

Accurate Chiral Discrimination of Acidic- and Amino acidic-Chiral Drugs by Indirect GC and Direct CE Enantiomeric Separation Methods

Kyoung-Rae Kim

College of Pharmacy, Sungkyunkwan University, Suwon 440-746, Korea

Because of the differences between biological and pharmacological properties of chiral drugs in human body, accurate determinations of their optical purities have been in great need. There are two major approaches in chiral separation: indirect method performed under achiral condition, and direct method under the chiral environment. We have been conducting chiral separation of acidic chiral compounds and also amino acidic chiral compounds employing indirect GC methods and direct CE enantiomeric separation methods.

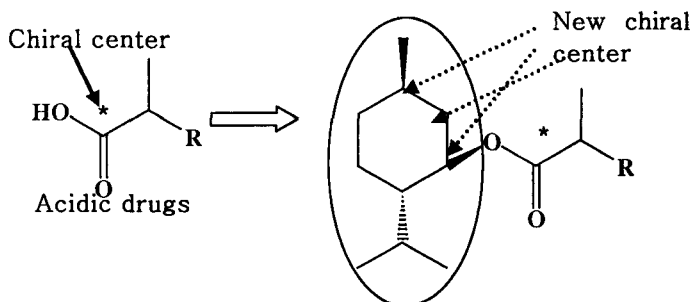
1. Indirect GC method

Chiral acidic- and amino acidic-compounds as volatile diastereomeric derivatives were analyzed directly by GC on achiral DB-5 and DB-17 dual-capillary columns of different polarities. The dual-columns were complements each of the other for the complete chiral separation. The enantiomers unresolved on DB-5 column were resolved on DB-17 column, while the enantiomers unresolved on DB-17 column were well resolved on DB-5. Moreover, the temperature-programmed retention index (*I*) values measured on both columns were characteristic of each enantiomer and thus simple *I* matching with the reference values was useful in cross-checking for the chemical identification and the chiral discrimination as well.

Prior to chiral separation, acidic enantiomers and amino acidic enantiomers were converted to appropriate diastereomeric derivatives under each optimum condition.

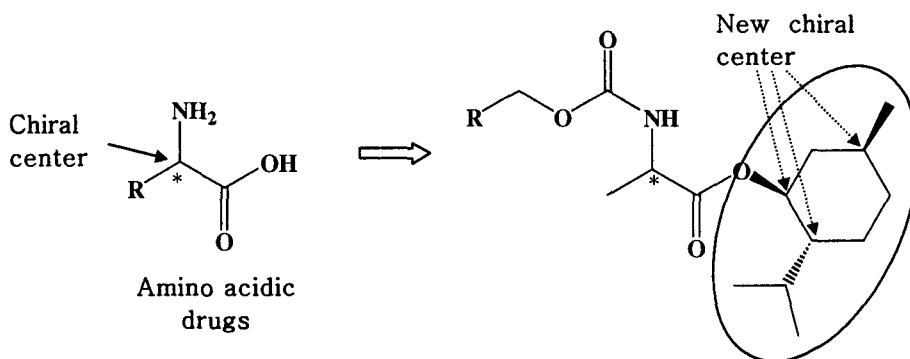
[1] Acidic drugs

Second chiral center was introduced into carboxyl groups of chiral acidic compounds by reacting with chiral alcohol such as (-)-menthol and the remaining hydroxyl groups were acylated.



[1] Amino acidic drugs

Two-phase extractive alkoxycarbonyl reaction with alkyl chloroformate present in the organic solvent phase was performed to recover zwitterionic amino acidic drugs from alkaline aqueous solutions. The resulting *N* (*O*, *S*)-alkoxycarbonylated amino acids were extracted into an organic solvent after acidification and then second chiral center was introduced into carboxyl groups by reacting with chiral alcohol such as (-)-menthol and the remaining hydroxyl groups were acylated.



2. Direct CE method

Enantioseparation of chiral aromatic acidic drugs and chiral amino acidic drugs that are labile in the GC system was achieved without derivatization by CE employing neutral cyclodextrin and charged cyclodextrin as the dual-chiral selectors. Dual-selector CE modes provided excellent separation of enantiomers under each optimal chiral environments. Moreover, migration orders of enantiomers on the two selectors of different enantioselectivities were very different and the relative migration time set measured was thus characteristic, enabling to crosscheck the chemical identification of each drug and also its accurate chirality.

References

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