1. Paraben mixtures (methyl paraben and propyl paraben) were used in most cases. (90 a 159 samples)
2. In case of methyl and propyl paraben being used, capsules showed a higher concentration than any other shape of drugs.
3. The sum of paraben (methyl paraben and propyl paraben) concentration was 0.06~0.28% in creams, 0.03~0.11% in syrups, 0.111% in suppositories 0.02~0.054% in ophthalmics solutions, 0.051~0.15% injections, 0.15~5.32mg/cap in capsules and 0.08~0.12% in solutions.

[PD4-8] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Chiral separations of β-blockers by HPLC using (S)-(+)-TBMB-COOH

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The fluorescent chiral derivatizing agent, (S)-(+)-TBMB carboxylic acid was applied for highly sensitive HPLC analysis of enantiomeric β-blockers. Racemic β-bolckers were derivatized with (S)-TBMB-COCl in pyridine-CH3CN solution and subjected to normal phase silica column HPLC for the separations of the derived diastereomeric di-(S)-TBMB-carboxylated β-blocker derivatives.
Optically pure (S)-TBMB-COCl was synthesized and its CH3CN solution was successfully used for the determination of the optical purities of β-blockers as their diastereomeric di-(S)-TBMB derivatives without any racemization. Optimum reaction conditions, reaction time, temperature and the concentration of (S)-TBMB-COCl, and HPLC conditions were examined using a normal phase silica column(4.6×250mm). The eluents were monitored by fluorescent detection at Ex. 310nm and Em. 380nm and the detection limits of (S)-TBMB-derivatized β-blockers were 0.1 pmole on column.
In this study, we have successfully demonstrated for the chiral separations of various β-blockers by normal phase HPLC using fluorescent chiral derivatization agent, (S)-(+)-TBMB-COOH, and the extension of the present method is underway.

[PD4-9] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Studies on the Chiral Separation Mechanism of Amine Moiety Drugs using chiral CBH column

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Enantioseparation of chiral drugs are sometimes laborious and time-consuming study and the chiral stationary phase is very expensive. Therefore, if the prediction of chiral separation of the drug is possible by their 3-dimensional molecular structure, it is certain that will be a very useful tool in studing the chiral separation of drugs and separation mechanism of chiral stationary phases. Especially, all beta blockers have chiral center in their molecule and most of them are marketed as racemic mixtures. It has been well documented that the single enantiomers of beta blocking agents, as well as several other drugs, differ largely in their pharmacodynamic and pharmacokinetic profiles. (S)-propranolol is more than 100 times potent in blocking beta receptors than the corresponding (R)-enantiomer. In this study, eleven of the most popular beta-blockers and some other drugs which have very similar structure with amine moieties were chosen as model drugs.
Firstly, in order to study the prediction of the chiral separation of some amine moiety drugs, influence on enantioselective retention of several mobile phase parameters, e. g., types of organic modifier, i.e., 2-propanol, acetonitrile, concentration of organic modifier, mobile phase buffer pH,

column temperature were studied using chiral CBH column. The structure of CBH, contains three regions, a catalytically active core, an inter-connecting region, and a cellulose-binding domain consisting of 36 amino acids forming two disulfide-bridged loops. Especially the retention factors as well as the enantioselectivity of amine were strongly dependent on pH. Especially betaxolol and pindolol weren't separated at pH 7.0, but as the pH was decreased to 6.0 and 5.0, chromatographic parameters were markedly increased. And most of the amine have the pKa values above 7.0. This means that they mainly are present as cations in the pH range studied. Thus the amines should be retained by electrostatic attraction or as a neutral complex(ion-pair) with an ion of opposite charge. Therefore, in this study electrostatic interaction was more important than hydrophobic interaction in chiral separation mechanism of amine moiety drugs using chiral CBH column.

[PD4-10] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Water-Methanol Mixture Analysis using NIR Spectral Data and ITTFA

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Water-methanol mixture is frequently used as an HPLC solvent and strong hydrogen bonding between water and methanol is well-known. But a detailed aspect of water-methanol mixture has not been shown with direct spectral evidence. Recently, near infrared spectroscopy and chemometric data refinery have been successfully combined in many applications. On the basis of factor analytical methods, the spectral features of water-methanol mixtures were studied to reveal the detail of mixtures.
Eleven water-methanol mixtures were prepared with varying concentration of each constituent and near infrared spectral data were acquired in the range of 1100-2500nm with 2-nm interval. The data matrix(11 by 700) was analysed with ITTFA(Iterative Target Transform Factor Analysis) algorithm implemented as MATLAB codes written in-house.
As a result, the concentration profiles of water, methanol and two different water-methanol complexes were resolved and the spectra of water-methanol complexes were calculated, which cannot be acquired with pure complexes. Those complexes cannot be isolated by any physical separation but their complete NIR spectra were acquired by ITTFA algorithm. The concentration profiles of two complexes were different by added amount of water and methanol. Those results will be shown on poster.

[PD4-11] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

A dipyridylamine-metal membrane sensor for potentiometric determination of metal ion

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A liquid membrane electrodes for metal ion Fe^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+} were investigated. The electroactive substance of the membrane electrode consists of ternary complex of tetraphenylborate and metal-dipyridylamine. The dipyridylamine-metal(II) complex reacts with tetraphenylborate to form a water insoluble ion association complex soluble in some plasticizer mediators. The liquid membrane was plasticized with nitrophenyl ether derivatives. The sensor exhibits fast Nernstian response for dipyridylamine-metal ion with a cationic calibration slope of Fe^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+} were 27.0±0.1 mV/dec., 26.7±0.1 mV/dec., 29.5±0.1 mV/dec., 25.2±0.1 mV/dec. down to 4×10^{-7} mol/L dipyridylamine-metal ion at pH 5~10.
Interferences from common inorganic cations were negligible.