Antibiotic

INTRODUCTION

The term “ antibiotic” was put forward by Vuillemin in 1889, to designate the active component involved in the process of ‘ antibiosis’ or to the opposition of one living micro-organism to another . According to another school of thought – ‘ antibiotics are nothing but the microbial metabolites which in relatively high dilution may inhibit the growth of micro-organisms’ .

Waksman proposed the widely cited definition that – ‘ an antibiotics or an antibiotics substance is a substance produced by the micro-organisms , which has the capacity of inhibiting the growth and even destroying other micro-organism’ .

However , the restriction that an antibiotic must be a product of micro-organism is not keeping with common use.

Classification

The antibiotics will be discussed explicitly under the following four main heads , namely :

1. β – Lactum antibiotics
2. Aminoglycoside antibiotics
3. Chloramphenicol
4. Tetracyclines

β – LACTUM ANTIOBIOTICS

Beta – lactam anitibiotics are substrates for beta-lactamases and the interaction results in the destruction of thr antibiotics . There arenow known as agents which bind to the beta – lactamase enzymes and inactivate them, thus sparing β – lactam antibiotics from destruction .

The β – Lactum antibiotics may be further divided into two categories , namely :

(a) Penicillins

(b) Cephalosporins

1) Penicillins

Penicillin is the name assigned to the mixture of natural compounds having the molecular formula C16H18N2O4S

The different only in the nature of ‘ R’.

Various silent features which ultimately determine the general structure of all penicillins :

1. The penicillins are all strong monobasic acids i. e., they form salts .

2. The penicillins are hydrolysed by hot dilute inorganic acids ; one carbon atom is eliminated as carbon dioxide and two products are obtained in equimolecular proportions , one being an amine , Penicillamine and the other an aldehyde , penniloaldehyde .

$C_9H_{11}O_4N_2SR + 2H_2O \longrightarrow CO_2 + C_5H_{11}O_2NS + C_3H_4O_2NR$

3. Combination of penicillamine and Penilloaldehyde in Penicillin

It has been observed that the hydrolysis of penicillin with dilute alkali or with the enzyme(penicillinase) yields penicillonic acid (a dicarboxlic acid), which readily eliminates a molecule of cabon dioxide to form penilloic acid, thereby suggesting that a carboxyl group is present in the β – position with regard to a negative group .

4. Probablen structures for penicillin

Based on the foregoing chemical evidences probable structures for penicillin are there:

Since penicillin is prone to undergo abrupt molecular rearrangement, e. g., on treatment with dilute acid, penicillin rearranges to penillic acid .

Therefore, it was absolutely necessary to examine the molecule by physical methods (thereby leaving the molecule intact). In fact, an intensive study of the penicillins was carried out with respect to their infra-red and X-ray diffraction analysis.

Different types of penicillin

Chemical reaction using penicillin

Semisynthetic Penicillins

- Penicilinase-resistant penicillins
- Carbapenems: very broad spectrum
- Monobactam: Gram negative
- Extended-spectrum penicillins
- Penicillins + b-lactamase inhibitors

2) Cephalosporins

The best known family of β – lactams are termed as the cephalosporins , wherein the β – lactam ring is strategically fused to a 6-membered dihydrothiazine ring system . The thiazine ring fusion makes the β – lactam system more stable but not fully resistant to opening by acids and penicillinase .

Classification

The cephalosporins may be classified under the following four categories :

- First generation
- Second generation
- Third generation
- Fourth generation

First generation

Cephalexin

Cefazolin

Cephalothin

Cephradine

Active against G+ cocci (except. enterococci & MRSA): s. pneumoniae, s. pyogenes, s. aureus, s. epidermidis

Indicated for streptococcal pharyngitis (e. g. cephalexin)

Commonly used (eg. Cefazolin) as prophylacic for surgical procedures.

Modest activity against G- bacteria

Second generation

Cefoxitin (mefoxin)

Cefuroxime (zinacef)

Cef. axetil (zinnat)

Cefaclor (ceclor)

Cefprozil (cefzil)

Mainly effective against G- bacteria

Modest activity against G+ bacteria

Cefoxitin active against bowel anaerobes (B. fragilis)

Cefuroxim active against H. influenzae, M. catarrhalis, S. pneumoniae

Cef. Axetil- oral form of cefuroxim

Cefaclor active against H. influenzae, M. catarrhalis &E. coli

Cefprozil- similar to cefaclor, c. axetil and augmentin- Liked by children

Second Generations are used primarily for URTIs (acute otitis media, sinusitis) and Lower RTIs (acute exacerbation of chronic bronchitis).

Third generation

Cefotaxime (claforan)

Cetazidime (fortum)

Cefoperazone (cefobid)

Cefixime (suprax)

They have enhanced G- activity, H. influenzae, N. meningitidis, N. gonorrhea, P. aeruginosae, M. catarrhalis, E. coli, most Klebsiella

Ceftriaxone has long half-life . Not advised in neonates (interferes with bilirubin metabolism)

Cefotaxime preferred in neonate (does not interfere with bilirubin metabolism), as may ceftriaxone.

Ceftazidime & cefoperazone have excellent activity against p. aeruginosae.

Cefixime has similar activity to amoxicillin & cefaclor for actute otitis media

Fourth generation

Cefipime

Active against G+ bacteria > than cefazolin against s. pyogenes, s. pneumoniae but lower against s. aureus.

Similar to cefotaxime against E. coli & K. pneumoniae but AMINOGLYCOSIDE ANTIBIOTICS

The aminoglycoside antibiotics constitute an important category of antibacterial agents in the therapeutic armamentarium , e. g., streptomycins , neomycins , paramomycin and the corresponding derivatives of these antibiotics .

These are a bunch of closely related chemically basic carbohydrates that are mostly water-soluble . Their respective hydrochlorides and sulphates are crystalline in nature . They are found to be effective in inhibiting the growth of gram-positive as well as gram-negative bacteria . They are also effective to a great extent against mycobacteria .

A few examples are discussed below :

(a) Streptomycin is chiefly employed in the treatment of tuberculosis in conjunction with each other drugs such as isoniazid and rifampicin .

Streptomycin and penicillin exerts a synergistic action against bacteria and are usually employed together in the treatment of subacute bacterial endocarditis caused by streptococcus faecalis

Mechanism of Action: The ‘ drug’ exerts its maximum effectiveness against the organism Mycobacterium tuberculosis . Interestingly , the antibiotic is not a cure itself but has proved to be an excellent and valuable adjunct to other modalities of therapeutic treatment for tuberculosis . It acquires a rapid development with respect to certain strains of microorganisms. The combined administration of streptomycin and penicillin has been suggested to combat infection which may be due to organisms that are sensitive to both these antibiotics . The ‘ drug’ is neither absorbed nor destroyed appreciably the GI tract .

(b) Neomycin is mostly used in a wide variety of local infection such as burns , ulcers , wounds , impetigo , infected dermatoses , furunculosis etc . It is employed as an adjuvant in topical steroid preparations to control secondary infections in the case of inflammatory disorders .

Structure of Neomycin

Mechanism of Action: The ‘ drug’ usually gets absorbed very rarely from the digestive system ; therefore , its oral administration primarily fails to produce any substantial effect .

CHLORAMPHENICOL ANTIBIOTICS

Chloramphenicol is a levorotatory broadspectrum antibiotic originally produced from a several streptomycetes , namely : S. venezualae , S. omiyamensis and S. phacochromogenes var. chloromyceticus . It has been reported to be the drug of choice for the treatment of typhus and typhoid fever .

However , chloramphenicol is of paramount interest owing to the following three reaons :

1. It is naturally occurring aromatic nitro compound of which there is only one previously recorded example of hiptagin , obtain form the root bark of Hiptage madablota Gaertn is noteworthy .
2. It is capable of exerting its effect against viral diseases as well as those due to bacterial invasion and opens up the whole field of the chemotherapy of virus and rickettsial infections in man including typhus, undulant fever , Salmonella septicaemia , whooping cough , gastroenteritis , lymphogranuloma inguinale , typhoid and paratyphoid . So far , chloramphenicol-fast strains have not been isolated .
3. It is amenable to synthesis on an industrial scale .

Structure of Chloramphenicol

The structure of chloramphenicol has been established on the basis of the following vital chemical evidence . They are :

1. The molecular formula of chloramphenicol is C11H12Cl2N2O5 .
2. Its absorption spectrum is similar to the nitrobenzene .

3. The presence of nitro group was revealed by the reduction of chloramphenicol with tin(Sn) and hydrochloric acid , followed by diazotization and then coupling to yield an orange precipitate with β-napthol .
4. When reduced catalytically(with palladium , Pd) it gives a product which has an absorption spectrum very similar to that of para-toluidine and the resulting solution gives a positive test for ionic chlorine

Synthesis of Chloramphenicol

Acetone

Acetic acid

Chloramphenicol Methanol

TRETACYCLINES ANTIBIOTICS

Tetracyclines are a group of broad spectrum antibiotics whose general usefulness has been reduced with the onset of bacterial resistance . Despite this they remain the treatment of choice of some specific indication .

Structure of Tetracycline Charaterstics of Tetracyclines

1. The tetracycline are obtained by fermentation procedures from streptomyces species or by the chemical transformation of the natural products .
2. The important members of this family are essentially derivatives of an octahydronaphthacene , i. e., a hydrocarbon made up of a system of four-fused rings .
3. The antibiotic spectra and the chemical proprerties of these compounds are quite similar but not identical .

4. The tetracyclines are amphoteric compounds , i. e., forming salts with either acids or bases . In neutral solutions these substances exist mainly as Zwitter ion .
5. The corresponding hydrochloride salts are used most commonly for oral administration and are usually encapsulate owing to their bitter taste .
6. The water soluble salts are obtained from bases such as sodium/potassium hydroxides or formed with divalent/polyvalent metals , e. g., Ca++ . The former ones are not stable in aqueous solution , while the latter ones , e. g., Calcium salt give tasteless products that may be employed to prepare suspensions for liquid oral dosage forms .

ADVANTAGES OF ANTIBIOTICS

Antibiotics have revolutionized the modern medical arena and saved countless lives. Antibiotics are beneficial for those patients who are suffering from the bacterial diseases because it only effects and cure the bacterial diseases such as tuberculosis, etc. There are also broad-spectrum types of antibiotics which work equally well on bacteria and fungus. It is cost effective and readily available as compared to others. There are over a 100 of types of antibiotics but the majority of the diseases can be cured from few types. Each antibiotic is effective only for some types of disease and your doctor knows the best.

In most cases, the doctor prescribes antibiotics with less side-effect which suits your body phenomena. Suppose if you are suffering from pneumonia, the doctors knows well how to treat this by an antibiotic and which bacteria

caused this respiratory system disease. It is necessary in antibiotics to take care of the dosing because in antibiotic medications, doctor prescribes patient the whole course of the antibiotics and it will be harmful for the patient if he or she doesn't act accordingly. If the right antibiotic is taken as prescribed, it will cure the disease in the shortest span of time.

DISADVANTAGES OF ANTIBIOTICS

As there are many advantages of the antibiotics, there are also many disadvantages of using antibiotics. Excess of everything is bad. The first and the major demerit of the antibiotics are in the form of side effect. Some of the most common side effects are: Diarrhea, mild stomach upset, vomiting, soft stools, etc. and in serious cases the side effects will be: Severe watery diarrhea and abdominal cramps, Allergic Reaction, Shortness of breath, vaginal itching or discharge, etc. So, if patient have any of these side effects, they must consult their physician immediately.

The antibiotics were first given only to those patients who had minor diseases like tummy upset, etc. but is has been proved that the repetition of the antibiotics is harmful and may cause serious diseases like Cancer. Many of the medical research centers has declared that the over use of the antibiotics is harmful for the human body as the frequent use , effects and disturb the human internal ecology and homeostasis.

In most cases, if doctors don't know about the bug, they prescribe their patients BROAD-SPECTRUM antibiotics and it harms because it removes all the bacteria either they are beneficial or harmful, therefore in this way BROAD-SPECTRUM antibiotics are harmful for human. Doctor prescribes

children tetracycline antibiotic and due to the side effects of these antibiotic medicines, it decreases the level of iron, calcium, magnesium and can also cause psoriasis. Excessive use of antibiotics can result in depletion of iron content resulting in sickle-cell anemia.

In a nutshell, after considering all the advantages and disadvantages, we can clearly infer that the frequent and over use of antibiotic drugs is harmful for us. Medicines are for our welfare but there are also some side effects associated with them. Medical Science is working to reduce the side effects but we should take care while dealing with antibiotics.