

Textbook of Pharmacology

B. C. BOSE, M.D., D.SC., F.A.M.S.

Ex-Dean & Professor of Pharmacology, Emeritus Scientist, Professor Emeritus M.G.M. Medical College, Indore (M.P.)

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SECTION

I

GENERAL PHARMACOLOGY

CHAPTER

1

SCIENCE OF PHARMACOLOGY

(EVOLUTION, RELATION AND SCOPE)

[Man's inquisitiveness for understanding the mysteries of nature, from which science and medicine have developed, must have been as old as life itself on the planet. It is believed that the homosapiens or the first race of 'ape-man' might have lived about 10°, the second race about 10° and the third race about 50,000 B.C. The concepts of 'Gods' and 'Demons' might have appeared in the neolithic period only. The primitive man hurt by an 'external foe' dealt with him physically. When afflicted by an illness, he took it to be the mischief of an 'internal foe' or 'demon' whom he tried to get rid of by placation or trephining. The mother found her baby unwell and applied a cold sponge for its relief. These thus were the starting points of medical, surgical and nursing cares in the prehistoric days. It was much later, that, when in search of food, he found out poisonous plants and used them against diseases and foes.

The earliest records of medical practice are traceable in Sumarian, Persian, Egyptian, Chinese and Indian systems. Though some of them had attained a good stature in medical, surgical and Public Health measures, modern medicine started from the Greco-Roman School with Hippocrates, Dioscorides and Galen, between 4th century B.C. to 2nd century A.D. Then followed a long period of over 1,000 years of 'Middle' or 'dark age' during which, the dogmatic teachings of Galen along with 'Arab alchemy', prevailed. Renaissance in medicine, started with Paracelsus in the 15th century A.D., followed by methodical studies of anatomy, physiology, mathematics, physics and chemistry. Nevertheless, progress was still very slow in the 17th and 18th centuries and scientific advances in medicine, started mostly in the 19th century, by which time, pure and basic medical sciences had sufficiently advanced.

Pharmacology like biochemistry, needed the prior development of chemistry and physiology for its scientific advancement. From the beginning of the last century, plant constituents were isolated and studied by animal experimentations with the help of gradually developed physiological techniques and instruments. The work was further facilitated by the discovery of hypodermic needle in the middle of the last century. The initial works of Magendie, Claude Bernard, Ludwig, Buchheim, Schmiedberg, Abel, Dixon and Cushny are of special significance in establishing the science of pharmacology on the sound footing. Towards the latter part of the last and the first half of the present century, with remarkable advances in biochemistry, drug synthesis, microbiology, knowledge of vitamins and hormones, it became

possible to understand the quantitative and cellular nature of drug action, which gradually led to the introduction of chemo and specific therapies, which are now eclipsing all other methods of treatment of diseases in the present era.

The subject of pharmacology comprises of pharmacognosy, pharmaceutics, pharmacodynamics, toxicology, bioassay and therapeutics. It is interrelated with botany, chemistry, physiology and biochemistry on the one hand and with pathology, microbiology, medicine and therapeutics on the other. Its scope has much increased during the last fifty years and it is being oriented more towards specific therapies, in all directions, including systemic, infective, malignancy, immunosuppressive, genetic and fertility problems, with more or less selective actions.]

Use of drugs is as old as diseases. In the earlier days, mostly herbal and chemical drugs were in empirical use and the subject providing relevant information about these drugs was known as materia medica. At a later stage, due to the advancement of basic sciences, knowledge of diseases and of experimental techniques, scientific study of drug action was possible. Since then the subject is known as pharmacology or the science of drugs.

Due to the advancement of physiology, biochemistry and allied disciplines, this new branch of medicine has developed beyond all proportions during the last one century, so much so that at present, not only drug action in many cases has been established on scientific and quantitative basis but their sites of action, metabolism actions at cellular or enzymatic levels, intricate mechanisms subscribing to the specificity of action as in the cases of chemotherapeutic, antibiotic, vitamins, hormones and other specific drugs have also been determined.

In the light of all these advances, it is now possible to consider and study the subject under the following aspects:

- (1) General pharmacology,
- (2) Special pharmacology,
- (3) Systemic pharmacology.

EVOLUTION

The history of pharmacology is intimately connected up with that of medicine. Struggle for health, struggle against illnesses and struggle for immortality have always been the fanciful dreams of human minds. History of medicine and drugs is thus traceable through different periods of growth of civilization, viz. (a) prehistoric era, (b) earlier periods, (c) middle ages, (d) renaissance, (e) medicine and pharmacology of modern times.

SECTION

I

GENERAL PHARMACOLOGY

CHAPTER

.1

SCIENCE OF PHARMACOLOGY

(EVOLUTION, RELATION AND SCOPE)

[Man's inquisitiveness for understanding the mysteries of nature, from which science and medicine have developed, must have been as old as life itself on the planet. It is believed that the homosapiens or the first race of 'ape-man' might have lived about 10°, the second race about 10° and the third race about 50,000 B.C. The concepts of 'Gods' and 'Demons' might have appeared in the neolithic period only. The primitive man hurt by an 'external foe' dealt with him physically. When afflicted by an illness, he took it to be the mischief of an 'internal foe' or 'demon' whom he tried to get rid of by placation or trephining. The mother found her baby unwell and applied a cold sponge for its relief. These thus were the starting points of medical, surgical and nursing cares in the prehistoric days. It was much later, that, when in search of food, he found out poisonous plants and used them against diseases and foes.

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features in Nidan and other treatises of Ayurvedic medicine are as follows:

- (a) Theory of Tridosha referring to the imbalance in 'vayu', 'pitta' and 'kapha', causing various disorders, which are reflected on the radial pulse and the diagnosis of diseases made therefrom. This is known as the 'science of pulse'.
 - (b) Monumental work, for those days, in medicine and surgery, as embodied in Susruta and Charak, compiled about 1000 B.C., the former dealing with surgery and the latter with internal medicine.
 - (c) A beautiful Materia Medica embodying 'Dravyaguna' and descriptions of 107 medicinal plants and inorganic chemicals.
 - (d) Knowledge of hygiene and public health, as contained in Manu Sanghita.
 - (e) Use of 'Sammohini' as an anaesthetic in the Buddhic period.
 - (f) Description of tuberculosis, infectious diseases, malaria, leprosy and practice of couching and trephining operations are found in these records.

This ancient medicine, however progressive in those days, could not be claimed to be scientific. Any attempt to integrate it with modern medicine would, therefore, fail as the basic concepts are not scientifically tenable. It is true that some amount of scientific researches on the chemico-pharmaco-therapeutic values of some of these ancient drugs could be carried out but in the light of experience already gained, it is for consideration whether this study should have the priority, as is being given to it in our country at present.

Greco-Roman School: This laid the real foundation of modern scientific medicine. Aesculapius (1143 B.C.), known as the son of Appollo, and his daughter, Hygeia, can be considered to be the earliest recorded figures. He was so famous in his time that he, it is alleged was slewn by Zeus with the apprehension that he might render all men immortal. To him, we owe the knowledge of the tonic properties of iron and the 'medical emblem' of the 'Snake and the Wand'.

Hippocrates (460-400 B.C.) is the father of modern medicine. Before him, medicine was a curious blend of mystic philosophy and predestined observations. It was the genius of Hippocrates to make it rational, ethical and an objective study. His contributions pervaded practically all aspects of medical science, public health and medical ethics. Diseases like tuberculosis, tetanus, epilepsy, hysteria and many others were masterly described by him and similarly, a large number

Plate I SOME EARLY PIONEERS



Fig. 1. Aesculapius (1143 B.C.). A mythical figure; son of Apollo and endowed with the secret of immortality. The medical emblem, 'Snake and Wand' comes from him.



Fig. 3. Dioscorides (A.D.56)
Author of De Universa
Medicina and the first
to systematise knowledge
of 800 medicinal plants.



Fig. 2. Hippocrates (360—400 B.C.). Undoubted founder of modern medicine, who advocated objective study and left sermons and hippocratic collections behind him.



Fig. 4. Galen (130—200 A.D.).

A supreme authority, whose doctrine and dogma remained unchallenged upto the 15th century. His polypharmacy and galenical preparations are still known.



Fig. 5. Paracelsus (1493—1541
A.D.). Rightly named as 'Luther of Medicine', who strongly decried Galen's dogmatic teachings, spared Hippocrates and advocated chemical study of diseases and medicines. He brought renaissance in medicine.

of drugs—opium, hyoscyamus, scilla and cantharis, to cite a few only, were studied and used. His method of treatment was simple —'vis medicatrix' or nature cure advocating the value of pure air, dietetic treatment, use of simple purgatives and cholagogues or drugs increasing excretion of bile. Hippocrates was also a saintly man and his ethical rules for the profession embodied in the Sermons of Hippocrates, are ostentatiously followed even today. More than 100 books, collectively known as Hippocratic Collections or Corpus were written by him or probably by his school. His school, however, was weak in theory, but strong advocates of observations, which was partially responsible for bringing the dogmatic Roman School of Galen at a later stage. It may be noted that Aristotle (384-322 B.C.) applied Hippocratic methods of observations in his study of general sciences.

School of Alexandria: With Herophili, as its central figure, it initiated some anatomical studies during this period. *Dioscorides* (A.D. 56) who belonged to the Roman School of Medicine contributed a good deal in therapeutics. He compiled the first extensive *Materia Medica* and described individual crude drugs—vegetable, animal and minerals used in medicine, in alphabetical orders. He also described their methods of preparation, administration and therapeutic values.

In his monumental work *De Universa Medicina*, he incorporated about 800 vegetable and 90 mineral remedies: (a) aromatic plants, (b) organotherapeutic remedies, (c) aloes and scammony as purgatives, (d) male fern for worms, (e) sulphur in pulmonary disease, and (f) castor oil as purgative. He had travelled extensively with the army of *Nero* and collected newer drugs from other countries, which he systematically arranged and described. The *Doctrine of Signature*, i.e. one medicine for one disease, which had further developed during this period, could be considered to be the starting point of pharmacognosy or identification of drugs of today.

Galen (A.D. 130-200) belonged to the Roman School of Medicine and was considered to be the supreme authority in medicine and pharmacy for nearly 15 centuries. He was the last scholar of the Alexandrian School and undoubtedly the most prominent figure after Hippocrates. Though his name in Greek meant calm, he was a man of great dynamism and drive and also vain and sophisticated. Unlike Hippocratic teachings which stressed observations and not theories, Galen's teachings were rich in theories and dogmas and had thus an initial appeal to the profession.