บทความที่น่าสนใจประจำเดือน พฤษภาคม 2558

สาขาวิทยาศาสตร์สุขภาพ

Title :	Improvement in oral bioavailability and dissolution of tanshinone IIA by preparation of solid dispersions with porous silica
Author :	Hong-mei Yan, E Sun, Li Cui, Xiao-bin Jia and Xin Jin
Journal :	Journal of Pharmacy and Pharmacology: Article first published online, 5 MAY 2015 | DOI: 10.1111/jphp.12423
Abstract :	Objectives This study aims to evaluate the oral bioavailability and dissolution of tanshinone IIA (tanIIA) by preparation of solid dispersions (SDs) with porous silica. Methods SDs of tanIIA were prepared using a solvent method. The physicochemical properties, dissolution property, drug stability and in-vivo performance of the SDs prepared were all evaluated. Key findings Compared with tanIIA alone and corresponding physical mixtures, tanIIA from SDs showed remarkably improved in-vitro dissolution rate. After forming the SDs, tanIIA changed into an amorphous state, which can infer from differential scanning calorimetry (DSC) and X-ray powder diffraction (XRPD). Fourier transform infrared spectroscopy (FTIR) also revealed the presence of interactions between tanIIA and porous silica in SDs. During the stability study, there is no significant decreasing in either the in-vitro dissolution or the drug content, which was observed following storage at room temperature for 12 months. The results of a pharmacokinetic study in rats showed the areas under the concentration–time curve from 0 h to 24 h (AUC0–24h) for the SDs and tanIIA were 1019.87 ± 161.819 mg/h per litre and 343.70 ± 75.628 mg/h per litre, respectively.

	Conclusions SDs with porous silica as carrier could achieve superior oral bioavailability by improving drug dissolution, whereas drug stability could be maintained.
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Title :	Differential Hematopoietic Activity in White Adipose Tissue Depending on its Localization
Author :	Elodie Luche, Coralie Sengenès, Emmanuelle Arnaud, Patrick Laharrague, Louis Casteilla and Beatrice Cousin
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 18 MAY 2015 05:51PM EST | DOI: 10.1002/jcp.25045
Abstract :	White adipose tissue (WAT) can be found in different locations in the body, and these different adipose deposits exhibit specific physiopathological importance according to the subcutaneous or abdominal locations. We have shown previously the presence of functional hematopoietic stem/progenitor cells (HSPC) in subcutaneous adipose tissue (SCAT). These cells exhibit a specific hematopoietic activity that contributes to the renewal of the immune cell compartment within this adipose deposit. In this study we investigated whether HSPC can be found in visceral adipose tissue (VAT) and whether a putative difference in in situ hematopoiesis may be related to anatomical location and to site-specific immune cell content in VAT compared to SCAT. Therein, we identified for the first time the presence of HSPC in VAT. Using both in vitro assays and in vivo competitive repopulation experiments with sorted HSPC from VAT or SCAT, we showed that the hematopoietic activity of HSPC was lower in VAT, compared to SCAT. In addition, this altered hematopoietic activity of HSPC in VAT was due to their microenvironment, and may be related to a specific combination of secreted factors and extracellular matrix molecules expressed by adipose derived stromal cells. Our results indicate that WAT specific hematopoietic activity may be generalized to all adipose deposits, although with specificity according to the fat pad location. Considering the abundance of WAT in the body, this emphasizes the potential importance of this hematopoietic activity in physiopathological situations.

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Title :	GLP-2 as Beneficial Factor in the Glucose Homeostasis in Mice Fed a High Fat Diet
Author :	Sara Baldassano, Francesca Rappa, Antonella Amato, Francesco Cappello and Flavia Mulè
Journal :	Journal of Cellular Physiology: Accepted manuscript online: 12 MAY 2015 01:42PM EST | DOI: 10.1002/jcp.25039
Abstract :	lucagon like peptide-2 (GLP-2) is a gastrointestinal hormone released in response to dietary nutrients, which acts through a specific receptor, the GLP-2 receptor (GLP-2R). The physiological effects of GLP-2 are multiple, involving also the intestinal adaptation to high fat diet (HFD). In consideration of the well-known relationship between chronic HFD and impaired glucose metabolism, in the present study we examined if the blocking of the GLP-2 signaling by chronic treatment with the GLP-2R antagonist, GLP-2 (3–33), leads to functional consequences in the regulation of glucose metabolism in HFD-fed mice. Compared with animals fed standard diet (STD), mice at the tenth week of HFD showed hyperglycaemia, glucose intolerance, high plasma insulin level after glucose load, increased pancreas weight and β cell expansion, but not insulin resistance. In HFD fed mice, GLP-2 (3-33) treatment for four weeks (from the sixth to the tenth week of diet) did not affect fasting glycaemia, but it significantly increased the glucose intolerance, both fasting and glucose-induced insulin levels, and reduced the sensitivity to insulin leading to insulin-resistance. In GLP-2 (3-33)-treated HFD mice pancreas was significantly heavier and displayed a significant increase in β-cell mass in comparison with vehicle-treated HFD mice. In STD mice, the GLP-2 (3-33) treatment did not affect fasted or glucose-stimulated glycemia, insulin, insulin sensitivity, pancreas weight and beta cell mass. The present study suggests that endogenous GLP-2 may act as a protective factor against the dysregulation of the glucose metabolism that occurs in HFD mice, because GLP-2 (3-33) worsens glucose metabolism disorders.
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Title :	Complementary and alternative medicine for the prevention and treatment of migraine headache: an overview of systematic reviews
Author :	Paul Posadzki, Abdullah MN AlBedah, Mohamed MK Khalil, Meshari S AlQaed, Myeong S Lee, Edzard Ernst and Josip Car
Journal :	Focus on Alternative and Complementary Therapies: Volume 20, Issue 2, pages 58–73, June 2015
Abstract :	Background Complementary and alternative medicine (CAM) is very popular among migraineurs. Objectives The aim of this article is to summarise and critically evaluate the evidence from systematic reviews (SRs) of CAM for the prevention and treatment of migraine headache. Method Ten electronic databases were searched from 1946 to August 2014. Retrieved papers were also hand-searched for relevant references. Systematic reviews were eligible for inclusion if they reported the prevention and treatment of migraine headache using any type of CAM. Oxman criteria were used to appraise the methodological quality of the included SRs. Results Thirty-three SRs, with a total of 45 886 migraine sufferers, were included in the analyses. The majority (64%) of the SRs were of high methodological quality (mean Oxman score=4.87, SD=3.96). Most (60.6%) SRs arrived at positive conclusions (16 of which were of high quality); two (6.0%) SRs arrived at negative conclusions (of which one was of high quality), and 11 (33.3%) arrived at equivocal conclusions (of which four were of high quality). The majority of the high-quality SRs (Oxman score=6–9) were based on moderate-quality RCTs. For multiple SRs, unanimously positive conclusions were reached for acupuncture and biofeedback. There was conflicting evidence regarding the effectiveness of homeopathy, herbal medicines

	such as Petasites hybridus and Tanacetum parthenium L., and spinal manipulative therapy. Conclusion The evidence from SRs evaluating the effectiveness of CAM for the prevention or treatment of migraine headache is mostly positive. However, several caveats should be taken into account, and only for acupuncture and biofeedback are the conclusions unanimously positive.
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Title :	Making polymeric membranes antifouling via “grafting from” polymerization of zwitterions
Author :	Qian Li, Joseph Imbrogno, Georges Belfort, Xiao-Lin Wang
Journal :	Journal of Applied Polymer Science: Volume 132, Issue 21 June 5, 2015
Abstract :	Protein-fouling of membranes has negative effects on the wide applications of membrane materials, such as poly(vinylidene fluoride) (PVDF), poly(ether sulfone) (PES)/polysulfone (PSf). Zwitterionic materials have recently been used and identified from high throughput screens of large libraries of monomers to modify membranes due to their stable anti-protein-fouling properties. “Grafting from” polymerization is a technique involving monomers that are polymerized using an initiation reaction on the membrane surface. It is regarded as a simple, useful, and versatile modification approach to increase the anti-fouling properties of a membrane. This strategy provides controllable introduction of graft chains with a high density and a long-term chemical stability due to covalent attachment of graft chains. Graft density, chemistry, chain length, and conformation are all important parameters that need to be considered. This article presents a mini-review of recent progress on the “grafting from” polymerization of zwitterionic monomers on the surfaces of PVDF and PES/PSf membranes, including an introduction of zwitterions and methods of graft polymerization. Various approaches such as free radical graft polymerization, photo-induced graft polymerization, and plasma-induced graft polymerization were compared based on uniformity and amount of grafted zwitterionic polymer, relative flux of modified membranes, simplicity and

	environment pollution of operation, and cost of technique. The application of different approaches and the performance of poly(zwitterion)-grafted PVDF and PES/PSf membranes are summarized according to recent research.
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Title :	Encapsulation of enzyme via one-step template-free formation of stable organic–inorganic capsules: A simple and efficient method for immobilizing enzyme with high activity and recyclability
Author :	Renliang Huang, Mengyun Wu, Mark J. Goldman and Zhi Li
Journal :	Biotechnology and Bioengineering: Volume 112, Issue 6, pages 1092–1101, June 2015
Abstract :	Enzyme encapsulation is a simple, gentle, and general method for immobilizing enzyme, but it often suffers from one or more problems regarding enzyme loading efficiency, enzyme leakage, mechanical stability, and recyclability. Here we report a novel, simple, and efficient method for enzyme encapsulation to overcome these problems by forming stable organic–inorganic hybrid capsules. A new, facile, one-step, and template-free synthesis of organic–inorganic capsules in aqueous phase were developed based on PEI-induced simultaneous interfacial self-assembly of Fmoc-FF and polycondensation of silicate. Addition of an aqueous solution of Fmoc-FF and sodium silicate into an aqueous solution of PEI gave a new class of organic–inorganic hybrid capsules (FPSi) with multi-layered structure in high yield. The capsules are mechanically stable due to the incorporation of inorganic silica. Direct encapsulation of enzyme such as epoxide hydrolase SpEH and BSA along with the formation of the organic–inorganic capsules gave high yield of enzyme-containing capsules (~1.2 mm in diameter), >90% enzyme loading efficiency, high specific enzyme loading (158 mg protein g−1 carrier), and low enzyme leakage (<3% after 48 h incubation). FPSi-SpEH capsules catalyzed the hydrolysis of cyclohexene oxide to give (1R, 2R)-cyclohexane-1,2-diol in high yield and concentration, with high specific activity (6.94 U mg−1 protein) and the same high enantioselectivity as the free enzyme. The immobilized SpEH demonstrated also excellent operational stability and recyclability: retaining 87% productivity after 20 cycles with a total

	reaction time of 80 h. The new enzyme encapsulation method is efficient, practical, and also better than other reported encapsulation methods.
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Title :	Heat shock protein 27 overexpression in CHO cells modulates apoptosis pathways and delays activation of caspases to improve recombinant monoclonal antibody titre in fed-batch bioreactors
Author :	Janice G.L. Tan, Yih Yean Lee, Tianhua Wang, Miranda G. S. Yap, Tin Wee Tan and Say Kong Ng
Journal :	Biotechnology Journal -- Special Issue: Vaccine Biotechnology, Volume 10, Issue 5, pages 790–800, May 2015
Abstract :	CHO cells are major production hosts for recombinant biologics including the rapidly expanding recombinant monoclonal antibodies (mAbs). Heat shock protein 27 (HSP27) expression was observed to be down-regulated towards the late-exponential and stationary phase of CHO fed-batch bioreactor cultures, whereas HSP27 was found to be highly expressed in human pathological cells and reported to have anti-apoptotic functions. These phenotypes suggest that overexpression of HSP27 is a potential cell line engineering strategy for improving robustness of CHO cells. In this work, HSP27 was stably overexpressed in CHO cells producing recombinant mAb and the effects of HSP27 on cell growth, volumetric production titer and product quality were assessed. Concomitantly, HSP27 anti-apoptosis functions in CHO cells were investigated. Stably transfected clones cultured in fed-batch bioreactors displayed 2.2-fold higher peak viable cell density, delayed loss of culture viability by two days and 2.3-fold increase in mAb titer without affecting the N-glycosylation profile, as compared to clones stably transfected with the vector backbone. Co-immunoprecipitation studies revealed HSP27 interactions with Akt, pro-caspase 3 and Daxx and caspase activity profiling showed delayed increase in caspase 2, 3, 8 and 9 activities. These results suggest that HSP27 modulates apoptosis signaling pathways and delays caspase activities to improve performance of CHO fed-batch bioreactor cultures.
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Title :	Evolution of fluorinated enzymes: An emerging trend for biocatalyst stabilization
Author :	Hernan Biava andNediljko Budisa
Journal :	Engineering in Life Sciences - -Special Issue: New and synthetic bioproduction systems, Volume 14, Issue 4, pages 340–351, July 2014
Abstract :	Nature uses remarkably limited sets of chemistries in its repertoire, especially when compared to synthetic organic chemistry. This limits both the chemical and structural diversity that can ultimately be achieved with biocatalysis, unless the powers of chemical synthesis are merged with biological systems by integrating nonnatural synthetic chemistries into the protoplasma of living cells. Of particular interest, here is the fluorous effect that has recently established the potential to generate enzymes with an increased resistance toward both high temperature and organic solvents. For these reasons, we are witnessing a rapid development of efficient methodologies for the incorporation of fluorinated amino acids in protein synthesis, using both in vivo and in vitro strategies. In this review, we highlight relevant and trendsetting results in the design and engineering of stable fluorinated proteins and peptides along with whole-cell biocatalysis as an economically attractive and convenient application with exclusive focus on industrial biocatalysis. Finally, we envision new strategies to improve current achievements and enable the field to progress far beyond the current state-of-the-art.
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Title :	An evaluation of salt screening methodologies
Author :	Ana Fernández Casares*, W. Mieke Nap, Glòria Ten Figás, Pieter Huizenga, Richard Groot andMarcel Hoffmann
Journal :	Journal of Pharmacy and Pharmacology - - Special Issue: Selection of Solid-State Forms for New Chemical Entities. Guest Editor: Christoph Saal, Volume 67, Issue 6, pages 812–822, June 2015
Abstract :	Objectives In this study, the advantages and disadvantages of three salt screening methodologies have been explored, and recommendations are put forward as to when each method is most appropriate.

	Methods Three salt screening methodologies have been investigated: the in-situ salt screen, the saturated solution or rational screen approach, and the cooling-evaporative or high-throughput method. Two Active Pharmaceutical Ingredients (APIs) with significant differences in aqueous solubility have been chosen for this study, namely aripiprazole and desvenlafaxine (see Figure 1). Key findings The in-situ salt formation screen appears to be a good method for early stage salt selection based on aqueous solubility, although this approach does not work for all APIs, as demonstrated in the comparison between aripiprazole and desvenlafaxine. The saturated solution method or rational approach demonstrated a valuable overview of the different salts that can be formed in an efficient and cost-effective manner. The cooling-evaporative screening method involved a complete examination of salt formation, including indication of polymorphism of the salts produced. Conclusions The three salt formation approaches are methods that deliver crystalline salts. The choice of salt screen approach depends on the physical properties of the drug substance, development stage and objective of the screen.
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Title :	The Influence of Single-Dose and Short-Term Administration of Quercetin on the Pharmacokinetics of Midazolam in Humans
Author :	Mai Anh Nguyen, Petra Staubach, Siegfried Wolffram and Peter Langguth
Journal :	Journal of Pharmaceutical Sciences: Article first published online: 18 MAY 2015 DOI: 10.1002/jps.24500
Abstract :	Quercetin is a plant flavonol that is available from both daily diet and nutraceuticals. To investigate the effect of acute and short-term intake of high-dose quercetin on CYP3A-mediated metabolism, 10 healthy volunteers received 7.5 mg oral

	midazolam without, with a single dose of 1500 mg quercetin and after 1-week supplementation with 1500 mg quercetin daily. A substudy was performed in three subjects to explore the impact of repeated quercetin intake on intravenously administered midazolam. Coadministration with a single dose of quercetin did not significantly alter the pharmacokinetics of midazolam and its 1′-hydroxymetabolite, but following short-term quercetin intake, there was a trend to reduced midazolam exposure (geometric mean ratio of test–control area under the plasma concentration–time curve ($AUC_{0-\infty}$): 0.82; 90% confidence interval: 0.61–1.10) and midazolam–metabolite $AUC_{0-\infty}$ ratios were decreased by 9.7%–47.6% from control in seven subjects. The tendency was opposite when midazolam was given intravenously. We conclude that a single dose of quercetin would not provoke any toxic adverse events when coadministered with midazolam, whereas repeated quercetin intake can reduce systemic exposure to the orally given drug by increasing its CYP3A-catalyzed metabolism. As the effect deviated after intravenous drug administration, different mechanisms of interaction may be involved at the intestinal site compared with the liver.
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