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Introductory Chapter: Chemistry and Biological Activity of Steroids - Scope and Overview

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1. Introduction

Steroid compounds are widely present in living organisms playing an important role in their vital activities.

The steroidal basic structure is constituted by a common chemical skeleton of four fused rings, consisting of three six-membered rings and a five-membered ring. This hydrocarbon scaffold contains 17 carbons and has the cyclopentanoperhydrophenanthrene basic structure [1, 2]. The four steroid rings are labelled as A, B, C and D, and their carbon atoms are numbered according to the universal convention (International Union of Pure and Applied Chemistry/International Union of Biochemistry Joint Commission on Biochemical Nomenclature). Angular methyl groups at C13 and C10 are designated as 18-CH₃ and 19-CH₃, respectively, and alkyl substituents at C17 are the steroid side chain. The 18- and 19-methyl groups stand above the plane of the steroid skeleton and, by convention, have β -configuration. Therefore, other atoms or substituents located above this plane also have β -configuration, while those below it have α -configuration [3].

Steroids interact with enzymes and receptors in a strikingly specific manner. Small changes in the steroid structure afford major biological differences.

Several natural and synthetic steroids are important therapeutic tools for a wide range of diseases [4, 5]. The steroid classes present in drug therapy include, among others, corticosteroids, neurosteroids, sexual hormones, bile acids, vitamin D and cardiotonic steroids [4].

Hundreds of steroid compounds have been isolated from natural sources, and many thousands of them have been obtained synthetically over the last decades, and their chemical and biological investigation continues to be very active. In fact, the steroid scaffold continues to be the structural basis of new drugs for a variety of targets and diseases.

The book *Chemistry and Biological Activity of Steroids* aims to provide an updated overview of the recent advances in the medicinal chemistry of steroids.

Novel synthetic methods of steroids through the use of microorganisms as carriers of strikingly selective enzyme catalysts, able to promote reactions that would be very difficult by conventional chemical methods, continue to be an area of intensive research and enormous industrial interest. Several biotransformations at industrial scale have been applied in the production of steroids, through chemo-, regio- and stereoselective reactions, namely, hydroxylations. The chapter concerning steroid biotransformations gives an overview of the recent achievements in this field.

The steroid hormones were discovered almost a century ago and have been found to be involved in important physiopathological conditions, being therefore important starting points for the development of drugs.

Oestrogens and androgens are two classes of steroid sex hormones responsible for female and male differentiation, respectively, and continue to be a source of questions and opportunities in deciphering the mechanisms of homeostasis and disease.

A chapter concerning the discovery of novel inhibitors of oestrone sulphatase, a clinically validated drug target in oestrogen-dependent cancers, presents the medicinal chemistry rational behind the design, synthesis and safety assessment of anticancer drug candidates for this pharmacological target. Furthermore examples of dual aromatase-sulfatase inhibitors are given, disclosing the potential of a synergistic dual inhibition.

On the other hand, sex steroids have important physiological actions, not limited to the reproductive organs. They exert important physiological roles, including the regulation of somatotrophic-liver axis, intermediate metabolism or gender dimorphism. This is in part because the liver is a sex steroid-responsive organ where sex steroid- and growth hormone-dependent signalling pathways connect to regulate complex gene expression networks. Deficiency of sex steroid- and GH-dependent signalling pathways has an impact on the mammalian liver physiology. This interesting and vast topic is discussed in Chapter 4.

Finally, the usefulness of steroids in the cutting-edge technology of supramolecular systems and nanomaterials for biomedical application is discussed in the fifth chapter. The renewable and economic natural steroid compounds can be employed as building blocks in the design and construction of steroid-based supramolecular systems. Interesting characteristics of steroids, concerning physicochemical and biological properties, biocompatibility and bioactivities, make them attractive as building blocks of supramolecular systems to be employed in biomolecular recognition/sensing and biomolecular transportation.

The chemical and biological properties of steroids include a large variety of topics. This book contributes with a selection of different chapters that give updated information and critical discussions, illustrating the novelty of this old class of molecules.

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