METHODS IN PHARMACOLOGY

Volume 3
Smooth Muscle

Edited by
Edwin E. Daniel and David M. Paton

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METHODS IN PHARMACOLOGY

Volume 3
Smooth Muscle

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Edited by: **Edwin E. Daniel** and **David M. Paton**

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Preface

The study of the actions of drugs on smooth muscle has been a preoccupation of many pharmacologists almost from the beginning of the discipline. To a considerable degree, the development of theories to explain drug actions on smooth muscle has occurred somewhat independently of the development of our knowledge of the physiology, biochemistry, and biophysics of smooth muscle. This knowledge has developed rapidly in the past decade, and some of its consequences for our understanding of drug–receptor interactions in smooth muscle have not always been fully appreciated or accepted. One of the purposes of this volume is to provide pharmacologists with some understanding of the physiology, biophysics, and biochemistry of smooth muscle and of related advances in methodology so as to facilitate the incorporation of such knowledge and related methods into future pharmacological studies of smooth muscle and drug interactions.

Another purpose of the book is to provide both graduate students and investigators in pharmacology and related disciplines with a summary of the numerous methods that have evolved or are available for the study of drug and smooth muscle interactions, and, in particular, to highlight their possible uses and limitations. Perhaps, because of the diversity in content and difficulty of these methods, there has to our knowledge never been a previous attempt to bring them together in one place. We have not, of course, succeeded entirely in this objective. However, we believe our contributors have provided accounts of a large number of methods in this area. Consequently, we hope that this book will provide a ready reference for those contemplating or involved in studies of interactions of drugs with smooth muscle.

This book has been organized into sections, with more or less related methods juxtaposed. To some degree, of course, the selection of those to be included in any given section is arbitrary. However, we hope that we have placed the chapters together in such a fashion as to facilitate their use and to introduce readers to methods they may not be using that might provide additional or deeper insights into their problems.

As editors, we have to acknowledge our complete dependence upon the contributions of the authors of this volume. Without their expertise it would never have been possible; yet we must accept the responsibility for whatever failings there are

in exposition or content, and in the selection of material. The editing of this volume has been a stimulating and rewarding task, and we hope that those who use it will benefit similarly.

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Edwin E. Daniel and David M. Paton

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Contents

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Ultrastructure

Chapter 1

Ultrastructure of Smooth Muscle

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I. INTRODUCTION

Identification of the anatomical sources of the increased intracellular free calcium that activates contraction in smooth muscle has been a major objective of cell pharmacology. The extracellular fluid, the space between the basement membrane and the plasma membrane, the plasma membrane itself, and intracellular organelles each has been considered as a possible source and sink of calcium during, respectively, excitation and inhibition (for reviews see Bohr, 1964; Daniel, 1965; Goodford, 1965; A. P. Somlyo and Somlyo, 1968; 1970; Hurwitz and Suria, 1971; Johansson, 1971). In the striated (twitch skeletal) muscles the sarcosplasmic reticulum is the intracellular "site" that accumulates calcium during relaxation and from which the calcium that activates contraction is released by the action potential (for reviews see Bianchi, 1968; A. F. Huxley, 1971). Recent studies have shown that some smooth muscles can be stimulated to contract even if the extracellular calcium concentration is reduced below the levels that can activate contraction (Bozler, 1969; A. P. Somlyo and Somlyo, 1970; A. P. Somlyo *et al.*, 1971b; Devine, Somlyo, and Somlyo, 1972; Keatinge, 1972), indicating the existence of an intracellular source of activator calcium. Recent electron microscopic studies have therefore been directed toward determining whether there is in smooth muscles a sarcoplasmic reticulum that may serve as an intracellular calcium storage site.

Some of the techniques for fixation and localization of the sites that accumulate divalent cations in smooth muscle will be discussed in this chapter. Ultimately, it is