



THE RISK OF HUMAN EXPOSURE TO ANTIBIOTIC RESIDUES FROM FOOD OF BOTH ANIMAL AND PLANT ORIGIN

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ABSTRACT

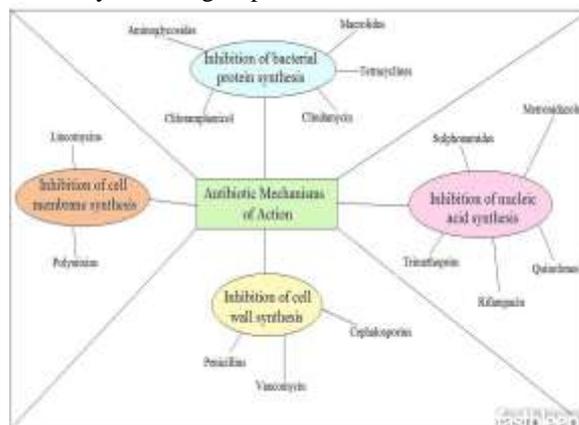
The misuse of antibiotics in agriculture could yield dramatic effects on both human and environmental health. Antibiotics were commonly used in agriculture treatments of either animal or plant production. Antibiotics used as veterinary drugs, therapeutic, prophylactic and feed additives in many countries to enhance and maximize the production of farm livestock's and aquaculture. As well, antibiotics are applied to plants in order to prevent or treat bacterial diseases. Estimates of the amounts of antibiotics used in agriculture production worldwide are not available, but in USA (2011) a collected data revealed that about 14.000 metric tons were sold for use in animal feeding only and about 3 folds of such quantity were used in preventive and curative programs of livestock breeding. As well. 36.000 metric tons were applied to different plant crops (McManus, 2014). Roughly about 100 thousand metric tons of antibiotics were applied in only USA annually. Such great amounts of antibiotics lead to review about the fate of these hazards and exposure of all plant, animal and human to these therapeutic chemicals and finally to follow the effect of antibiotic residues on environmental, animal, plant and human micro-flora. As well to follow how pathogenic bacteria become antibiotic resistant bacteria.

KEYWORDS: antibiotics–antimicrobials–pharmaceutical drugs–hazards–risk.

Classification of antibiotics

Antibiotics are classified according to their mode of action into 7 main classes; aminoglycosides, chloramphenicol, macroloides, beta-lactames, sulfa drugs, tetracyclines, fluoroquinolones and others. The 1 st and most common class of these compounds are the aminoglycosides including streptomycin and gentamycin which act by interfering with protein synthesis of bacteria. Streptomycin is effective against the bacterial species of *Brucella*, *Salmonella*, *Klabsiella*, *Shigella* and *Mycobacterium*. It is used in large animals to combat leptospirosis and in poultry to prevent chronic respiratory diseases and infections. The 2 nd class is chloramphenicol which acts by inhibiting cell wall synthesis in bacteria. It is effective against bacteria of brucellosis, salmonellosis and pneumonia of most of farm livestock. The 3 rd class is macroloides, which used as an alternative to other antibiotics when bacteria develop resistance. Erythrocin is a common example used as bacteriostatic agent to inhibit growth, not necessarily kill the microorganisms. The 4 th class is penicillin's, which are commonly used to treat wide range of bacterial infections. The 5 th class is sulfa drugs, the oldest known antibiotics ever used, they are used to control urinary tract infections in large ruminants. The 6 th class is tetracycline's which are classified as broad spectrum antibiotics commonly

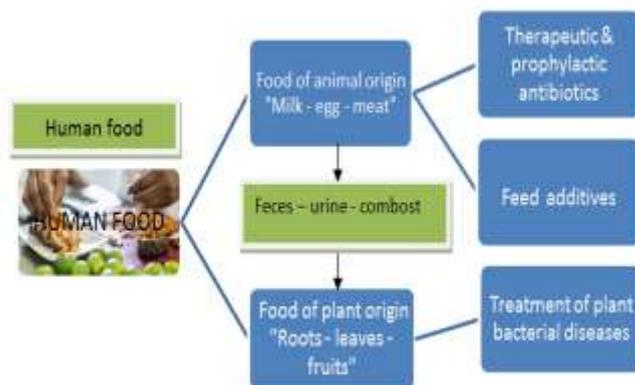
described against wide variety of bacterial diseases and infections threaten human and animal health. It's worthy to differentiate between 2 terms; antibiotics and antimicrobials. Antimicrobials are broader term refers to any compound, including antibiotics, sanitizers, disinfectants and other compounds that acts to inhibit and/ or kill microorganisms. Antibiotics are only targeting bacterial diseases and infections, or in other words they are sub-group of antimicrobials.



Antibiotics classification according their mode of action "By Rebecca Sankey Manchester University. www.fastbleep.com/medical-notes

Animal exposure to antibiotics

The animal husbandry industry based on pre-arranged protocols to apply specific and certain drugs for the treatment of diseases that may threaten the herd health and productivity. Antibiotics are drugs commonly used to prevent and treat mainly the bacterial infections and diseases. Application of antibiotics in animal husbandry followed one of the 3 categories; therapeutic, prophylactic and / or growth promoters. Therapeutic treatments are those when drugs used to treat or cure certain bacterial diseases or conditions, while prophylactic treatment means the administration of the drug to animals aiming to prevent or minimize the probability of disease occurrence (Timothy et al., 2012). Growth promoting application aims to enhance growth and productivity facilitating the efficiency of feed utilization processes in which feed is converted to muscle mass within short feeding period. Bacteria become resistant to antibiotics through over exposure to them (WHO, 2014). Hardly strains of bacteria survive the exposure and pass on that resistant trait to successive generations. Also, they could pass the trait to other unrelated bacteria including most of the common pathogens threaten human health. Eventually, the antibiotic resistant bacteria will survive and remains and the drugs will be no longer effective. As resistant bacteria emerge, they have easy passage to human. As an example, campylobacter carried out into kitchens on poultry and could cause illness when people consumed undercooked poultry meat. The center for diseases and control (CDC) estimated that the annual campylobacter infections in USA are ranged between 2-4 million cases, resulting in many deaths as well. Furthermore, campylobacter infection could lead to Gullian-Barre' syndrome which leads consequently to paralysis. They use of quinolones in poultry industry developed resistant campylobacter strains. The same phenomenon happened and repeated in Europe with the antibiotic vancomycin which used to treat life-threatening infections. The collected data suggests the rising levels of vancomycin resistant bacteria resulted from the previous usage avoparcin in agriculture. Because both avoparcin and vancomycin are similar in structure (CDC, 2014). However, the link between animal agriculture and human diseases are complicated, but there are strong evidence lead scientists and public health organizations to believe and doing their best to reduce the use of antibiotics in agriculture. The CDC stated that in USA, antibiotics use in food animals is the dominant source of antibiotic resistance among food-borne pathogens (CDC, 2014).



"Human exposure to antibiotic residues"

Plant exposure and uptake of antibiotics

Antibiotic residues could reach human food of plant origin through many indirect routes rather than the direct exposure of spraying specific antibiotics to treat bacterial diseases and infections (Kipper et al., 2010). Composting or aerobic biological treatment of organic wastes is an old way to reduce the mass of field wastes and maximize its benefits by recycling and re-usage processes. Such organic wastes contain organic matter and nutrients that are very essential for plant growth and production. Organic wastes including sewage sludge composting enables good quality compost could be used as a soil modifier, conditioner and fertilizer. The quality of compost depends on its environmental compatibility with quality criteria. The criteria involve the absence of toxic organic and inorganic compounds that may enter food chain through pre-harvest processes. Undoubtedly, the consumed quantities of antibiotics in agriculture rise from year to year. Over the past decade, the problems of antibiotic residues had become increasingly interested in the impacts of food contamination and human health (Xuedi et al., 2013). Antibiotics characterized by the necessary properties to bioaccumulate and provoke changes in ecosystems. Plants, unlike animals have no solid or liquid excretions, therefore drug residues could accumulate and resulting concentrations of drug residues in edible plant tissues could exceed the recommended maximum residue levels (MRL) of food of animal origin. So far, no limits were established for antibiotic residues in plants. Cheng et al. (2015) studied the occurrence of 15 antibiotics in soil and manure samples from 11 large scale greenhouse vegetable productions in China. They found that the greenhouse soils were ubiquitously contaminated with antibiotics and that antibiotic concentrations were significantly higher in greenhouses than in open field soils. The estimated the mean concentrations of 4 antibiotic classes found to be tetracyclines, quinolones, sulfonamides and macroloides being 102, 86, 1.1 and 0.62 ug/ kg soil, respectively. The concluded that fertilization with manure and especially animal feces might be the primary source of antibiotic residues. A risk assessment study based on the calculated risk quotients (RQ's) demonstrated that oxytetracycline, chlortetracycline, norfloxacin and

ciprofloxacin could pose a high risk to soil organisms. Veterinary medicine, including antibiotics is widely used in farm livestock treatment will reach to the soil either directly through feces and urine or indirectly through application of manure as fertilizer. A range of antibiotics have been detected in soil as well as in surface and ground waters (Alistair et al., 2006). Although, the reported concentrations of antibiotics were generally low, the antibiotics have been observed throughout the year and across different hydrological climatic and land-use settings. The authors concluded that antibiotics have been shown to be released to soil and capable to persist in the environment. They added that the studied antibiotics are likely to occur in soil for at least 5 months following application of manure containing antibiotic residues. There is a selective properties to uptake, absorb and accumulate certain antibiotics in different edible plants. The antibiotics of florfenicol, levamisole and trimethoprim were taken up by lettuce, whereas, diazenone, enrofloxacin, florfenicol were detected in carrot roots. Also, Carter et al. (2014) confirmed that pharmaceuticals have been detected in the soil environment where there is the potential for uptake into crops. They found that each drug had a specific pattern to be absorbed and accumulated in different plant tissues. Carbamazepine was taken up to the greatest extent in both the radish and ryegrass being 52, 33 ug/ kg, respectively, whereas sulfamethazine dropped below the limit of quantitation (LOQ) being < 0.01 ug/g. They added that the concentration of dichlofenac and sulfamethazine dropped below the LOQ after 7 days. Their data and results demonstrated the ability of plant species to accumulate pharmaceuticals including antibiotics from soils with uptake apparently specific to both plant species and chemical properties. Lin et al., (2013) showed that high antibiotic concentrations > 10 g/L. leads to toxic effects on the plant roots and affect leaf chlorophyll. The retained portion of antibiotics was varied depending upon the chemical behavior of the drug, therefore the retained drugs were descendingly ordered as follows; ciprofloxacin> oxytetracycline> sulfamethazine and the distribution of the same antibiotics in plant parts followed the sequence of root> leaf> stem. Similarly, Hawker et al. (2013) proved that antibiotics are emerging organic environmental contaminants. Uptake from soil by plants and the soil/water matrix occurs simultaneously with degradation in the soil/ water matrix. Under farming conditions, winter wheat was cultivated on manure-fertilized soil. The manure was obtained from medicated livestock's with 3 antibiotics; chlortetracycline, sulfadiazine and trimethoprim. All the 3 antibiotics were readily taken up by the roots and then translocated within the plants into stems and leaves (Manfred et al., 2007).

Occurrence and developing antibiotic-resistant bacteria

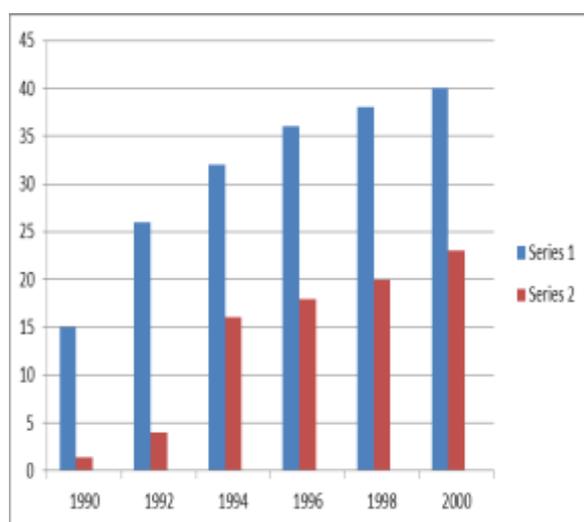
Antibiotic resistance occurs when one microorganism is able to survive and multiply in the presence of antibiotics. This instance is considered natural

phenomenon, because many microorganisms have intrinsic genes that code resistance to antibiotics that they produce themselves. Antibiotic resistance represents a serious and growing human and environmental health problem extended to threat aquatic environment. Many studies supported the basic idea that the overuse and misuse of antimicrobial agents could lead to the selection of drug-resistant microorganisms. Bacteria may become resistant by developing genetic mutation that provides survival advantage. If a food-borne disease requires treatment with antibiotic and the bacteria are resistant to it, then the severity of the disease could increase with many consequences such as lengthening of the disease period, increased rates of hospitalization or in other cases increased risk of death (WHO, 2014).

Organisms resistant to antibiotics are developed by genes that are either carried on the bacterial chromosomes or on DNA plasmid which direct the synthesis of the traits that protect bacteria from antibiotics. Certain resistance genes code for enzymes that degrade antibiotics or chemically modify them to be inactivated. Other resistance genes may cause bacteria to modify or replace molecules that are normally bound by an antibiotic removing the drug target (Davies and Davies, 2016). Evolution of resistant bacteria could occur through mutations when some bacteria will develop genes that help to protect them against antibiotic attack mechanisms. Few bacteria will survive with favorable traits and reproduce, Resistant bacteria consequently leads to the concentration of the resistant trait in the population and environment. The selective advantage conferred by the resistant trait will, unfortunately cause natural selection and eventually population will be entirely resistant to the treatment (Joes, 2014).

Antibiotic resistance refers especially to the resistance to antibiotics that occurs in common bacteria that cause infections, while antimicrobial resistance, as broader term, encompassing resistance to all drugs treated infections of other microbes such as parasites (malaria), viruses (HIV), and fungi (Candida). New resistance mechanisms emerge and spread globally threatening our ability to cure common infectious diseases, leads to death and disability of individuals who could continue a normal course of life. Without effective anti-infective treatment, many standard medical treatment and protocols will fail or turn into very high risk procedures. As an example, the death rate for patients with serious infectious caused by common bacteria treated in hospitals could be about twice that of patients with infections caused by the same non-resistant bacteria. Sure, when infectious become resistant to first line antibiotics, a series of negative consequences were obtained including the need to use more expensive therapies, longer duration of illness and treatment, increasing health care costs, besides the economic burden on families and societies (WHO, 2016). Bacterial resistance develops when potentially harmful bacteria change in a way that reduce or eliminates the

effectiveness of antibiotics. Undoubtedly, the extraordinary genetic capacities of microbes have benefitted from the overuse and misuse of antibiotics. The horizontal gene transmission had multiple mechanisms of resistance for each and every antibiotic introduced into clinical and/or agricultural practices. A wide range of biochemical and physiological mechanisms may be attributed especially with antibiotics. The complexity of the processes that contribute to emergence and dissemination of resistance cannot be emphasized, and the lack of the knowledge on these items and details are the primary reasons that there has been little achievement in the effective prevention and control of resistance development (Davies and Davies, 2016).



Series: 1 Normal strains & Series 2. penicillin-resistant strains Penicillin resistance with *Streptococcus pneumoniae* in the United States (Source: uihealthcare.com/news/currents/vol5)

Undoubtedly, the most dangerous and dramatic effects due to the misuse of antibiotics in agriculture is developing antibiotic-resistant bacteria. The fore mentioned example showed that the penicillin resistance bacteria of *Streptococcus pneumoniae* were multiplied by more than 200% within 10 years (Klugman et al., 2008).

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