ALTANT MODIPHY

INTRODUCTION

Phytochemicals are attractive substitutes for antibiotics. Until now anti-microbial activities were reported for various phytochemical compounds and some of them are already marketed as feed additives.
Most pathogens enter their hosts through the mucosal tissues of lung and gut. Critical immune defense mechanisms in the mucosa were elucidated only recently. These mechanisms now interconnect the activity of 1) innate immunity, such as macrophages, natural antibodies and stress proteins with 2) acquired immunity, such as specific antibodies and T cells including T regs to control the so-called collateral tissue damage and energy consumption caused by unproductive inflammation. By stimulating 1) and controlling 2) such molecules can be an aid in controlling the consequences of pathogenic infections at acceptable energy cost. The MODIPHY (Modulation with Immune-stimulating Phytochemicals) consortium consists of experts in phytochemistry, food science, infectious diseases, toxicology, immunology and animal health.

TARGET

The target of MODIPHY is to select phytochemicals or combinations thereof, which are able to combine 1) direct antimicrobial activities and 2) indirect (immune-mediated) antimicrobial activities and 3) activities to improve host immune preparedness. This multivalent strategy may result in more robust animals and is probably better suited to overcome resistance mechanisms of micro-organisms which are the major problem of current antibiotics.

RESULTS

MODIPHY developed a panel of *in vitro* test assays to test direct and indirect antimicrobial and immunemediating activities of phytochemicals under standard conditions with appropriate controls. In addition, phytochemicals were evaluated *in vivo* for their potential to improve host immune preparedness in a coccidiosis (*E. acervulina*) and colibacillosis (*E.coli*) infection model in poultry.
In vitro analysis of phytochemicals alone or in combination revealed interesting properties for three out of six compounds tested. Direct anti-microbial effects and attraction of neutrophils was found for compound A. Recruitment and activation of phagocytes and immuneregulating properties were found for a mixture of compound A and B. Interestingly, this combination of compounds also inhibited invasion of *E. tenella* in cultured cells, which in turn was enhanced by adding compound C. In addition, enhanced phagocytosis of *E.coli* was found in response to compound B and compound C.
In vivo, significant effects on reduction of mortality and enhanced body weights of chickens have not been found consistently for any of the single compounds tested. However, since combinations of compounds A-C displayed antimicrobial and/or immune mediating properties *in vitro*, these combinations are currently being evaluated *in vivo* and data are expected to be generated in the next months.
Possibilities for patent protection are being investigated.

PROPOSITION

Direct anti-microbial effects of phytochemicals have been demonstrated, but cannot compete with the classic antibiotics. However, the attractiveness of applying some of the phytochemicals described in this study is their secondary effect on stimulating the inherited defense system. This additional feature may further increase the robustness of treated animals to withstand the clinical consequences of pathogenic infections and thereby reduce or even overcome the use of classic antibiotics. Although positive effects have been found *in vivo*, consistency lacked so far, possibly due to the limited bioavailability of the products in the present formulation.

The consortium therefore seeks partners that support the idea of the application of these (combinations of) active molecules and jointly develop these in suitable products.
The formulations may be improved by proprietary technology of the partner, whereby the set of proven assays will be a unique tool to validate the efficacy of the formulations.

Project is open for participation

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