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論文題名　：Study on analysis of the rheumatoid arthritis therapeutic drug for identifying drug-interactions

区　　分　：甲

論　文　内　容　の　要　旨

●Introduction

In this study, we developed simple and rapid HPLC assay of rheumatoid arthritis (RA) therapeutic drug available for identifying drug-interactions. In Chapter 1, we developed the assay as a measurement object in non-steroidal anti-inflammatory drugs (NSAIDs) used together with representative methotrexate (MTX) for the purpose of reducing symptoms such as sharp pain with the joint pain, the swelling as RA therapeutic drug at the HPLC same time. In Chapter 2, we developed the HPLC native fluorescence detection method of serum TCZ as a simple and rapid blood concentration assay of TCZ which was biological disease-modifying anti-rheumatic drugs (bDMARDs) developed in Japan.

●Chapter 1.　Development of the HPLC simultaneous assay of MTX and NSAIDs

NSAIDs for the measurement included adaptation in RA and chose a selective COX-2 repressor or celecoxib which was high in COX-2 selectivity, diclofenac, loxoprofen, lornoxicam, meloxicam besides. Because each these had plane structure, we adopted phenyl hexyl in a stationary phase and improved stability, and HPLC separated using the Gemini C6-Phenyl column which improved selectivity by π-π interaction again. In addition, the detection was to set it for the absorption wavelength that was most suitable for a measurement object, and high sensitivity aimed at becoming it. As a result, separation, the detection was possible, and the results that linearities of calibration curves, reproducibilities and detection limits had good was provided within 25 min. After applying to human serum, recovery and accuracy results good together were provided.

●Chapter 2.　Development of the TCZ assay by the HPLC native fluorescence detection method

At first we tried the HPLC native fluorescence detection of the TCZ authentic sample. After performing separation (HT-RPLC) using the Presto FF-C18 column which was non-Paula ska lamb for a high temperature reverse phase, a sharp single peak was provided within 11 minutes. After examining separation of IgG1 which was TCZ and a subclass successively, it was shown that we could isolate TCZ and IgG1 by simple and easy pretreatment. Finally after developing the assay of blood TCZ concentration using commercial human serum, in the thing that we preprocessed using avian propylamine, we could remove a foreign element derived from blood IgG1 well and were able

to assay serum TCZ concentration.

●Conclusion

As for serum MTX and the simultaneous assay and the assay of serum TCZ of NSAIDs that we developed this time, it is thought that we are useful in elucidating interaction at the time of the combination with NSAIDs and DMARDs of not only the prevention of an adverse event of TCZ and the confirmation of the therapeutic effect but also the RA treatment patient.