Recent Approaches as Alternative Growth Promote to Replace Antibiotic in Animal Nutrition

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Summary

The purpose of this short article is to focus on the possible alternatives to antibiotic in animal nutrition for producing safe products and limit the negative effects of antibiotics on the environment.

Introduction

Worldwide, animal products are main sources of protein, and poultry are the fastest growing sources of meat, representing nearly one fourth of all the meat produced globally. The modern production unit can produce market ready broiler chickens in about five weeks. This development arose from genetic selection, improved feeding and health management practices involving usage of antibiotics as therapeutic agents to treat bacterial diseases in intensive farming systems. They may also be used as prophylactic agents in the water of healthy chicks and as growth promoters at sub-therapeutic concentrations in feed. Bacitracin, chlortetracycline, tylosin, avoparcin, neomycin, ox tetracycline, Virginiamycin and others are used for these purposes. Sub-therapeutic dosing in feed increase the rate of weight gains and improves the efficiency of converting feed to meat. The recommended levels of antibiotics in feed were 5-10g/kg in the 1950's and have increased by ten to twenty folds since then.

During the last 50 years antibiotics were extensively used worldwide (Figure 1 & 2) as growth enhancer to improve animal performance, fight pathogens and eliminate culling [1-10]. The Maps above shows the widespread of using antibiotics as growth promoters in animal nutrition. However, during the last two decades there were public and governmental pressures to mimic the use of AGPs in animal nutrition. Thus, as shown in Table 1, some of the members of the Organization for Economic Co-operation and Development (OECD) countries have banned the use of antibiotic as growth enhancers in animal nutrition to eliminate health hazards and sustainable agriculture and environment.

Table 1 shows the regulation of the use of antibiotic growth enhancers in animal nutrition in the Organization for Economic Co-operation and Development OECD countries (source: as cited by

Kumar P et al., 2018; Antibiotic Free Chicken, <https://en.engormix.com/poultry-industry/articles/antibiotic-free-chicken-t41857.htm>, accessed March 27, 2018) from Teillant and Laxminarayan, 2015, Teillant, Aude and Laxminarayan R, 2015. Economics of antibiotic use in US swine and poultry production, CHOICES 1st Quarter 2015, 30(1): 1-11).

Figure 1: Antimicrobial consumption in chickens (A) and pigs (B) in 2010. Purple indicates new areas where antimicrobial consumption will exceed 30kg per 10km² by 2030. Van Boeckel et al. [9].

Figure 2: Global antimicrobial consumption in livestock in milligrams per 10 km² pixels (Top) and average SD of estimates of milligrams per PCU Van Boeckel et al. (9).

Table 1: The regulation of the use of antibiotic growth enhancers in animal nutrition in the organisation for economic co-operation and development OECD countries (source: as cited by Kumar P 2018).

OECD Country	Ban Of Antibiotic Growth Enhancer	Prescription Required To Use Antibiotic In Animals
Australia	No, but some AGPs ARE BANNED (fluoroquinolones, avoparcin, virginiamycin, etc.) [Australian Commission on safety and Quality in health care, 2013, https://www.safetyandquality.gov.au/].	Nearly all veterinary antibiotic can be sold on a veterinarian prescription
Canada	No. The Canadian government issued a notice in April 2014 to stakeholders mimicking the FDA approach to voluntarily phase out use of medically important antibiotic as growth promoters [Government of Canada, 2014, Federal action plan on antimicrobial resistance and use in Canada, http://healthycanadians.gc.ca/alt/pdf/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/action-plan-daction-eng.pdf?_ga=2.119983503.664858479.1519725596-573225208.1519725596]	No. Plan to develop options to strengthen the veterinary oversight of the use antibiotic
Chile	No data	No data
EU States	Yes. All AGPs was prohibited in 2006 [European Union, 2003; http://europa.eu/rapid/press-release_IP-05-1687_en.htm]	Yes
Israel	No data	No data
Japan	No [10]	Yes
Mexico	Yes, AGPs were banned in 2007 with some exceptions (avoparcin, vancomycin, bacitracin, tylosin, virginiamycin, etc [10]	Yes
New Zealand	Yes, for the critically and highly important antibiotics listed by both WHO and OIE (MAF New Zealand, 2011, A baseline survey of antimicrobial resistance in bacteria from selected New Zealand foods, 2009-2010]	Yes, for antibiotics identified with the potential for resistance problems.
South Korea	Yes, since 211, AGPs use have been discontinued until a veterinary oversight system can be put in place [USDA, 2011 https://www.ers.usda.gov/amber-waves/2015/november/restrictions-on-antibiotic-use-for-production-purposes-in-us-livestock-industries-likely-to-have-small-effects-on-prices-and-quantities/]	Yes, the veterinary oversight system is currently being developed.
Turkey	No	No data
USA	No, the FDA released voluntary guidelines for the industry to withdraw the use of medically important antibiotics as growth promoters [U.S. Food and Drug Administration, 2013, http://www.nytimes.com/2013/12/12/health/fda-to-phase-out-use-of-some-antibiotics-in-animals-raised-for-meat.html]	No, under the new FDA guidelines for industry, use of medically impotent antibiotics will be under the oversight of licensed veterinarians.

Phytogenic called photobiotic or botanicals, included herbs, spices and their products such as essential/volatile oils and plant excretes are a group of natural growth promoters [NGPs] used as feed additives. They derived from herbs, spices or other plants to enhance livestock productivity, stimulation of appetite, improvement of digestibility by increasing endogenous digestive enzyme secretion and thus nutrient absorption, antioxidant, immune stimulant, antimicrobial and anthelmintic influences [1-3]. Phytogenic plants are good source of anti oxidants [4-6]. Additionally, they are safe for both living organisms and the environment, but the photogenic composition may vary widely due to method of processing, botanical origin, agronomical and environmental factors [7-10]. Medicinal herbs and their derivatives have many components that have anti-microbial, anti-oxidative, anti-allergic, anti-cancer, anti-mutagenic, hepato-protective and immune-modulate, they may also enhance economic performance, to gut eco-system, production yield, food quality, and fertility [2-3].

For example, Milk thistle [*Silybum marianum* L. Gaert., Asteraceae] seeds and Rosemary [*Rosmarinus officinalis* L.] leaves are new feed additives that may have promising effects. Milk Thistle has been utilized for long times by Theophrastus [4th century BC] who was possibly the first to define it under the name of "Pternix" and later it was cited by Dioskurides in his "Materiamedica" and by Plinius [1st century AD] [11-13]. Silymarin is a flavonoids mixture extracted from milk thistle seeds (MTS), which contains silybin, silydianin and silychristin; molecules that show estrogenic effect in ovariectomized rats [14] and its major component, silibinin, bind to cytosolic estrogen receptors [15]. Milk thistles process powerful anti-oxidants [16]. Silymarin is the active constituent in milk thistle seeds and represent about 4-6% of the milk thistle seed extract [17]. Other beneficial health components in MTS are fixed oil and free fatty acids and proteins, silybonol, apigenin, flavonolignans and betaine. The MTS was utilized in Europe for many centuries for liver and gall bladder dysfunction treatments [18]. The enhancing effect of silymarin is mediated through increasing endogenous antioxidant defenses, such as those mediated by glutathione system and superoxide dismutase [SOD] [19]. Silymarin is an outstanding scavenging reactive oxygen species [ROS], antioxidant. In addition, repeated doses of extract of milk thistle extract significantly decreased biomarker [enzymes] of liver leakages while increased antioxidant enzymes of rat liver homogenate, showing free radical scavenger potential [20]. Also, lipid peroxidation controlling, thereby defending cells against oxygen species [21].

Another example of potential phytogenic with multipurposes application is the *Rosemary leaves*. Rosemary is rich source of antioxidant substances such as rosmarinic acid and caffeic acid [22]. Rosmarinic acid is well absorbed in the gut and from the skin, decreases the creation of leukotriene B4 in human polymorph nuclear leukocytes and prevents the complement system [23]. Furthermore, revealed that rosemary essential oil enriches rat hepatocytes' resistance against DNA-damaging oxidative agents and effective agent for scavenging free radicals [24]. Caffeic

acid and rosmarinic acid have a potential for inflammatory diseases and hepatotoxic treatments [25]. Rosemary is rich in photochemical derivatives such as triterpenes, flavonoids and apolyphenol. Carnosol, rosmanol and epirosmanol phenolic diterpenes of rosemary control peroxidation of unsaturated lipids [26]. Moreover, rosemary significantly decreased the elevation in peroxidation of unsaturated lipids and boosted the levels of reduced glutathione and antioxidant enzyme actions in the kidney and testis in comparison to aspartame controls [27].

Conclusion

Research for alternative to antibiotic is an essential task in animal nutrition and can lead to replace antibiotic, safe animal products and econ-friendly environment. However, it seems that looking for complex formulas based on their active substances of different photogenic plan and/or their products may lead to constant and better results [28]. The use of probiotics, prebiotics, synbiotic, enzymes and organic acids are possible alternatives although further research is essential. The future of using phylogenic could be extended to alleviate the stressful condition and improve immunity [5,28].

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