Mechanisms of bacteria resistance to antibiotics biology essay

Science, Biology

Human population has been faced throughout history with infections that have been the major cause of diseases. The use of antibiotics ameliorated the spread of diseases and their discovery was a turning point in human history. Regrettably, the widespread use of antibiotics is increasingly complicated by the ability of bacterial species to develop numerous mechanisms that render bacteria resistant to some, and in certain cases, nearly all antibiotics (Livermore, 2003). Bacteria can become resistant to antibiotics by either one or some to the mechanisms enumerated below: Direct Antibiotic Inactivation: Bacteria can acquire resistance to an antibiotic by producing enzymes that degrade or modify the drug. These enzymes inactivate the antibiotic by hydrolysis of susceptible chemical bonds (e. g. esters and amides), transfer of a phosphoryl or acetyl group to the periphery of the antibiotic molecule or by a redox modification of the antibiotic such as the oxidation of the tetracycline antibiotics by the TetX enzyme. These cause the antibiotics to be inactivated before they reach their target within the bacteria or affect their binding to their targets. The hydrolytic amidases are the β-lactamases that cleave the β-lactam ring of the penicillin and cephalosporin antibiotics. Recently, extended-spectrum β-lactamases (ESBLs) have been discovered to mediate resistance to all penicillin, third generation cephalosporin and aztreonam (Kotra and Mobashery, 1999). Modification of Target: Resistance can also be achieved by modification of the antibiotic target site so that the antibiotic interacts most unfavourably with the modified target. The peptidoglycan component of the bacterial cell wall presents an excellent selective target for antibiotics. The presence of mutations in the penicillin-binding domain of penicillin-binding proteins

(PBPs) results in decreased affinity to β-lactam antibiotics (Winn et al, 2009). Resistance to vancomycin is achieved by altering the amino acid composition at the C-terminus from D-Ala-D-Ala to D-alanyl-D-lactate. Therefore, the affinity of the drug for the new C-terminus is 1000 times lower than the native peptidoglycan precursor. Furthermore, resistance to antibiotics that interfere with protein synthesis such as aminoglycosides, tetracyclins, streptomycins; or transcription via RNA polymerase such as rifamycin, is also brought about by modification of the specific target. Resistance to the macrolide, lincosamide and streptogramin B groups of antibiotics (known as MLS (B) type resistance) results from a posttranscriptional modification of the 23S rRNA component of the 50S ribosomal subunit. Mutations in the 16S rRNA gene confer resistance to the aminoglycoside (Weisblum, 1995). Efflux pumps and outer membrane (OM) permeability. Bacteria also acquire resistance through mechanisms that ensure a low intracellular concentration of the antibiotic. This is achieved by a combination of membrane proteins (efflux pump) that actively export the antibiotics out of the cell, as well as reduced outer membrane permeability that results in reduced uptake of the antibiotic. Though efflux pumps affect all classes of antibiotics, those that target intracellular processes like protein synthesis and DNA biosynthesis are especially susceptible. Many efflux systems are multidrug transporters that are capable of expelling a wide variety of structurally unrelated drugs. This has been identified to contribute significantly to multidrug resistance in bacteria (MDR). According to Dzidic et. al, (2008), inducible multidrug efflux pumps are responsible for the intrinsic antibiotic resistance of many organisms and mutation of the

regulatory elements that control the production of efflux pumps can lead to an increase in antibiotic resistance. Furthermore, the composition of the outer membrane plays a major role in determining the concentration of the antibiotic that enters the bacterial cell. This is seen more commonly in Gram-negative bacteria that possess an outer membrane consisting of an outer layer made of the lipid A moiety of lipopolysaccharide (LPS) and an inner layer containing phospholipids. Mutations: Bacteria can also acquire resistance to antibiotics through a mutation occurring in different chromosomal loci as well as through the acquisition of resistant genes from other microorganisms in a process known as horizontal gene transfer. Most often, strains of bacteria carrying resistance-conferring mutations are selected by antimicrobial use, which kills the susceptible strains but allows the newly resistant strains to survive and grow. Acquired resistance that develops due to chromosomal mutations and selection is termed vertical evolution. Some antibiotic-resistant mutations may arise in the absence of any selective pressure. These growth-dependent spontaneous mutation events occur randomly as replication errors or an incorrect repair of a damaged DNA in actively dividing cell, resulting in nucleotide point mutation that are able to produce a resistance phenotype. Furthermore, the overproduction of antibiotic-inactivating enzymes may also be achieved through mutational events. Horizontal Gene Transfer: Horizontal transfer of genetic material through conjugation, transformation or transduction is a principal mechanism for the spread of antibiotic resistance. This presents a mechanism for the spread of multiple drug resistance because resistance genes can be found in clusters and transferred together to the recipient

enabled by the existence of DNA elements known as integrons. These DNA elements have the ability to capture one or more genes (cassettes) especially those encoding antibiotic resistance, by site-specific recombination. Integron are usually located on the bacterial chromosome or on broad host range plasmids. These gene cassettes can encode many types of resistance including resistance to trimethoprim, chloramphenicol, β-lactams, aminoglycosides, fosfomycin and quinolones. Horizontal transfer of the resistance genes can be achieved when an integron is incorporated into a host range plasmid. A plasmid with a pre-existing resistance gene cassette can acquire additional resistance gene cassettes from donor plasmids, thus spreading multiresistance.