



## APPLICATION OF MICROBIAL AGENTS TO CONTROL DISEASES IN AGRICULTURE WITH A FOCUS TO BEEKEEPING: A REVIEW

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### ABSTRACT

This review describes the system of the biocontrol of diseases using microorganisms with specific regard to potential use in beekeeping. Diseases are caused mainly by microorganisms. The gut microbiota has a special important role in animal health. A hypothesis assumes that the use of other microorganisms can provide effective protection against diseases. In our review we focused on probiotics as a supplementary agent in animal nutrition with positive results on intestinal microbiota. The four main mechanisms on how they work are: direct antagonism, competition for nutrients/energy, occupation of susceptible receptors and stimulation of immunity. The probiotics group includes various bacteria, yeasts, filamentous fungi or bacteriophages. The best known representatives are lactobacilli and bifidobacteria. The use of probiotics in nutrition of poultry, cattle, pigs, lambs, aquatic animals as well as bees was tested. The lactic acid bacteria specific for honey bee, with the main representative *Lactobacillus kunkeei*, have confirmed strong antimicrobial activity against pathogens, e.g. *Paenibacillus larvae*, causative agent of American Foulbrood. However, these bacteria were not effective in field studies. Successful use of probiotics in beekeeping depends on various factors, including high level of pesticides or contaminants in bee surrounding, which could negatively influence bee microbiota.

**Key words:** bee immunity; probiotics; antagonism; *Lactobacillus kunkeei*; prophylaxis

### INTRODUCTION

Several studies about integrated pest management (IPM) with microorganisms are focused only on plant protection (Fuentealba *et al.* 2015; Stenberg *et al.*, 2015; Ondráčková, 2015; Bellutti *et al.*, 2018; Francis *et al.*, 2020). The term "pests" is generally used in relation to plants as their damaging agents. In animal science, there is a problem with diseases often caused by microorganisms, which result in the

death of animals. Chemical treatment against harmful microorganisms has been used for many years, including antibiotic use as a prevention of diseases. However, the disadvantages of such treatments are similar compared to the use of fertilizers and pesticides in plant science (i.e. negative impact on food security and environment). This paper overviews current research on biocontrol of diseases using microorganisms, especially probiotics, including the new perspective of their use in beekeeping.

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## BIOCONTROL OF DISEASES IN AGRICULTURE

The term "disease" could be found in plant as well as in animal kingdom. Plants and animals have evolved sophisticated surveillance mechanisms to recognize various bacterial pathogens. In particular, plants recognize distinct effectors from pathogenic bacteria, whereas animals recognize conserved "molecular patterns" derived from lipopolysaccharides (LPS) or peptidoglycans (Staskawicz *et al.*, 2001).

### Biocontrol of plant diseases

Several action modes for the biocontrol of plant diseases are known: microorganisms act as parasites of the pathogens' resting structures, such as sclerotia of *Sclerotinia sclerotiorum* (Lib.) de Bary<sup>b</sup>, and eggs and/or juveniles of nematodes *Meloidogyne Göeldi*<sup>®</sup> sp.; other microorganisms produce antibiotic compounds that protect the plant tissue (such as the plant growth-promoting rhizobacteria that colonize plant roots and release antibiotics that tackle damping-off-causing pathogens); some agents consume free nutrients on the plant and scavenge them from the pathogen; and upon colonization of the plant tissue, receptors from the cell membrane perceive the microbial colonization and trigger an induced resistance that result in broad-spectrum plant protection that is resulted in combination of more than one mode of action in current largely used biocontrol strategies (de Medeiros and da Silva, 2019).

### Biocontrol of animal diseases

Three types of livestock diseases are of special concern: epidemic or outbreak diseases, which are highly contagious and liable to spread rapidly; endemic diseases, which are consistently present in a given population; zoonotic diseases, which are transmissible between animals and people (Grace, 2020). Infectious diseases refer to diseases that are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi and can directly or indirectly spread from an infected host to another susceptible host (WHO, 2019, cit. Raji, 2020). Viruses, bacteria and parasites are the three main infectious factors causing animal diseases (Chen, 2020). Farrell and Davies (2019) used a global dataset of >4,000 case-fatality rates for 65 infectious diseases (caused by microparasites and macroparasites) and 12 domesticated host species and showed that

the average evolutionary distance from an infected host to other mammal host species is a strong predictor of disease-induced mortality and found that as parasites infected species outside of their documented phylogenetic host range, they were more likely to result in lethal infections, with the odds of death doubling for each additional 10 million years of evolutionary distance.

Antibiotics as prevention of diseases (or antibiotic growth promoters) were banned in animal production in the European Union and scientists have tested various preparations of natural origin, including probiotics, prebiotics, enzymes or organic acids to keep the animals in good state (Falcão-e-Cunha *et al.*, 2007). Probiotic microorganisms play a primary role against other microorganisms including parasites. Aldayel (2019) indicated that the success of biological control depends on the selection of effective microbial strains against pathogens, such as the production of microbial strains that have the ability to resist pathogenic microbes, the ability to withstand various environmental conditions and the ability to produce secondary compounds eliminating pathogenic microorganisms.

### Probiotics

#### Characterization

Different environmental factors may affect the gut microbial ecology. They include diet, medication, stress, age and general living conditions (Vlková *et al.*, 2009). Fuller (1989; cit. Fuller, 1994) defined probiotics as "a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance". Various biological properties have been reported for probiotics, including antimicrobial activity (Silva *et al.*, 2020).

#### Important representatives

Often we have heard about lactobacilli and bifidobacteria. Wang *et al.* (2016) performed experimental trials with probiotics: 25 with animals and 15 with humans, while in most studies bacterial genus were used as following: *Bifidobacterium* Orla-Jensen<sup>a</sup>, e.g. *B. longum* Reuter<sup>a</sup>, *B. breve* Reuter<sup>a</sup>, *B. infantis* Reuter<sup>a</sup>, and genus *Lactobacillus* Beijerinck<sup>a</sup>, e.g. *L. helveticus* (Orla-Jensen) Bergey *et al.*<sup>a</sup> and *L. rhamnosus* (Hansen) Collins *et al.*<sup>a</sup>, at doses of 9.00 – 10.00 log CFU.g<sup>-1</sup> for 2 weeks in animals and 4 weeks in humans.

Fuller (1994) stated that probiotics include bacteria, yeasts, moulds and bacteriophages, which have all been shown to have effects on disease resistance, nutrition and growth.

### **Mode of action**

Probiotics applied in animal nutrition have the similar principles comparing IPM, i.e. microorganisms and their metabolites are used for the health of the host (animals, humans). When ingested in adequate quantities, probiotics may modulate biological functions with health benefits (Silva *et al.*, 2020). There are several modes of action that probiotics cause on hosts: direct antagonism (by producing inhibitory compounds), competition for nutrients and energy, competition for adhesion receptors and stimulation of immunity (Fuller, 1994; Verschuere *et al.*, 2000). The main four modes of action are the same compared with action modes of agents against plant diseases (described above). Verschuere *et al.* (2000) reported additional mode of action, when probiotics are used in aquaculture – the improvement of water quality and interaction with phytoplankton.

Niode *et al.* (2020) explained role of probiotics in wound healing. Formic acid and lactic acid produced by symbiotic lactic acid bacteria (LAB) could decrease the environmental pH of wounds, therefore, preventing the growth of pathogenic microbes, because volatile compounds produced by LAB are also toxic for them, while small amount of H<sub>2</sub>O<sub>2</sub> is needed for optimal wound recovery.

The host-specific nature of microbial gut colonisation makes it unwise to transpose results between any animal species without considering very carefully the different factors which may be operating (Fuller, 1994). On the example of poultry, the wide range of conditions under which poultry is produced (geographic location, feed ingredients, types of litter and environmental temperature) affect the types of native bacteria present in the intestinal tracts and a culture would have to be effective under these conditions (Nava *et al.*, 2005).

### **Isolation**

The ideal probiotic would be one, which could establish itself permanently in the intestine and produce its active agents *in situ* (Fuller, 1994). Vlková *et al.* (2009) isolated bifidobacteria from faecal

samples of lambs during the milk-feeding period using modified TPY agar with mupirocin (100 mg.L<sup>-1</sup>) and glacial acetic acid (1 mL.L<sup>-1</sup>) according to Rada and Petr (2000). They identified bifidobacteria according to morphological, biochemical and molecular-genetic properties, tested functional properties *in vitro* (acid and bile tolerance and antimicrobial activity against potential pathogens) and produced bifidobacterial "cocktail" from strains with appropriate properties.

### **Case studies**

Probiotics are used in animal feeding in order to improve zootechnical traits such as average daily gain, feed conversion rate and quality of animal products (Vlková *et al.*, 2009). Probiotics added to nutrition of poultry, cattle and pigs improved health state of animals as well as the meat quality (Nava *et al.*, 2005; Taras *et al.*, 2007; Siggers *et al.*, 2008; Liu *et al.*, 2013; Pinloche *et al.*, 2013; Uyeno *et al.*, 2015; Kelsey and Colpoys, 2018; Haščík *et al.*, 2020). Vlková *et al.* (2009) tested special bifidobacteria on lambs. Some of bifidobacteria survived for 30 days in the gastrointestinal tract of treated lambs, however none of the tested strain was able to colonise the lamb's tract permanently. Verschuere *et al.* (2000) demonstrated that probiotics are also beneficial in aquaculture. From current combined research, Redweik *et al.* (2020) proved combined treatment (recombinant attenuated *Salmonella* Lignieres<sup>a</sup> vaccines (RASV) and probiotics) as a feasible method to reduce infection by avian pathogenic *Escherichia coli* (Migula) Castellani and Chalmers<sup>a</sup> (APEC) and *Salmonella* in chickens, which are threatened by these bacterial infections.

## **BIOLOGICAL CONTROL OF BEE DISEASES**

Shimanuki and Knox (2000) classified bee diseases according to microbial causative agent into 4 groups: bacterial (American foulbrood, European foulbrood, powdery scale, septicemia, spiroplasmosis), fungal (chalkbrood, stonebrood), protozoan (*Nosema* Nägeli<sup>b</sup> disease, *Amoeba* Bory de Saint-Vincent<sup>b</sup> disease and other protozoa) and viral (sacbrood, chronic bee paralysis, filamentous virus, acute paralysis bee virus and Kashmir bee virus) diseases. In Slovakia, the most common causes of bee death and worsening of bee colonies vitality are varroosis,

American foulbrood, nosematosis, viroses and poisonings of bees (Chlebo, 2017). The main current methods for controlling American foulbrood (AFB) in honeybees, caused by the bacterial pathogen *Paenibacillus larvae* (White) Ash *et al.*<sup>a</sup>, are enforced incineration or prophylactic antibiotic treatment, but neither of which is fully satisfactory (Lamei *et al.*, 2020). In Slovakia, hives and all equipment from colonies with clinical symptoms of AFB are for burning. Natural relationships between the pathogenic and mutualistic microorganisms of the honeybee microbiome are observed (Lamei *et al.*, 2020). The honeybee immune system consists of a complex of interlinked reactions that are mostly activated by microbial pathogens (viruses, fungi and bacteria) and as a social insect, honey bees can also employ mechanisms of social immunity (Dostálková *et al.*, 2021).

### Bacteria

Gut bacteria influence the development of different pathologies caused by bacteria, fungi and parasitoids in insects (Polenogova *et al.*, 2019). In general, bacteria are better invaders than fungi (Albright *et al.*, 2020). Diverse gut microbiota can provide a strong line of defence for bees against biotic stressors while improving worker bee lifespan (Geldert *et al.*, 2021). Honeybees possess an abundant, diverse and ancient LAB microbiota in their honey crop with beneficial effects for bee health defending them against microbial threats (Vásquez *et al.*, 2012).

Probiotic bacteria have been tested in terms of bees' nutrition and immunity using *in vitro* and *in vivo* experiments in numerous studies. There has been a conflict between the results of laboratory and field tests. From the current research, *Lactobacillus* sp., especially *Lactobacillus kunkeei* Edwards *et al.*<sup>a</sup>, *L. crispatus* (Brygoo and Aladame) Moore and Holdeman<sup>a</sup> and *L. acidophilus* (Moro) Hansen and Mocquot<sup>a</sup>, showed the strongest antimicrobial activity against *Paenibacillus larvae*, the causal agent of AFB (Kačániová *et al.*, 2020). On the other side, although individual laboratory larval assays have clearly demonstrated the antagonistic effects of hbs-LAB (honey bee specific lactic acid bacteria) on *P. larvae* infection, the experiments indicated that direct conversion of such practice to colony-level administration of live hbs-LAB is not

effective (Lamei *et al.*, 2020). Different results of probiotic use in the field conditions can be influenced by application of some pesticides. Motta *et al.* (2018) observed that the active substance glyphosate negatively affects intestinal microbiota.

Albright *et al.* (2020) stated that microbial probiotics often fail to establish in a pre-existing microbiome, while this is a species invasion problem and the relative importance of the two major factors controlling establishment in this context, propagule pressure (inoculation dose and frequency) and biotic interactions (composition of introduced and resident communities), is unknown. Ptaszyńska *et al.* (2016) found that honeybees fed with sugar syrup supplemented with a commercial probiotic and probiotic + prebiotic were more susceptible to *Nosema ceranae* Silva *et al.*<sup>b</sup> infection and their lifespan was much shorter. They concluded that the supplementation of honeybee diet with improper probiotics or probiotics + prebiotics can disturb the natural microbiota composition, which is important in maintaining metabolic homeostasis in bee intestines. It can deregulate the immune system and, in consequence, may promote pathogen infections and increase honey bee mortality. Concerning immunity, Dostálková *et al.* (2021) evaluated immune response in short-living summer bees and long-living winter bees, and found that winter bees exhibited a more intense response including higher expression of antimicrobial genes and antimicrobial activity and significant decrease of vitellogenin gene expression and its concentration in the haemolymph.

### Other microorganisms

Among other microorganisms tested in bee nutrition, Ricigliano (2020) proposed application of microalgae during the substitute diet, because microalgae are prolific sources of plant-based nutrition with many species exhibiting biochemical profiles that are comparable to natural pollen.

## CONCLUSION

According to available publications, probiotics play the main role in prevention against diseases to strengthen immunity and keep the animals in good health. Probiotics are living organisms and, therefore,



result of their action is influenced by various factors, e.g. microbial strain, its origin, dose of microorganisms, host and its properties and environmental surrounding including presence of contaminants.

Bee microbiota could be positively influenced by probiotic use. Lactic acid bacteria (LAB) specific for honey bee is a special group of LAB with a potential to become the appropriate bee probiotic. Published results of laboratory experiments showed that probiotic organisms inhibited the bee pathogens. However, these results were not confirmed by field studies. Therefore, bee surrounding and its quality are considered as the important factors for bee life.

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