

REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE
OF NICARBAZIN IN FEEDINGSTUFFS FOR POULTRY

Opinion expressed 14 April 1982

TERMS OF REFERENCE (December 1977)

The Scientific Committee for Animal Nutrition is requested to give an opinion on the following questions :

1. Does the use of the coccidiostat nicarbazin in feedingstuffs for poultry under the conditions of use authorized (see Background), result in the presence of residues in animal products? If so, what is the nature and the amount of these residues? Could these residues be harmful to the consumer?
2. Could the excreted products, derived from the additive, be prejudicial to the environment? If so, what is the nature of the risks?
3. In the light of the answers to the above questions, should the conditions of use authorized for this additive be maintained or should they be modified?

BACKGROUND

In accordance with the provisions of Council Directive 70/524/EEC, of 23 November 1970, concerning additives in feedingstuffs (1), as last amended by the twentieth Commission Directive of 7 December 1977 (2), Member

(1) OJ No L 270, 14.12.1970, p. 1

(2) OJ No L 18, 24.01.1978, p. 7

States are authorized to use nicarbazin, by way of derogation up to 31 December 1978, under the following conditions set out in Annex II, Section B, of the Directive :

Species of animal : poultry

Minimum and maximum content in complete feedingstuffs : 100-125 ppm (mg/kg).

Other provisions : use prohibited from laying age onwards and at least seven days before slaughter.

OPINION OF THE COMMITTEE

1. Nicarbazin is an equimolecular crystalline complex composed of 67.4-73.0% 4,4'-dinitrocarbanilide (DNC) and 27.7-30.0% 2-hydroxy-4,6-dimethylpyrimidine (HDP).

Studies of the metabolism of nicarbazin were carried out using ¹⁴C-labelled molecules either in the DNC moiety or in the HDP moiety in colostomised chickens, permitting separate collection of urine and faeces. With chickens fed during 3 days on a diet containing 125 mg of the product/kg feed 96-110% of the radioactivity was excreted within the 3 following days in faeces and urine; 9,7% of the DNC and 98,7% of the HDP were recovered in the urine. The HDP component is absorbed and excreted or metabolised more rapidly than the DNC component. Immediately on withdrawal, residues in the various tissues and organs ranged from 1.6 to 3.2 mg/kg for HDP and from 3.3 to 32.4 mg/kg for DNC. Five days after withdrawal, the residues has disappeared from all tissues and organs (limit of detection : 0.02-0.10 mg/kg) except the liver where traces of DNC were still present on the 8th day.

In other experiments on chickens feed on diets containing 100-800 mg nicarbazin/kg feed, HDP could only be detected in the liver and had disappeared 24 hours after withdrawal of the supplemented feed, except at the dose-level of 800 mg/kg feed. DNC residues in the various tissues and organs had disappeared 48 hours after withdrawal except in the liver where they ranged from 2.4 to 4.7 mg/kg according to the dose-level in the feed (100-800 mg/kg feed). Small amounts of the metabolite diacetylamidocarbanilide, derived from DNC, were also detected in the liver.

After prolonged feeding of nicarbazin to laying hens (50-400 mg nicarbazin/kg feedingstuff during 32-36 weeks) residues of DNC of 10-32 µg/ml were found in egg yolks.

There are few data available on residues resulting from the use of nicarbazin under presently authorized conditions. They refer to DNC (the longer persisting component of the complex) in chicken tissues. These residues were estimated five days after withdrawal at 0.1-0.2 mg/kg in the liver and less in other tissues. It should be noted, however, that these values were obtained by extrapolation of results obtained by a polarographic method of low sensitivity (limit of detection : 1 mg/kg).

Nicarbazin was investigated in short- and long-term toxicological studies in laboratory animals. In the long-term and reproduction studies a mixture of DNC and HDP (ratio : 3/1) was used. These studies were carried out in the period 1965-1970 and do not satisfy all the requirements of current toxicological testing; nevertheless, they suffice for the evaluation of the ADI. The no-effect level was estimated at 50 and 60 mg DNC/kg body weight in the rat and the dog

respectively. Using a safety factor of 250 (to compensate for some experimental gaps), the ADI was evaluated at 0.20-0.24 mg/kg body weight. There is thus a large margin of safety between the ADI and the amount of residues which may persist in edible chicken products after a withdrawal period of at least 7 days (< 0.2 mg DNC/kg animal product).

2. No data were available to the Committee on the biodegradation of HDP, DNC and their possible metabolites in poultry manure, soil and water nor on their toxicity to soil micro-organisms. As DNC exhibits only slight solubility in water (0.02 mg/l), a contamination of water streams seems unlikely. The toxicity of DNC and HDP to water organisms was tested in the unicellular alga Chlorella pyrenoidosa, the water flea Daphnia magna and in two fish species : Poecilia reticulata and Salmo gairdnerii. The acute toxicity of HDP was in all cases very low. For DNC, no toxic effects were observed at the concentration of 0.02 mg/l (maximum solubility in water).

3. In the light of the available information, the Committee is of the opinion that the use of nicarbazin as feed additive should be limited to feedingstuffs for fattening chickens. No data are available to justify the use of this product in chickens reared for laying or other poultry species. The dose-levels of 100-125 mg/kg complete feedingstuff and the withdrawal period of at least 7 days before slaughter appear acceptable. However, a reassessment of this additive is needed, after more extensive studies on the metabolism of nicarbazin in chickens, biodegradation of excreted products and their possible effects on soil micro-organisms have been carried out.

Note

According to Neshavarz and McDougald (1981), chickens fed a diet containing nicarbazin are more sensitive to stress caused by heat. Under these conditions, there is an increase of mortality in chickens when 18-29 days old.

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