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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 to be 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 drugs specification. In order to get correlation coefficient between weight variation and content uniformity, assay, weight variation and content uniformity were tested on drugs with single active ingredient of 148 lots and drugs with multiple active ingredients of 144 lots on the domestic market; of which classified into groups based upon the number of active ingredients, content(%), and content uniformity test of their specifications. The ratio of products that lie within KP criteria of weight variation and content uniformity is 97.6% and 78.1% respectively. This results means that the survaillance of content uniformity of oral solid dosage forms is needed. Drugs with single active ingredient showed more correlation than ones with multiple active ingredients. Study also showed that differences in correlations were more influenced by each active ingredient than their weight of active ingredients. 53% of drugs with single active ingredient showing content(%) of 2% or more appeared to be correlated. Since this study was not based upon sufficient sample numbers of each test group, more research works on coated tablets and capsule are required to suggest the guideline of content uniformity tests

[PE1-2] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Effetcs of Adhesives and Permeation Enhancers on the Skin Permeation of Captopril

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In order to formulate TDDS of captopril, matrix-type patches containing 20% captopril and various pressure-sensitive adhesives (PSAs) and permeation enhancers were prepared using a labcoater. The effects of PSA and permeation enhancers on skin permeation rate of captopril from the prepared patches were evaluated using Franz diffusion cells fitted with excised rat skins. Among 6 polyacrylate copolymers studied, D-2287 resulted in the highest permeation rate of captopril. Fatty alcohols resulted in pronounced enhancing effect on the skin permeation of captopril, while DMSO, NMP, oleic acid, Transcutol and polysorbate 20 showed no significant enhancing effect. The permeation enhancing effect of fatty alcohols reached the maximum at the level of 10%. The results indicate that matrix-type TDDS of captopril can be developed with further optimization.

[PE1-3] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Formulation of Cefatrizine-Containing Matrix Tablet with Short-Term Duration

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Cefatrizine(CFT) has very short half-life that it is recommended to take it four times a day, therefore it needs to sustain the release. Even though this urging necessity, it has been widely reported that this kind of formulation is nearly impossible because its absorption window, like other most cephalosporines including general β-lactam antibiotics, is so narrow, i.e., at the region of the upper

small intestine. Accordingly, formulating this kind of drugs with too much release time resulted in very low bioavailability.
So, we tried to formulate the matrix tablet containing CFT with short-term sustained release so that we should minimize the portion of the unabsorbed drug through the small intestine. We chose various hydroxypropylmethylcelluloses (HPMC) as a matrix carrier and estimated how the drug to polymer ratio and polymer type had an influence on the release of the drug. In more, we evaluated not only the effect of various diluents and lubricants, but also the influence of granulation on the release of the drug.
As a result of our research, we could formulate the robust short-term sustained release tablet with the duration time of about 2 hours. It is supposed to make other similar drugs, which has the narrow absorption window, a sustained release form with relatively high bioavailability than ever since.

[PE1-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

PREPARATION AND EVALUATION OF MICROEMULSION CONTAINING IBUPROFEN

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PREPARATION AND EVALUATION OF MICROEMULSION CONTAINING IBUPROFEN
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Oleic acid, linoleic acid, and several kinds of glycerides and triglycerides were used as an oil phase with several surfactants, which consist of saturated polyglycolized glycerides (Labrasol) , diethylene glycol monoethyl ether(Transcutol) , and polyoxyethylene(4) lauryl ether(Brij 30). The solubilities of ibuprofen in oils and surfactants were about 100 times higher than that of water. The three phase diagrams show o/w microemulsion domain. When oleoyl macroglycerides EP(Labrafil) or caprylic/capric triglyceride polyethylene glycol-4 complex(Labrafac) as oil phase and diethylene glycol monoethyl ether(Transcutol) or saturated polyglycolized glycerides (Labrasol) as surfactant were used, the domain of microemulsion was wide. In dissolution test, it was showed 23.7 %, 24.3%, 19.1 % and 15.4 % for caprylic/capric triglyceride polyethylene glycol-4 complex (Labrafac), oleoyl macroglycerides EP(Labrafil), linoleic acid and suspension, respectively. Following oral administration of microemulsion containing ibuprofen, the Cmax was more increased and the Tmax was more rapid than these of suspension. The relative bioavailability of microemulsion was increased as 165.5 %, 166.1 % and 134.8 % for caprylic/capric triglyceride polyethylene glycol-4 complex(Labrafac), oleoyl macroglycerides EP(Labrafil), linoleic acid and suspension, respectively.

[PE1-5] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Synthesis and characterization of a ketoprofen prodrug

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The objective of this study is to prepare ketoprofen (KP) - polyethylene glycol (PEG) conjugate and to study its degradation kinetics and solution behavior. KP-PEG conjugate were synthesized from ketoprofen and PEG methylester by esterification in the presence of DCC. The KP-PEG conjugate (KPEG750) was characterized by IR, ^{1}H-NMR spectroscopy. The quantitation and separation of KPEG750 were performed by HPLC with mobile phase consists of acetonitril/ammonium phosphate buffer (pH 3.0). The conjugation between KP and PEG could be observed by the disappearance and appearance of some specific IR bands: ① the disappearance of very broad peak by hydrogen