บทความที่น่าสนใจประจำเดือน มีนาคม 2557

Title :	Stereomicroscopic Imaging Technique for the Quantification of Cold Flow in Drug-in-Adhesive Type of Transdermal Drug Delivery Systems
Author :	Yellela S.R. Krishnaiah, Usha Katragadda, Mansoor A. Khan
Journal :	Journal of Pharmaceutical Sciences: Article first published online, 1 MAR 2014 DOI: 10.1002/jps.23915
Abstract :	Cold flow is a phenomenon occurring in drug-in-adhesive type of transdermal drug delivery systems (DIA-TDDS) because of the migration of DIA coat beyond the edge. Excessive cold flow can affect their therapeutic effectiveness, make removal of DIA-TDDS difficult from the pouch, and potentially decrease available dose if any drug remains adhered to pouch. There are no compendial or noncompendial methods available for quantification of this critical quality attribute. The objective was to develop a method for quantification of cold flow using stereomicroscopic imaging technique. Cold flow was induced by applying 1 kg force on punched-out samples of marketed estradiol DIA-TDDS (model product) stored at 25°C, 32°C, and 40°C/60% relative humidity (RH) for 1, 2, or 3 days. At the end of testing period, dimensional change in the area of DIA-TDDS samples was measured using image analysis software, and expressed as percent of cold flow. The percent of cold flow significantly decreased ($p < 0.001$) with increase in size of punched-out DIA-TDDS samples and increased ($p < 0.001$) with increase in cold flow induction temperature and time. This first ever report suggests that dimensional change in the area of punched-out samples stored at 32°C/60%RH for 2 days applied with 1 kg force could be used for quantification of cold flow in DIA-TDDS.
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Title :	Mechanisms and effects of "fat taste" in humans
Author :	Robin M. Tucker, Richard D. Mattes and Cordelia A. Running
Journal :	BioFactors: Article first published online: 4 MAR 2014 | DOI: 10.1002/biof.1162
Abstract :	Evidence supporting a "taste" cue from fat in the oral cavity continues to accrue. The proposed stimuli for fat taste, non-esterified fatty acids (NEFA), are released from food through hydrolytic rancidity and lipase activity derived from foods or saliva. NEFA must then be released from the food matrix, negotiate the aqueous environment to reach taste cell surfaces, and interact with receptors such as CD36 and GPR120 or diffuse across cell membranes to initiate a taste signal. Knowledge of these processes in non-gustatory tissues should inform understanding of taste responses to NEFA. Additionally, downstream effects of oral triglyceride exposure have been observed in numerous studies. Data specific to effects of NEFA versus triglyceride are scarce, but modified sham feeding trials with triglyceride document cephalic phase responses including elevations in serum lipids and insulin as well as potential, but debated, effects on gut peptides, appetite, and thermogenesis. In this review, we highlight the mechanisms by which NEFA migrate to and interact with taste cells, and then we examine physiological responses to oral fat exposure.
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Title :	A novel method for the immobilization of a thermostable fungal chitinase and the properties of the immobilized enzyme
Author :	Muthu Prasad and Peramachi Palanivelu
Journal :	Biotechnology and Applied Biochemistry: Article first published online, 1 MAR 2014 | DOI: 10.1002/bab.1179
Abstract :	The recombinant thermostable fungal chitinase of Thermomyces lanuginosus was immobilized on the phenyl Sepharose matrix, and the properties of the immobilized chitinase were studied. The immobilized enzyme was optimally active at pH 6.0 and 50 °C and showed improved activity in the acidic range of pH values when compared with the soluble enzyme. The recombinant thermostable immobilized enzyme showed remarkable thermostability at 50 °C by retaining about 45% of the activity for more than 6 H. The KM and Vmax values were 1.3 mM and 4.5 mol/min/mg of protein, respectively. Both the free and immobilized forms of the enzymes were inhibited significantly by Ag+ but behaved similarly to various other metal ions, detergents, and additives. The immobilized enzyme was stable for at least 1 month at 4 °C.
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Title :	Peptide microarrays enable rapid mimotope optimization for pharmacokinetic analysis of the novel therapeutic antibody IMAB362
Author :	Karsten Schnatbaum, Hans-Ulrich Schmoldt, Matin Daneschdar, Laura M. Plum, Janina Jansong, Johannes Zerweck, Yvonne Kühne, Antonia Masch, Holger Wenschuh, Markus Fiedler, Özlem Türeci, Ugur Sahin and Ulf Reimer
Journal :	Biotechnology Journal: Article first published online, 7 MAR 2014 DOI: 10.1002/biot.201300456
Abstract :	As membrane proteins play an important role in a variety of life-threatening diseases, the development of therapeutic monoclonal antibodies against membrane proteins is of significant interest. Among many other requirements, the process of antibody drug development requires a set of tailor-made assays for the characterization of the antibodies and for monitoring their activity. Designing assays to characterize antibodies directed to membrane proteins is challenging, because the natural targets are often not available in a format that is compatible with a biochemical assay setup. Thus, alternatives that mimic the targeted membrane proteins are needed. In this study, we developed optimal peptidic mimotopes for the ELISA-based detection of the novel therapeutic antibody IMAB362 in biological samples. Initial hits were identified using phage display and these hits were optimized with the help of structure-activity relationship analysis on peptide microarrays. The optimized peptides showed binding constants in the low nanomolar to picomolar range, an improvement by a factor of up to 30 compared to the initial hits. The best mimotope (apparent KD = 0.15 nM) was successfully used for the ELISA-based quantification of IMAB362 in samples from a mouse pharmacokinetic study. The process described allows the rapid discovery of mimotopes for target proteins that are difficult to produce or handle, which can then be used in pre-clinical and clinical assays or for the purification of biological products.
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Title :	Gene regulatory networks and epigenetic modifications in cell differentiation
Author :	Siddhartha Roy and Tapas K. Kundu
Journal :	IUBMB Life Article first published online, 27 FEB 2014 DOI: 10.1002/iub.1249
Abstract :	It is becoming increasingly clear that the functionalities of an organism are mostly derived from regulation of its gene repertoire. Specialized cell types are created from pluripotent stem cells by regulating expression of genes. In eukaryotes, genes are primarily regulated by gene regulatory networks consisting of highly sequence-specific transcription factors and epigenetic modifications. The former mode of regulation is more readily reversible and non-heritable across cell generations, whereas the latter mode is less reversible and heritable. In this article, we explore the relationship between cell differentiation and the two modes of regulation of gene expression, focusing primarily on pluripotent and multipotent stem cells. Recent studies suggest that stem cells execute different gene expression programs, probably driven by one or more gene regulatory network(s). It is now also evident that as stem cells differentiate to more specialized progeny cells, rewriting of epigenetic marks occurs in parallel with the change in the pattern of gene expression. A conceptual framework is put forward in which it is proposed that the cell fate determining gene regulatory network in a pluripotent or multipotent cell has the capability to exist in multiple stationary states with each stationary state dictating a particular pattern of gene expression. We also propose that the broad pattern of gene expression in each stationary state, termed the lineage biased state or LIBS, resembles that of a more differentiated progeny cell. The differentiation process leading to a particular progeny cell involves rewriting of epigenetic marks that result in upregulation of genes in a LIBS and silencing of genes involved in alternative LIBS; thus selecting a particular pattern of gene expression and making a lineage commitment.
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Title :	Evaluation of a kinetic model for computer simulation of growth and fermentation by Scheffersomyces (Pichia) stipitis fed D-xylose
Author :	P. J. Slininger, B. S. Dien, J. M. Lomont, R. J. Bothast, M. R. Ladisch and M. R. Okos
Journal :	Biotechnology and Bioengineering: Article first published online, 4 MAR 2014 | DOI: 10.1002/bit.25215
Abstract :	Scheffersomyces (formerly Pichia) stipitis is a potential biocatalyst for converting lignocelluloses to ethanol because the yeast natively ferments xylose. An unstructured kinetic model based upon a system of linear differential equations has been formulated that describes growth and ethanol production as functions of ethanol, oxygen, and xylose concentrations for both growth and fermentation stages. The model was validated for various growth conditions including batch, cell recycle, batch with in situ ethanol removal and fed-batch. The model provides a summary of basic physiological yeast properties and is an important tool for simulating and optimizing various culture conditions and evaluating various bioreactor designs for ethanol production. Biotechnol. Bioeng. 2014;9999: 1–9.
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Title :	Coeliac disease and the gluten-free diet in New Zealand: The New Zealand Coeliac Health Survey
Author :	Kiri Sharp, Heather Walker and Kirsten J. Coppell
Journal :	Nutrition & Dietetics: Article first published online, 21 FEB 2014 | DOI: 10.1111/1747-0080.12105
Abstract :	Aim The aim of the present study was to describe the health and dietary treatment of people with coeliac disease in New Zealand. Methods The New Zealand Coeliac Health Survey was a self-administered cross-sectional survey adapted, with permission, from the Canadian Celiac Health Survey. All members of Coeliac New Zealand Incorporated (n = 2720) were surveyed, primarily online (n = 2383). Surveys were posted to those without an email address (n = 337). Results The overall response rate was 46.5% (n = 1264). This analysis included biopsy-positive respondents aged 16 years and over (n = 936). Mean age at diagnosis was 43.5 (SD: 15.5) years. The median time between reported onset of symptoms and diagnosis of coeliac disease was 5 years (IQR 1–16). Most (88.4%) described their diet as being strictly gluten free, yet many had incomplete recovery from symptoms. Of 81.6% reported being referred to a dietitian, 19.9% considered the information they received to be fair or poor. Following a gluten-free diet was very difficult for 6.2%, and moderately difficult for 29.8%. Common problems included finding good quality gluten-free foods and identifying whether foods were gluten free or not from the label. More than one-third (36.3%) avoided travelling because of coeliac disease at least some of the time, and one-quarter (25.6%) never or rarely ate at restaurants. Conclusions Although coeliac disease is a common condition in New Zealand, ongoing symptoms among patients suggest that dietary management is inadequate. Knowledge of a gluten-free diet and its implementation among dietitians, and the preparation of commercial and restaurant gluten-free foods could be improved.
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Title :	A Novel Inhalable Form of Rifapentine
Author :	John G. Y. Chan, Colin C. Duke, Hui Xin Ong, Joseph C. Y. Chan, Anneliese S. Tyne, Hak-Kim Chan, Warwick J. Britton, Paul M. Young, Daniela Traini
Journal :	Journal of Pharmaceutical Sciences: Article first published online, 1 MAR 2014 DOI: 10.1002/jps.23911
Abstract :	Recent murine studies found that rifapentine, dosed daily, at least halved tuberculosis treatment times compared with standard rifampicin and isoniazid-containing regimens. However, in humans, an inhalable form of rifapentine may be necessary to considerably shorten treatment duration because of the physiological barriers associated with oral therapy. The current study compares two inhalable rifapentine dry powders—a novel pure crystalline form and an amorphous form—by a series of in vitro tests. The crystalline and amorphous powders had a mass median aerodynamic size of 1.68 ± 0.03 and 1.92 ± 0.01 μm, respectively, associated with a fine particle fraction of 83.2 ± 1.2% and 68.8

	± 2.1%, respectively. A quinone degradation product was identified in the amorphous powder stored for 1 month, whereas the crystalline form remained chemically stable after storage at both 0% and 60% relative humidity, 25°C, for at least 3 months. Solubilized rifapentine was well tolerated by pulmonary tissue and macrophage cells up to approximately 50 μM. The accumulation of rifapentine within alveolar macrophage cells was significantly higher than for rifampicin, indicating enhanced delivery to infected macrophages. The novel inhalable crystalline form of rifapentine is suitable for targeted treatment of tuberculosis infection and may radically shorten treatment duration.
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Title :	Attitudes to weight and weight management in the early teenage years: a qualitative study of parental perceptions and views
Author :	Wendy J. Wills and Julia Lawton
Journal :	Health Expectations: Article first published online, 25 FEB 2014 | DOI: 10.1111/hex.12182
Abstract :	Background As most young teenagers grow up in families, parents might be well situated to facilitate and support their weight management and thereby prevent or manage obesity prior to adulthood. Aim This paper explores parents' perceptions of, and views about, their teenage children's weight and the factors that influence parents' weight management strategies. Design, setting and participants We conducted two qualitative studies in Scotland, UK, involving in-depth interviews with the parents of overweight/obese and 'normal' weight 13–15 year olds (n = 69). Findings Parents' concerns about their own weight provided useful context for understanding their attitudes or actions with regards to their teenage child. Some parents described their teenager's weight as being of concern to them, although puberty often introduced confusion about a child's weight status. Genetic explanations were very often put forward as a way of making sense of teenage weight or body size. Frustration about advising teenagers about weight management was expressed, and some parents worried about giving their growing child a 'problem' if they directly raised concerns about weight with them. Discussion Parents' views about their own weight as well as social and moral norms about labelling a teenager as overweight or as needing help with their weight could usefully inform patient-centred service development. Parent/teenage partnerships and supporting parents to create a healthy home in which teenagers can make healthier choices are suggestions for intervention development. Conclusion The study highlights the importance of taking parents' perceptions into account when developing family-based interventions to address teenage overweight and obesity.

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Title :	Brain-derived neurotrophic factor promotes angiogenic tube formation through generation of oxidative stress in human vascular endothelial cells
Author :	T. Usui, A. Naruo, M. Okada, Y. Hayabe and H. Yamawaki
Journal :	Acta Physiologica: Article first published online, 10 MAR 2014 | DOI: 10.1111/apha.12249
Abstract :	Aim Brain-derived neurotrophic factor (BDNF), a major type of neurotrophins, plays a role in the regulation of synaptic function. Recent studies suggest that BDNF promotes angiogenesis through its specific receptor, tropomyosin-related kinase B (TrkB). However, the detailed mechanisms for this still remain to be determined. Reactive oxygen species (ROS) generation contributes to the regulation of angiogenesis. Thus, we investigated the mechanisms by which BDNF regulates angiogenesis with focusing on ROS in cultured human vascular endothelial cells (ECs). Methods and results In human umbilical vein ECs, BDNF increased ROS generation as measured fluorometrically using 2′ 7′-dichlorofluorescein diacetate as well as NADPH oxidase (NOX) activity as measured by lucigenin assay. BDNF-induced ROS generation and NOX activity were inhibited by K252a, a TrkB receptor inhibitor. BDNF induced phosphorylation of p47 phox, a regulatory component of NOX, which was inhibited by K252a as measured by Western blotting. BDNF increased angiogenic tube formation in ECs, which was completely inhibited by K252a or gp91ds-tat, a NOX inhibitor. BDNF caused Akt phosphorylation in ECs, which was inhibited by K252a or gp91ds-tat. Conclusion The present results for the first time demonstrate that BDNF induces NOX-derived ROS generation through activation of p47 phox in a TrkB receptor-dependent manner, which leads to the promotion of angiogenic tube formation possibly via Akt activation.
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