Asian Journal of Pharmaceutical Technology and Innovation

Editorial

Editorial on ADEK Studies

Frank Orlowski

Director, Government & Commercial Strategic Operations at Latham BioPharm Group.

ε-Polylysine is a homopolymer of L-lysine, containing approximately 30 L-lysine subunits, as synthesized in aerobic bacterial fermentation by Streptomyces albulus. ε-Polylysine is approved for food use in Japan as an antimicrobial preservative. A series of pharmacokinetic and metabolic profile studies on ε-polylysine have been conducted in rats in order to provide a better understanding of the reason for its lack of toxicological effects in subchronic and chronic feeding bioassays using relatively high concentrations in the diet up to 50,000 ppm. As reported in this article, ε-polylysine was practically non-toxic in an acute oral toxicity study in rats, with no mortality up to 5 g/kg and was not mutagenic in bacterial reversion assays. Absorption, distribution, metabolism and excretion (ADME) studies on 14C-radiolabeled ε-polylysine, given in a single dose to fasted male rats at 100 mg/kg, revealed low absorption from the gastrointestinal tract. All but trace amounts of the dosed radioactivity was eliminated by excretion within 168 h and over 97% was accounted for in urine (1.2%), feces (92.9%), or expired air (3%) by 48 h. The sum of the cumulative excretion with routes associated with absorption in urine, expired air and carcass was 6.4% of total recovered radioactivity; approximately 94% of the dose of ε-polylysine passed unabsorbed through the gastrointestinal tract in the feces. Whole body autoradiography did not show concentration of absorbed ε-polylysine in any tissue or organ. Excretion half-lives of ε-polylysine equivalents in blood and plasma were 20 and 3.9 days, likely prolonged by the incorporation into protein of cleaved L-lysine. Metabolic profiles by HPLC analysis of plasma samples suggest that L-lysine is the predominant early metabolic by-product, likely from protease activity in the upper GI tract; only 0.2% of the administered parent compound was found in plasma. At 8–72 h, HPLC profiles show diminishing levels of ε-polylysine and L-lysine in plasma, accompanied by a shift to larger peaks of homopolymer fragments of varying subunit length, presumably from microbial degradation of ε-polylysine in the lower gut. HPLC profiles of urine and feces collected from 0 to 24 h post-dosing revealed three distinct peaks in urine, the first peak likely to be ε-polylysine and ε-polylysine less a few amino acid subunits, and the second, L-lysine and the third, a metabolite of L-lysine. Radiolabeled L-lysine was reduced from 67.2% of the radioactivity in plasma at 30 min to 7.5% at 4 h, indicating that L-lysine is readily removed from plasma from essential amino acid incorporation into protein. Based on the findings of the ADME studies and lack of toxicity in safety studies, the proposed use of ε-polylysine as a preservative in foods is considered to be safe.

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Editorial

Market Analysis on Generic Medicine

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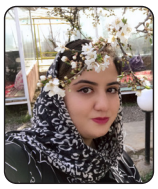
A large number of studies have focussed on the determinants of the entry of generics in the pharmaceuticals market. Most of them focus on the United States market. Much less evidence is found about heavily regulated pharmaceutical markets, such as the Portuguese market. This study uses data from Portugal, for the period 2000–2015. Based on a sample of 50 reimbursable outpatient drugs, that face potential entry of generics, two econometric models were estimated aiming to identify the determinants of entry and penetration of generics. The active substances included were chosen among those that represent the highest financial burden to the National Health System or are the most sold (in volume). To each of those active substances, the most sold pharmaceutical form, dosage, and package size was chosen. Our results suggest that market size is the main determinant of the generics entry. Concerning market penetration, our results show that it is determined by the number of marketed generics, as well as by price differences between brands and generics.

Asian Journal of Pharmaceutical Technology and Innovation

Abstract



Challenges of In vitro Genome Editing with CRISPR/Cas9 and Possible Solutions: A Review

Vida Ebrahimi

Shahid Beheshti University of Medical Sciences, Iran

Abstract:

Microbial production of bio-based ingredients often requires metabolically engineered bacterial strains with the edited genome. Genome editing tools are also essential for gene identification and investigating genotype-phenotype connections. Currently, one of the most common tools of genome editing is based on a natural bacterial adaptive immune system known as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas9 (CRISPR-associated protein 9) due to its simple, rapid, and efficient activities. Although successful in some in vitro systems, its application as an approach of metabolic engineering and genome editing is still not so extensive. Here, we discuss existing barriers and challenges of the CRISPR/Cas9 editing tool for in vitro systems. Firstly, we aim to briefly introduce the CRISPR/Cas9 method as an in vitro gene editing tool. Next, we discuss existing obstacles to CRISPR-based editing in bacterial and in vitro model systems and offer guidelines to help achieve editing in an expanded range of in vitro systems. Keywords: CRISPR/Cas9, Genome editing, Challenges, Bacteria, In vitro model systems.

Biography:

Vida Ebrahimi currently works at the Department of Pharmacognosy and Pharmaceutical Biotechnology, Shahid Beheshti University of Medical Sciences. Vida does research in Cell Biology, Bioinformatics and Biotechnology. Their most recent publication is 'The Effects of Genistein on Renal Oxidative Stress and Inflammation of Ovariectomized Rats'.

Recent Publications:

1. Polycyclic aromatic hydrocarbons degradation by aquatic bacteria isolated from Khazar Sea, the world's largest lake.
2. Epigenetic Modifications in Gastric Cancer: Focus on DNA Methylation.
3. Overview of ultraviolet‐based methods used in polycyclic aromatic hydrocarbons analysis and measurement.

Webinar on Pharmaceutical Sciences, November 30,2020 | Rome, Itly

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Asian Journal of Pharmaceutical Technology and Innovation

Abstract

Analytical chemisytry, analytical method development

Ali Khorramdoust

Supervisor of quality control at Medvac

Abstract:

Achieving radical tumor resection while preserving disease-free tissue during breast-conserving surgery (BCS) remains a challenge. Here, mass spectrometry technologies were used to discriminate stromal tissues reported to be altered surrounding breast tumors, and build tissue classifiers ex vivo. Additionally, we employed the approach for in vivo and real-time classification of breast pathology based on electrosurgical vapors. Breast-resected samples were obtained from patients undergoing surgery at MUMC+. The specimens were subsequently sampled ex vivo to generate electrosurgical vapors analyzed by rapid evaporative ionization mass spectrometry (REIMS). Tissues were processed for histopathology to assign tissue components to the mass spectral profiles. We collected a total of 689 ex vivo REIMS profiles from 72 patients which were analyzed using multivariate statistical analysis (principal component analysis-linear discriminant analysis). These profiles were classified as adipose, stromal and tumor tissues with 92.3% accuracy with a leave-one patient-out cross-validation. Tissue recognition using this ex vivo-built REIMS classification model was subsequently tested in vivo on electrosurgical vapors. Stromal and adipose tissues were classified during one BCS. Complementary ex vivo analyses were performed by REIMS and by desorption electrospray ionization mass spectrometry (DESI-MS) to study the potential of breast stroma to guide BCS. Tumor border stroma (TBS) and remote tumor stroma (RTS) were classified by REIMS and DESI-MS with 86.4% and 87.8% accuracy,

respectively. We demonstrate the potential of stromal molecular alterations surrounding breast tumors to guide BCS in real-time using REIMS analysis of electrosurgical vapors.

Biography:

PhD in Biophysics; Analytical Development of Pharmaceutical Biotechnology, Quality control of pharmaceutical products. MedvacInstitute of Iran • Supervisor of quality control • Medvac.

Recent Publications:

1. 1.Finding the best angle, between the carbon nanotubes and Four groups of antibiotics, using methods computational using.

Webinar on Pharmaceutical Sciences, November 30,2020 | Rome, Itly

Citation: Ali Khorramdoust, Analytical chemisytry, analytical method development, Webinar on Pharmaceutical Sciences.

Asian Journal of Pharmaceutical Technology and Innovation

Abstract

Non clinical studies in development of new drug delivery technologies; are they predictive or indicative?

Bijay Kumar Padhi
Unichem Laboratories Limited, India

Abstract:
Increasing demand in new and complex delivery technologies for differentiated formulations urges to identify early indicative or predictive non clinical methods. Predicting in-vivo performance of dosage forms is critical to the development of new drug delivery approaches. Physiological factors that influence in-vivo performance of formulations include gastrointestinal condition, mechanical stress, effects of food, enzymatic or pH related degradation of drug and its excipients, in-vivo drug release profile and the direct influence of some excipients on drug metabolism and transport etc. Practicality of non-clinical studies during product development is discussed with case studies on novel oral lipid based formulations, nasal sprays and long acting depot formulations. Absorption studies in animal models are discussed on early stage formulations. Primary pharmacokinetic parameters of interests; partial AUCs [e.g. (AUC0-15min), (AUC0- 30min), (AUC0-60min) etc.] , AUC from baseline through Tmax of reference products (AUC0-RefTmax), relative percentage of AUC0-T with respect to reference exposure values and Cmax were evaluated to rank order various formulation approaches. Translation of preclinical pharmacokinetic parameters and dosage form performance in humans are also discussed. Pharmacokinetics studies in appropriate animal models provide useful insights for further formulation development and help in minimizing both development-time and risks.

Biography:

Bijay Kumar Padhi has completed his PhD from The M.S.University of Baroda, INDIA on Pharmaceutics and Drug Delivery. He is the Associate Vice President and Head Formulation R&D at Unichem Laboratories Limited, INDIA. He has more than 18 years of industrial and research experience in formulation and drug delivery. He is the inventor for 5 USA granted patents, 1 Australian patent and more than 20 patent pending applications.

Recent Publications:

1. .Modified release doxycycline composition
2. .Effect of Food on the Pharmacokinetics of 2 Formulations of DRL□17822, a Novel Selective Cholesteryl Ester Transfer Protein (CETP) Inhibitor, in Healthy Males

Webinar on Pharmaceutical Sciences, November 30,2020 | Rome, Itly

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