



A REVIEW OF DERIVATIVES OF BETA LACTAM ANTIBIOTICS

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Abstract: The review is based on the different types of derivatives of beta lactam antibiotics. The antibiotics are the metabolic product of one micro- organism used to kill other micro- organisms is called as antibiotics. But most of the bacteria are the resistance to antibiotics. So that the different derivatives form to kill or static them. This micro-organism produces diseases in our body like fever, chills, runny nose, head-ach, etc. so in this review we synthesized the derivative of penicillin called as penicillin M.

Keywords: Penicillin M, Antibiotics, Beta Lactam, Resistance, Gram Negative bacteria.

I. INTRODUCTION

The human body harbors a large number of bacteria and many micro-organism's but their localization in healthy individuals is normally restricted to sureindividual body surfaces such as the skin, the mucosa of buccal and nasal cavities, vagina and most primly, the gastrointestinal tract. The inner tissues are normally aseptic. In some time, however, some opportunistic pathogens are able to enter the host by taking advantage of injuries or breaches in one of the different host barriers. In adding, *bona fide* bacterium have developed mechanisms to across host protective's and goes inner organs or tissues where they multiply and see to danger disease for their host. We will narrate the diversity of mechanisms used by bacterial micro-organisms to colonize and invade human organs. We will first focus on the capacity of these bacteria to adhere and to multiply at the surface of host cells and tissues, in the face of a wide-range of defense mechanisms used by the individual. We will then present how some bacteria are gifted to enter and to multiply inner individual cells. Finally we will discuss the new beta lactam drugs or their derivatives.[1]Emergence of antibiotic resistance-Antibiotic resistance was described to happen when a drug loses its capacity to inhibit bacterial growth productively. Bacteria enhance 'resistant' and start to multiply in the present of the antibiotics[2].Bacteria, when copy uniform in the present of the antibiotics, are called resistant bacteria. The origin of antimicrobial resistance was seen some after the launch of new antimicrobial compounds. Antibiotic resistance can occur as a natural selection procedure where nature licensesall bacteria with some degree of low resistance [3]. For example, one study established that sulfamethoxazole and trimethoprim, ampicillin and tetracycline that were frequently used in past years, but now have no longer role in use of non-cholera diarrhea disease in Thailand. At the same time, another study lead inBangladesh showed the success of the same drugs in use of them successfully. In fact, resistance was noted even before the beginning of the usage of the antibiotics in treat the infection. Unbiased use of antibiotic is fault of making microbes resistant. However, sulfonamide resistance was noted in the 1930s, which tell the same mechanism of resistance that still work even now, more than 80 years later. In six years of the making of the aminoglycosides, aminoglycoside-resistant strains of *Staphylococcus aureus* was developed. Emergence in 1961, Methicillin was the first of the semi-synthetic penicillinase resistant penicillin to target strains of penicillinase producing *Staphylococcus aureus*. However, resistance to methicillin was noted soon after its start. In the 1980 fluoroquinolones resistance later revealed that these drugs were also used to treat Gram-positive infections[4]Antibiotics; either are deadly to the micro-organisms, permitting the body's natural defenses, such as the immune system, to kill them. They often act by preventing the synthesis of a bacterial cell, synthesis of proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), by a membrane disorganizing agent, or other particular actions[5]. Antibiotics may also enter inside the cell wall of the bacteria by attach to them, using the energy-dependent transport mechanisms in ribosomal sites, which starts to the inhibition of the protein synthesis. To fight against infections or microbes, no doubt antibiotics are a favor to humans that has saved millions of people life.At the time, there was a cheerful reliance that communicable disease was nearly coming to a complete finish. The dawn of new 'antibiotic era' was analogous related with two names Alexander Fleming and Paul Ehrlich [6]. A detail history of the antibiotic era, scripture learned and dare for the future[7]. The time from the 1950 to 1970 was thus considered as the golden era for the discovery of new antibiotics classes[8]. In the developing world, almost all the antibiotics are obtainable over the counter and can be bought without any prescription which is one of the most important factors in causing the resistance. Therefore, if the

resistance to the antibiotics needs to be hold back, the only way shall be to educate the patients and the public. The review is showing the evaluation and possible future of antibiotic resistance and existing regulation to reduce the antibiotic resistance problems.

II. CLASSIFICATION OF ANTIBIOTICS

There are different number of antibiotics are in market. Some are resistance to all type of bacterial infection and some are resist the micro-organism (table 1). In some of them the beta lactams are very potential to kill all type of bacteria.

table 1- classification and MOA of antibiotics

Antibiotic class	Example(s)	Mode(s) of resistance
P-Lactams	Penicillin's, Cephalosporin's, Penems, Monobactams	Hydrolysis, outflow, altered target
Aminoglycosides	Gentamicin, Streptomycin, Spectinomycin	Phosphorylation, acetylation, nucleotidylation, outflow, altered target
Glycopeptides	Vancomycin, Teicoplanin	Reprogramming peptidoglycan biosynthesis
Tetracyclines	Minocycline, Tigecycline	Monooxygenation, outflow, altered target
Macrolides	Erythromycin, azithromycin	Hydrolysis, glycosylation, phosphorylation, outflow, altered target
Lincosamides	Clindamycin	Nucleotidylation, outflow, altered target
Streptogramins	Synercid	Carbon-Oxygen lyase, acetylation, outflow, altered target
Oxazolidinones	Linezolid	outflow, altered target
Phenicol	Chloramphenicol	Acetylation, outflow, altered target
Quinolones	Ciprofloxacin	Acetylation, altered target
Pyrimidines	Trimethoprim	altered target
Sulfonamides	Sulfamethoxazole	altered target
Rifamycins	Rifampin	ADP-ribosylation, altered target

III. PENICILLIN AS BETA LACTUM ANTIOTBIOTICS

The effort at the Northern geographical Research Laboratory also discloses that different strains, culture conditions, and media result in the manufacture of different penicillin compounds. Penicillin from the United States strain was flourishingly crystallized and analyzed at E.R. Squibb & Sons [9] and Florey's group later crystallized the compound from the English strain. Florey and partners display that their strain used for the English clinical trials was primarily 2-pentenylpenicillin (Penicillin F or I) while the United States penicillin was mainly benzyl-penicillin. It was later shown that both forms of penicillin contained β -lactam rings (Fig. 1).

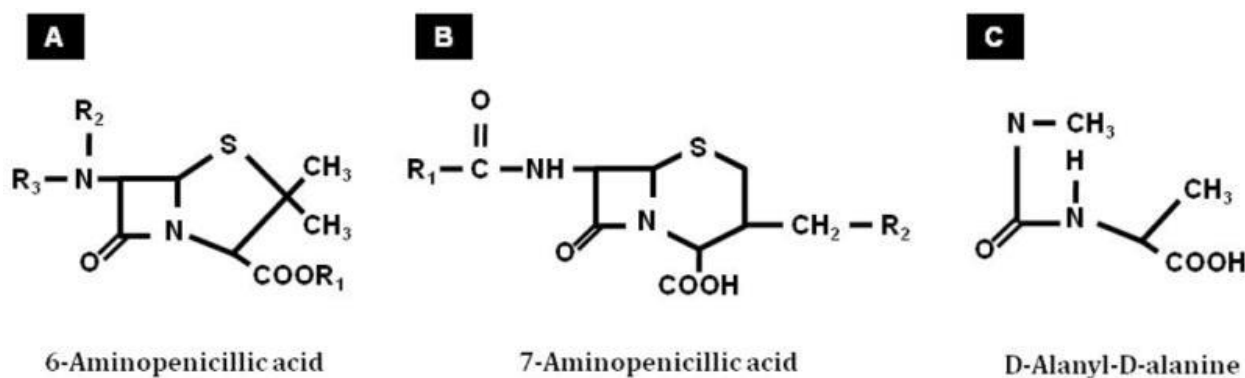


figure 1: structure of derivatives of penicillin.

IV. BETA LACTUM DERIVATIVES

Varying chemical structure of β -lactam molecules and their particular antibacterial potency, chemists were anxious to look far away what nature had contributed, and how science could contribute and substitute. Untimely work using different fermentation conditions were not very successful [10]. The β -lactam nucleus, 6-aminopenicillanic acid show to be the key in penicillin synthesis and modification. The Penicillin V by acylation of chemically synthesized 6-APA. This main piece of chore opened up the barricade where new beta-lactam agents could be mass-produced by adding abnormal side chains to 6-APA. Thereafter, semi-synthetic β -lactam compounds have been developed continuously and systematically [11]. Though the production of semi-synthetic compounds presented a great moment, natural sources continued to be investigate. Using 7-ACA as the precursor, several generations of cephalosporins with dominant broad-spectrum activity have been synthesized. Derivatives of these compounds, either naturally-occurring or semi-synthetic, further dilate the spectrum of β -lactam agents [12].

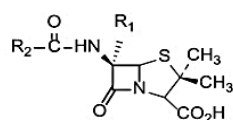
V. MECHANISM OF ACTION

The β -Lactam antibiotics are kill the bacteria that break in bacterial cell-wall formation as a result of covalent binding to vital penicillin-binding proteins (PBPs), enzymes that are participated in the end steps of peptidoglycan cross-linking in both Gram-negative and Gram-positive bacteria. The inhibition of bacterial peptidoglycan transpeptidation by penicillin was express spontaneously in old paper by who noted a structural similarity of penicillin G to the terminal D-Ala-D-Ala dipeptide of the developing peptidoglycan in the dividing bacterial cell. The occurring inactive acyl enzyme may then slowly hydrolyze the antibiotic to form a microbiologically inactive structure. In Gram-negative bacteria, essential PBPs comprise the high-molecular-weight PBPs 1a and 1b that are involved in cell lysis, PBP2, the inhibition of which results in a end of cell division and the formation of spherical cells, and PBP3 for which inhibition bust cell division, resulting in filamentation. Cell kill occur as a result of preventing of these PBP.

VI. PENICILLIN AND ITS DERIVATIVES

Benzylpenicillin was the first β -lactam to be used medically, more regularly to treat streptococcal contaminations for which it had high potency. Naturally arise penicillin, penicillin V, in an oral formulation is still used therapeutically and preventively for mild to moderate infections caused by susceptible *Streptococcus* spp. However, the choice of penicillin-resistant penicillinase-producing staphylococci in patients treated with penicillin G guide to decreased use of this agent, and evokes the search for more penicillin with higher stability to the staphylococcal β -lactamases. Penicillins with improved activity against Gram-negative pathogens comprise the orally bioavailable ampicillin and amoxicillin, both of which were introduced in the 1970s. Carbenicillin was the first antipseudomonal penicillin to be introduced, but short of stability to β -lactamase hydrolysis and was less potent than piperacillin or ticarcillin, after antipseudomonal penicillins. These latter drugs were considered to be dominant broad-spectrum

penicillins that included penicillin-susceptible staphylococci, enteric bacteria, anaerobes, and *P. aeruginosa* in their spectrum of activity. They were used extensively to treat serious nosocomial infections, mostly when combined with a β -lactamase inhibitor [12].



Name	R ₁	R ₂	Route of administration	Approval date ^{b,c}	Status
Benzylpenicillin (penicillin G)	—H		IM or IV	1946	Approved worldwide
Phenoxymethylpenicillin (penicillin V)	—H		Oral	1968	Approved worldwide
Methicillin	—H		IV	1960	No longer available; of historical interest
Oxacillin	—H		Oral, IV	1962	Widely available, but not in the United Kingdom
Cloxacillin	—H		Oral, IV	1974	Widely available, but not in the United Kingdom
Ampicillin	—H		Oral, IV	1963	Widely available
Nafcillin	—H		IV	1970	Limited availability

figure 2: penicillin and its derivatives

VII. P-ANISIDINE PENICILLINE

It is also called as the penicillin M in this the P-Anisidine group is attach to the R2 position of the penicillin. It is the active agent against the gram negative as well as gram positive bacteria. The following steps of synthesis of the p-anisidine penicillin.

GENERAL STRUCTURE

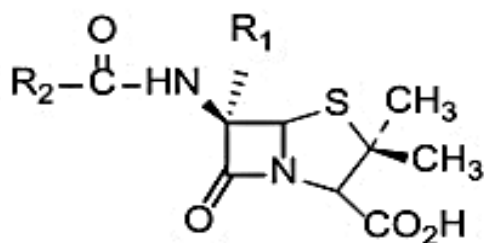
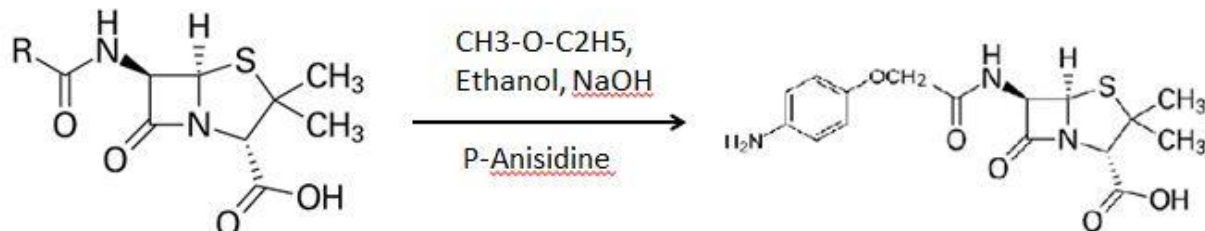


figure 2: structure of penicillin

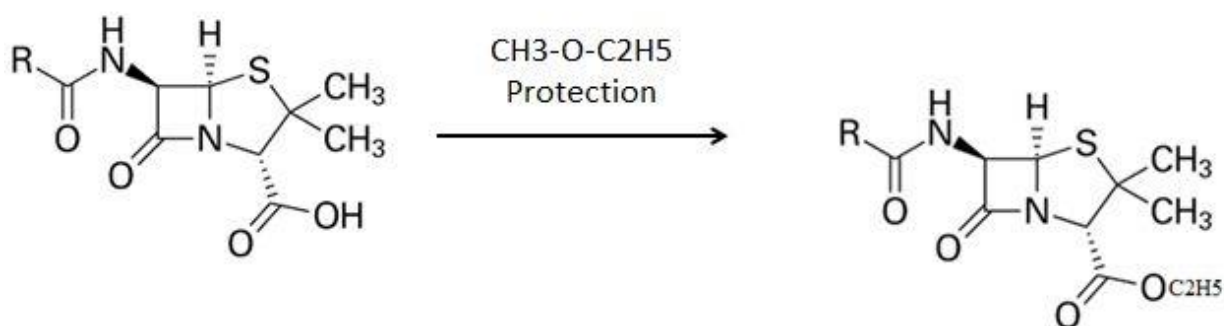
GENERAL REACTION

In this reaction they are commonly followed three step first one is the protection of the carboxylic group then next step the addition of p-anisidine and final step is de-protection.



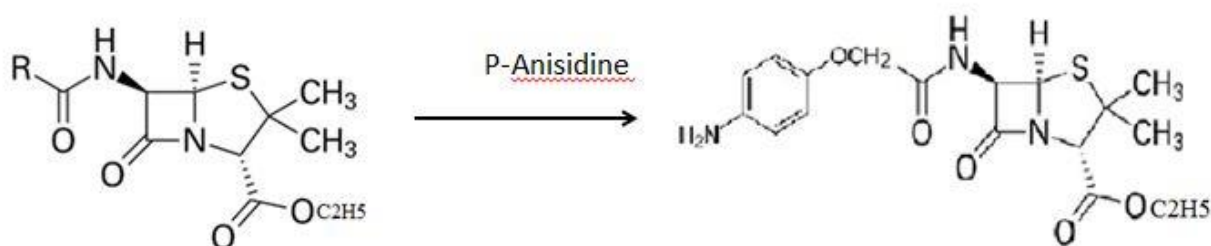
STEPWISE REACTION-

STEP 1

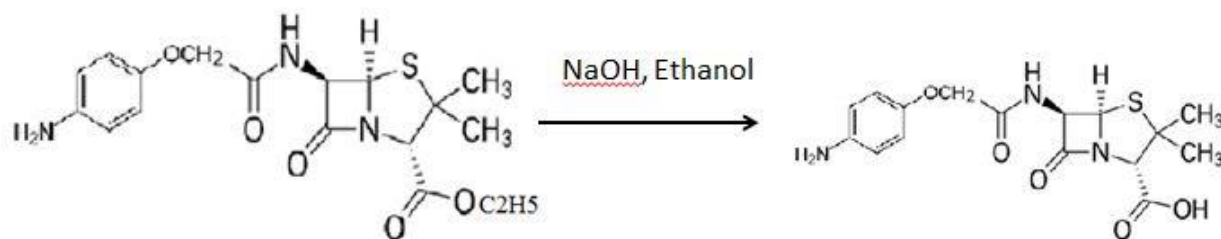


In the step 1 the penicillin is react with the methyl ethyl ether under the temperature of 25 degree centigrade. This is important step also called protective step because of the protection of carboxylic acid group in penicillin in step 2 attack or gives the proper orientation.

STEP 2



Step 2 – in this the protective penicillin undergoes the attack of p-anisidine the anisidine is attach to the R group of penicillin and formation of complex product.

STEP 3

This is the final step 3 in this the complex compounds is reacted with the NaOH gives the sodium salt of penicillin M compound after that is treated with the ethanol we will gives the final product called as penicillin M.

VIII. CONCLUSION

In this review based on the different derivatives of the penicillin and I was actually made up of the derivatives of penicillin called as penicillin M. Penicillin is the antibiotics. The structure is closely related to the beta lactam antibiotics. Beta lactam antibiotics used to kill gram positive as well as gram negative bacteria. Antibiotics is a metabolic substances used to kill another micro-organism life which are produced diseases in our body.

IX. CONFLICTS OF INTEREST

The authors do not have any conflict of interest to declare.

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