

Ahn Moon Kyu , Lee Dong Hyuk , Lee Mi Na , Lee Un Kyung , Moon Hyun Sook , Jung Moon Mo, Hur Moon Hye

Department of pharmacy, Kyungsoong Univ.608-736, Pusan, Korea \* Pusan regional Food & Drug Administration, 608-080, Pusan, Korea

A poly(vinylchloride) membrane ion-selective electrode for determining the acidic drugs is described. The sensing membrane of the electrode consists of acidic drug-metal(II)-dipyridylketone oxime as an ion-exchanger site in a PVC matrix plasticized with nitrophenyl ether group. In a borate buffer solutions of pH 8.9, the electrode exhibits a fast, stable and linear response for  $2 \times 10^{-5} \sim 10^{-2}$  mol dm<sup>-3</sup> acidic drug with an anionic slope of near 55 mV decade<sup>-1</sup>. Potentiometric selectivity measurements revealed negligible interferences from several different anions. The electrode displays useful analytical characteristics for the direct determination of acidic drugs such as fenemates, ibuprofen, naproxen and diclofenac in pure form and in pharmaceutical preparations.

[PD4-10] [ 10/19/2001 (Fri) 09:00 - 12:00 / Hall D ]

### **Novel chiral derivatizing agent, (+)-2,4-dimethyl-1,3-benzodioxole-2-acetic acid**

Ko Mi Young<sup>o</sup>, Kim Jeong-Hwan, Lee Jae Young , Mar Woongchon, Kim Kyeong Ho

College of Pharmacy, Kangwon National University, National Product Research Institute, Seoul National University

A carboxylic acid with a 1,3-benzodioxole skeleton, (+)-2,4-dimethyl-1,3-benzodioxole-2-acetic acid ((+)-DMBA) was prepared. The potential as a chiral derivatizing agent was evaluated in terms of the HPLC analysis of (±)-methylbenzylamine. With more than 50 times molar excess of (+)-DMBA chiral derivatization reaction was completed within one hour at 70°C. Diastereomeric derivatives of (±)-methylbenzyl amine were well resolved on the silica column using n-hexane-ethyl acetate as a mobile phase.

[PD4-11] [ 10/19/2001 (Fri) 09:00 - 12:00 / Hall D ]

### **Chiral derivatization of (±)-methyl benzylamine with (+)-2-t-butyl-2-methyl-1,3-benzodioxole-4-carboxylic acid as a chiral derivatizing agent**

Lee Jae Young<sup>o</sup>, Kim Jeong-Hwan, Ko Mi Young, Seo Sang Hun, Kim Kyeong Ho

College of Pharmacy, Kangwon National University, Department of Production, Yuhan Corporation

The applicability of (+)-2-t-butyl-2-methyl-1,3-benzodioxole-4-carboxylic acid ((+)-TBMB) as a chiral derivatizing agent for the enantioseparation of a compound containing an amino group such as (±)-methyl benzylamine and some β-blockers was investigated. Diastereomeric derivatives were prepared and confirmed by NMR and Mass. Diastereomeric derivatives were analyzed by normal phase high-performance liquid chromatography. Condition of derivatization (temperature, reagent excess and reaction time) were optimized and compared to each other.

[PD4-12] [ 10/19/2001 (Fri) 09:00 - 12:00 / Hall D ]

### **Chiral Analysis of Baclofen by Capillary Electrophoresis using Highly Sulfated γ-Cyclodextrins as Chiral Selectors**

Ahn Sungyeon<sup>0</sup>, La Sookie, Kim KyoungRae, Kim JungHan

College of Pharmacy, Sungkyunkwan University, Department of Biotechnology, College of Engineering and Bioproducts Research Center, Yonsei University

Baclofen (4-amino-3-p-chlorophenylbutyric acid), a p-chlorophenyl analogue of  $\gamma$ -aminobutyric acid, is widely used in the treatment of spastic disorders as a skeletal muscle relaxant. The enantiomers of baclofen differ in their pharmacodynamic and toxicological properties: the R-( $-$ )-enantiomer is much more active but also more toxic than the S-( $+$ )-enantiomer. Besides, the "ineffective" S-( $+$ )-enantiomer antagonizes the action of the effective R-( $-$ )-enantiomer, so that the R-( $-$ )-enantiomer is also substantially more effective than racemic baclofen. Because the kinetic disposition of the two enantiomers may be different, the investigation of the pharmacokinetic behavior of both enantiomers is often desirable. In this study, the optimal enantiomeric separation of baclofen and the validation of the method for its accurate and precise assay in human plasma will be discussed by capillary electrophoresis using highly sulfated  $\gamma$ -cyclodextrins as chiral additives.

[PD4-13] [ 10/19/2001 (Fri) 09:00 - 12:00 / Hall D ]

### **New reagent for the enantiospecific analysis of primary or secondary amino group via High-Performance Liquid Chromatography**

Lee KyoungJune<sup>0</sup>, Youm JeongRok

Division of Pharmacokinetics and Drug Metabolism, ChoongWae Pharma Corp., Kyungkido, South Korea  
College of Pharmacy, ChungAng University, Seoul, South Korea

The synthesis and analytical testing of new ultraviolet active chiral derivatizing agent, (S)-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-2,5-dioxo-pyrrolidin-1-yl ester were investigated. In a rapid, one-step procedure, the compound reacts with primary or secondary amino group of  $\beta$ -blockers (acebutolol, arotinolol, betaxolol, bisoprolol, celiprolol, metoprolol, pindolol and propranolol) to form stable asymmetric urea derivatives. Studies on derivatization conditions demonstrate excellent derivative yield in mild organic base solutions. With excess of 20 times molar or more of chiral derivatizing agent, chiral derivatization reactions were completed within one hour at room temperature. Diastereomeric derivatives of  $\beta$ -blockers were well resolved in the ODS-C8 column using acetonitrile-methanol-water as mobile phase.

A reversed-phase high performance liquid chromatographic method was developed to determine the optical purity of propranolol enantiomers. The enantiomers were converted to diastereomeric derivatives using this new chiral derivatizing agent. Separation of the enantiomers as diastereomers was achieved by reversed phase HPLC within 35 min using Develosil C8 column. This method allowed determination of 0.05% of either of the enantiomers in the presence of its stereoisomer and method validation showed adequate linearity over the required range. Owing to the reaction condition during the derivatization with (S)-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-2,5-dioxo-pyrrolidin-1-yl ester, the possibility of racemization had to be established. Different ratios of (R)-(+)-propranolol and (S)-(-)-propranolol were prepared. Enantiomeric separation of these mixtures took place on a Chiralcel OD column or, after derivatization with (S)-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-2,5-dioxo-pyrrolidin-1-yl ester, on a Develosil C8 column. The results from these two independent separation systems were compared with trace racemization and were in very good agreement. No racemization was found during the experiment.

[PD4-14] [ 10/19/2001 (Fri) 09:00 - 12:00 / Hall D ]

### **Influence of temperature and time differences on contents of cefaclor in dried-syrup.**

Park WonHee, Chae YoungZoo