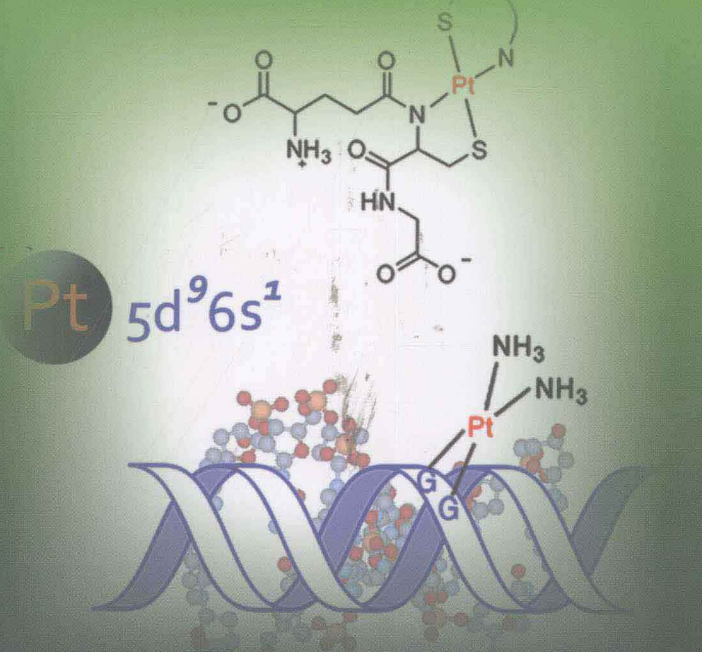
医学教育改革系列教材

首都医科大学 CAPITAL MEDICAL UNIVERSITY 1960

General Chemistry

Chief Editor Ming Zhao



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Foreword

Global developments in medicine and health shape trends in medical education. And in China education reform has become an important focus as the country strives to meet the basic requirements for developing a medical education system that meets international standards. Significant medical developments abroad are now being incorporated into the education of both domestic and international medical students in China, which includes students from Hong Kong, Macao and Taiwan that are taught through mandarin Chinese as well as students from a variety of other regions that are taught through the English language. This latter group creates higher demands for both schools and teachers.

Unfortunately there is no consensus as to how to improve the level and quality of education for these students or even as to which English language materials should be used. Some teachers prefer to directly use original English language materials, while others make use of Chinese medical textbooks with the help of English language medical notes. The lack of consensus has emerged from the lack of English language medical textbooks based on the characteristics of modern medical education in China.

In fact, most Chinese teachers involved in medical education have already attained an adequate level of English language usage. However, English language medical textbooks that reflect the culture of the teachers would in fact make it easier for these teachers to complete the task at hand and would improve the level and quality of medical education for international students. In addition, these texts could be used to improve the English language level of the medical students taught in Chinese. This is the purpose behind the compilation and publishing of this set of English language medical education textbooks.

The editors in chief are mainly experts in medicine from Capital Medical University (CCMU). The editorial board members are mainly teachers of a variety of subjects from CCMU. In addition, teachers with rich teaching experience in other medical schools are also called upon to help create this set of textbooks. And finally some excellent scholars are invited to participate as final arbiters for some of the materials.

The total package of English medical education textbooks includes 63 books. Each textbook conforms to five standards according to their grounding in science; adherence to a system; basic theory, concepts and skills elucidated; simplicity and practicality. This has enabled the creation of a series of English language textbooks that adheres to the characteristics and customs of Chinese medical education. The complete set of textbooks conforms to an overall design and uniform style in regards to covers, colors, and graphics. Each chapter contains learning objectives, core concepts, an introduction, a body, a summary, questions and references that together serve as a scaffold for both teachers and students.

The complete set of English language medical education textbooks is designed for teaching overseas undergraduate clinical medicine students (six years), and can also serve as reference textbooks for bilingual teaching and learning for 5-year, 7-year and 8-year programs in clinical medicine.

We would like to thank the chief arbiters, chief editors and general editors for their arduous labor in the writing of each chapter. We would also like to acknowledge all the contributors. Finally, we would like to acknowledge Higher Education Press. They have all provided valuable support during the many weekends and evening hours of work that were necessary for completing this endeavor.

President of Capital Medical University
Director of English Textbook Compiling Commission
Zhaofeng Lu
August 1st, 2011

Preface

So far, a drug can do its intended job for treating a disease only when it gets to the right place in the human body. That is where chemistry can play its role, in tweaking molecules to interact appropriately with the body. Many factors, including chemical makeup, stability and solubility (how well it dissolves in water or body fluids), determine a molecule's potential as a drug. Chemistry is an important part of medications, either as a diagnostic tool or as a treatment tool. On the other hand, the stable levels of numerous endo-generous substances of the human body are vital for the life, failure of keeping the stability of the levels may result in failure of supporting the biological processes in the body.

Relying on the chemical knowledge, the medical labs in hospitals are able to analyze the blood, urine, etc. for proteins, sugars (glucose in the urine is a sign of diabetes), other metabolic substances and inorganic substances like potassium and sodium. Through these analyses the doctors know at which level and what kinds of the endo-generous substances are wrong, and consequently are able to give a treating strategy.

Most of the medications are involved by inhibiting a specific enzyme or the expression of a gene. Blocking an active site of an enzyme requires a specifically designed blocker that can consequently limit the function of the enzyme. This depends on the interaction between blocker and target enzyme, therefore requires chemistry. Though RNA interference (RNAi) depends more on the biological concept, the engineering of chemicals to inhibit the translation of mRNA into an amino acid sequence by ribosomes needs chemical technique. In RNAi, a designed piece of double-stranded RNA literally chops up mRNA and can prevent mRNA translation. In this context this text book would like to give medical students a sound basis of chemistry.

Ming Zhao

August, 2011

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Chapter 1

Introduction

▪ Objectives

To define chemistry

To give an overview of historical and present day information regarding topics of medical chemistry

To list the SI base units and to derive unit conversion factors

To define the atomic mass unit

To define the mole

To calculate the molar mass of any elementary entities

To express the concentration of a solution in several different ways

To convert between different concentration units

▪ Key concepts

SI Unit; Mole; Molarity; Mass Concentration; Molality; Mole Fraction

Have you ever wondered how our bodies use food to maintain life and combat invading viruses. Chemistry provides answers for these questions and countless others like these. Definition of Chemistry (from Webster's Dictionary): chem is try: (1) the science that systematically studies the composition, properties, and activity of organic and inorganic substances and various elementary forms of matter. (2) chemical properties, reactions, phenomena, etc.: the chemistry of carbon. (3) a. sympathetic understanding; rapport. b. sexual attraction. (4) the constituent elements of something; the chemistry of love. Chemistry is a science. Chemists often arrive at new results by nonscientific means (like luck or sheer creativity), but their work is not chemistry unless it can be reproduced and verified scientifically. Chemistry is a systematic study. Chemists have devised several good methods for solving problems and making observations. For example, analytical chemists often make a plan (thoroughly tested recipes) for determining the concentrations of substances in a sample, then observe and write down the experimental phenomenon and data, take statistics, finally obtain the conclusion. Now Chemists use high technology like spectroscopy and chromatography to study the concentration and chemical structure of new or unknown substances. Certain forms of matter such as wood and glass, water and gasoline, salt and sugar, coal and granite, and iron and gold differ remarkably from each other in many properties. Chemistry is the study of the composition and properties of matter. Matter is the physical material of the universe; it is anything that has mass and occupies space. Your books, your pens, the air you are breathing are all samples of matter. Chemistry answers questions like, 'What kind of stuff is this sample made of? How does the structure of the material determine its properties? How do the properties of the material change when altering temperature, pressure, or some other environmental variables?' Actually the tremendous variety of matter in our world is due to combinations of only about 100 very basic or elementary substances, called elements. Each element is composed of a unique kind of atom, the almost infinitesimally small building block of matter. We will understand how the arrangements of these atoms to form the structure of a molecule or matter. Chemistry is the study of connections between the everyday world and the molecular world. Chemists use atoms and molecules to explain properties and behaviors of matter. What changes in matter are taking place when iron rusts, milk sours, a storage battery produces an electric current, and food is digested and assimilated by the body? Chemistry is the study of the reactivity of substances. One material can be changed into another by a chemical reaction. A complex substance can be made from simpler ones. Chemical compounds can break down into simpler substances. That fuels burning, food cooking, leaves turning color in the fall, cells growing, and medicines curing all involve chemical reactions. Chemistry is concerned with the essential processes that make these changes happen.

1.1 History of Chemistry

By 1000 B.C., ancient civilizations used technologies that would eventually form the basis of the many utilizations of chemistry. Examples include extracting metals from ores, making pottery and glazes, fermenting beer and wine, making pigments for cosmetics and painting, extracting chemicals from plants for medicine and perfume, making cheese, dying cloth, tanning leather, rendering fat into soap, making glass, and making alloys like bronze. **Alchemy** is an early protoscientific or pseudoscience practice combining the content and form of chemistry, physics, astrology, art, semiotics, metallurgy, medicine, mysticism, and religion. There were three main goals many alchemists sought for. First, the most renowned goal of alchemy is the transmutation of any metal into either gold or silver. Second, they also tried to create universal panacea, a remedy that would cure all diseases and prolong life indefinitely. The philosopher's stone was the key in these goals, a legendary substance, allegedly capable of turning inexpensive metals into gold. It was sometimes believed to be an elixir of life, useful for rejuvenation and possibly for achieving immortality. The Chinese alchemists were interested in the preparation of artificial cinnabar, which they believed to become celestial being with the 'life-giving' red pigment. The third goal was to create human life. Aristotle taught that all matter consisted of four fundamental constituent factors or elements—air, water, earth, and fire. All matter was supposed to incorporate these four elements in different combinations and proportions. Thus, alchemy ultimately gave rise to modern chemical thought and, gradually, the goals of alchemy were abandoned. In a broad sense, alchemy can be regarded as the precursor of the modern science of chemistry prior to the formulation of the scientific method.

The **history of chemistry** may be said to begin with the distinction of chemistry from Alchemy by Robert Boyle (1627–1697) in his work, *The Skeptical Chymist* (1661). Chemistry became a full-fledged science when Antoine Lavoisier (1743–1784) discovered oxygen and the law of conservation of mass, and thereby refused to accept the phlogiston (Phlogiston was supposed to be an imponderable substance liberated by flammable materials in burning.) theory of combustion in 1783. In 1789, Lavoisier published his textbook 'Elementary Treatise on Chemistry'. So, while both alchemy and chemistry are concerned with the nature of matter and its transformations, only the chemists apply the **scientific method**. The history of chemistry was intertwined with the history of thermodynamics, especially through the work of Willard Gibbs.

After the debate on the nature of combustion was settled, another dispute, about the vitalism and the essential distinction between organic and inorganic substances, was revolutionized by Friedrich Wöhler's accidental synthesis of an organic compound outside a living system, urea, from inorganic substances in 1828.

$$\mathrm{Pb(OCN)_2 + 2\ NH_3 + H_2O \longrightarrow PbO + NH_4OCN \longrightarrow H_2NCONH_2}$$

It was Wöhler's synthesis of urea that led to the demise of the theory of vitalism. This opened a new research field in chemistry, and by the end of the 19th century, scientists were able to synthesize hundreds of organic compounds.

Although such proponents of the atomic theory as Amedeo Avogadro and Ludwig Boltzmann made great advances in explaining the behavior of gases, this dispute was not finally settled until Jean Perrin's experimental investigation of Einstein's atomic explanation of Brownian motion in the first decade of the 20th century. Well before the dispute had been settled, Svante Arrhenius had begun to investigate the internal structure of atoms with his theory of ionization. This was carried much further by Ernest Rutherford, who established the study of the substructure of the atom as a branch of physics, but was awarded the Nobel Prize in chemistry, not physics, for his work.

In 1869, Lothar Meyer compiled a Periodic Table of 56 elements based on the periodicity of properties such as molar volume when arranged in order of atomic weight. Mendeleev also published his periodic table & law in 1869, but he also forecasted the properties of missing elements. Both Meyer and Mendeleev constructed periodic tables independently that are credited as being the basis of the modern table. Meyer was more impressed by the periodicity of physical properties, while Mendeleev was more interested in the chemical properties. The most impressive thing was Mendeleev's use of the table to predict the existence and the properties of germanium, gallium, and scandium. Mendeleev made his prediction in 1870; gallium was discovered in 1875, and was found to have roughly the same properties that Mendeleev predicted for it.

The exhaustion of the oil supplied from whaling before the exploitation of the petrochemicals of the earth emerged on the later part of the 19th century. Systematic production of refined materials provided a ready supply of products which not only provided energy, but also synthetic materials for clothing, medicine, and everyday disposable resources, by the 20th century.

In 1939, the American chemist, Linus Pauling accomplished his ambition by publishing the seminal textbook *The Nature of the Chemical Bond* on the subject. It was based primarily on his work in this area that he was awarded the first of his two Nobel prizes in 1954 'for his research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances'.

By the 20th century, the integration of physics and chemistry was completed, with chemical properties explained as the result of the electronic structure of the atom; Linus Pauling's book of *The Nature of the Chemical Bond* used the principles of quantum mechanics to deduce bond angles in ever-more complicated molecules. Pauling had formulated a model for the structure of hemoglobin in which atoms were arranged in a helical pattern, and applied this idea to proteins in general. This helical arrangement suggested the double helix for deoxyribonucleic acid (DNA). In1953 James Watson (1928–2004) and Francis Crick (1916–1953) discovered the molecular structure of DNA. Their helical structure was simultaneously confirmed by Rosalind Franklin's X-ray crystallography. Their work on the structure of DNA was performed with the knowledge of Chargaff's ratios of the bases in DNA and some access to the X-ray crystallography of Maurice Wilkins (b.1916) and Rosalind Franklin at King's College, London. Combining all of this work led to the deduction that DNA exists as a double helix. Crick, Watson and Wilkins shared the 1962 Nobel Prize for Physiology or Medicine. Franklin died of cancer in 1958. Biology milestone: James Watson and Francis Crick proposed the double helix—a twisted ladder structure—as the form of DNA, it led to the modern science of molecular biology and the understanding on how genes control processes within cells. Soon the Miller-Urey experiment demonstrated that basic constituents of DNA, simple amino acids, could themselves be built up from simpler molecules in a simulation of primordial processes on the Earth.

GENERAL CHEMISTRY includes the three branches of Chemistry, namely, **INORGANIC CHEMISTRY** concerned with the chemistry of the elements other than carbon and their compounds; **PHYSICAL CHEMISTRY** primarily concerned with the structure of matter, energy changes, the laws, principles, and theories which explain the transformations of one form of matter into another, and **ANALYTICAL CHEMISTRY** concerned with the identification, separation, and quantitative determination of the composition of different substances.

1.2 Chemistry in Medicine

> The task of chemistry is not to make gold or silver, but to prepare medicines. —Paracelsus (1493–1541)
>
> Discovery consists of seeing what everybody else has seen and thinking what nobody else has thought.
> —Albert Szent-Györgyi (1893–1986)

Malaria-Quinine; Artemisinin

Malaria is one of the worst sicknesses to affect humankind for thousands of years. Currently, malaria kills more than a million children a year in Africa alone. Malaria is caused by a microscopic parasite called *Plasmodium* that infects humans when they are bitten by an infected female *Anopheles* mosquito. Inside the human host, the parasite multiplies in the liver and in red blood cells, which periodically release more parasites, concomitantly causing fever. These organisms can infect any mosquito that feeds on the host's blood, thus helping to spread the disease. For centuries there was no specific treatment until the 17th century when Spanish colonizers brought back from Peru the tree bark from which quinine was later extracted. The label on the bottle translates from French as 'Produced by J. Pelletier'. In 1820, the two French Chemists Pierre-Joseph Pelletier (1788–1842) and Joseph Caventou (1795–1877) discovered and isolated the compound in cinchona bark that made the bark so effective against malaria. They named the compound quinine. Since then improvements in production techniques have given us more effective quinine-based drugs against malaria. Many new synthetic drugs, including chloroquine, primaquine, proguanil, and artemisinins, were deployed against malaria.

A herb frequently mentioned in Chinese materia medica (called ben cao in Chinese) as of value in the treatment of intermittent fever is Artemisia annua or sweet wormwood (qing hao in Chinese). In the Chinese medical *Handbook of Prescriptions for Emergency* (approx. 333 AD) by the alchemist and physician Ge Hong, the method to treat malaria was described in his statement of treating fever: 'a handful of qin hao, *Herba Artemisiae Annuae* L, is added to two litres of water and pounded into juice to take'. In 1970s-Chinese Cultural Revolution, this preparation was tried by Chinese scientists as part of Project 523, using the herb to make a tisane (pouring boiling water for a few minutes) or infusion (pouring room temperature water for a while) and carefully filtering off the solid material, as it is a common practice with herbal remedies. They found that the tisane had no antimalarial properties whatsoever. Removal of the solvent left with the colorless crystals that proved to be very effective in killing the malaria parasite in animal models. Further research work revealed that the active compound is qing hao su or, for the benefit of Westerners, artemisinin (or, more rarely, arteannuin), which was first purified and its structure was determined by a group of Chinese scientists. After numerous studies on its chemistry, pharmacology, and toxicology, and the investigations carried out in clinics, artemisinin was proven to be effective and have a rapid action and low toxicity against malaria. The isolation and characterization of artemisinin from *A. annua* L. was considered one of the most important discoveries in contemporary herbal medicine research. Then the drug-design research of pharmaceutical chemistry revealed that Artemether is a methyl ether derivative of artemisinin and it is more active than artemisinin.

Scurvy-Vitamin C

For centuries scurvy had been the scourge of sailors or pirates on long sea voyages, and the illness was an extremely important issue. Scurvy can lead to the formation of spots on the skin, spongy gums, and bleeding from the mucous membranes. The spots are most abundant on the thighs and legs, and a person with the ailment looks pale, feels depressed, and is partially immobilized. In advanced scurvy there are open, suppurating wounds and loss of teeth. It was described by Hippocrates (c. 460 BC–c. 380 BC), and herbal cures for scurvy have been known in many native cultures since prehistory. Fresh fruit was too easily putrid to keep on board, whereas boiling it down to juice allowed easy storage but destroyed the vitamin (especially if boiled in copper kettles). James Lind (1716–1794), a surgeon on a ship of the British Royal Navy, first attempted to give scientific basis for the cause of this disease. While at sea in May 1747, Lind isolated 12 sailors suffering from scurvy and treated them with six different remedies. He provided six crew members with two oranges and one lemon per day along with their normal rations. He found oranges and lemons to be the most effective cures. In the history of science this is considered to be the first occurrence of a controlled experiment, comparing results on two populations of a factor applied to one group only with all other factors the same. The results conclusively showed that citrus fruits prevented the disease. In 1754, Lind published *A Treatise of the Scurvy*. In spite of Lind's works, his advice about giving sailors citrus fruits to prevent scurvy was not taken seriously by the British Navy until after his death. In the next year, 1795, the Royal Navy adopted the practice of giving seamen citrus fruits and juices as part of their diets. Scurvy promptly vanished from the Royal Navy. The name 'antiscorbutic' was used in the eighteenth and nineteenth centuries as general term for those foods known to prevent scurvy, even though there was no understanding of the reason for this. These foods included but were not limited to: lemons, limes, oranges, sauerkraut, cabbage, malt, and portable soup.

In 1932, Albert Szent-Györgyi's group discovered that paprika peppers (a common spice in the Hungarian diet) was a rich source of hexuronic acid (vitamin C, the L-enantiomer of ascorbic acid), the antiscorbutic factor, by then named ascorbic acid, in honor of its activity against scurvy. Also during this time, Szent-Gyorgi continued his work on cellular respiration, identifying fumaric acid and other steps in what would be known as the Krebs cycle. In 1937, he received the Nobel Prize in Physiology or Medicine 'For his discoveries in connection with the biological combustion process with special reference to vitamin C and the catalysis of fumaric acid'.

Haworth made fundamental contributions to carbohydrate chemistry. He introduced, in 1925, the correct cyclic model for glucose, and structures of monosaccharides, disaccharides, and eventually the polysaccharides. Haworth also established the correct structure of ascorbic acid (vitamin C), and his synthesis constituted the first synthesis of any vitamin. Haworth was awarded the 1937 Nobel Prize in Chemistry (shared with Paul Karrer) for his research on carbohydrates and vitamin C. He was the first British organic chemist to receive the Nobel Prize.

In 1933, the Swiss chemist Tadeus Reichstein succeeded in synthesizing the vitamin C, making it the first to be artificially produced. This made possible the cheap mass-production of what was then known as vitamin C and it was produced from glucose. The Reichstein process, a combined chemical and bacterial fermentation sequence still used today to produce vitamin C, retained Reichstein's name. Vitamin C was commercially synthesized in 1934. The modern two-step fermentation process, originally developed in China in the 1960s, uses additional fermentation to replace part of the later chemical stages.

Analgesics-Aspirin (Acetylsalicylic acid)

In the 5th century B.C., Hippocrates, the father of modern medicine, recommended willow bark for pain relief. The medicine men of every Native American tribe would use the bark of willow trees (usually in the form of tea) to treat pain and fever. Ancient Egyptians took an infusion of dried myrtle leaves to treat muscle pain. When chemists analyzed willows and myrtle leaves in the last century, they discovered salicylic acid. In 1758, English clergyman Edward Stone chewed a twig of white willow to ease pain and fever. He was so impressed with its effect that he wrote to the Royal Society in 1763 to alert them to its benefits. The true beginnings of pain **Chemotherapy** (the chemical treatment of disease) came with the isolation of salicylic acid from willow bark in 1860. An additional source of salicylic acid was found in 1835 by the German chemist Karl Jakob Lowig. This new wonder pain killer was found in Meadowsweet (Spiraea ulmaria), a wild flowering plant that grows on riverbanks over much of Europe. Twenty years later salicylic acid was successfully synthesized in the laboratory, enabling mass production for the first time. Unfortunately, salicylic acid has a very sour taste and cause severe irritation to the mouth and throat. It upsets stomachs as well.

In 1897, Felix Hoffmann, a pharmaceuticals graduate working at the German pharmaceutical company Bayer, invented acetyl salicylic acid (ASA)—a new formulation of salicylic acid which did not have the unpleasant side effects of its predecessor, because he had an arthritic father who could not tolerate salicylic acid. But much to Hoffmann's surprise, his new discovery was shelved. Bayer was far more interested in Hoffmann's another discovery, diacetylmorphine, a drug Bayer wanted to use in cough medicines. Given the brand name 'Heroin', it is now a Class A Controlled Drug. It was not until January 1899, after further successful tests, ASA was given its brand name, Aspirin.

In 2003, the World Health Organization (WHO) included acetylsalicylic acid, the active ingredient in Aspirin®, in its 'List of essential medicines'.

Anesthesia-Nitrous Oxide (N_2O, Laughing Gas)

Like analgesics, anesthetics relieve pain, but unlike analgesics, they produce a complete or partial lack of feeling. Joseph Priestley (1733–1804) synthesized nitrous oxide in 1775. Joseph Priestley had announced that nitrous oxide was poisonous. As it turned out, impure nitrous oxide gas contained corrosive nitric acid, which damaged the mucous membrane in the mouth because it was prepared by treatment of copper or iron with diluted nitric acid. **Humphry** Davy (1778–1829) was a rare genius, later, Davy found out that only purified nitrous oxide was safe to inhale. Pure nitrous oxide gave him soaring euphoria and later unconsciousness, which he exclaimed to be an absolutely intoxicating sensation. Davy called nitrous oxide 'laughing gas' because many people involuntarily started laughing uncontrollably after inhalation. In 1800 Davy published a flamboyant and widely read book on nitrous oxide titled *Researches, Chemical and Philosophical; Chiefly Concerning Nitrous Oxide and Its Respiration*. Davy presciently suggested in his book: 'As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations'. A dentist, Horace Wells (1815–1848) noticed the connection between nitrous oxide and pain relief. Wells tried his idea and had his former student extracted a bothersome wisdom tooth of his. Wells woke up and did not feel any pain. 'A new era in tooth-pulling!' Little did he know that event would change the medical history. On January 24, 1848, he cut the femoral artery in his left thigh under the influence of chloroform.