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Data Mining via Internet Key to Identifying Human Genes

ARLINGTON, Va. - An article published in the American Association of Pharmaceutical Scientists' (AAPS) online journal, *AAPS PharmSci*, www.pharmsci.org, describes how novel human genes can be found on the Internet, and what type of information can be gleaned from public data before the first laboratory experiment is done.

The paper contains interactive figures that illustrate how gene sequences are found and spliced together - a benefit of an online-only journal.

The authors use the intestinal peptide transporter, proteins embedded in cell membranes that translocate substances such as drugs across the membrane, as an example of how gene sequence data can be found on the Internet. The authors explain that antibiotics have proven highly effective in treating infectious diseases. Whereas some antibiotics need to be injected, many can be taken orally. To be absorbed into the body, the main oral antibiotics with peptide-like structure need to be absorbed from the intestines through transporter proteins. The intestinal peptide transporter is encoded by a known gene, termed hPepT1, but it is currently unknown whether there are more human genes with similar functions, assisting in drug absorption and distribution to infected sites in the body. With the sequencing of the human genome nearing completion, the authors explain that most if not all related probable peptide transporter genes can now be found from sequence data publicly available on the Internet. Such data mining is the key to recent advances publicized by genomics companies.

The article, entitled "Human Proton/Oligopeptide Transporter (POT) Genes: Identification of Putative Human Genes Using Bioinformatics," appears in *AAPS PharmSci*, Volume 2, Issue 2. The article's authors include Christopher W. Botka, Thomas W. Wittig, Richard C. Graul, Carsten Uhd Nielsen, Kazutaka Higaki, Gordon L. Amidon, and Wolfgang Sadée.

The full text of the article can be viewed at www.pharmsci.org/transportergenes. AAPS PharmSci is an exclusively online journal of AAPS. AAPS PharmSci offers a forum for the rapid exchange and dissemination of scientific knowledge in the pharmaceutical sciences. AAPS is a professional, scientific society of more than 10,000 members employed in academia, industry, government and other research institutes worldwide. Founded in 1986, AAPS aims to advance science through the open exchange of scientific knowledge, serve as an information resource, and contribute to human health through pharmaceutical research and development. For more information about AAPS, visit AAPS Online at www.aaps.org.

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Volume 1 Issue 3 Highlights

Prediction of Adsorption from Multicomponent Solutions by Activated Carbon Using Single Solute Parameters

Dale Eric Wurster, Khouloud A. Alkhamis, and Lloyd E. Matheson.

The adsorption of 3 barbiturates— phenobarbital, mephobarbital, and primidone— from simulated intestinal fluid (SIF), without pancreatin, by activated carbon was studied using the rotating bottle method. The concentrations of each drug remaining

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in solution at equilibrium were determined with the aid of a high-performance liquid chromatography (HPLC) system employing a reversed-phase column. The competitive Langmuir-like model, the modified competitive Langmuir-like model, and the LeVan-Vermeulen model were each fit to the data. Excellent agreement was obtained between the experimental and predicted data using the modified competitive Langmuir-like model and the LeVan-Vermeulen model. The agreement obtained from the original competitive Langmuir-like model was less satisfactory. These observations are not surprising because the competitive Langmuir-like model assumes that the capacities of the adsorbates are equal, while the other 2 models take into account the differences in the capacities of the components. The results of these studies indicate that the adsorbates employed are competing for the same binding sites on the activated carbon surface. The results also demonstrate that it is possible to accurately predict multicomponent adsorption isotherms using only single-solute isotherm parameters. Such prediction is likely to be useful for improving in vivo/in vitro correlations.

The Potential of Organic-Based Amylose-Ethylcellulose Film Coatings as Oral Colon-Specific Drug Delivery Systems

Lee F. Siew, Abdul W. Basit, and J. Michael Newton.

Amylose-ethylcellulose film coatings obtained from organic-based solvents were investigated as potential vehicles for colonic drug delivery. Amylose, in the form of an amylose-butan-1-ol dispersion, and ethylcellulose, dissolved in either ethyl lactate, ethanol, or propanol and plasticized with dibutyl sebacate, were mixed in various proportions and applied using a fluidized bed coater to achieve a range of film thicknesses on 5-aminosalicylic acid pellets. Drug release from the coated pellets was assessed under gastric and small intestinal conditions in the presence and absence of pepsin and pancreatin using dissolution methodology, and also within a simulated colonic environment involving fermentation testing with human feces in the form of a slurry. Under upper gastrointestinal tract conditions, the rate and extent of drug release were found to be related to the thickness of the coating and the ratio of amylose to ethylcellulose within the film. Modeling of the drug release data revealed that the ratio was more important than coat thickness in controlling drug release, irrespective of the solvent used for coating. Coatings with a thick film and/or low amylose content were relatively impermeable and able to delay drug release under conditions mimicking the upper gastrointestinal tract. Furthermore, drug release was unaffected by the presence of pepsin and pancreatin and by long-term storage. Under simulated colonic conditions, drug release was more pronounced from coating formulations containing higher proportions of amylose. Colon-specificity can therefore be achieved using such systems by judicious choice of the appropriate ratio of amylose to ethylcellulose and coat thickness.

Structural Analysis of Microparticles by Confocal Laser Scanning Microscopy

Alf Lamprecht, Ulrich Schäfer, and Claus-Michael Lehr

This study demonstrates the potential of confocal laser scanning microscopy (CLSM) as a characterization tool for different types of microparticles. Microparticles were prepared by various methods including complex coacervation, spray drying, double emulsion solvent evaporation technique, and ionotropic gelation. Protein drugs and particle wall polymers were covalently labeled with a fluorescent marker prior to particle preparation, while low molecular weight drugs were labeled by mixing with a fluorescent marker of similar solubility properties. As was demonstrated in several examples, CLSM allowed visualization of the polymeric particle wall composition and detection of heterogeneous polymer distribution or changes in polymer matrix composition under the influence of the drug. Furthermore, CLSM provides a method for three-dimensional reconstruction and image analysis of the microparticles by imaging several coplanar sections throughout the object. In conclusion, CLSM allows the inspection of internal particle structures without prior sample destruction. It can be used to localize the encapsulated compounds and to detect special structural details of the particle wall composition.