บทความที่น่าสนใจประจำเดือนมิถุนายน 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	The stage-specific in vitro efficacy of a malaria antigen cocktail provides valuable insights into the development of effective multi-stage vaccines
Author :	Holger Spiegel, Alexander Boes, Robin Kastilan, Stephanie Kapelski, Güven Edgue, Veronique Beiss, Ivana Chubodova, Matthias Scheuermayer, Gabriele Pradel, Stefan Schillberg, Andreas Reimann and Rainer Fischer
Journal :	Biotechnology Journal: Article first published online, 26 MAY 2015 | DOI: 10.1002/biot.201500055
Abstract :	Multicomponent vaccines targeting different stages of Plasmodium falciparum represent a promising, holistic concept towards better malaria vaccines. Additionally, an effective vaccine candidate should demonstrate cross-strain specificity because many antigens are polymorphic, which can reduce vaccine efficacy. A cocktail of recombinant fusion proteins (VAMAX-Mix) featuring three diversity-covering variants of the blood-stage antigen PfAMA1, each combined with the conserved sexual-stage antigen Pfs25 and one of the pre-erythrocytic-stage antigens PfCSP_TSR or PfCelTOS, or the additional blood-stage antigen PfMSP1_19, was produced in Pichia pastoris and used to immunize rabbits. The immune sera and purified IgG were used to perform various assays determining antigen specific titers and in vitro efficacy against different parasite stages and strains. In functional in vitro assays we observed robust inhibition of blood-stage (up to 90%), and sexual-stage parasites (up to 100%) and biased inhibition of pre-erythrocytic parasites (0–40%). Cross-strain blood-stage efficacy was observed in erythrocyte invasion assays using four different P. falciparum strains. The quantification of antigen-specific IgGs allowed the determination of specific IC50 values. The significant difference in antigen-specific IC50 requirements, the direct correlation between antigen-specific IgG and the relative quantitative representation of antigens within the cocktail, provide valuable implementations for future multi-stage, multi-component vaccine designs.
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Title :	Topical Application of a Novel Oxycodone Gel Formulation (Tocopheryl Phosphate Mixture) in a Rat Model of Peripheral Inflammatory Pain Produces Localized Pain Relief Without Significant Systemic Exposure
Author :	Maree T. Smith, Bruce D. Wyse, Stephen R. Edwards, Mahmoud El-Tamimy, Giacinto Gaetano and Paul Gavin
Journal :	Journal of Pharmaceutical Sciences: Article first published online, 20 MAY 2015 | DOI: 10.1002/jps.24502
Abstract :	This study was designed to assess the analgesic efficacy and systemic exposure of oxycodone administered topically in a novel tocopheryl phosphate mixture (TPM) gel formulation, to the inflamed hindpaws in a rat model of inflammatory pain. Unilateral hindpaw inflammation was induced in male Sprague–Dawley rats by intraplantar (i.pl.) injection of Freund's complete adjuvant (FCA). Mechanical hyperalgesia and hindpaw inflammation were assessed by measuring paw pressure thresholds and hindpaw volume, respectively, just prior to i.pl. FCA and again 5–6 days later. The analgesic effects of oxycodone administered topically (1 mg in TPM gel) or by i.pl. injection (50 μg), were assessed. Systemic oxycodone exposure was assessed over an 8-h postdosing interval following topical application. Skin permeation of oxycodone from the gel formulation was assessed in vitro using Franz diffusion cells. Oxycodone administered topically or by i.pl. injection produced significant ($p < 0.05$) analgesia in the inflamed hindpaws. Systemic oxycodone exposure was insignificant after topical dosing. The in vitro cumulative skin permeation of oxycodone was linearly related to the amount applied. Topical TPM/oxycodone gel formulations have the potential to alleviate moderate to severe inflammatory pain conditions with minimal systemic exposure, thereby avoiding central nervous system (CNS)-mediated adverse effects associated with oral administration of opioid analgesics.
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Title :	Analgesia enhancement and prevention of tolerance to morphine: beneficial effects of combined therapy with omega-3 fatty acids
Author :	Graciela E. Escudero, Carolina B. Romañuk, María E. Toledo, María E. Olivera, Ruben H. Manzo and Carlos H. Laino
Journal :	Journal of Pharmacy and Pharmacology: Article first published online, 25 MAY 2015 | DOI: 10.1111/jphp.12416
Abstract :	Objectives Recent evidence associates omega-3 fatty acids (O3) with pain reduction. The aim of this work was to evaluate the antinociceptive effect of O3, either alone or in combination with morphine after acute and chronic administration in rats. As well, a new pharmaceutical mixture that allows the concomitant administration of O3 and morphine as an oral solution was developed. Methods Animals were fed on a control or an experimental diet supplemented with O3. They were subjected to the hot-plate test to assess analgesic effect and tolerance to the analgesic effect of morphine. The open-field test was carried out to determine if the differences in the response latency can be related to non-specific sedative effects. Key findings O3 dietary supplementation increased the response latency compared with the control group. Acute treatment with morphine in these groups resulted in an additive antinociceptive effect not related to locomotor activity. Chronic coadministration of morphine with O3 attenuated the development of tolerance. Oral administration of the new pharmaceutical mixture showed analgesic activity with a subtherapeutic dose of morphine. Conclusion This finding suggests a role for O3 as adjuncts to opioids in pain therapy and might contribute to the reduction of the occurrence of morphine side-effects.
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Title :	A Novel On-Package Sticker Sensor Based on Methyl Red for Real-Time Monitoring of Broiler Chicken Cut Freshness
Author :	Bambang Kuswandi, Jayus, Revi Oktaviana, Aminah Abdullah andLee Yook Heng
Journal :	Packaging Technology and Science: Volume 27, Issue 1, pages 69–81, January 2014
Abstract :	A novel sticker sensor has been fabricated based on methyl red, and tests have been conducted to detect the freshness of broiler chicken cuts. Methyl red was immobilized onto a bacterial cellulose membrane via absorption method. The methyl red/cellulose membrane as a freshness sensor worked based on pH increase as the basic spoilage volatile amines produced gradually in the package headspace, and subsequently, the colour of the sensor will change from red to yellow for spoilage indication, which is easily visible to the naked eye. The results show that the sticker sensor could be used to determine the degree of chicken cut freshness, as the relationship between the colour change of methyl red as a sensor response and the chicken cut freshness follows a similar trend. Therefore, the spoilage of the chicken cut could be detected visually. A sticker sensor indicates the chicken cut freshness by its colour change in real time. Thus, the sticker sensor can be used as an effective tool for monitoring the microbial quality of packaged fresh poultry meat. Finally, the methyl red/cellulose membrane was successfully used as a sticker sensor for the real-time monitoring of chicken cut freshness in ambient and chiller conditions.
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Title :	Comparison of erythropoietin resistance in hemodialysis patients using calcitriol, cinacalcet or paricalcitol
Author :	Baris Afsar, Erhan Agca and Suleyman Turk
Journal :	The Journal of Clinical Pharmacology: Accepted manuscript online, 1 JUN 2015 04:35AM EST | DOI: 10.1002/jcph.556
Abstract :	The erythropoiesis stimulating agent (ESA) hyporesponsiveness index (EHRI) calculated as the weekly dose of EPO divided by weight (kg) divided by hemoglobin level (g/dL) has been considered useful to assess the ESA resistance. Recent

	evidence suggests that active vitamin D, cinacalcet and paricalcitol use may be related with lower ESA resistance. We conducted this observational cross-sectional study to investigate ESA resistance calculated by EHRI among patients using calcitriol, cinacalcet and paricalcitol. Participants underwent medical history taking, physical examination, measurement of biochemical analysis, calculation of dialysis adequacy and EHRI. 65 patients did not receive any treatment regarding vitamin D, paricalcitol and cinacalcet (Group 1), 41 were taking only vitamin D (Group 2), 50 were taking only paricalcitol (Group 3), 19 were taking only cinacalcet (Group 4) and 21 were taking paricalcitol + cinacalcet (Group 5). The EHRI values for Group 1,2,3,4 and 5 were 11.36 ± 8.72, 11.58 ± 5.72, 8.29 ± 5.54, 9.49 ± 4.61, 8.91 ± 4.44 respectively (P: 0.034). Post hoc analysis showed that EHRI was different between Group 1 and Group 3 (P:0.017), and between Group 2 and Group 3 (P:0.006). In linear regression analysis, use of paricalcitol was independently associated with EHRI. In conclusion, paricalcitol use was associated with lower EHRI levels as a measure of ESA resistance.
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Title :	A Novel Role for Thrombopoietin in Regulating Osteoclast Development in Humans and Mice
Author :	Monique Bethel, Calvin L.T. Barnes, Amanda F. Taylor, Ying-Hua Cheng, Brahmananda R. Chitteti, Mark C. Horowitz, Angela Bruzzaniti, Edward F. Srour and Melissa A. Kacena
Journal :	Journal of Cellular Physiology: Volume 230, Issue 9, pages 2142–2151, September 2015 (Article first published online: 26 MAY 2015 | DOI: 10.1002/jcp.24943)
Abstract :	Emerging data suggest that megakaryocytes (MKs) play a significant role in skeletal homeostasis. Indeed, osteosclerosis observed in several MK-related disorders may be a result of increased numbers of MKs. In support of this idea, we have previously demonstrated that MKs increase osteoblast (OB) proliferation by a direct cell–cell contact mechanism and that MKs also inhibit osteoclast (OC) formation. As MKs and OCs are derived from the same hematopoietic precursor, in these osteoclastogenesis studies we examined the role of the main MK growth factor, thrombopoietin (TPO) on OC formation and bone resorption. Here we show that TPO

	directly increases OC formation and differentiation in vitro. Specifically, we demonstrate the TPO receptor (c-mpl or CD110) is expressed on cells of the OC lineage, c-mpl is required for TPO to enhance OC formation in vitro, and TPO activates the mitogen-activated protein kinases, Janus kinase/signal transducer and activator of transcription, and nuclear factor-kappaB signaling pathways, but does not activate the PI3K/AKT pathway. Further, we found TPO enhances OC resorption in CD14+CD110+ human OC progenitors derived from peripheral blood mononuclear cells, and further separating OC progenitors based on CD110 expression enriches for mature OC development. The regulation of OCs by TPO highlights a novel therapeutic target for bone loss diseases and may be important to consider in the numerous hematologic disorders associated with alterations in TPO/c-mpl signaling as well as in patients suffering from bone disorders.
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Title :	Skin delivery of antioxidant surfactants based on gallic acid and hydroxytyrosol
Author :	Cristina Alonso, Ricardo Lucas, Clara Barba, Meritxell Marti, Laia Rubio, Francesc Comelles, Juan Carlos Morales, Luisa Coderch and José Luís Parra
Journal :	Journal of Pharmacy and Pharmacology: Volume 67, Issue 7, pages 900–908, July 2015
Abstract :	Objectives The aim of this study has been to investigate the dermal absorption profile of the antioxidant compounds gallic acid and hydroxytyrosol as well as their derivatives, hexanoate (hexyl gallate and hydroxytyrosol hexanoate) and octanoate (octyl gallate and octanoate derivative) alkyl esters (antioxidant surfactants). Previously, the scavenging capacity of these compounds, expressed as efficient dose ED50, has also determined. Methods The percutaneous absorption of these compounds was obtained by an in vitro methodology using porcine skin biopsies on Franz static diffusion cells. The antiradical activity of compounds was determined using the 1,1-diphenyl-2-picrylhydrazyl free radical method.

	Key findings The percutaneous penetration results show the presence of antioxidants in all layers of the skin. The content of the cutaneously absorbed compound is higher for the antioxidant surfactants (ester derivatives). This particular behaviour could be due to the higher hydrophobicity of these compounds and the presence of surface activity in the antioxidant surfactants. Conclusions These new antioxidant surfactants display optimum properties, which may be useful in the preparation of emulsified systems in cosmetic and pharmaceutical formulations because of their suitable surface activity and because they can protect the skin from oxidative damage.
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Title :	Thermal, X-ray Structural, and Dissolution Characteristics of Solid Forms Derived from the Anticancer Agents 2-Methoxyestradiol and 2-Methoxyestradiol-3,17-O,O-Bis-Sulfamate
Author :	Mino R. Caira, Susan A. Bourne and Halima Samsodien
Journal :	Journal of Pharmaceutical Sciences - - Article first published online: 12 JUN 2015 | DOI: 10.1002/jps.24545
Abstract :	The aim of the study was to generate alternative solid forms of 2-methoxyestradiol (2ME) and its sulfamoylated derivative 2-methoxyestradiol-3,17-O,O-bis-sulfamate (2MES), both of which are potent anticancer agents with no significant history of solid-state investigation. Screening for polymorphs and solvates by a variety of procedures yielded four distinct species: a crystalline form of 2ME, an amorphous form of 2ME, a chloroform solvate 2ME·(CHCl3)2, and the hemihydrate of the bis-sulfamate, 2MES·(H2O)0.5. Hydrogen-bonded assembly of 2ME molecules into layers in both crystalline 2ME and its chloroform solvate was established using single-crystal X-ray diffraction. This technique also revealed disorder of the sulfamate group at position 17 in both molecules comprising the asymmetric unit in the crystal of 2MES·(H2O)0.5. The thermal stabilities of the crystalline phases were

	recorded using hot-stage microscopy, thermogravimetry, and differential scanning calorimetry, and the results were reconciled with the crystal structures. Aqueous dissolution rates measured at 37°C generally decreased in the order 2MES·(H2O)0.5 > 2ME(amorphous) > 2ME(crystalline).
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Title :	Effects of age and sex on the pharmacokinetics of LCZ696, an angiotensin receptor neprilysin inhibitor
Author :	Lu Gan, Thomas Langenickel, Jesika Petruck, Kiran Kode, Iris Rajman, Priya Chandra, Wei Zhou, Sam Rebello and Gangadhar Sunkara
Journal :	The Journal of Clinical Pharmacology - - Accepted manuscript online: 12 JUN 2015 04:41PM EST | DOI: 10.1002/jcph.571
Abstract :	LCZ696, a novel angiotensin receptor neprilysin inhibitor, is in development for the treatment of heart failure. Administration of LCZ696 results in systemic exposure to sacubitril (inactive prodrug of LBQ657), LBQ657 (neprilysin inhibitor), and valsartan (angiotensin II receptor blocker). We investigated the potential effect of age and sex on the pharmacokinetics of LCZ696 analytes (LBQ657 and valsartan) in an open-label, single oral dose (400 mg), parallel group study in healthy subjects. Among 36 enrolled subjects, there were 19 male and 17 female subjects; 18 subjects were 18-45 years old (young), and 18 subjects were 65 years of age or older (elderly). Compared to young subjects, the AUCinf and T1/2 for LBQ657 were 42% and 30% greater in elderly subjects, respectively. The Cmax for LBQ657 was similar between age groups. The AUCinf, Cmax, and T1/2 for valsartan were 30%, 24% greater, and 3.35 hours longer in elderly when compared to young subjects, respectively. All pharmacokinetic parameters of LCZ696 analytes (LBQ657 and valsartan) were similar between male and female subjects, indicating no effect on the pharmacokinetics of LCZ696 analytes based on sex. Considering the magnitude of change and its clinical significance, dose adjustment based on age or sex is not considered necessary.
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Title :	Challenges to consumers travelling with multiple medicines
Author :	Jacqueline Tudball, Lorraine Smith, Kath Ryan, Margaret Williamson and Elizabeth Manias
Journal :	Journal of Pharmaceutical Health Services Research - - Article first published online: 8 JUN 2015 | DOI: 10.1111/jphs.12097
Abstract :	Objectives The need to maintain medicine adherence when travelling is irrefutable, yet how people achieve this goal and the challenges they encounter in doing so have seldom been explored in previous research. This study examined how consumers residing in Australia experience and manage their multiple medicines while travelling. Methods Face-to-face, narrative interviews were conducted in participants' homes or workplaces and were audio and video-recorded. The coding schema was devised with the input of an Advisory Panel with expertise in multiple medicines. Data were analysed using the constant comparative method. Key findings Participants who had experienced medicines mishaps when travelling had learnt to take greater care when planning and preparing for future trips. Prior to travelling, they rarely sought advice regarding their regular medicines from health professionals. Organising and packing their medicines could be extremely time-consuming and confusing; younger participants especially lamented the reduced spontaneity this imposed on their lives. Replicating their usual routines was a successful strategy for many; however, this was challenged by unforeseen events and the lack of privacy. Conclusions Travel comprised inherent risks to the users of multiple medicines and often required intensive and complicated preparation. Community pharmacists and other health professionals are well placed to advise and assist consumers with complex

	regimens who are planning to travel, as well as raise general awareness concerning the need for utmost care with multiple medicines.
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