

codeine.

At this time, opium is assigned as narcotics in Korea according to the rule concerning narcotics control, and its major component morphine and codeine too.

The concentration of opiate alkaloids, morphine and codeine was measured to classify it from extra-narcotics used in medical treatment.

In this research, we confirmed and measured the content of morphine and codeine in 'bokbanggamchopyeon'

30 species of seized 'bokbanggamchopyeon' tablets were used for test and qualitative and quantitative analysis of morphine and codeine were performed by GC/MS.

As a result, all of 30 samples showed about 10 times higher concentration of morphine and codeine than extra-narcotics according to the rule concerning narcotics control.

[PD4-18] [04/18/2003 (Fri) 13:30 – 16:30 / Hall P]

Determination of Glimepiride in Human Plasma by LC-MS/MS

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This study established a sensitive novel quantification method for detecting glimepiride in human plasma using LC-MS/MS for pharmacokinetic studies. The mobile phase used after degassing was composed of 10 mM ammonium acetate and acetonitrile (20:80, pH 3.0), with flow rate of 200 μ L/min. One mL plasma were pipetted into glass tubes and spiked with 0.1 mL of internal standard solution. After adding 6 mL of diethyl ether – ethyl acetate (1:1, v/v), the plasma sample was then shaken for 15 min. A centrifuged upper layer was then evaporated and reconstituted with 120 μ L mobile phase and 20 μ L of sample were injected into LC-MS/MS. Glimepiride produced a protonated precursor ion ($[M+H]^+$) at m/z 491 with a major product ion at m/z 352. On the other hand, internal standard produced a protonated precursor ion ($[M+H]^+$) at m/z 446 with a major product ion at 321. Based on a signal-to-noise level (S/N) of 9–11, the limit of quantification for glimepiride was found to be 0.1 ng/mL. Validation experiments have shown that the assay has good precision and accuracy over a wide concentration range. This simple, rapid and robust assay will enable the complete processing of large sample for pharmacokinetic studies of glimepiride in human plasma.

[PD4-19] [04/18/2003 (Fri) 13:30 – 16:30 / Hall P]

Chiral Separation of Non-Steroidal Inflammatory Drugs as Dual Diastereomeric Derivatives with (R)- and (S)-Phenylethylamines

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The carboxylated acidic non-steroidal anti-inflammatory drugs (NSAIDs) constitute the principal class of agents for controlling the pain and inflammation of the rheumatic diseases. It is mostly administered as a racemic mixture like most other drugs with asymmetric carbon atoms. However enantiomers of many racemic drug substances have been shown to possess different pharmacological toxicological properties. Therefore, production of active NSAIDs in enantiomerically pure forms and their optical purity control have become important tasks. In this study, each enantiomer of nine NSAIDs (ibuprofen, suprofen, flurbiprofen, fenoprofen, piroprofen, indoprofen, carprofen, ketoprofen and naproxen) was activated with ethyl chloroformate, followed by conversion into diastereomeric amide either with (R)-(+)-phenylethylamine or (S)-(-)-phenylethylamine. The resulting derivative extracted with ethyl acetate in acidic condition was

concentrated to dry residue and reconstituted in ethyl acetate for direct analyses by capillary column gas chromatography. Chiral amidation was optimized and validated for the simultaneous assay of multi NSAID enantiomers in a single run. The present method will be useful for the simultaneous chiral separation of commercial products such as ibuprofen, naproxen and fenoprofen.

[PD4-20] [04/18/2003 (Fri) 13:30 – 16:30 / Hall P]

Studies on the quantification of sobrerol by high-performance liquid chromatography

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This study was designed to develop and validate an isocratic reversed phase high performance liquid chromatographic(HPLC) method for the quantitation of sobrerol in drug preparations, and obtain the data pool that can be used in the revision of pharmacopoeia. The separation of sobrerol and the other compounds (S-carboxymethylcysteine, acetaminophen, methyl paraben, propyl paraben, and sobrerol degradants) was achieved in a C18 column with an acetonitrile-methanol-water (24.5:10.5:65.0) mobile phase. The detection was performed at 200nm. The linearity of peak area responses versus concentrations was demonstrated from 20 ~ 60 $\mu\text{g}/\text{mL}$ of sobrerol by a correlation coefficient of 0.9995. The limit of detection (LOD) and quantitation(LOQ) was 0.6 $\mu\text{g}/\text{mL}$ and 2 $\mu\text{g}/\text{mL}$, respectively. Recovery from excipients was 100.8% (drug substance), 101.1%(capsule), and 99.5%(syrup), respectively. The precision of this method showed RSD of 0.9%(drug substance), 1.9% (capsule), and 1.6% (syrup), respectively. According to a recovery and precision study, this method was shown to be quantitative, and sobrerol in analytical solutions was stable for 1 day. A comparison study of HPLC and GC showed that validation parameters were similar to each other except the range of linearity.

[PD4-21] [04/18/2003 (Fri) 13:30 – 16:30 / Hall P]

Sensitive Determination of Felodipine in Human Plasma by LC-MS/MS

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This study established a highly sensitive novel quantification method for detecting felodipine in human plasma using LC-MS/MS. The mobile phase used after degassing was composed of 1 mM ammonium acetate and acetonitrile (20:80, pH 6.0), with flow rate of 200 $\mu\text{L}/\text{min}$. One mL plasma were pipetted into glass tubes and spiked with 0.1 mL of internal standard solution. After adding 6 mL of diethyl ether, the plasma sample was then shaken for 15 min. A centrifuged upper layer was then evaporated and reconstituted with 120 μL mobile phase and 20 μL of sample were injected into LC-MS/MS. Felodipine produced a protonated precursor ion ($[\text{M}+\text{H}]^+$) at m/z 384 with a major product ion at m/z 338. On the other hand, internal standard produced a protonated precursor ion ($[\text{M}+\text{H}]^+$) at m/z 347 with a major product ion at m/z 315. Based on a signal-to-noise level (S/N) of 9-10, the limit of quantification for felodipine was found to be 0.05 ng/mL. Validation experiments have shown that the assay has good precision and accuracy over a wide concentration range. This method is not only selective and reliable also faster and simpler compared to other recently reported methods. Likewise, this method has been successfully applied to preliminary pharmacokinetic studies.