

could be formulated. However, it should be noted that dissolution rate of poorly water-soluble drugs were highly dependent on drug properties, solubilizing compositions and polymeric carriers. Supported by ministry of health & welfare (02-PJ1-PG11-VN02-SV01-0002).

[PE1-13] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

A study on the Physico-chemical Properties of CB-ph, a New Anti-cancer drug

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Purpose To investigate the physico-chemical properties of CB-ph[2-benzoyloxycinnamaldehyde], an anticancer drug obtained from *Cinnamomum cassia* using methylenechloride, and its stability in various aqueous solutions. Results CB-ph was rarely soluble in water but soluble in methanol and very soluble in ether. Kinetic salt effect on degradation of CB-ph in buffer solutions at pH 4.0 and 60°C showed a linear relationship having a positive slope that means reactions between hydronium ions and protonated substrates. By plotting the logarithm of the degradation rate constants of CB-ph as a function of temperature(40-80°C) in aqueous solutions vs. 1/temperature was obtained a linear relationship and the t_{90} of CB-ph was calculated from Arrhenius plot. From the pH-rate profile, it was found that CB-ph was most stable in pH range of 2 - 4 at 60°C. The weight change of CB-ph in desiccator storage for 5 weeks under various relative humidity(21 to 88%) were not found. Conclusions Melting point of CB-ph was 82.5°C. The solubilities of CB-ph were 0.4ug/mL in water, 18mg/mL in methanol, and 49mg/mL in ether. The pH-rate profile of CB-ph at 60°C showed a general acid-base catalysis reaction in the range of pH 1-9. The degradation rate constants(K) of CB-ph at 60°C and pH 1, 4, 5 and 9 were 0.0041, 0.0004, 0.0019 and 1.5828 h⁻¹, respectively. t_{90} of CB-ph in distilled water at 20°C was approximately 170 days. The degradation of CB-ph in buffer solutions at pH 4.0 and 60°C may be affected through both of a primary and a secondary salt effect.

[PE1-14] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Pharmacokinetics of New Solubilizer in Intravenous Micelle Formulation of Paclitaxel in Mice

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Paclitaxel is an antitumor agent with poor water solubility and its pharmacokinetics are nonlinear. Cremophor EL, a surfactant used in the formulation of paclitaxel, may cause adverse effects. New solubilizer(Aceporol 460) was developed to reduce side effects of Cremophor EL and to increase the effect of drug as surfactant used in the intravenous micelle formulation of anticancer drug paclitaxel. We studied easy, rapid quantitative determination of Aceporol 460 in mouse plasma samples, which was achieved by complexation of the compound with the Coomassie brilliant blue G-250 dye in protein-free extracts. The binding of the dye to Aceporol 460 caused a shift of the absorption maximum in 400-700nm. Pharmacokinetics of New solubilizer were studied by this method. Mice were treated with Cremophor EL, Aceporol 460, each at dose levels of 0.83, 0.625, 0.417mL/kg(29.3, 22.1, 14.7mL/m²). Mouse samples were collected up to 90 minute after injection. AUCs(0-90) of Aceporol 460 were 85.46 μ Lmin/mL(at 0.417mL/kg), 194.83 μ Lmin/mL(at 0.625mL/kg), 252.99 μ Lmin/mL(at 0.83mL/kg).

[PE1-15] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Tissue Distribution of Novel Polymeric Micellar Paclitaxel in Mice

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Paclitaxel is a diterpenoid isolated from *Taxus brevifolia* and is an active anticancer drug for the treatment of ovarian cancer, breast cancer and Kaposi's sarcoma. Due to its low solubility in water, it is dissolved in Cremophor EL (polyethoxylated castor oil) and ethanol, which cause serious side effects including hypersensitivity. BLK460 was developed as a novel polymeric micellar paclitaxel formulation containing Aceporol460 as solubilizer. In this study, We evaluated tissue distribution of BLK460 in mice. BLK460 or reference formulation was administered to ICR mice by i.v. injection at a dose of 20 mg/kg as paclitaxel. At 5 min, 0.5 hr, 1 hr, 2 hr, 4 hr, and 8 hr after injection of BLK460 or reference formulation, the mice were sacrificed by cervical dislocation under ether anesthesia. Samples of blood, liver, kidney, lung, heart and spleen were collected. Paclitaxel was extracted from the biological samples using acetonitrile and analyzed using reverse phase HPLC with UV detection at 227 nm. Significant amounts of paclitaxel were detected in blood, liver, kidney, lung, heart and spleen following intravenous administration of BLK460.

[PE1-16] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

DEVELOPMENT OF FAST-DISSOLVING TABLET(FDT) CONTAINING ONDANSETRON HYDROCHLORIDE (Onseran™)

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To improve the compliance of oral administration of drugs in cancer patients, who are unable to swallow tablets, FDT containing ondansetron HCl(Onseran™) was developed with a low-cost manufacturing process. Onseran™ was prepared from ondansetron, mannitol, crospovidone, and others with a direct compression method. The disintegration time and dissolution rate of Onseran™ were assessed according to the USP method. The results were compared with those of the reference drug (Zofran™). Also in comparison with Zofran™, bioequivalence (BE) of Onseran™ was performed according to the guidelines of KFDA. Twenty-six healthy male volunteers of 20-40 years of age were divided into two groups and a randomized 2×2 cross-over design was employed. After oral administration of the tablet containing 8 mg of ondansetron to each subject blood was taken at predetermined time intervals, and the plasma concentrations of ondansetron were determined using HPLC. The disintegration time in the oral cavity of the Onseran™ was within a minute. The dissolution profiles of Onseran™ were similar to that of Zofran™. The differences in AUC₀₋₂₄ and C_{max} between two tablets were 6.9% and -8.7%, respectively and these two parameters met the BE criteria of the KFDA guideline. This result indicates that Onseran™ tablet is biologically equivalent to Zofran™ tablet.

[PE1-17] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Standardization of uniformity of dosage unit for oral dosage forms

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To secure the safety of drugs without compromising drug efficacy, it can not be more important to administer the exact intended amount of active ingredients to patients. Even if the correct amount of drugs are taken in the correct manner, drug can be overdosed or less-dosed without intention unless the content uniformity of the unit dose were secured. Especially, it can be a serious problem when it comes to drugs with narrow therapeutic windows or a strong pharmacological activity at a small dose. In this study, evaluation of uniformity and correlations between weight and content were reviewed to prepare the guideline for establishing the content uniformity test in the drug specification. In order to get a correlation coefficient between weight variation and content uniformity, assay, weight variation and content uniformity were tested on drugs with single active ingredient of 560 lots : which were classified into groups based upon content of active ingredients and dosage forms. This study showed that surveillance of content uniformity is needed in products containing less than 2 % or 2 mg of active ingredient and sugar coated tablets.