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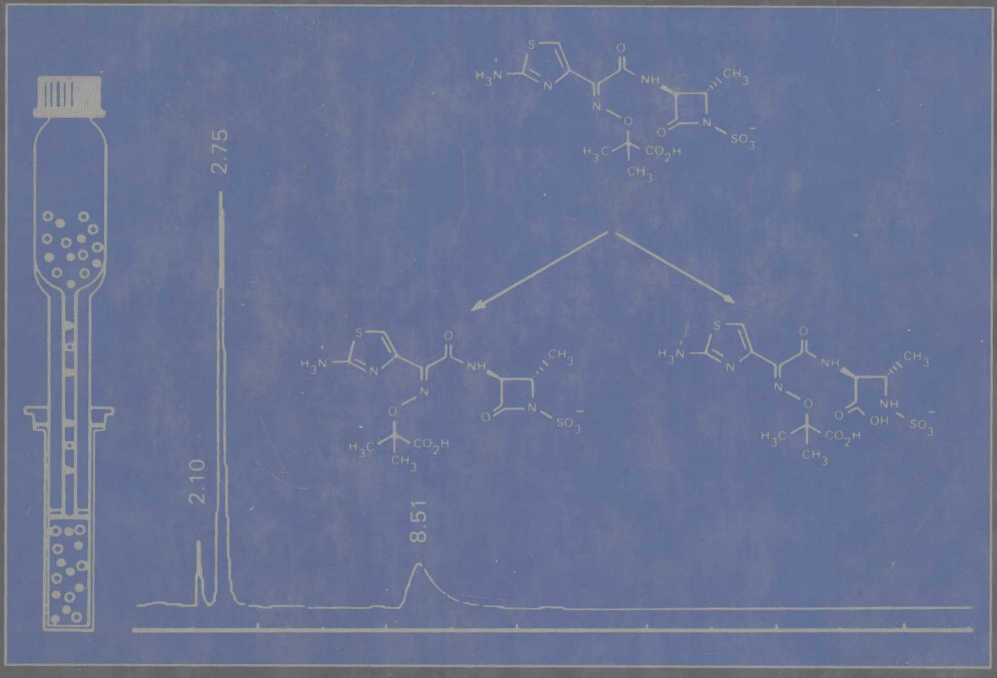
Chromatographic Analysis of Pharmaceuticals



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Preface

Over the last fifteen years, chromatographic methods have been used extensively in the pharmaceutical industry for the measurement of drugs, impurities, and excipients in preparations (tablets, ointments, etc.). The aim of this volume is to bring together all these procedures so that the practitioner of chromatography will have a handy reference source. This book is directed to chemists with analytical development, pharmaceutical development, quality control, or chemical process responsibilities.

Relevant subjects such as the FDA regulations and sample handling are covered extensively since they have a direct impact on the nature of a chromatographic method. Chromatographic theory and solvent properties are not covered. Numerous references are included to provide the interested reader with additional information.

Part I contains an overview of the various regulatory stages of a drug candidate. The determination of valid chromatographic methods is also discussed.

Part II is devoted to sample handling procedures. Chapter 2 reviews the various sample handling techniques that have been used in the chromatographic assay of formulations. The following chapter emphasizes automated instrumental sample handling approaches.

In Part III, chapters are devoted to thin-layer chromatographic, gas chromatographic, and high-performance liquid chromatographic technology and their respective approaches to methods development. The chapter on headspace analysis gives an alternative approach to the assay of pharmaceuticals.

The last and most extensive portion of this book (Part IV) is a comprehensive tabulation of chromatographic methods used in the analysis of drugs. The drug name, sample matrix analyzed, sample handling procedure, column sorbent, mobile phase, mode of detection, and reference are listed for each drug. The pharmacopoeias of the United States, Great Britain, Europe, and Japan, and literature references up to 1988 were used to compile this section.

I would like to thank the contributors to this volume and the useful criticism provided by R. Hartwick, L. Treiber, J. Karten, K. Himes, B. Cooley, J. Florence, G. Diegnan, K. Shields, K. C. Van Horne, and J. D. Pipkin, as well as K. J. Robison, who provided the most technical criticism. The resources provided to me by Cytogen Corporation are also appreciated.

John A. Adamovics

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REGULATORY CONSIDERATIONS

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Regulatory Considerations for the Chromatographer

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I. INTRODUCTION

Analysis of pharmaceutical preparations by chromatography can be traced back to 1922 [1]. By 1955, descending and ascending paper chromatography had been described in *The United States Pharmacopeia* (USP) for the tentative identification of drug products [2]. Subsequent editions introduced gas chromatographic methods. High-performance liquid chromatographic methods were introduced in the 1975 edition of the USP. Chromatographic methods clearly have assumed a dominant role in the USP with over 700 methods listed in the 1985 edition.

The following section describes the analytical concerns that arise during the developmental phase of a new drug. Section III describes the new technologies of recombinant DNA and monoclonal antibodies with their unique requirements. The remaining sections discuss the current state of method validation and system suitability tests of chromatographic systems.

II. NEW DRUG DEVELOPMENTS

In their search for new drug candidates, researchers at pharmaceutical companies synthesize new compounds, modify existing compounds, and extract compounds from natural sources. These new drug candidates are subjected to a biological screening process which may involve pharmacological, toxicity, and biochemical testing. The