

Resistance of bacterial to antimicrobial agents

[Science](#), [Biology](#)



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Introduction

Bacterial resistance to antibiotics is a global problem in the treatment of bacterial infection. Bacterial resistance is a mechanism by which bacterial are able to overcome antibiotic meant to destroy or kill them, these bacterial multiply to cause disease in humans figure 1 (Patrick, 2003)

Figure1 the non antimicrobial resistance and non antimicrobial resistance

Although the most resistant bacterium can be inhibited or destroyed by using a high concentration of antibiotic, subjects on the other hand may not be able to bear the high concentration of antibacterial agents that may be required treat some bacterial infection or disease. Bacterial species differ in their susceptibility to an antibiotic or antibiotics. For instance some strains of *Streptococcus pneumonia* in Britain are inhibited by 0. 01mg/l of benzyl penicillin thus the minimum inhibitory concentration, and that of *Escherichia coli*, a dose 32-64mg/l is needed to inhibit the growth or kill the bacterial but

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this becomes highly toxic to the human body cannot manage. This opens the view of clinical resistance, which is based on the on effect antibiotics on humans and misuse of antibiotics. Clinical resistance is therefore a process by which the type of infecting pathogenic bacterium, its point of attachment in the body, the distribution of antimicrobial in the body, its concentration at site of infection and the immune status of the subject interact (Gerard, 2011). Bacterium uses enzymes, efflux pump, gene, helix ring as well as plasmid to defend itself or to develop resistant to antibiotics. (figure2)

Figure2 structure of a resistant bacterium

Beta- lactamase

Beta-lactams are of copies penicillin, a large group of antibiotics that are made up of all the antibiotic agents with a four ring in their molecular structure. The bacterial cell wall serves as a protective tool for the bacterial against any foreign substances such as antibacterial agents, from entering inside the bacterial to destroy its internal protective structures. The beta-lactam antibiotic works by blocking the cell wall synthesis of the bacterial. Douglas (2002), but bacterial develop resistance to beta lactam by attacking the four ring structure shown in blue in figure of the beta-lactam through an enzymatic reactions (figure1). Bacterial produce beta lactamase enzyme to breaks the beta-lactam ring of the antibiotic and makes the antibiotic ineffective to block the bacterial cell wall synthesis and hence a resistance to the antibiotic (Miller et al., 2004).

Figure3 structure of beta-lactam ([www. users. rcn. com/jkimball. ma. ultranet/Biology/pages/A/Antibiotics](http://www.users.rcn.com/jkimball.ma.ultranet/Biology/pages/A/Antibiotics))

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Mutation at the target sites

Some antibiotics such as Streptomycin inhibits bacterial protein synthesis by binding to the 16SrRNA and blocks the function of the ribosome but bacterial changes the 16SrRNA gene and limit the attraction of streptomycin to the 16S molecule bacterial mutate and acquire a new DNA. In imipenem resistant, *Pseudomonosa aeruginosa*, lack the specific D2 porin and imipenem cannot break through the cell. Changing the main site of action may change the drug target in that antibiotic may enter the cell but may miss the target and may not be able to bind, the antibiotic may not be metabolised. This makes the antibiotic inactive in the bacteria and as result the bacterial develop tolerance (Springer et al., 2001).

Enzymatic modification

Ciprofloxacin act together with an enzyme gyrase to block its enzymatic action. An alteration in each the gene that is gyraseA or gyraseB would change the molecular arrangement of the gyrase and as such limit the binding affinity of the enzyme for ciprofloxacin. It therefore prevents the antibiotic from blocking the gyrase and this process enables the bacteria cell more resistant to the antibiotic (ciprofloxacin) (Gerard, 2005)

Efflux of antibiotics from the cell by pump

Other bacterial such as the *Escherichia coli* create a multiple antibiotic resistance (MAR) outflow pump gives the bacterial with resistance to antibiotics such as tetracycline, erythromycin or nalidic acid. The pump drives out the antibiotic from the cytoplasm of the bacterial cell and allows the bacterial to maintain the intracellular levels below the toxic or lethal

concentration The MAR pump is made of proteins MarA and MarB, whose production is blocked by the controlling protein Mar. Poole (2000) These changes get rid of the suppression control of Mar and leads to much production of the Mar A and B efflux pump. The bacterial cell wall is able to get rid of higher concentrations of antimicrobial agents and as such become resistant to the antibiotic (Cohen et al., 1988).

Acquired Resistance by alternate metabolic pathways

Resistance in bacteria may be acquired when a bacterium is been exposed to antibiotic for a long period of time for example vancomycin resistance in *Escherichia coli*. This may be by mutation or by gaining a new DNA. Plasmids are copying pieces portion of DNA, slighter than the bacteria genome which programme their transfer by copying into another bacterial strain. These bacteria may then carry and transfer resistance gene which as part of the DNA. Viruses that infects bacterial bacteriophages can pass on resistance, especially in *staphylococcus*, DNA is released when bacterial dead bacterial is taken up by a viable bacterial and this is possibly route for the spread of penicillin resistance in *Streptococcus pneumonia*. Bacteria possesses range of biochemical genetic systems for warranting the progression and diffusion of antibiotic resistance. Genes can appear by rapid transformation (Penrose, 1998).

' Superbugs' are used to describe a bacterium or microorganism that is able to resistant more than one or more commonly used antibiotics. Bacteria resistance to antibiotics are grouped according to the type of antimicrobial agent that they resist. The most common groups are:

MRSA (Staphylococcus aureus strains resistant to methicillin)

VRE (Enterococcus species resistant to vancomycin); these type of bacteria live in the bowel and usually cause infection such as pneumonia, heart or wound in subjects with weak immune system or subjects with chronic disease such as diabetes.

PRSP (Streptococcus pneumoniae strains resistant to penicillin);

ESBLs (Escherichia coli and other Gram-negative bacteria resistant to cephalosporin and

Monobactams) (Gerard, 2011)

Treatment of superbugs

MRSA is a type of Staphylococcus aureus has developed a resistant to antibacterial activity of methicillin and the other penicillins Staphylococcus aureus may cause infection in the blood or on the skin disease such.

Vancomycin is a glycopeptide that is effective for the treatment of MRSA. It is a hard and large molecule that blocks the last step of bacterial cell wall synthesis through hydrogen bonds with D-alanyl-D-alanine end of the peptidoglycan (PDG) side chains (Reynolds, 1989). Subjects infected with MRSA are treated with vancomycin but very painful through the intramuscular route and a rapid administration into the veins may cause an allergic reaction called the red-man syndrome, therefore a slow infusion of 50mg/kg is given two times daily for 7 days. Daptomycin is a broad spectrum antibiotic that has been approved by the American Food and Drug Administration for the treatment of MRSA, VRE and PSBP. It binds irreversibly to the bacterial cell membrane and depolarises it and more Potassium ions

move out of the cell to create an imbalance of the ion-concentration gradient. Currently, Daptomycin shows no cross-resistance. A dose of 4-6mg/kg is administered once daily for 7 days. It is not metabolised in the liver. Daptomycin interacts with the HMG-6A reductase inhibitors such as statin. Nausea, constipation and headache are the main side effects associated with the use of Daptomycin. Quinupristin was well used in the year 2000 for the treatment of hospital acquired infection. Quinupristin main function was to interfere with both the early and the last phase of bacterial protein synthesis but the major problem was that it has to required slow infusion for a large volume fluid just as vancomycin and as such could only be used for inpatients subjects(Despoina and Jordi, 2006)). Dancer, an oral Streptogramin has been was developed and out 53 subjects 39 were successfully cured of MRSA infection. A new glycopeptide, MDL63246 with a similar mechanism of action and pharmacokinetics as vancomycin is under early stages of development and would be more effective at lower dosages than vancomycin and less side effects. (Franz-Joseph and Mark, 1997)

A new approach for VRE treatment is the blocking of oxazoliddines from flowing out of the bacterial cell and broad spectrum pumps of Gram negative bacterial is being studied for future treatment of VRE. (Livermore, 2003). Linezolid belongs to the oxazolinones class of antibiotics and it binds to the 50S ribosomal segment and blocks bacterial protein synthesis. can be administered intravenously or orally . Through the oral administration, a subject is given 600mg two times daily for 10-14 days and 600mg 30-120 minutes twice daily for one week for intravenous route.

Moxifloxacin is a drug of choice for the treatment of PRSP. It works by inhibiting DNA synthesis by enhancing cleavage of DNA of the bacterial DNA enzyme complex of the DNA gyrase and type IV topoisomerase. The dose regime is based on the type of infection, for the treatment of acute bacterial sinusitis a 400mg of Moxifloxacin is given daily for 10 days and 400mg daily dose of Moxifloxacin for 7-14 days is used to treat community acquired pneumonia by *Streptococcus* sp.

Figure 3 the mechanism of action of Fluoroquinolones

(www.mecriticalcare.net/downloads/Dcourse/AntimicrobialAgents)

Tigecycline is currently used to treat ESBLs, Gram negative enteric rods such as *E. coli* and Gram negative bacilli such as the *Pseudomonas* spp.

Tigecycline interferes with the bacterial protein synthesis by attaching to the 30S of the ribosomal subunit and this 100mg load dose is given initially and 50mg subsequent dose of every 12 hours is administered for seven days (figure 3). (Wunderink et al., 2003)

Figure 3 Tigecycline binding to Ribosome 30S subunit at: www.mecriticalcare.net/AntimicrobialAgent.

Conclusion

Bacteria or microbes are constantly reproducing at a faster rate and becoming resistant to antimicrobial agents. Antimicrobial resistance is a global crisis and new and more potent antibiotics would have to be developed to overcome the problem of antibiotic resistance. Identification of natural products and

knowing their biosynthesis from the bacterial source would enable scientist to find well defined antibiotic structures to that could kill or destroy all kinds of bacterial. Scientist may target ribose DNA, RNA or the peptodoglycan.

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