

History and development of medicinal chemistry

Dr. Gopal Krishna Padhy

Introduction to medicinal chemistry

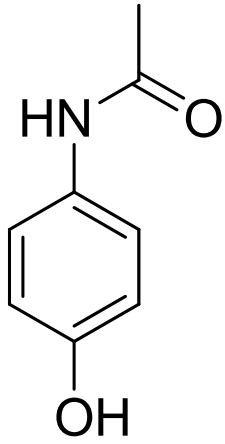
- ❖ Medicinal chemistry and pharmaceutical chemistry are disciplines of chemistry, especially synthetic organic chemistry, pharmacology and other biological specialization, where they are involved with design, chemical synthesis and development of pharmaceutical agents, or bio-active molecules (drugs).
- ❖ Medicinal chemistry in its most common practice—focus on synthetic organic chemistry, natural products and computational chemistry in close combination with chemical biology, enzymology and structural biology, together aiming at the discovery and development of new therapeutic agents.

History and development of medicinal chemistry

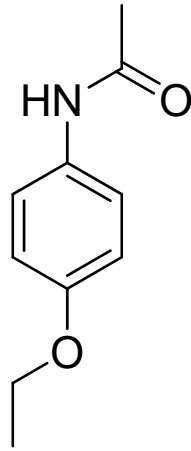
- ❖ There is a long history of plants being used to treat various diseases. They figure in the records of early civilizations in Babylon, Egypt, India and China. The therapeutic properties of plants were described by the Ancient Greeks and by the Romans and are recorded in the writings of Hippocrates and Galenus. Some metals and metal salts were also used at that time.
- ❖ In the Middle Ages various 'Materia Medica and pharmacopeas brought together traditional uses of plants. The herbals of John Gerard (1596), John Parkinson (1640) and Nicolas Culpeper (1649) provide an insight into this widespread use of herbs. Exploration in the seventeenth and eighteenth centuries led to the addition of a number of useful tropical plants.

- ❖ General anesthetics like diethyl ether (1842), nitrous oxide (1845) and chloroform (1847) were introduced in surgery from 1842 onwards. Antiseptics such as iodine (1839) and phenol (1860) also made an important contribution to the success of surgery. The hypnotic activity of chloral (trichloroethanal) (1869) was also reported.
- ❖ Although the use of willow bark as a pain-killer was known to the herbalists, the analgesic activity of its constituent salicylic acid was discovered in the 1870s. p-Hydroxyacetanilide (paracetamol) and phenacetin (1886) were also recognized as pain-killers. Acetylation of salicylic acid to reduce its deleterious effect on the stomach led to the introduction of aspirin in 1899. However its mode of action was not established until 1971.

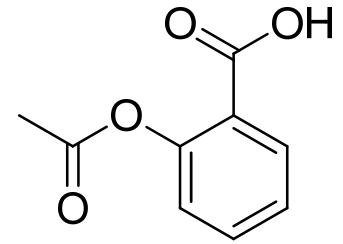




Paracetamol



Phenacetin

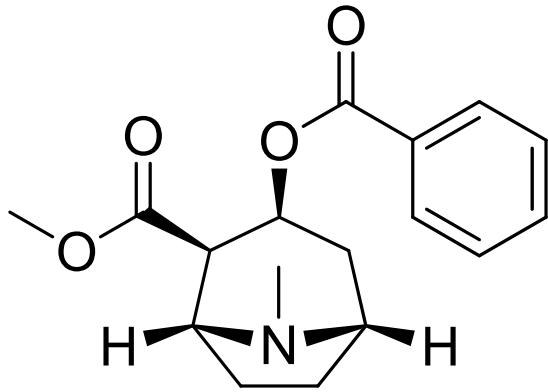


Aspirin

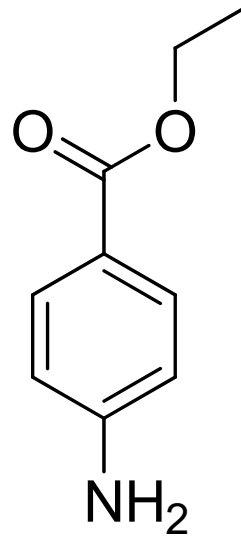


- ❖ The local anaesthetic action of cocaine was reported in 1884 although its structure was not known at the time. Various modifications of cocaine led to discovery of benzocaine (1892) and procaine (1905).
- ❖ In the mid-nineteenth century, the first theories of the relationships between chemical structure and biological activity began to emerge. Thus Crum-Brown and Fraser (1869) noted that a 'relationship exists between the physiological action of a substance and its chemical composition' leading to the idea that cells can respond to the signals from specific molecules.
- ❖ In the 1890s Ehrlich put forward the idea that there were specific receptors for biologically active compounds and there exist a lock and key' relationships between them.

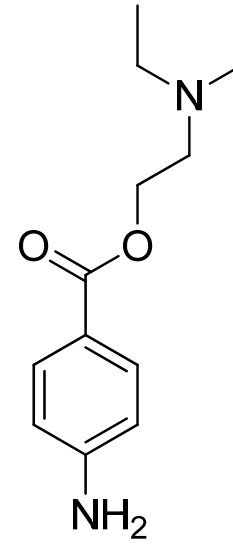




Cocaine



Benzocaine



Procaine



- ❖ 20th century saw the recognition of vitamin deficiency diseases and the elucidation of the structure of various vitamins. Subsequently synthetic anti-malarials such as pamaquine (1926), mepacrine (1932) and later chloroquine were introduced as quinine replacements.
- ❖ A number of developments took place in structures of various vitamin and structures of various vitamin the 1960s, which changed medicinal chemistry.
- ❖ It was found that a drug, thalidomide which had been introduced as a sedative, when used by pregnant women, led to the birth of deformed children (S isomer). The consequences of this teratogenic effect brought about a major tightening of the regulations regarding drug registration and the safety of medicines.
- ❖ Secondly in 1964 Hansch published correlations between substituent effects (Hammett parameters) and the biological activity of some aromatic compounds. These QSAR began to provide a framework for the systematic development of drugs and for decisions to be made in the planning of a research programme.