sequencing improve, biomedical research will increasingly use this method to draw inferences based on comparisons between the genetic data of a set of individuals thought to be related to each other. Cases in which genomic sequencing will be very useful include those in which a child has a rare or undiagnosed disease that might have an underlying genetic etiology. Researchers will be able to sequence the pediatric proband and both parents to compare their genomes in hopes of finding novel variants that point toward a diagnosis and perhaps to treatment. However, researchers are sure to discover that, in a growing number of cases, the assumed biological relationships between the individuals do not actually exist. Consequently, they will have to grapple with decisions about whether to return incidental findings of misattributed genetic parentage on a much larger scale than ever before. While we make no normative claims about whether individuals ought to value genetic relationships, the disclosure of information about misattributed parentage has the potential to affect familial relationships and notions of personal identity in many ways. Researchers need a decision-making framework about disclosing this information that accounts for nonclinical factors alongside factors that the incidental findings literature already emphasizes as relevant.</p>

	<p>We argue that nondisclosure should be the default position for researchers. We begin by assessing the limited guidance that can be found in the literature on incidental research findings and on disclosure of misattributed parentage in the clinical setting. We then sketch the normative argument that underlies our position, providing a taxonomy of the possible harms and benefits of disclosure. We close by considering three objections: that nondisclosure may cause false beliefs in participants, that researchers may have relationships of trust with their participants that entail a duty to disclose, and that participant preferences should be solicited and followed. We close by suggesting ways in which the consent process could minimize possible harms related to nondisclosure.</p>
Database :	Wiley Online Library

Title :	Warfarin-drug interactions: An emphasis on influence of polypharmacy and high doses of amoxicillin/clavulanate
Author :	Mahmoud I. Abdel-Aziz, Mostafa A. Sayed Ali, Ayman K. M. Hassan and Tahani H. Elfaham
Journal :	The Journal of Clinical Pharmacology: Accepted manuscript online, 2 JUL 2015 05:48PM EST DOI: 10.1002/jcph.583
Abstract :	<p>The objective of this study was to investigate the effect of polypharmacy and high doses of amoxicillin/clavulanate on warfarin response in hospitalized patients.</p> <p>Prospective cross-sectional observational study on 120 patients started from July 2013 to January 2014. Potentially interacting drugs were classified according to their tendency of increasing INR or bleeding risk. 87.5% patients prescribed high dose amoxicillin/clavulanate (10-12 g daily) compared with 28.9% patients prescribed normal dose (up to 3.6 g daily) had INR values ≥ 4 during hospital stay ($p = <.001$). Increased number of potentially interacting drugs that are known to increase INR was a significant predictor of having INR values ≥ 4 (OR, 2.5 [95% CI, 1.3-4.7]) and increased number of potentially interacting drugs that are known to increase bleeding risk was a significant predictor of experiencing bleeding episodes (OR, 3.1 [95% CI, 1.3-7.3]).</p>

	<p>High doses of amoxicillin/clavulanate were associated with a higher risk of over anticoagulation when combined with warfarin than normal doses. Increased risk of having INRs ≥ 4 and bleeding events was associated with the increased numbers of potentially interacting drugs prescribed indicating that polypharmacy is a problem of concern. Frequent monitoring of warfarin therapy along with patient's medications is necessary to avoid complications.</p>
Database :	Wiley Online Library

Title :	Coenzyme Q10 in combination with triple therapy regimens ameliorates oxidative stress and lipid peroxidation in chronic gastritis associated with H. pylori infection
Author :	Asghar Rahmani, Ghobad Abangah, Atefeh Moradkhani, Mohammad Reza Hafezi Ahmadi and Khairollah Asadollahi
Journal :	The Journal of Clinical Pharmacology: Volume 55, Issue 8, pages 842–847, August 2015 \
Abstract :	<p>Chronic gastritis associated with H. pylori infection causes oxidative stress in the stomach. This study aimed to evaluate the therapeutic effects of coenzyme q10 among gastric patients infected by H. pylori. By a clinical trial, chronic gastric patients infected by H. pylori were randomly divided into 2 groups: intervention and placebo. The placebo group received a standard triple therapy regimen, and the intervention group received the triple regimen + coenzyme Q10 (CoQ10). Mean inflammation score; serum levels of 3 serum markers were then compared. A total of 100 participants of whom 67% were female were evaluated. The mean age of participants was 59.4 ± 11.4 years. The mean inflammation score was considerably decreased at the end of the study, in the intervention group. The mean levels of total antioxidant capacity (TAC) and glutathione peroxidase (GPx) at the end of the study were reduced among the triple therapy group ($P < .05$, $P = .03$ respectively). The mean levels of TAC and GPx were significantly higher among the intervention group at the end of the study compared with those at the start of the study. The combination of triple therapy with CoQ10 demonstrated an effective outcome on the mucosal inflammation, and stress oxidative in patients with chronic gastritis.</p>

Database :	Wiley Online Library
-------------------	----------------------

Title :	Alterations in Skeletal Muscle Oxidative Phenotype in Mice Exposed to Three Weeks of Normobaric Hypoxia
----------------	---

Author :	Ilse G.M. Slot, Annemie M.W.J. Schols, Chiel C. de Theije, Frank J.M. Snepvangers and Harry R. Gosker
-----------------	---

Journal :	Journal of Cellular Physiology: Accepted manuscript online, 30 JUN 2015 05:54PM EST DOI: 10.1002/jcp.25083
------------------	--

Abstract :	<p>Skeletal muscle of patients with chronic respiratory failure is prone to loss of muscle mass and oxidative phenotype. Tissue hypoxia has been associated with cachexia and emphysema in humans. Experimental research on the role of hypoxia in loss of muscle oxidative phenotype however has yielded inconsistent results. Animal studies are frequently performed in young animals, which may hinder translation to generally older aged patients. Therefore in this study we tested the hypothesis that hypoxia induces loss of skeletal muscle oxidative phenotype in a model of aged (52 weeks) mice exposed to three weeks of hypoxia. Additional groups of young (4 weeks) and adult (12 weeks) mice were included to examine age effects. To verify hypoxia-induced cachexia, fat pad and muscle weights as well as muscle fiber cross-sectional areas were determined. Muscle oxidative phenotype was assessed by expression and activity of markers of mitochondrial metabolism and fiber-type distribution. A profound loss of muscle and fat was indeed accompanied by a slightly lower expression of markers of muscle oxidative capacity in the aged hypoxic mice. In contrast, hypoxia-associated changes of fiber-type composition were more prominent in the young mice. The differential response of the muscle of young, adult, and aged mice to hypoxia suggests that age matters and that the aged mouse is a better model for translation of findings to elderly patients with chronic respiratory disease. Furthermore, the findings warrant further mechanistic research into putative accelerating effects of hypoxia-induced loss of oxidative phenotype on the cachexia process in chronic respiratory disease.</p>
-------------------	--

Database :	Wiley Online Library
-------------------	----------------------

Title :	Genetic and Functional Analysis of Polymorphisms in the Human Dopamine Receptor and Transporter Genes in Small Cell Lung Cancer
Author :	Emanuela Cherubini, Arianna Di Napoli, Alessia Noto, Giorgia Amira Osman, Maria Cristina Esposito, Salvatore Mariotta, Rossella Sellitri, Luigi Ruco, Giuseppe Cardillo, Gennaro Ciliberto, Rita Mancini and Alberto Ricci
Journal :	Journal of Cellular Physiology: Accepted manuscript online, 16 JUN 2015 05:46PM EST DOI: 10.1002/jcp.25079
Abstract :	<p>The regulatory role of dopamine (DA) in endocrine, cardiovascular and renal functions has been extensively studied and used for clinical purposes. More recently DA has been indicated as a regulatory molecule for immune cells and malignant cell proliferation. We assessed the expression and the functional role DA, DA receptors and transporters in primary small cell lung cancer (SCLC). By HPLC DA plasma levels were more elevated in SCLC patients in comparison with NSCLC patients and healthy controls. SCLC cell expressed DA D1- and D2-like receptors and membrane and vesicular transporters at protein and mRNA levels. We also investigated the effects of independent D1- or D2-like receptor stimulation on SCLC cell cultures. DA D1 receptor agonist SKF38393 induced the increase of cAMP levels and DARPP-32 protein expression without affecting SCLC growth rate. Cell treatment with the DA D1 receptor antagonist SCH23390 inhibited SKF38393 effects. In contrast, the DA D2 receptor agonist quinpirole (10μM) counteracted, in a dose and time dependent way, SCLC cell proliferation, it did not affect cAMP levels and decreased phosphorylated AKT that was induced by DA D2 receptor antagonist sulpiride. However, in only one SCLC line, stimulation of DA D2 receptor failed to inhibit cell proliferation in vitro. This effect was associated to the existence of rs6275 and rs6277 polymorphisms in the D2 gene. These results gave more insight into DA control of lung cancer cell behavior and suggested the existence of different SCLC phenotypes.</p>
Database :	Wiley Online Library

Title :	Pharmacokinetics of sufentanil during long-term infusion in critically ill pediatric patients
----------------	---

Author :	Alicja Bartkowska-Śniatkowska, Agnieszka Bienert, Paweł Wiczling, Jowita Rosada-Kurasińska, Marzena Zielińska, Justyna Warzybok, Agnieszka Borsuk, Dick Tibboel, Roman Kaliszan and Edmund Grześkowiak
Journal :	The Journal of Clinical Pharmacology: Accepted manuscript online, 23 JUN 2015 06:47PM EST DOI: 10.1002/jcph.577
Abstract :	<p>The aim of this study was to develop a population pharmacokinetic model of sufentanil and to assess the influence of covariates in critically ill children admitted to pediatric intensive care unit (PICU). After institutional approval 41 children were enrolled into the study. Blood samples for PK assessment were collected from routinely placed arterial catheters, during and after discontinuation of infusion. Population nonlinear mixed-effect modeling was performed using NONMEM. A two-compartment model described sufentanil PK sufficiently. Typical values of the central and peripheral volume of distribution, and the metabolic and inter-compartmental clearance for a theoretical patient of 70 kg weight were $VC = 7.90$ l, $VT = 481$ l, $Cl = 45.3$ l/hr, and $Q = 38.3$ l/hr. High inter-individual variability of all PK parameters was noted. Allometric/isometric principles to scale sufentanil PK revealed that to achieve the same steady-state sufentanil concentrations in plasma for pediatric patients of different body weights, the infusion rate should follow the formula (infusion rate for a 70 kg adult patient, $\mu\text{g/h}$)*(Body Weight/70 kg)^{0.75}. Severity of illness described by PRISM score, the monitored physiological and laboratory parameters, and co-administered drugs such as vasopressors were not found to be significant covariates.</p>
Database :	Wiley Online Library

Title :	Holidays, celebrations, and commiserations: measuring drinking during feasting and fasting to improve national and individual estimates of alcohol consumption
Author :	Mark A Bellis, Karen Hughes, Lisa Jones, Michela Morleo, James Nicholls, Ellie McCoy, Jane Webster and Harry Sumnall
Journal :	BMC Medicine 2015, 13:113 doi:10.1186/s12916-015-0337-0
Abstract :	Background

Accurate measures of alcohol consumption are critical in assessing health harms caused by alcohol. In many countries, there are large discrepancies between survey-based measures of consumption and those based on alcohol sales. In England, surveys measuring typical alcohol consumption account for only around 60% of alcohol sold. Here, using a national survey, we measure both typical drinking and atypical/special occasion drinking (i.e., feasting and fasting) in order to develop more complete measures of alcohol consumption.

Methods

A national random probability telephone survey was implemented (May 2013 to April 2014). Inclusion criteria were resident in England and aged 16 years or over. Respondents (n = 6,085) provided information on typical drinking (amounts per day, drinking frequency) and changes in consumption associated with routine atypical days (e.g., Friday nights) and special drinking periods (e.g., holidays) and events (e.g., weddings). Generalized linear modelling was used to identify additional alcohol consumption associated with atypical/special occasion drinking by age, sex, and typical drinking level.

Results

Accounting for atypical/special occasion drinking added more than 120 million UK units of alcohol/week (~12 million bottles of wine) to population alcohol consumption in England. The greatest impact was seen among 25- to 34-year-olds with the highest typical consumption, where atypical/special occasions added approximately 18 units/week (144 g) for both sexes. Those reporting the lowest typical consumption (≤ 1 unit/week) showed large relative increases in consumption (209.3%) with most drinking associated with special occasions. In some demographics, adjusting for special occasions resulted in overall reductions in annual consumption (e.g., females, 65 to 74 years in the highest typical drinking category).

Conclusions

Typical drinking alone can be a poor proxy for actual alcohol consumption. Accounting for atypical/special occasion drinking fills 41.6% of the gap between

	<p>surveyed consumption and national sales in England. These additional units are inevitably linked to increases in lifetime risk of alcohol-related disease and injury, particularly as special occasions often constitute heavy drinking episodes. Better population measures of celebratory, festival, and holiday drinking are required in national surveys in order to adequately measure both alcohol consumption and the health harms associated with special occasion drinking.</p>
Database :	BMC Medicine

~~XXXXXXXXXXXXXXXXXXXX~~