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药物化学

Medicinal Chemistry

(英中双语注解版)

李绍顺 主编



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内 容 简 介

本书是药学教学领域编写和出版的第一本英中双语教材。全书共分 16 章,前 5 章为总论,主要介绍药物研发的基本理论和基本方法,如药物设计学的基础知识、药物代谢和前药设计的基本方法等;第 6~16 章为各论,按目前新药研究的重点领域进行分类,主要讲授神经系统药物、胃肠道系统药物、心血管系统药物、抗肿瘤药物等。

本书可供进行药物化学双语教学的师生使用,也可作为药物化学专业的研究生、技术人员的参考用书。

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前 言

目前,国内主要的药学院校都把培养国际化、研究型创新人才作为教学目标。教育部提倡在一些重要的专业课教学中采用双语教学。我们近几年在药物化学教学中进行了双语教学尝试,但面临的主要问题之一是没有合适的教材。使用英文原版书籍存在几方面问题:一是内容与教学大纲的要求差别较大,不太适合作为教科书使用;二是学生对大量专业名词术语的理解存在一定的困难;三是价格较贵,加重学生经济负担。为解决上述问题,规范双语教学过程,使教学形式和内容完整、统一,我们尝试编写了这本《药物化学》双语教材。

本教材以科学出版社引进出版的 John B Taylor and David J Triggler 主编的 *Organic Chemistry of Drug Design and Drug Action* 和 Richard B Silverman 主编的 *Comprehensive Medicinal Chemistry* 两本导读版为蓝本,选取适合教学大纲要求的重要内容加以编辑,对药名和关键名词术语加以中文注释,以便于学生阅读和理解。全书共分 16 章,前 5 章为总论部分,主要讲授药物研发的基本理论和基本方法,内容包括新药研究中先导化合物的发现和结构优化、药物设计学的基础知识、受体及酶抑制剂的基本理论、药物代谢和前药设计的基本方法等。第 6~16 章为各论,按目前新药研究的重点领域进行分类,主要讲授神经系统药物、镇痛和麻醉药、代谢综合征治疗药、胃肠道系统药物、心血管系统药物、抗肿瘤、抗病毒、抗真菌、抗感染、抗寄生虫及免疫抗炎药等。每章中讲授的内容为疾病的基础、目前药物治疗现状、药物的作用机理、结构与活性关系、尚待解决的问题及新的治疗领域。每类药物列举 1~2 个代表性药物,给出它们的结构、化学名、合成路线、作用及药代动力学状况。在每章的最后对本章的重点内容进行归纳,以利于学生对重点内容的把握。本教材在内容的选取和编写体例上与国内目前在药物化学教学中使用的教科书有所不同,增加了药物研发和药物设计的相关内容,减少各论中药品的罗列,每个章节还包括最新的药物化学研究成果和趋势,以拓展学生的创新思路,力求使学生在掌握基本知识点的基础上能够举一反三、触类旁通,以满足培养研究型、创新型人才的需要。

参加本教材编写的老师(以编写章节顺序为序)有上海交通大学药学院李绍顺(第 1 章药物发现、设计与开发,第 4 章药物代谢,第 7 章镇痛和麻醉药),山东大学药学院徐文方(第 2 章受体),沈阳药科大学赵临襄(第 3 章酶和酶的抑制剂),北京大学药学院张亮仁(第 5 章前药和药物给药系统),复旦大学药学院叶德泳、李炜(第 6 章神经系统药物),上海交通大学药学院傅磊(第 8 章代谢综合征治疗药),吉林大学药学院杨晓虹(第 9 章胃肠道系统药物),中国药科大学尤启冬(第 10 章心血管系统药物),浙江大学药学院刘淘(第 11 章抗肿瘤药),广州中医药大学刘鹰翔(第 12 章抗病毒药),沈阳药科大学郭春(第 13 章抗真菌药),上海交通大学药学院周虎臣(第 14 章抗感染药,第 15 章抗寄生虫药),华东理工大学药学院邓卫平(第 16 章抗炎药)。上海交通大学药学院孟青青、周文、徐德锋承担了本教材编写的联络组织、文稿校对及其他一些事务性工作。另外,教材的编写得到上海交通大学药学院领导的支持,在此一并表示感谢。

本教材可供进行药物化学双语教学的教师和学生使用,也可供药物化学专业的研究生和

专业技术人员作为参考书使用。据我们目前了解到的情况，在药学教学领域中编写和出版双语教材还是第一次。希望本教材的出版能够对推进药物化学双语教学产生积极作用，同时对药学其他专业的双语教学也能有借鉴作用。由于是第一次尝试，加之时间、能力和经验所限，教材难免存在许多缺点和错误，诚挚欢迎使用本教材的教师、学生、其他读者以及本专业的各位同仁提出批评意见。

李绍顺

2009年6月

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Chapter 1 Drug Discovery, Design and Development

1.1 Drug Discovery

Drug discovery is a very time-consuming and expensive process. Estimates of the average time required to bring a drug to the market range from 12~15 years at an average cost of about \$800 million. For approximately every 10 000 compounds that are evaluated in animal studies, 10 will make it to human clinical trials in order to get 1 compound on the market. The clinical trials consist of three phases prior to drug approval: phase I (generally a few months to a year and a half) evaluates the safety, tolerability (dosage levels and side effects), pharmacokinetic properties, and pharmacological effects in 20~100 healthy volunteers; phase II phase III (about 1~3 years) assesses the effectiveness of the drug, determines side effects and other safety aspects, and clarifies the dosing regimen in a few hundred diseased patients in clinics and hospitals that establishes the efficacy of the drug and monitors adverse reactions from long-term use. Once the new drug application (NDA) is submitted to the Food and Drug Administration (FDA), it can be several months to several years before it is approved for commercial use. Phase IV studies are considered to be the results found with a drug that has already been allowed onto the drug market and is in general use. Drug candidates (or new chemical entities, NCE, as they are often called) that fail late in this process result in huge, unrecovered financial losses for the company. This is why the cost to purchase a drug is so high. It is not that it costs that much to manufacture that one drug, but that the profits are needed to pay for all of the drugs that fail to make it to market after large sums of research funds have already been expended.

In general, drugs are not discovered. What is more likely discovered is known as a lead compound. The lead is a prototype compound that has a number of attractive characteristics, such as the desired biological or pharmacological activity, but may have other undesirable characteristics, for example, high toxicity, other biological activities, absorption difficulties, insolubility, or

- 药物发现
- 药物被批准上市
- I 期临床
- 耐受性
- 药代动力学性质
- II 期临床
- 药物的临床疗效
- 给药方式
- 新药申请
- 食品药品监督管理局
- 候选药物
- 新化学实体
- 先导化合物