CHAPTER – 1

INTRODUCTION TO ANTIBIOTICS

ABSTRACT

A general introduction of antibiotics with reference to chemotherapy is given briefly. A classification of antibiotics is provided. The activities and uses of antibiotics are given briefly.
1.1 History of Antibiotics 1,2,3

Among the very few remarkable events in the history of microbial diseases, antibiotic discovery is the one. With the advancement of scientific research, one is almost free from deadly infecteous diseases and the surgery of medical science is no longer a desperate gamble with human life. This is primarily due to the antibiotic discovery. As a result of it people can live safely and healthily for a longer period. The meaning of the word antibiotic in Greek is "against life".

Antibiotics are chemical substances produced by various species of microorganisms and other living systems that are capable of inhibiting the growth of or killing bacteria and other microorganisms.

The recent progress made in the chemistry of natural products has also contributed to the development of the method now in use for the isolation of antibiotics. The period 1885 – 1939 may be considered as one in which the foundation was laid for the development of our knowledge of Antibiotics. The production of chemical agents came to be recognised as responsible for the inhibitory effect. These agents were at first designated as "lethal principles" and "Toxic Substances". Their designation as "antibiotics" is only of recent origin.

The first systematic search for, the study of, antibiotics, made by Gratia and Dath about 1924, resulted in the discovery of actinomycetin in strains of actinomycetes, and soil organisms. Actinomycetin was never used for the treatment of patients but was used to lyse cultures of bacteria for the production of vaccines.

In 1929, Fleming published his observations on the effect of a fungal contaminant, identified at that time as penicillin rubrum but later as penicillin
notatum, upon the growth of bacteria. Fleming designated the antibacterial product of
the fungus as penicillin. The foregoing observations, in the studies of mixed cultures
carried out before 1939, amply illustrated the fact that numerous types of micro-
organisms, especially the bacteria, fungi and actinomycetes possess the capacity to
inhibit the growth of other microorganisms. This inhibiting effect was shown to be
due to the production of specific chemical substances later designated as antibiotics.

A systematic search of antibiotic – producing microorganisms from soil was
undertaken. In 1939 Dubos\(^1\) isolated from soil a culture of bacillus brevis which
produced two valuable antibacterial substances, now known as gramicidin and
tyrocidin, that killed many gram positive bacteria. Soon afterwards Selman
Waksman discovered streptomycin, a product of streptomyces griseus. Some 2000
antibiotic substances have been isolated and studied, of which about 50 are useful
clinically.

Several thousand antibiotic substances have been isolated and identified since
1940. Many of them are of no practical importance as yet, but a few have changed
the entire concept of chemotherapy. The popularity of antibiotics is due to their
ability to destroy many kinds of pathogens and to their relatively nontoxic properties
to the host when given systemically. Few developments in the field of medicine have
had as dramatic an effect as have antibiotics in the treatment of microbial infections.

1.2 Antibiotics and chemotherapy:-

The treatment of a disease with a chemical substance is known as
chemotherapy. The chemical substance is called a chemotherapeutic agent.
Antibiotic is the discovery of a new and potent class of antibacterially active
chemotherapeutic agent. In general, naturally occurring substances are distinguished from synthetic compounds by the name antibiotics. Some antibiotics are prepared synthetically, but most of them are prepared commercially by microbial biosynthesis.

To be useful as a chemotherapeutic agent a substance must have selective toxicity for the parasite, which means a low toxicity for host cells and high toxicity for the parasite. For this and other reasons antiseptics, and germicides such as phenol are unsatisfactory as chemotherapeutic agents. So, antibiotics are used as chemotherapeutic agents.

1.3 Classification

Antibiotics are classified as:

a) The producing micro-organisms
b) Activity spectrum
c) Metabolic pathways of biosynthesis
d) Chemical structure.

Garrod, Lambert and O'Grady have classified Antibiotics on the basis of general similarity of chemical structure.

1) Penicillin and related Antibiotics:- All members of this group have a β-lactum ring in their structure. This group includes the natural penicillins the semisynthetic penicillins and cephalosporins.

2) Aminoglycoside Antibiotics:- All members of this group have amino sugars in glycoside linkage. This group comprises the streptomycins, neomycin, kanamycin, paromomycin gentamycin, tubramycin and amikacin.

3) Macrolide Antibiotics:- All these consist of a macro cyclic lactone ring to which sugars are attached. This group comprises erythromycin, oleandomycin and spiromycin.
4) **Tetracycline Antibiotics:** The Tetracyclines are derivatives of the poly cyclic napthacene carboxamide. This group consists of tetracycline, chlortetracycline, demeclocycline, oxytetracycline and minocycline.

5) **Chloramphenicol:** This antibiotic is in a class in itself. It is a nitrobenzene derivative of dichloroacetic acid.

6) **Peptide Antibiotics:** These antibiotics form a large group but very few have found therapeutic application. These antibiotics are composed of peptide-linked amino acids which commonly include both D-and L-forms. Antibiotics in this category include bacitracin, gramicidin and the polymyxins.

7) **Antifungal Antibiotics:** This group has two main sub-groups (1) polyenes which contain a large ring with a conjugated double bond system. In this group most important antibiotics are hystain and amphotericin B, (2) the other group including 5-fluro cytosine, clotrimazole and griseofulfin.

**Unclassified:** These antibiotics have varied structures. They are not classified among the main groups described above. Antibiotics in this group include cycloserine, tusidic acid, novobiocin, prasinnomycin, spectinomycin and vancomycin.

In preparations of medicines antibiotics are subdivided into the following seven groups. 1) Penicillins (including semi synthetic methicillin, oxacillin, ampicillin) and cephalosporins. 2) Broad-Spectrum antibiotics (tetracycline and their derivatives) 3) Streptomycin group (streptomycin, neomycin etc.) 4) Reverse antibiotics (erythromycin, chloramphenicol ristomycin, novobiocin) 5) Antifungal (levorin, nystatin etc) 6) antituberculous (streptomycin, kanamycin, phlorimycin, etc) 7) Antineoplastic (bruneomycin olivomycin etc)
1.4 Activity

The activity of antibiotics is expressed in international units (I.U). (One I.U of penicillin (oxford unit) is equivalent to 0.6 micrograms of pure benzyl penicillin. It is the smallest amount of preparation inhibiting the growth of a standard staphylococcus aureus strain. Recently the method of determining the activity of antibiotics according to the weight of the preparation has received wide application.

Antibiotics may act by 1) affecting cell wall peptidoglycon biosynthesis 2) affecting the cell membrane 3) inhibiting DNA synthesis and 4) inhibiting protein synthesis.

Certain antibiotics are effective only against a few types of bacteria and are known as narrow spectrum antibiotics. Others act against a large number of species, which may be unrelated. They are called broad spectrum antibiotics. Penicillin and streptomycin are narrow spectrum antibiotics while, tetracycline, chloramphicol are broad spectrum antibiotics.

1.5 Uses:

Antibiotics have been shown to be effective for many of the diseases of live stock. Antibiotic medication through the feed represents a convenient and effective means of treating certain specific disease conditions.

Medical Uses:

Now a days physicians control approximately 50% of all male and pathos. The number of patients being rescued from surgery by antibiotic medicine is increasing everyday.
Non-Medical Uses:

The application of antibiotics to animal was an outgrowth of the work in the human disease field. Certain antibiotics have found widespread use as animal feed supplements to promote growth in live stock. Additionally, antibiotics had some use in food preservation and spraying of crops to control specific crop diseases.

According to Lucken\textsuperscript{11} the reactivity of a molecule depends in the most general way on the polarization and polarizability of the different atoms of which it is composed. Hence it can be expected that a systematic study of the bond and molecular polarizability coefficients can throw light on the chemical characteristics. Similarly the knowledge of diamagnetic susceptibility ($\chi_m$) and molecular electron ionization cross section ($Q$), which gives a measure of the electronic interactions between molecule and the incoming field is also expected to have some bearing on the activity of Antibiotics. As such a systematic study of the $\alpha_m$, $\chi_m$ and $Q$ of a few antibiotics is being undertaken and the results are discussed in the present investigations.
References

10) Luther, H.G and Hawley, G.E “Antibiotics in Animal nutrition and diseases.” An health institute of scientific session (April) 1953