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^{TM})

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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^{TM}) was developed with a low-cost manufacturing process. Onseran^{TM} was prepared from ondansetron, mannitol, crospovidone, and others with a direct compression method.The disintegration time and dissolution rate of Onseran^{TM} were assessed according to the USP method. The results were compared with those of the reference drug (Zofran^{TM}).Also in comparison with Zofran^{TM}, bioequivalence (BE) of Onseran^{TM} 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^{TM} was within a minute. The dissolution profiles of Onseran^{TM} were similar to that of Zofran^{TM}. The differences in AUC_{0-24}, 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^{TM} tablet is biologically equivalent to Zofran^{TM} 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.