高 等 学 校 教 材

制药工程专业英语

大学英语专业阅读教材编委会组织编写

吴达俊 庄思永 主编
嵇汝运 主审

化学工业出版社
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全国部分高校化工类及相关专业
大学英语专业阅读教材编委会

前　言

组织编审出版系列的专业英语教材，是许多院校多年来共同的愿望。在高等教育面向21世纪的改革中，学生基本素质和实际工作能力的培养受到了空前的重视。对非英语专业的学生而言，英语水平和能力的培养不仅是构成其文化素质的重要部分，在很大程度上也是其综合能力的补充和延伸。在此背景下，教育部几次组织会议研究加强外语教学的问题，制订有关规范，使外语教学更加受到重视。教材是教学的基本因素之一，与基础英语相比，专业英语教学的教材问题此时显得更为突出。

国家主管部门的重视和广大院校的呼吁引起了化学工业出版社的关注。他们及时地与原化工部教育主管部门和全国化工类专业教学指导委员会请示协商后，组织全国十余所院校成立了大学英语专业阅读教材编委会。经过必要的调查研究后，根据学校需求，编委会优先从各院校教学（交流）讲义中确定选题，同时组织力量进行编审工作。本套教材涉及的专业主要包括化学工程与工艺、石油化工、机械工程、信息工程、生产过程自动化、应用化学和精细化工、生化工程、环境工程、制药工程、材料科学与工程和化工商贸等。

根据“全国部分高校化工类及相关专业大学英语专业阅读教材编审委员会”的要求和安排编写的《制药工程专业英语》教材可供制药工程及相关专业的本科学生使用，也可作为同等程度（通过大学英语四级）的专业技术人员自学教材。

本书分为5个部分（PART），每个部分中有5个单元（UNIT）。每个单元由一篇课文和一篇阅读材料构成。阅读材料提供与课文相关的背景知识，以进一步拓宽课文内容，为学生自学（开拓视野和训练阅读技能）提供合适的材料。课文还配有相应的练习题。各篇课文之间、课文与相应的阅读材料之间既有一定的联系，又可独立成章，教学时可根据不同学时数灵活选用。课文与阅读材料共计50篇，均选自原版英文教科书、科技报告、专著、大型参考书和专业期刊，大部分为80年代末和90年代以来的出版物。

PART 1 为药物化学的内容，包括药物的生产，药物的结构特点和药理活性的关系，化学治疗学和药物的研究开发等；

PART 2 为生物制药的内容，包括植物化学，胰岛素化学，新抗生素的寻找，β-内酰胺类抗生素，肝素的制备和纯化以及脱氧核糖核酸等；

PART 3 为工业药剂的内容，包括片剂，灭菌制剂，缓释制剂，药物制剂的动力学原理和稳定性试验等；

PART 4 为制药工程的内容，包括反应器，发酵，蒸馏，超临界液体萃取，结晶，干燥以及空气和水的净化等；

PART 5 为制药工程前沿的内容，包括手性药物，干扰素，海洋药物，催化抗体，合成有机化学中的酶，药物设计原理和计算机辅助药物设计等。

附录内容有：The General Principles for Nomenclature of Chinese Approved Drug Names（包括原料药和制剂的命名），INN 采用的词干及其中文译名，英汉对照新药名选编和总词汇表。

本书在编写过程中得到了化学工业出版社、全国部分高校化工类及相关专业大学英语专业阅读教材编委会、华东理工大学教务处和浙江工业大学教务处的大力支持；中国科学院上海药物研究所嵇汝运院士审阅了全书，并提出了许多宝贵意见；本书稿于1999年10月在北京化工大学召开的审稿会议上进行了讨论，与会专家对本书提出了许多宝贵的修改意见；对此一并表示衷心的感谢。

本书由华东理工大学和浙江工业大学合编。华东理工大学朱为宏、吴达俊编写第一部分，卓超编写第三部分，庄思永、何斌编写第四部分，吴达俊、庄思永编写附录及总词汇表，浙江工业大学项斌编写第二部分，赵军编写第五部分，华东理工大学硕士研究生潘海港、梁冰等参加了本书的文稿整理和文字处理工作。

本教材从结构到练习设计都是一种尝试。由于时间仓促和编者的水平有限，不妥之处希望使用本书的师生、读者提出宝贵意见。

编　者

2000年元旦

内 容 提 要

《制药工程专业英语》是根据《大学英语教学大纲（修订本）》（高等学校本科用）的专业阅读部分的要求编写的。供理工科制药工程专业（包括化学制药专业和药物制剂专业）或相关专业的三、四年级学生使用，也可供同等英语程度的科技人员学习。

本书包括课文及阅读材料共25个单元（50篇），均选自原版英文教科书、专著、大型参考书及专业期刊（大部分是国外80年代末及90年代以来的出版物）。其中第一部分1～5单元介绍药物化学；第二部分6～10单元介绍生物制药；第三部分11～15单元介绍工业药剂；第四部分16～20单元介绍制药工程，第五部分21～25单元介绍制药工程前沿的研究领域。每个单元由一篇课文和一篇阅读材料构成。附录有：The General Principles for Nomenclature of Chinese Approved Drug Names，INN采用的词干及其中文译名，英汉对照新药名选编和总词汇表。每篇课文均配有阅读理解练习和词汇练习。为便于学生自学，本书每单元均配有单词和词组表，并作了必要的注释。

Content

PART 1 MEDICINAL CHEMISTRY

Unit 1 Production of Drugs

Depending on their production or origin pharmaceutical agents can be split into three groups:

Ⅰ. Totally synthetic materials (synthetics),

Ⅱ. Natural products, and

Ⅲ. Products from partial syntheses (semi-synthetic products).

The emphasis of the present book is on the most important compounds of groups Ⅰ and Ⅲ -thus Drug *synthesis*. This does not mean, however, that natural products or other agents are less important. They can serve as valuable lead structures, and they are frequently needed as starting materials or as intermediates for important synthetic products.

Table 1 gives an overview of the different methods for obtaining pharmaceutical agents.

Table 1 Possibilities for the preparation of drugs

Methods	Examples
1. Total synthesis	—over 75% of all pharmaceutical agents (synthetics)
2. Isolation from natural sources (natural products):	
2.1 Plants	—alkaloids; enzymes①; heart glycosides; polysaccharides; tocopherol; steroid precursors (diosgenin, sitosterin); citral (intermediate product for vitamins A, E, and K)
2.2 Animal organs	— enzymes; peptide hormones; cholic acid from gall; insulin② from the pancreas; sera and vaccines
2.3 Other sources	— cholesterol from wool oils; L-amino acids from keratin and gelatine hydrolysates
3. Fermentation	— antibiotics; L-amino acids; dextran; targeted modifications on steroids, e.g. 11-hydroxylation; also insulin, interferon, antibodies, peptide hormones, enzymes, vaccines
4. Partial synthetic modification of natural products (semisynthetic agents):	
	— alkaloid compounds; semisynthetic β-lactam antibiotics; steroids; human insulin

Several therapeutically significant natural products which were originally obtained from natural sources are today more effectively -i.e. more economically -prepared by total synthesis. Such examples include **L-amino acids**, **Chloramphenicol**, **Caffeine**, **Dopamine**, **Epinephrine**, **Levodopa**, **peptide hormones**, **Prostaglandins**, **D-Penicillamine**, **Vincamine**, and practically all vitamins.

Over the last few years fermentation - i.e. microbiological processes - has become

extremely important. Through modern technology and results from genetic selection leading to the creation of high performance mutants of microorganisms, fermentation has already become the method of choice for a wide range of substances. Both Eukaryonts (yeasts and moulds) and Prokaryonts (single bacterial cells, and actinomycetes) are used as microorganisms. The following product types can be obtained:

1. cell material (single cell protein),
2. enzymes,
3. primary degradation products (primary metabolites),
4. secondary degradation products (secondary metabolites).

Disregarding the production of dextran from the mucous membranes of certain microorganisms, e. g. *Leuconostoc mesenteroides*, classes 2 and 3 are the relevant ones for the preparation of drugs. Dextran itself, with a molecular weight of 50,000～100,000, is used as a blood plasma substitute. Among the primary metabolites the L-amino acids from mutants of *Corynebacterium glutamicum* and *Brevibacterium flavum* are especially interesting. From these organisms some 350,000 tones of monosodium L-glutamate (food additive) and some 70,000 tones of L-lysine (supplement for vegetable proteins) are produced. Further important primary metabolites are the purina nucleotides, organic acids, lactic acid, citric acid, and vitamins, for example vitamin B_{12} from *Propionibacterium shermanii*.

Among the secondary metabolites the antibiotics must be mentioned first. The following five groups represent a yearly worldwide value of US-$ 17 billion:

penicillins③ (*Penicillium chrysogenum*),

cephalosporins (*Cephalosporium acremonium*),

tetracyclines (*Streptomyces aureofaciens*),

erythromycins (*Streptomyces erythreus*),

aminoglycosides (e. g. streptomycin from *Streptomyces griseus*).

About 5000 antibiotics have already been isolated from microorganisms, but of these only somewhat fewer than 100 are in therapeutic use. It must be remembered, however, that many derivatives have been modified by partial synthesis for therapeutic use; some 50,000 agents have been semisynthetically obtained from β-lactams alone in the last decade. Fermentations are carried out in stainless steel fermentors with volumes up to 400 m^3. To avoid contamination of the microorganisms with phages etc. the whole process has to be performed under sterile conditions. Since the more important fermentations occur exclusively under aerobic conditions a good supply of oxygen or air (sterile) is needed. Carbon dioxide sources include carbohydrates, e. g. molasses, saccharides, and glucose. Additionally the microorganisms must be supplied in the growth medium with nitrogen-containing compounds such as ammonium sulfate, ammonia, or urea, as well as with inorganic phosphates. Furthermore, constant optimal pH and temperature are required. In the case of penicillin G, the fermentation is finished after 200 hours, and the cell mass is separated by filtration. The desired active agents are isolated from the filtrate by absorption or extraction processes. The

cell mass, if not the desired product, can be further used as an animal feedstuff owing to its high protein content.

By modern recombinant techniques microorganisms have been obtained which also allow production of peptides which were not encoded in the original genes. Modified E. *coli* bacteria make it thus possible to produce A- and B- chains of **human insulin** or **proinsulin** analogs. The disulfide bridges are formed selectively after isolation, and the final purification is effected by chromatographic procedures. In this way **human insulin** is obtained totally independently from any pancreatic material taken from animals.

Other important peptides, hormones, and enzymes, such as **human growth hormone (HGH)**, **neuroactive peptides**, **somatostatin**, **interferons**, **tissue plasminogen activator (TPA)**, **lymphokines**, calcium regulators like **calmodulin**, **protein vaccines**, as well as **monoclonal antibodies** used as diagnostics, are synthesized in this way.

The enzymes or enzymatic systems which are present in a single microorganism can be used for directed stereospecific and regiospecific chemical reactions. This principle is especially useful in steroid chemistry. Here we may refer only to the microbiological 11-α-hydro xylation of **progesterone** to 11-α-hydroxyprogesterone, a key product used in the synthesis of **cortisone**. Isolated enzymes are important today not only because of the technical importance of the enzymatic saccharification of starch, and the isomerization of glucose to fructose, They are also significant in the countless test procedures used in diagnosing illness, and in enzymatic analysis which is used in the monitoring of therapy.

A number of enzymes are themselves used as active ingredients. Thus preparations containing proteases (e. g. chymotrypsin, pepsin, and trypsin), amylases and lipases, mostly in combination with synthetic antacids, promote digestion. Streptokinase and urokinase are important in thrombolytics, and asparaginase is used as a cytostatic agent in the treatment of leukemia.

Finally mention must be made of the important use of enzymes as 'biocatalysts' in chemical reactions where their stereospecificity and selectivity can be used. Known examples are the enzymatic cleavage of racemates of N-acetyl-D, L-amino acids to give L-amino acids, the production of 6-aminopenicillanic acid from benzylpenicillin by means of penicillinamidase and the aspartase-catalysed stereospecific addition of ammonia to fumaric acid in order to produce L-aspartic acid.

In these applications the enzymes can be used in immobilized forms——somehow bound to carriers - and so used as heterogeneous catalysts. This is advantageous because they can then easily be separated from the reaction medium and recycled for further use.

Another important process depending on the specific action of proteases is applied for the production of semisynthetic human insulin. This starts with pig insulin in which the alanine in the 30-position of the B-chain is replaced by a threonine tert-butyl ester by the selective action of trypsin. The insulin ester is separated, hydrolyzed to human insulin and finally purified by chromatographic procedures.

Sources for enzymes include not only microorganisms but also vegetable and animal

materials.

In Table 1 it was already shown that over 75% of all pharmaceutical agents are obtained by total synthesis. Therefore knowledge of the synthetic routes is useful. Understanding also makes it possible to recognize contamination of the agents by intermediates and by-products. For the reason of effective quality control the registration authorities in many countries demand as essentials for registration a thorough documentation on the production process. Knowledge of drug syntheses provides the R&D chemist with valuable stimulation as well.

There are neither preferred structural classes for all pharmaceutically active compounds nor preferred reaction types. This implies that practically the whole field of organic and in part also organometallic chemistry is covered. Nevertheless, a larger number of starting materials and intermediates are more frequently used, and so it is useful to know the possibilities for their preparation from primary chemicals. For this reason it is appropriate somewhere in this book to illustrate a tree of especially important intermediates. These latter intermediates are the key compounds used in synthetic processes leading to an enormous number of agents. For the most part chemicals are involved which are produced in large amounts. In a similar way this is also true for the intermediates based on the industrial aromatic compounds toluene, phenol and chlorobenzene. Further key compounds may be shown in a table which can be useful in tracing cross-relationships in syntheses.

In addition to the actual starting materials and intermediates solvents are required both as a reaction medium and for purification via recrystallization. Frequently used solvents are methanol, ethanol, isopropanol, butanol, acetone, ethyl acetate, benzene, toluene and xylene. To a lesser extent diethyl ether, tetrahydrofuran, glycol ethers, dimethylformamide (DMF) and dimethyl sulphoxide (DMSO) are used in special reactions.

Reagents used in larger amounts are not only acids (hydrochloric acid, sulfuric acid, nitric acid, acetic acid) but also inorganic and organic bases (sodium hydroxide, potassium hydroxide, potassium carbonate, sodium bicarbonate, ammonia, triethylamine, pyridine). Further auxiliary chemicals include active charcoal and catalysts. All of these supplementary chemicals (like the intermediates) can be a source of impurities in the final product.

In 1969 the WHO published a treatise on 'Safeguarding Quality in Drugs'. Appendix 2 is concerned with the 'Proper Practice for Reparation and Safeguarding Quality in Drugs' (WHO Technical Report No. 418,1969, Appendix 2; No. 567, 1975, Appendix 1A). This has in the meantime become known as 'Good Manufacturing Practices' or GMP rules, and these should now be obeyed in drug production. They form the basis for mutual recognition of quality certificates relating to the production of pharmaceuticals and for inspections of the production facilities.

For a long time the US drug authority, the Food and Drug Administration (FDA)[4], has issued regulations for the preparation of drugs analogous to the WHO rules, and it applies these strictly. Exports of drugs to the USA, like those of finished products, require regular inspection of the production facilities by the FDA .

It may merely be noted here that such careful control applies not only to the products, but also to the raw materials (control of starting materials), and also to the intermediates. Clearly the technical and hygienic equipment of the production and the storage areas have to fulfill set conditions.

Since only a few compounds, such as acetylsalicylic acid, paracetamol and vitamins, are prepared in large amounts, most of the actual production takes place in multi-purpose (multi-product) facilities. Special care has to be taken to avoid cross-contamination by other products what can be effected by good cleansing of used apparatus. A careful description and definition of all stored intermediates and products is needed.

Selected from H. J. Roth and A. Kleemann, *Pharmaceutical Chemistry*, Vol. 1, *Drug Synthesis*, Ellis Horwood Limited, England, 1988.

Words and Expressions

pharmaceutical [ˌfɑːməˈsjuːtikəl] *a.* 制药的，药学的；*n.* 药品，药剂
alkaloid [ˈælkəlɔid] *n.* 生物碱
enzyme [ˈenzaim] *n.* 酶
polysaccharide [pɔliˈsækəraid] *n.* 多糖，多聚糖
precursor [priˈkəːsə] *n.* 前体
steroid [ˈstɛrɔid] *n.* 甾类
peptide [ˈpeptaid] *n.* 肽，缩氨酸
hormone [ˈhɔːməun] *n.* 激素，荷尔蒙
gall [gɔːl] *n.* 胆汁
insulin [ˈinsjulin] *n.* 胰岛素
pancreas [ˈpæŋkriəs] *n.* 胰腺
serum [ˈsiərəm] *n.* 血浆
vaccine [ˈvæksiːn] *n.* 疫苗，牛痘疫苗
cholesterol [kəˈlesterəul] *n.* 胆固醇
gelatine [ˌdʒeləˈtin] *n.* 骨胶，明胶（亦作：gelatin）
antibiotic [ˌæntibaiˈɔtik] *a.* 抗生的，抗菌的；*n.* 抗生素
interferon [ˌintəˈfiərɔn] *n.* 干扰素
antibody [ˈæntiˌbɔdi] *n.* 抗体
fermentation [fəːmenˈteiʃən] *n.* 发酵
therapeutical [ˌθerəˈpjuːtikəl] *a.* 治疗（学）的
Caffeine [ˈkæfiːn] *n.* 咖啡因，咖啡碱
dopamine [ˈdəupəˌmiːn] *n.* 多巴胺（一种神经递质）
yeast [jiːst] *n.* 酵母
mucous [ˈmjuːkəs] *a.* 粘液的，分泌粘液的
plasma [ˈplæzmə] *n.* 血浆，淋巴液，等离子体
Penicillin [ˌpeniˈsilin] *n.* 青霉素

Streptomycin [ˌstreptə'maisin] *n.* 链霉素
derivative [di'rivətiv] *n.* 衍生物
sterile ['sterail] *a.* 不能生育的，无细菌的
aerobic [eiə'rəubik] *a.* 需氧的，有氧的
feedstuff ['fi:dstʌf] *n.* 饲料
lymph [limf] *n.* 淋巴，淋巴液
starch [stɑ:tʃ] *n.* 淀粉
regiospecific reaction 区域专一性反应
stereospecific reaction 立体专一性反应
glucose ['glu:kəus] *n.* 葡萄糖
streptokinase ['streptəu'kaineis] *n.* 链球葡萄激酶
immobilize [i'məubilaiz] *vt.* 固定化
heterogeneous ['hetərəu'dʒi:niəs] *a.* 不均匀的，多相的
trypsin ['tripsin] *n.* 胰蛋白酶
contamination [kənˌtæmi'neiʃən] *n.* 玷污，污染，污染物
hygienic [hai'dʒi:nik] *a.* 卫生学的，卫生的
intermediate [ˌintə'mi:diət] *n.* 中间体
extraction [ik'strækʃən] *n.* 萃取，提取
recrystallization [riˌkristəlai'zeiʃən] *n.* 重结晶
xylene ['zaili:n] *n.* 二甲苯
toluene ['tɔlju:n] *n.* 甲苯
ether ['i:θə] *n.* 醚
benzene ['benzi:n] *n.* 苯

Notes

① Enzyme——酶，一类由生物体产生的具有高效和专一催化功能的蛋白质。在生物体内，酶是参与催化几乎所有的物质转化过程，与生命活动有密切关系；在体外，也可作为催化剂进行工业生产。在工业生产中，酶主要从微生物发酵获得。

② Insulin——胰岛素，胰岛 β-细胞分泌的蛋白质激素，由两条肽链共 51 个氨基酸组成。胰岛素主要是促进碳水化合物的代谢，增加肝糖元和肌糖元的贮存，降低血糖，并能抑制脂肪的分解，减少酮体生成。胰岛素分泌不足会引起糖尿病。

③ Penicillin——青霉素，一种抗革兰氏阳性细菌的 β-内酰胺类抗生素，是 6-氨基青霉烷酸（简称 6-APA）的酰化衍生物。由青霉素产生菌培养所得的天然青霉素有多种成分。

④ FDA——美国联邦食品及药物管理局（The Federal Food and Drng Administration）。

Exercises

1. Answer the following questions:

(1) How many groups can pharmaceutical agents be split into depending on their production or origin?

(2) Can you illustrate any significant examples of pharmaceutical agents obtained by

total synthesis?

(3) What is the difference between the synthetic drugs and traditional Chinese herbal medicine?

2. Put the following into English:

生物碱	中间体	起始原料	重结晶	胆固醇
吡啶	甲苯	萃取	胰岛素	醛

3. Put the following into Chinese:

polysaccharide	peptide	hormone	vaccine	heterogeneous catalyst
contamination	plasma	steroid	penicillin	metabolite

4. Fill in the blanks with the following verb words:

derive *term* *distinguish* *present* *compose*

Nucleic acids are polyanionic molecules of high molecular weight. These polymers are _____of a sequence of subunits or nucleotides so that the whole is usually _____ a polynucleotide. The nucleic acids are of two main varieties, ribonucleic (RNA) and deoxyribonucleic (DNA). DNA is found primarily in the chromatin of the cell nucleus, whereas 90% of RNA is _____ in the cell cytoplasm and 10% in the nucleolus. The two classes of nucleic acids are _____ primary on the basis of the five-carbon atom sugar or pentose present. Two general kinds of bases are found in all nucleic acids. One type is a derivative of the parent compound purine. Principle examples are guanine and adenine. The second class of bases found in all nucleic acids is _____ from the parent compound pyrimidine.

Reading Material 1

Past Approaches to Discovering New Drugs as Medicines

1 Introduction

New medicines are mainly developed by the modern pharmaceutical industry where also most of the new drugs have been discovered. To put the present situation into context it is helpful to recall some of the main approaches to drug discovery which have been taken in the relatively recent past. Broadly speaking, there are four main sources for new drug leads. These are:

- Natural products
- Existing drugs
- Screens
- Physiological transmitters

2 Drugs Derived from Natural Products

Natural products provide the oldest source for new medicines. Natural selection during

evolution, and competition between the species, has produced powerful biologically active natural products which can serve as chemical leads. For example, moulds and bacteria produce substances that prevent other organisms from growing in their vicinity, *e. g.* Penicillin. The discovery of penicillin gave rise to the concept of seeking naturally occurring antibiotics and to its further development by microbiologists who argued that bacteria that cause infections in humans do not survive for long in soil because they are destroyed by other soil-inhabiting microbes. Extensive soil screening research programs have led to many antibiotics which have provided some very potent life-saving drugs, *e. g.* Streptomycin, Chloramphenicol, Chlortetracycline, and Erythromycin.

Microbial fermentation products may also provide leads to other types of drug when combined with a suitable screen. A classic example is that of the novel cholecystokinin (CCK)antagonist, obtained from *Aspergillus alliaceus* fermentation broths which served as the starting point for scientists at Merck Sharp and Dohme to develop very specific and potent nonpeptide antagonists at CCK-A and CCK-B receptors respectively. Screening against the binding of [^{125}I]CCK-33 to a membrane preparation from rat pancreas furnished a substance. Asperlicin, which had $IC_{50}=1.4$ μm; its structure was determined and served as a lead (Fig. 1). Structure-activity exploration led to a very potent synthetic inhibitor (MK-329, devazepide), having $IC_{50}=0.008$nm, *i. e.* over 10000 fold increase in potency; a non-peptide antagonist of a peptide. Fermentation broths contain hundreds, if not thousands, of chemicals and are a potentially rich source of novel enzyme inhibitors and receptor blockers.

Venoms and toxins are used by animals as protection or to paralyse their prey; some are extremely potent, requiring only minute doses, *e. g.* tetrodotoxin (from puffer fish) which blocks sodium channels, charybdotoxin (from scorpion venom) which blocks Ca-activated potassium channels, α-bungarotoxin (from snake venom) which combines with acetycholine receptors, and batroxobin (from the venom of a pit viper) which is a thrombin-like enzyme. They have served as starting points for investigation of ion channels, hormone receptors, or enzymes. Recent subjects for study include frogs, spiders and sponges. Indeed, marine life offers a vast untapped resource for future investigation.

Another fruitful means for identifying pharmacologically active natural products has been the folk law remedies, which are mainly plant products. Alkaloids such as Atropine and Hyoscine (from plants of the Solanaceae family known to the ancient Greeks), Morphine (from the opium poppy known in ancient Egypt), and Reserpine (from *Rauwolfia serpentina*, the snakeroot popular in India as a herbal remedy), and non-nitrogenous natural products such as salicylates, *e. g.* salicin from the willow tree (genus *Salix*, botanical sources known to Hippocrates), and the glycosides, *e. g.* Digitoxin and Digoxin in digitalis from the foxglove (in folk use in England for centuries).

Natural products continue to provide a fruitful source of drug leads. A recent example is the anticancer drug, taxol, isolated from the pacific yew tree. Testing the natural products has become much more efficient now that the procedure can be coupled with robotic screens based on modern pharmacological or biochemical procedures, *e. g.* for enzyme inhibitors or