hydroxybutyric acid was in R configuration.

[PD4-19] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Studies on the Quality Evaluation of Pharmaceuticals(II) - Method Validation of Endotoxin Test in Pharmaceutical Injections.

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Limulus Amebocyte Lysate(LAL) test (endotoxin test) is supposed to be a alternative to the rabbit pyrogen test in that the former is more convenient, specific and inexpensive. We applied the LAL test to the detection of bacterial endotoxins in 5 pharmaceutical injections (dextrose injection, saline injection, mannitol injection, NaCl injection and KCl injection) using gel-clot method and kinetic turbidimetric method and validated the methods by investigating LAL reagent sensitivity, interferences, calibration curve, reproducibility and recovery.
The determined LAL reagent sensitivity was 0.0605 EU/mL and the calibration curve of endotoxin standard solutions was linear over the entire range from 0.0078125 to 50 EU/mL. The linear regression coefficient of determination was 0.9997 and the limit of detection was 0.005 EU/mL. In all 5 injections, the amount of endotoxin estimated by the LAL test (gel-clot method and kinetic turbidimetric method) was well recovered and there are no significant inteference (both enhancement and inhivition) factors. These results suggest that the LAL test was useful method for quantitative estimation of endotoxin, the probable major cause of pyrogenicity and expected for the substitutive method for pyrogen test in examined 5 injections.

[PD4-20] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Studies on the Quality Evaluation of Pharmaceuticals (II) - Comparative Analysis of Pyrogen and Endotoxin Test in Pharmaceutical Injections.

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Limulus Amebocyte Lysate(LAL) test (endotoxin test) is supposed to be a alternative to the rabbit pyrogen test in that the former is more convenient, specific and inexpensive. To compare the LAL test with the rabbit pyrogen test, we prepared spiked samples of 5 injections(dextrose injection, saline injection, mannitol injection, NaCl injection and KCl injection) with concentration of 0.25, 0.5, 1.0 EU/mL and tested those by pyrogen and endotoxin test simultaneously. The LAL test was accomplished by using 2 different methods, gel-clot method and kinetic turbidimetric method and the pyrogen test was accomplished by using KP official pyrogen test method.
In our results, the LAL test was about 14 times more sensitive than the rabbit pyrogen test in the case of gel-clot method and about 95 times more sensitive than the rabbit pyrogen test in the case of kinetic turbidimetric method. The amounts of endotoxin in 5 injections estimated by the LAL test was well recovered and correlated with the rise of body temperature in rabbit pyrogen test. These results suggest that the LAL test could be used as an alternative method for the rabbit pyrogen test to examined 5 injections.

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

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 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