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Antibiotic and synthetic growth promoters in animal diets: Review of impact and analytical methods

Manuel Gonzalez Ronquillo [a, *], Juan Carlos Angeles Hernandez [b, c]

[a] Departamento de Nutricion Animal, Facultad de Medicina Veterinaria y Zootecnia, Universidad Autonoma del Estado de México, Instituto Literario 100, 50000 Toluca, Mexico
[b] Programa de Maestría y Doctorado en Ciencias de la Producción y de la Salud Animal, Facultad de Medicina Veterinaria y Zootecnia, Universidad Nacional Autonoma de México, Circuito Exterior, Ciudad Universitaria, Delegacion Coyoacan 04510, Mexico
[c] Departamento de Nutrición Animal y Bioquímica, Facultad de Medicina Veterinaria y Zootecnia, Universidad Nacional Autónoma de México, Circuito Exterior, Cuidad Universitaria, Delgacion Coyoacan 04510, Mexico

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Clenbuterol (PubChem CID: 16048573)
Chloramphenicol (PubChem CID: 5959)
Monensin (PubChem CID: 441145)
Oxytretacycline (PubChem CID: 54675779)
Ractopamine (PubChem CID: 56052)
Salbutamol (PubChem CID: 2083)
Tretacycline (PubChem CID: 54675776)
Tylosin (PubChem CID: 5280440)
Zeranol (PubChem CID: 216284)

ABSTRACT

Food quality and safety have been a significant and pressing issue in recent years. In light of the FAO's definition of food security – the physical, social and economic access to sufficient and nutritious food – food safety plays a fundamental role. Animal feed and feeding is pivotal to the livestock industry, but the use of veterinary antibiotics (VAs) and synthetic growth promoters (SGP) diminishes the sustainability of the diets and can cause an accumulation of residues in animals (meat, milk and eggs) and the environment (water and soil pollution). Wastewater systems are another major pathway through which antibiotics and hormones can enter the environment, with negative consequences. In order to protect the planet through more sustainable feeding, the reduction of antibiotics and synthetic growth promoters is a key aim, in particular with the goal of reducing antibiotic resistance and allergies. Analytical methods play a crucial role in food analysis, to determine the presence of antibiotics and other additives. Recent methods are based on liquid chromatography with ultraviolet, fluorescence, or mass spectrophotometry detection, which is recognized as an essential technique in food analysis, able to identify more than 300 compounds in feed samples. In general, a monitoring program put in place to educate the population on the hazards of residues in animal products is necessary, in conjunction with a continuous decrease in the use of antibiotics and synthetic growth promoters in animal diets.

1. Introduction

Food quality and safety have been a significant and pressing topic in recent years. In light of the FAO's definition of food security – the physical, social and economic access to sufficient and nutritious food – food safety plays a fundamental role. The concern about food safety on the part of scientists, food experts and informed consumers can be defined as the probability of not falling ill as a consequence of consuming a certain food (Grunert, 2005). This concern naturally includes the potential risks from consuming foodstuffs of animal origin.

Animal feed plays a large role in the sustainability of animal production systems. It is estimated that about 70% of animal-production costs are attributable to the cost of feed. The choice of diet on the farm affects the animal production chain, because feed management must take into account such factors as genetic animal potential, agro-ecological conditions, market demand, management practices and the social and economic environment.

The “Sustainable Animal Diets” (StAnD) concept was developed

* Corresponding author.
E-mail address: mrg@uaemex.mx (M. Gonzalez Ronquillo).

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by the Food and Agriculture Organization of the United Nations (FAO) in consultation with a large international group of experts (Makkar & Ankers, 2014) to resolve issues of sustainable animal feed. The StAnD concept is based on the three dimensions of sustainability: Planet, People, and Profit.

To understand the notion of StAnD, it is first necessary to transcribe the concept of sustainability into a conceptual model based on clearly identified objectives and elements. The Planet dimension considers 15 elements that are considered essential for a sustainable animal diet. For example: "production of StAnD and its feeding should not use antibiotics or synthetic growth promoters".

Antibiotic growth promoters (AGP) can be defined as any medicines that destroy or inhibit bacterial growth and are administered at a low subtherapeutic dosage (Hughes & Heritage, 2004). The use of these components has risen with the intensification of livestock farming as a consequence of increased consumer demand and improvements in the efficiency of conversion of natural resources to food animal products.

A wide range of veterinary antibiotics (VA) – natural, synthetic or semi-synthetic compounds with antimicrobial activity that can be administered orally (Phillips et al., 2004) – are used for disease control, as feed additives, or as synthetic growth promoters (SGP) within various sectors such as livestock farming, aquaculture and agricultural activities (Aust et al., 2008; Gao et al., 2012; Zuccato, Castiglioni, Bagnati, Melis, & Fanelli, 2010). Agricultural activities represent a large proportion of the usage of antibiotics in worldwide antibiotic consumption.

The growth-promoting effects of antibiotics were discovered in the 1940s when chickens were fed feed containing by-products of tetracycline fermentation. In this case, the chickens exhibited higher growth rates than chickens that were not fed feed containing by-products (Phillips et al., 2004). Since then, the use of growth promoters has been expanded to include a wide range of antibiotics that are applied to several species.

In pigs, the first evidence of the beneficial effects of AGP in productive animal performance was also observed in the 1940s, with the studies carried out by Cunha and Burnside (1949) and Stokstad, Jukes, Pierce, Page, and Franklin (1949), who found that the addition of dried mycelia from aerobic cultures of *Streptomyces aureofaciens* that contained chlortetracycline residues (previously called aureomycin) to the feed of pigs improved their growth (Castanon, 2007) (Fig. 1). The administration of antibiotics as growth promoters in the 1940s and 1950s was part of an initial approach of supplementation in animal feed known as the "animal protein factor" (APF). APF was described as an unidentified substance necessary for balanced swine and poultry rations; initially it was claimed that APF consisted of Vitamin B12 although later it was found that APF also contained growth-promoting factors (antibiotics).

Since pharmaceutical antibiotics do not bioaccumulate significantly (Thiele-Bruhn, 2003), a high proportion of VAs are excreted via urine, feces (Ostermanna et al., 2013), milk (Arikan, Mulbry, & Rice, 2009; Halling-Sorensen, Jensen, Tjornelund, & Montforts, 2001) and eggs (Idowu et al., 2010) as the non-metabolized parent compounds, or accumulate to a high concentration in tissues (Kim & Schrenk, 2012; Kwon et al., 2011). This may pose a real threat to the consumer, either through exposure to the residues, the transfer of antibiotic resistance (Butaye, Devriese, & Haesebrouck, 2003) or increased allergies resulting from antibiotic presence in foods. However, there are differing opinions regarding the level of risk that antibiotic residues pose to human health. Some researchers suggest that the actual danger is minimal and that banning antibiotics might prove more harmful to human and animal health. Furthermore, certain studies support the rational and prudent use of antibiotics in all contexts (Phillips et al., 2004).

It is not easy to establish and quantify the relationship between the use of AGP and possible negative effects on animal health, human health and the environment. However, in line with available information and the precautionary principle, AGP has been banned in some countries (Council Directive 96/22/EC). Barton (2000) notes that antibiotic resistance is already well-established in bacterial populations in animals, humans and the environment; Hao et al. (2014) show that the misuse and overuse of AGP may culminate in the development of drug-resistant pathogens, with severe consequences for the treatment of bacterial infections in patients.

Phillips et al. (2004) report that the low dosages of antibiotics used for growth promotion are a quantified hazard. To address the need for proper analysis of antibiotics usage, new techniques that combine chemical extraction, chromatographic separation and subsequent determination of antibiotic activity by microbial assays have been developed (Blasco, Torres, & Pico, 2007; Cronly et al., 2010; De Alwis & Heller, 2010; Sczesny, Nau, & Hamscher, 2003; Stolker, Zuidema, & Nielen, 2007).

Antibiotics are not the only substance added to animal feed by livestock farmers. Anabolic steroids (natural steroids, xenobiotics and synthetic steroids) and β-agonists have been largely used in intensive meat production to improve the integration of nutrient availability and animal performance in beef cattle (Vasconcelos et al., 2008), sheep (Mondragon et al. 2010) and swine (Shao et al., 2009), mainly through their endocrine systems; this produces meat which appeals to consumers in accordance with current human dietary guidelines.

Animal scientists have been interested in improving efficiency

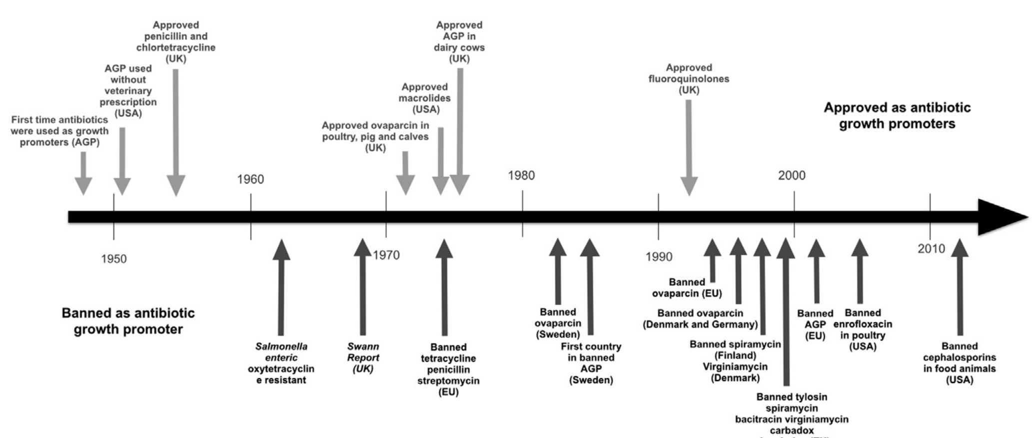

Fig. 1. Timeline of antibiotic growth promoters (AGP).