Antibiotic Resistance Factors and Alternatives to Antimicrobial Growth Factors within Animal Husbandry

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Abstract

The repercussions of antibiotic resistance in humans give scientists a vivid picture of the effects of microbial evolution. These repercussions can be felt economically and scientifically as the demand for stronger antibiotics grows stronger, yet the availability for such an effect remains low. Citizens must pay more money in order to access antibiotics from their healthcare providers; however, if treatment is not completed, bacteria become increasingly immune to antibiotics, closing off pathways to new antibiotics that are able to combat the bacterial immunity. Antibiotic resistance can stem from other areas aside from a doctor's office, where they are used not only for treating bacterial infections, but antibiotics that are utilized also to kill bacteria in agriculture and in animal husbandry, which remnants fall into the hands of the consumer when they consume the animal product. This review therefore looks at several mechanisms of such resistance transfer as well as alternatives to antibiotics to decrease the amount of antibiotic resistance in humans.

Key words: Antimicrobial Growth Factors (AGP), Integrons, Animal Husbandry

Introduction

The discovery of antibiotics deemed what was called the "Golden Age" in medicine, allowing individuals to successfully recover from what could have been fatal illnesses. Life expectancy and the quality of life were extended, and with its continued use, led to practical uses in the animal industry. Antibiotics served several purposes in animal husbandry: therapeutic use, the prevention of disease and most importantly as antimicrobial growth factors (AGP) (Lathers, C., 2002). Although scientists debate over the impact of antibiotic resistance from animals, we cannot ignore the seriousness of the severely limited production of new classes of antibiotics. Since the evolution of bacteria has caused a genetic multi-drug resistance, bacteria have now acquired a resistance to all classes of antibiotics (Chowdhury, et. al, 2014). In fact, the use of antibiotics as antimicrobial growth promoters (which help yield a higher production in animal products) can actually be thought to increase the prevalence of resistance in animal bacteria and in turn poses as a risk factor for the possibility of human antibacterial resistance for human pathogens (Chowdhury, et. al., 2014). Examining the mechanisms for transferal from animal to human and possible consequences is therefore important in combating antibiotic resistance as well as exploring possible alternatives to the use of antibiotics and AGPs in the animal industry.

Microbial populations develop resistance through several different mechanisms, of which include mutation and gene transfer. In general, mutations are determined by environmental factors, cell physiology, the genes of the bacteria and the population dynamics. These mutations manifest as point mutations, which affect only one base pair or may affect many base pairs at a time. Antimicrobial resistance in the bacteria may also be gained by horizontal gene transfer or the uptaking DNA form its surroundings in a process known as transformation. Bacteria also may uptake genes from plasmids between other bacteria from physical contact in a process known as conjugation. Transduction, another gene transfer mechanism, allows bacteriophages to inject their DNA in the host bacterium and replicates itself into the host DNA. However most importantly, transposons, which serve as form of horizontal gene transfer, allows itself to move from different parts of the genome through self-excison and reinsertion. It has been suggested that these transposons may play a significant role in the development of resistance because of their resitance genes, including integrons Matthew, A. et. al, 2007).

Antibiotic Resistance and Mechanisms

I. Integrons

Resistance integrons carry genes that encode for resistance to antibiotics and disinfectants, and are divided in three classes. Class I of these resistance integrons (the most common variety) are commonly associated with livestock (Matthew, A., et. al., 2007). Studies have shown that toxin producing *E. coli* that were isolated from poultry, cattle, swine and humans possed class I integrons that conferred resistance to ampicillin, tetracycline and other antibiotics. These class I integrons are also commonly found in *Salmonella*, which can easily be contracted by humans and cause illness. Functionally, these integrons are composed of promoter-less open reading frames and a recombination site. These integrons most frequently contain multiple genes called "cassete arrays" that can be expressed by a single promoter. This allows the integrin to effectively jump from one spot in the DNA to the other (Matthew, A., et.al, 2007). The risks posed to humans by antibiotic use in livestock production can influence human health by means of foodborne transfer of bacteria carrying resistance genes, as direct animal to human transfer of resistant bacteria has been reported.

II. Studies on Antibacterial Growth Factors

A study conducted in 1997 noted that the presence of vancomycin-resistant enterococci (VRE) had been recorded in the stools of asymptomatic individuals from a community that had not recently been in the hospital or had received any antibiotics. At the same time, avoparcin, a glycopeptide that had been used in Europe as an AGP in animal feed was also being dominantly used. This suggested that a possible link existed between the use of avoparcin, the selection of VRE and humans becoming colonized via the food chain. Scientists confirmed this as a rural area in Germany where the study was conducted noted that the vancomycin-resistant enterococci were not isolated from humans but found in animals. The study established that the VRE was spread through meat products and were also found in non-hospitalized humans. This wide use of antibiotics in animal husbandry and its links of cross-resistance of some antibiotics to their medical counterparts is therefore a concern to human medicine. By 2000, scientists have then postulated that the selective pressures exerted by the use of antibiotics as growth promoters in food animals appeared to create large reservoirs of transferable antibiotic resistance in humans because of extensive AGP use. The development of resistance precedes the use of antibiotics and shall continue to be a problem with the continual success of patient treatment. In the past several decades, multiple-resistant pathogenic bacteria have emerged worldwide and are of serious concern to healthcare today. The question raised is whether the development of new antimicrobial agents can be developed at a rate that is sufficient enough to combat the increasing number of multi-resistant bacteria. Health committees have recommended that antimicrobials that are used to treat human infections should not be approved for the growth promotion in food animals. Such antibiotics have become important in the treatment of infections in a last-resort scenario, including avoparcin, virginiamycin and avilamycin (Lathers, C., 2002). Such effects of abolishing the usage of antimicrobial agents as growth promoters may result in the reduction of antimicrobial resistance if selective pressures are removed.

Antibiotics within Agriculture Today

I. Benefits and Risks

Agriculture today often benefits from the usage of antibiotics. The treatment of disease, improvement of carcass quality, and the improvement of feed efficiency all have promoted the general hygiene of harvesting animal products and the food safety for the general public. The use of antibiotics has also garnered an economic gain for farms as they have maintained profitable margins and lowered manure output, thus decreasing the effects of animal wastes and pathogen loads on the environment. The introduction of probiotics has also benefited farmers as probiotics have been shown to prevent inflammation in the gut, reduce the incidence of meat contamination and promote growth, therefore serving as an seemingly preferable method over the use of antibiotic growth promoters. The probiotics serve as live microbial food supplements that beneficially affect the host by improving the intestinal microbial balance. They modify pH and antagonize pathogens through the production of antimicrobial and antibacterial compounds, compete for pathogen binding and receptor sites for available nutrient and growth factors (Lathers, C., 2002).

II. Measuring Benefits and Risk

Due to the risks presented by antibiotics and antimicrobial growth promoters, some alternatives have been suggested in order to alleviate pathogen load and reduce the risk of increasing the amount antibiotic resistance in humans. Tannins have been proposed to replace AGPs because of their performance promoting effects without the downside of increasing the risk of antibacterial resistance (Redondo, L., et. al, 2014). Tannins are plant derived compounds normally responsible for the color pigmentation but however, studies have been shown that there was significant potential in the use of tannins to enhance nutrition and animal health. The benefits in of tannins were shown to include anti-inflammatory, anti-carcinogenic, antiviral and antibacterial properties. Veterinary studies have also been shown to reduce the risk of livestock disease, induce better growth and reduced the transmission of zoonotic pathogens in an environmentally friendly manner. The tannins do not leave residue in animal products and therefore leaves fewer chances for resistance. The use however of such compounds should be closely monitored if added to animal feed to ensure that the same quality of the animal product stays consistent to health standards.

As previously mentioned, probiotics are effective as they serve as a live therapeutic agent as well as an analog to AGP to improve growth and performance. Researchers conducted a study evaluating the effect of *Saccharomyces boulardii* and *Bacillus subtilis* on ultrasound modulation and the mucosal immunity development in broiler chickens (Rajput, I. et. al, 2013). Three hundred broiler chickens were randomized into three groups. The control group was fed feed that contained an antibiotic, virginiamycin while the other groups were fed the antibiotic feed in addition to their respective probiotic *S. boulardii* and *B. subtilis*. The result of the experimental groups showed that there was a significant improvement in the ultrastructure of the gut, as well as the inducement of the immunity through cytokine production. Scientists postulated that although probiotics could be used as an alternative, further studies must be made in order to learn the mechanisms involved in the immunity development.

Conclusion

It is apparent that there must be more research in order to clearly define the risks associated with animal husbandry-linked antibiotic resistance, especially with resistance associated to AGP. However as we know the basic mechanisms to a microbe's pathogenicity, we are able to explore other options to help curb and reduce the amount of antibacterial resistance from animal products that are now a threat to human health. There are currently alternatives such as tannins and probiotics but more research must be invested into these two compounds in order to assert their functionality in the industry today.

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