Environmental Impact of Antibiotics and Tetracycline on Environmental Systems

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Abstract

Large-scale production of antibiotics began in the 1940's. Almost immediately, the use of antibiotics spread to agricultural uses. In livestock, antibiotics are used to reduce illness. However, a far more common use is to increase feed efficiency, resulting in better profits. (Coghlan, 1996 and Bonner, 1997) With the widespread use of antibiotics has come a variety of concerns. Primarily, fear that microbial resistance will render antibiotics useless against common illnesses. (UNEP/DEWA/Earthwatch 1996-2005) In the past decades, a large increase in the number of multi-resistant microbes has been discovered. In these cases, the antibiotic treatments have had significantly poorer results. One possible explanation for the development of this resistance is the excessive use of antibiotics. Particular concern arises in respect to agricultural uses since in these cases it is being used for productivity enhancement instead of saving lives. A commonly used antibiotic on the market is Tetracycline. In a variety of forms, tetracycline is used for both human and animal purposes. Research has shown this tetracycline can be excreted through feces and urine. Different concerns arise from the various ways we treat agricultural waste and human waste. However, it is evident that agricultural waste remains less impacted by the treatment process. In turn the environmental concern on this type of usage has only increased. The agricultural impact of antibiotics on microbes in the environment is just beginning to be examined, but at least in the case of Tetracycline, appears to increase the microbial resistance to the drug. Examination and consideration of the problems with current methods of livestock waste disposal may be a necessity to reduce the risk of human exposure to multi-resistant microbes.

Keywords

microbial resistance, antibiotics, Tetracycline, sewage

Introduction

In 1928 a Scottish scientist by the name of Alexander Fleming, discovered penicillin, which later became the first antibiotic. At the time he was keeping bacteria in a petri dish when a speck of mold fell in it. The mold grew into the agar which was feeding the bacteria. In time, the bacteria growth stopped. Fleming called the mold penicillin (called *Penicillium notatum*). He proceeded with trying a few simple experiments and wrote about them but quickly lost interest and moved onto other research.

The term antibiotic was first used in 1945 when Waksman defined it as a chemical substance of microbial origin that possesses antibiotic powers. (Origin of Antibiotics) Research on the topic of Penicillin continued through the work of Howard Florey. He read Fleming's reports about penicillin. Florey was a more persistent person than Fleming and decided to learn more about penicillin. He had great success with his research. Then in 1940 an Oxford team of Chain, Florey, Gardner, Heatley, Jennings, Orr-Ewing and Sanders made a dry powder which allowed toxicity and other biological tests to be conducted. (Origin of Antibiotics) Since that time few other antibiotics of such widespread effect suitable for use in humans have been found.

The British drug and chemical industry could not make the large amounts of penicillin made necessary by World War II. Therefore members of the Oxford team, Florey and Norman Heatley, got help from the American chemical manufacturers. Among the drug companies that worked on penicillin production and purification was Charles Pfizer. This Brooklyn firm had experience in producing chemicals by growing microbes in large volume. Using this experience Pfizer succeeded in being the first to make penicillin commercially. Penicillin appeared in limited quantities in 1943 for clinical tests and then in large quantities by 1944 as a result of the war.

(Origin of Antibiotics) Penicillin proved to be very valuable for bacterial infections during World War II.

Human bacterial infections

The origin for antibiotics was the treatment of human bacterial infections. Diseases which created fear and uncertainty prior to World War II were easily manageable by the development of antibiotics. Currently there is a wide variety of antibiotics available to consumers. Specific antibiotics will be discussed later.

Human antibiotic use is primarily for bacterial infections. An area of common concern within the health community is the over prescription of various antimicrobial agents which in theory result in microbial resistance. It is important to keep in mind the various uses of antibiotics when evaluating this theory since the majority of antibiotic use is not for human infections.

Commercially Used Antibiotics

More than half of the antibiotics used in the U.S. are used in livestock, not humans. The routine use of antibiotics in agriculture is economically beneficial because they prevent sickness and promote weight gain. (CSU) Antibiotics are used in agriculture for primarily two purposes. In animal agriculture, antibiotics are administered for therapeutic purposes to treat infections, prophylactic purposes in advance of observed symptoms, and nontherapeutic purposes to promote growth and improve feed efficiency (Wegener 2003).

The large use of antibiotics in livestock has become a highly debated topic. (Coghlan, 1996 and Bonner 1997) In general, antibiotics are administered at higher concentrations for therapeutic and prophylactic use and lower concentrations for nontherapeutic use (Wegener 2003). It has been estimated that the nontherapeutic use of antimicrobials in livestock production comprises 60-80% of total antimicrobial production in the United States (Mellon et al. 2001).

Types of Antibiotics and How they Work

Below, provided by ThinkQuest Educational Foundation, is a list of some useful antibiotics and information about each:

- **Cell wall synthesis inhibitors** usually stop bacteria from forming their cell walls. They kill bacteria and not human cells because human cells do not form cell walls. Examples of cell wall synthesis inhibitors are beta lactums, semisynthetic penicillins, and bacitracin.
- **Cell membrane inhibitors** kill bacterial cells by disorganizing the outer membranes of bacteria. An example of a cell membrane inhibitor is polymyxin.
- **Protein synthesis inhibitors** interfere with the process of translation in protein synthesis. Their action is usually on the ribosomes. Examples of protein synthesis inhibitors are tetracyclines, chloramphenicol, macrolides, and aminoglycosides.
- **Chemotheraputic agents affecting the synthesis of nucleic acids** block the division and growth of cells by inhibiting synthesis of DNA and RNA. Most of these agents affect both animal and bacteria cells, so they cannot be used as an antibiotic. However, nalidixic acid and rifamycins are selectively active towards bacteria.
- **Competitive inhibitors** are mostly synthetic. These drugs work by disrupting the metabolic rate of bacteria. Some examples include sulfonamides, isoniazid, paraaminosalicylic acid, and ethambutol.

Tetracyclines, listed above as a protein synthesis inhibitor, are one of the most successful classes of antibiotics used in the past 50 years. With the first identification of chlortetracycline in

1948, this class of antibiotic has been valuable in the treatment of bacterial infections. Its major benefits are its broad spectrum applicability, oral availability, and its low cost. (Yang, W. et al, 2004) Figure 1 below shows the tonnage of various antibiotics sold in EU in 1997. This provides a general idea of the quantity of tetracycline used in agriculture.

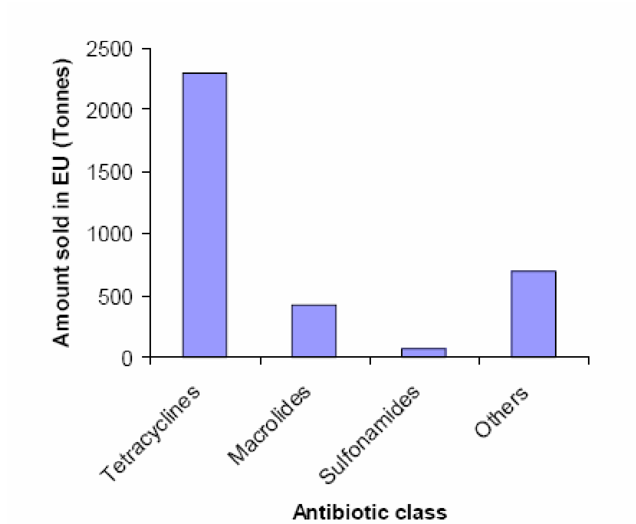

Figure 1: Quantity of Antibiotics sold for Agricultural uses. (Cranfield, 2003)

Tetracyclines are also widely used in agriculture to treat bacterial infections of plants, in aquaculture, and for animal growth. Tetracycline resistance has emerged over the past decades as a significant issue in the use of this class of antibiotic. Figure 2 shows the structure and nomenclature of Tetracycline antibiotics.

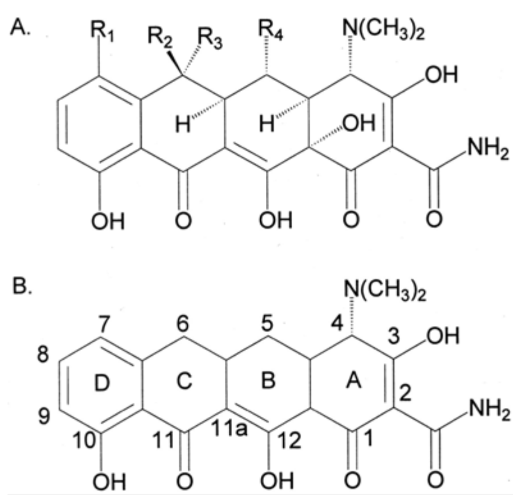

Figure 2: Structure and nomenclature of Tetracycline. (Cranfield, 2003)

Methods of Tetracycline Discharge

With the two major uses of Tetracycline being human and animal, there are several ways the antibiotic may be discharged into the environment. Below is a list of various ways Tetracycline can be released primarily through ground and surface waters (Atoyan, 2005).

- Human methods of discharge
    - Not fully metabolized Tetracycline can be wasted in urine, and enter the sanitary sewer system.
    - Disposal of drugs into the sewer system.

- Animal methods of discharge
    - Tetracycline present in the animal at its time of death can enter into the human discharge method after the consumption of meat treated with antibiotics.
    - Animal manure is spread over fields as fertilizer.
        - Runoff can result in direct stream influence.
        - Absorption into the soil can result in groundwater contamination.

Figure 3 below depicts exposure routes of veterinary drugs in the environment. (Jorgensen, 2000)

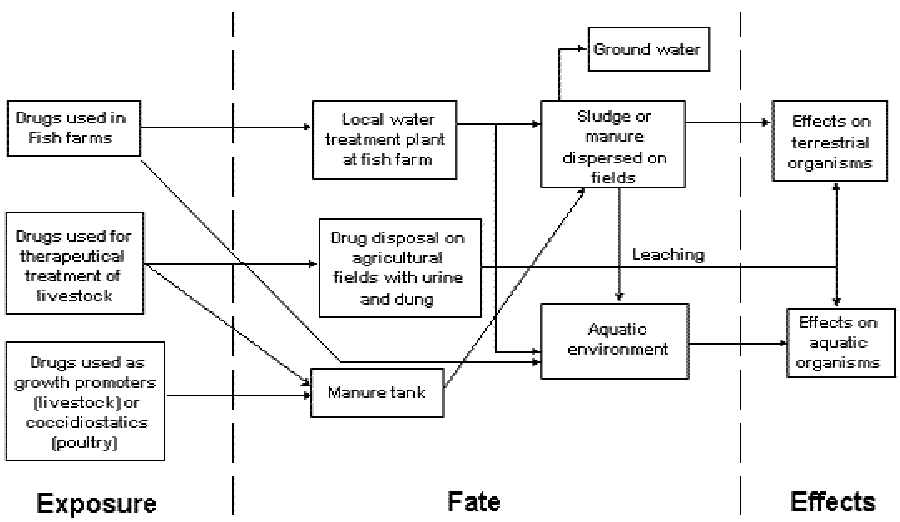

Figure 3: Anticipated exposure routes of veterinary drugs in the environment. (Jorgensen, 2000)

Areas of Impact
Obviously the locations of human discharge are from point sources, specifically wastewater treatment plants. However, agriculturally produced waste can be spread on fields and impact streams, reservoirs, and plant uptake. Greenhouse studies were preformed to see if plants gown in manure-applied soil absorb antibiotics present in manure. In the case of corn, green onions, and cabbage, all three crops absorbed chlortetracycline. The concentrations were low, but increased with increasing amount of antibiotics present in the manure. (Kumar, et al, 2005) These studies point out the potential health risks associated with consumption of fresh produce which contain antibiotics. Specific concerns result from human antibiotic allergies, as well as the development of microbial resistance through plant uptake. In another study, antibiotics have been shown to remain in soils for long periods of time once released as shown in Figure 4 (Cranfield, 2003).

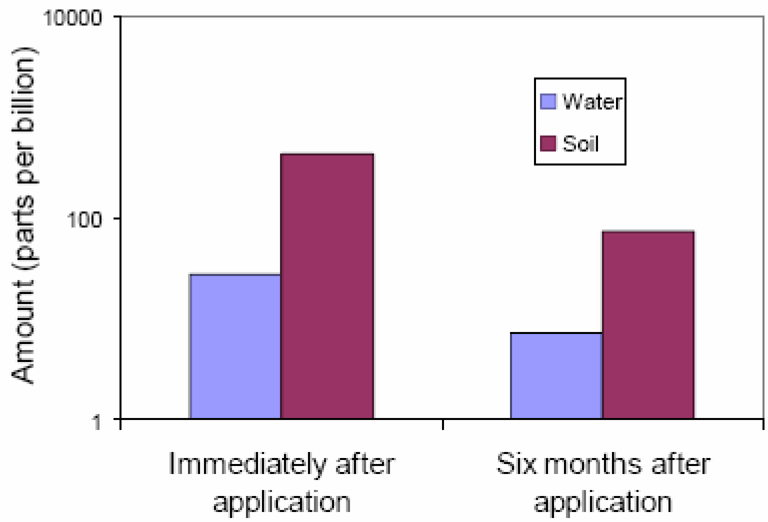

Figure 4: Concentrations of applied tetracycline in field studies. (Cranfield, 2003)

Furthermore, research has shown that the use of nontherapeutic levels of antibiotics in swine production can select for antibiotic resistance to tetracycline in airborne microbes as well. (Chapin, 2005) Thus showing antibiotics are capable of impacting not only water, but also air quality.

Environmental Impact

The development and persistence of multidrug-resistant bacteria pose increasing challenges to public health (Institute of Medicine 1998). The use of antibiotics in human medicine has influenced antibiotic-resistant bacteria; the use of antibiotics in animal agriculture has contributed to this critical problem as well (Cohen and Tauxe 1986; Gorbach 2001; Institute of Medicine 1998; National Research Council 1999; van den Boogard and Stobberingh 1999).

There is significant potential of drugs as environmental pollutants to create new pools of resistance which, given evidence of genetic transfers across species, could accelerate the development of resistance in many disease organisms. (UNEP/DEWA/Earthwatch 1996-2005) If new forms of resistance start to come not only from human treatments and hospital settings, but by inter-species transfers from the environment, the growing ineffectiveness of present forms of treatment and major epidemics is a possibility.

Industrialized countries have the highest antibiotic use, and so could be the first to see the development of environmental communities of resistance. However, with global travel, drug resistance can be expected to spread steadily to all parts of the world. Developing countries may in turn suffer the worst consequences because of the poor state of their health services and their inability to pay for alternatives to cheap antibiotics (UNEP/DEWA/Earthwatch 1996-2005).

A recent study conducted at State University of New York focused on the removal of antibiotics in wastewater. In addition, it addressed Tetracycline in the Activated Sludge Process. In Figure 5 below, the data shows a reduction of relative Tetracycline concentration as time increases allowing further biodegradation.

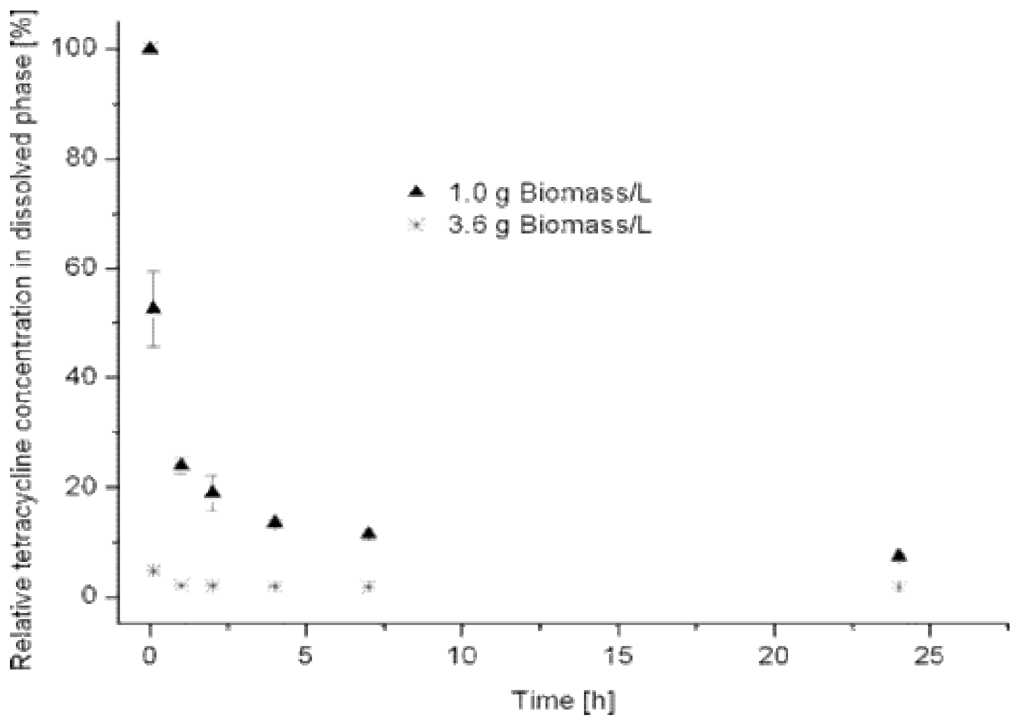

Figure 5: Tetracycline concentration versus time. (Sungpyo, 2005)

This reduction, observed in a single batch reactor, may be applicable to large-scale wastewater treatment as research is continued (Sungpyo, 2005).

Conclusion

Despite research which may support wastewater treatment options, controlled use of antibiotics remains the best method of controlling microbial resistance. (UNEP/DEWA/Earthwatch 1996-2005)

Continued research into the environmental impacts on natural microbial communities of heavy antibiotic exposure may support new forms of waste treatment. Currently the area lacks strong non-bias research which can assess the risks to public health and the environment. It is safe to say as a precautionary approach, the use of drugs/antibiotics should be reduced to the minimum necessary.

Other measures in the future may also be helpful, including drugs that could be developed to break down quickly in the environment; doctors could be assisted, perhaps by expert systems, to chose medicines and to adopt treatment methods that minimize the risk of creating or spreading resistance; waste treatment facilities that destroy drugs before they contaminate the environment could be installed in hospitals and other settings where drug use is high; and national and international legislation could be considered to prevent or limit the spread of drug resistance. (UNEP/DEWA/Earthwatch 1996-2005)

The issues surrounding microbial resistance and antibiotic use in humans and animals will continue to be a highly debated topic which will require international attention.

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