DEVELOPMENT OF ADVANCED STABILITY-INDICATING ASSAY METHODS FOR CERTAIN PHARMACEUTICAL COMPOUNDS

Thesis Presented By

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For the Degree of Philosophy Doctor
in
Pharmaceutical Sciences
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2011
Summary

The present thesis is devoted to the development of new methods for the stability indicating analysis of certain compounds of pharmaceutical interest, namely; loratadine, desloratadine, ziprasidone hydrochloride monohydrate, naftazone, methocarbamol and floctafenine. The experimental parameters affecting procedures were carefully studied and optimized. Furthermore, the data obtained were statistically analyzed and compared with those obtained by reference methods.

The developed methods were further applied to the determination of these drugs in their pharmaceutical preparation and human plasma.

The thesis comprises six main parts describing the theoretical and practical aspects of the investigated analytical methods:

PART I: General Introduction

This part included an introduction about stability-indicating assay methods and their importance in pharmaceutical development and industry. Also this part included the aim of the thesis.

PART II: Stability-Indicating Micelle-Enhanced Spectrofluorimetric Method for Determination of Loratadine and Desloratadine in Pure Form and Pharmaceutical Formulations

In this part, a sensitive and rapid spectrofluorimetric method was developed for the determination of loratadine and desloratadine in pure form and different pharmaceutical preparations. The method depended on enhancement of the native fluorescence of the two drugs using sodium dodecyl sulfate as a fluorescence enhancer. The fluorescence of the two compounds was measured at 438 nm after excitation at 290 nm. The suggested method was applied to investigate the inherent stability of the two studied drugs under different stress conditions. The results of the developed method were statistically analyzed and were in good agreement with those obtained by the official or the comparison
PART III: Stability-Indicating Spectrofluorimetric Method for Determination of Ziprasidone in Pure Form and Capsules

In this part a sensitive and rapid spectrofluorimetric method was developed and applied for the determination of ziprasidone in pure form and capsules. The developed method is based on the measurement of the native fluorescence of the studied compound in acetate buffer of pH 4.5 at 315/398 nm. Different experimental parameters were optimized and the method was validated and successfully applied to the determination of the studied compound in its capsules. The developed method was applied also to investigate the effect of different stress conditions on the stability of ziprasidone and to study the kinetics of its degradation. The obtained results were statistically compared with those obtained by the comparison method and were found to be in good agreement.


In this part, a sensitive and rapid high-performance liquid chromatographic method was developed for the determination of naftazone in pure form and tablets. The method was applied to investigate the stability of the drug under different stress conditions and to study its degradation kinetics. The method was also extended to content uniformity testing of naftazone commercial tablets and to drive the pH-rate profile curve of the drug.

PART V: Simultaneous Determination of Methocarbamol and its Degradation Product and Main Impurity (Guaifenesin) Using HPLC Method with Fluorescence Detection. Application to Pure Form, Tablets
and Therapeutic Drug Monitoring

In this part, a highly sensitive and accurate high-performance liquid chromatographic method was developed for the simultaneous determination of methocarbamol and its degradation product and main impurity (guaifenesin). Different chromatographic parameters were studied and the method was successfully applied for the analysis of methocarbamol in different pharmaceutical preparations. By virtue of its high sensitivity, the developed method was extended to investigate the pharmacokinetic profile of the studied compound following the oral administration of a tablet formulation. The obtained results were statistically analyzed and were in good agreement with those obtained by the official method.

PART VI: Simultaneous Determination of Floctafenine and its Degradation product and Major Metabolite (Floctafenic Acid) Using Micellar Liquid Chromatographic Method. Application to Pure Form, Tablets and Human Plasma

In this part, a sensitive and rapid high-performance liquid chromatographic method was developed and applied for the simultaneous determination of floctafenine and its degradation product and major metabolite (floctafenic acid). The developed method was applied to the determination of floctafenine in commercial and laboratory-prepared tablets. Also, the proposed method was extended to the determination of floctafenic acid in human plasma as a major metabolite of floctafenine. The results of the developed method were statistically compared with those obtained using a comparison method and were found to be in good agreement.