

Salinomycin is an important compound widely used in poultry production as a coccidiostat (an agent against a common parasitic disease). Lately, it has also been tested for potential application in anticancer treatment. Huge differences of salinomycin toxicity were observed among animal species. The lethal dose (in mg per kg b.w.) in turkeys is 100 times lower in comparison to chickens. The reasons for these differences are not fully known. Therefore, the main research objective of the project is to understand the mechanism of the toxicity of salinomycin, especially in the most sensitive species.

Two animal experiments will be conducted for both chickens and turkeys. The first experiment will establish a dose-effect relationship. The animals will receive 0; 0.03, 0.09; 0.3 and 0.9 mg/kg b.w. of salinomycin in feed for two weeks. In the second experiment, salinomycin at LOEL (Lowest Observed Effect Level) from experiment 1 will be administered together with monensin (another coccidiostat), tiamulin, or enrofloxacin (antibiotics) to study the interactions.

The batch of tests using both traditional toxicological methods and novel techniques will be performed. Thanks to this holistic and interdisciplinary approach, more data will be obtained that will help to fulfill project objectives. The following tests will be performed:

- Monitoring of clinical condition and production results;
- Histopathological analyses of tissues;
- Determination of biochemical markers of salinomycin intoxication in blood;
- Detection of salinomycin and its metabolites in biological samples;
- Description of the profile of gut microbiome (bacterial flora);
- Analysis of gene expression of muscle (as the target organ for toxic effects), liver (as the organ engaged in biotransformation), and small intestine (as the tissue responsible for absorption of both nutrients and drugs).

The results of the project could be further used in both agricultural and health protection fields. Intoxications of turkeys with salinomycin cause relevant economic losses. The risk assessment of this problem and consequent legal regulations were based on incomplete and sometimes inconsistent toxicological data. The determination of the safe dose of salinomycin could be an impulse for the European Food Safety Authority to reassess the risks.

A better understanding of the mechanism of salinomycin toxicity may also relate to human health. Salinomycin is a promising antiproliferative agent tested for potential application in cancer treatment, including leukemia, colon carcinoma and prostate cancer. So far, little is known about its toxicity to humans. The huge differences in susceptibility to this compound may suggest that there may be factors predisposing to the occurrence of toxic effects. Such factors may be common at an inter-species and inter-individual level and knowing them could help better design the therapy for cancer patients.