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Combination of Antibiotics and Plasmids with Broad Host Range, in Agriculture: A Threat to Human Health

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Successful employment of antibiotic therapy to treat infectious diseases is one of the great achievements in biomedical sciences. Antibiotics remained effective against disease causing pathogens for a long time but their overuse results in the emergence of antibiotic resistant bacteria. With each passing day new antimicrobial resistant strains are being reported, which increases the risk of complications and failure to cure the infections. Use of antibiotics in other than clinical practices is significantly accelerating the pace of resistance development in pathogens. For example in agriculture, antibiotics are generally employed for treatment of diseases and growth encouragement in food-producing animals. Oliver *et al.* (2011) reviewed literature with respect to use of antibiotics in dairy and its link with antimicrobial resistance to both human and animal pathogens. They found no strong evidences to support the theory that use of antibiotics in dairy industry is responsible for widespread emergence of antimicrobial resistance but found a positive link between use of antibiotics and increase in the number of antibiotic resistant bacteria. Moreover these antibiotics are not completely absorbed by the animal gut and unabsorbed antibiotic are excreted into the environment through animal manure (Kumar *et al.*, 2005). Food crops grown on soils that are supplemented with manure (derived from animals feed with antibiotics as supplements) can absorb significant amount of antibiotics, which indirectly increases the antibiotic intake by humans. Moreover, these manure derived pathogenic bacteria can transfer resistance to other soil-borne human pathogens.

Horizontal Gene Transfer (HGT) is the most common phenomena responsible for inter and intra-specie transfer of resistant genes. HGT mediated resistance involves several mechanisms for gene transfer: conjugation between cells; transformation of DNA or plasmid released by dead cells; transduction through phage. In most of the cases genes confer resistant against antibiotics are present on bacterial plasmids. Narrow host range is a limiting factor for the spread of resistance gene carrying plasmids but plasmids with broad range of hosts have significant role in spread of antibiotic resistance. IncP-1 plasmid is very versatile in terms of adoption to various hosts and that is the reason, why it is very common in our environment (Norberg *et al.*, 2011). This plasmid has been isolated from various human pathogens and is believed to be responsible for the development of antibiotic resistance. Backbone of this plasmid not only serve the purpose of its replication and stable transformation in host but also carries genes that confer resistance to host, against almost all clinically employed antimicrobial drugs (Schluter *et al.*, 2007). Recently Heuer *et al.* (2012) conducted a study and on a plasmid (IncP-1e) which belongs to the group of IncP-1 and isolated it from various samples of manure and arable soil. They found a positive correlation between antibiotic use and the abundance of IncP-1e plasmid and this correlation significantly increased even 127 days after the application of manure-containing sulfadiazine antibiotic. A total of fifty IncP-1e plasmids were isolated from different bacterial communities of manure and arable soil and

all plasmids showed the presence of sulfonamide resistance gene. They concluded that IncP-1ε plasmids play an important role for the spread of antibiotic resistance in agricultural ecosystem.

Genetic variation of bacteria acquired through the acquisition of foreign plasmids is mainly responsible for their adaptation to various environmental stresses and resistance to antibiotic is an important example of such adaptation, which have severe consequences on currently used antibiotic therapies. Transmissible plasmids carrying the antibiotic-resistance genes especially with broad host range are mainly responsible for the spread of antibiotic resistance and virulence traits in pathogenic bacteria. Abundance of plasmids with broader host range and antibiotic resistance genes in our ecosystem has resulted in the emergence of multidrug resistant pathogenic bacterial strains. The better understanding of such plasmids (IncP-1ε) will facilitate the efforts aiming to devise new strategies to cope with such multidrug resistant pathogenic bacteria.

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