national reference standard with a defined specific activity for use in biological and physico-chemical assays to enable the harmonized quality control of biological products. The candidate reference standard of KFDA for somatropin 98/674 was evaluated to determine the suitability of serving as the standard for somatropin by the collaborative study, in which 10 laboratories were participated. Physico-chemical analysis and in vivo bioassay were performed by direct comparison with the international somatropin standard 88/624. Data of identification by SDS-PAGE, IEF, peptide mapping, and HPLC indicated KS 98/674 was almost identical to IS 88/624. Determination of somatropin content by SE-HPLC yielded a mean estimate of 2.01 mg somatropin per ampoule. Data from the study also yielded mean values of 0.39±0.26 % for high molecular weight impurities by SE-HPLC and mean values of 2.13±1.29 % for somatropin related proteins by RP-HPLC. Estimates of relative potency IU by weight gain bioassay in the hypophysectomised rats showed one IU of IS 88/624 was equivalent to one IU of Korean Standard 98/674. Based on the results of the study, the candidate standard 98/674 is suitable to serve as a somatropin reference standard of KFDA.

[PD4-17] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Determination of Hair Polyamines as N,N-Ethyloxycarbonyl-Pentafluoropropionyl Derivatives by Gas Chromatography-Mass Spectrometry

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A noble method is described for the simultaneous determination of hair polyamines such as 1,3-diaminopropane, putrescine, cadaverine, spermidine, and spermine by gas chromatography-mass spectrometry (GC-MS). The method is based on the extractive two-phase ethyloxycarbonylation of amino functions in aqueous solutions combined with further pentafluoropropionylation of the remaining active protons for the direct analysis by GC-MS with the selected ion-monitoring (SIM) mode. This method showed a good overall accuracy (% bias) and precision (% CV) as 3.32~11.05 and 5.88~14.71, respectively. When applied to hydrolysates of human head hair samples from 11 male and 19 female normal subjects, all 5 polyamines were positively detected at the concentrations of 8.82~871.87 ng/g. The detection limits for SIM of the polyamines ranged from 0.02 to 0.2 ng, while their recovery rates varied in the range of 76.42~93.38%. The levels of polyamines except for cadaverine in hair specimens studied were found to be higher in men than in women.

[PD4-18] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Determination of the Absolute Configurations of Urinary Chiral Acids from Patients Suffering from Ornitine Transfer Carbamylase Deficiency, β-Ketothiolase Deficiency & Lactic acidosis by GC

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Chiral acids occurring in metabolic pathways are known as important biochemical indicators of specific enzyme deficiencies in inborn errors of metabolism and their accurate chiral determination is thus of utmost importance for the correct diagnosis. After extraction from urine samples of patients suffering from Ornitine Transfer Carbamylase (OTC) Deficiency, β-Ketothiolase Deficiency & Lactic Acidosis, chiral acids such as lactic, 2-hydroxybutyric and 3-hydroxybutyric acids were converted to diastereomeric O-trifluoroacetylated (1S, 2R, 5S)-(-)-menthyl esters and p-hydroxyphenyllactic acid was converted to diastereomeric O-trifluoroacetylated (S)-(+)-3-methyl-2-butyl ester for the direct GC analysis on achiral dual-capillary column system. In all cases of OTC, β-Ketothiolase and Lactic Acidosis, the absolute configurations of lactic, 2-hydroxybutyric and p-hydroxyphenyllactic acids were positively determined to be in their S-form, while 3-

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.

Kim HS, Lee SD, Kim HS, Kim MJ, Jin JS, Jung KS, Yang SJ, Jung HY and Jang SJ

Division of Drug Chemistry, Department of Drug Evaluation, KFDA

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