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The Absorption, Excretion and Environmental Fate of Nicarbazin

Basic Mechanism and Action

Chemically, nicarbazin is an equimolar complex of 4,4′-dinitrocarbanilide ("DNC") and 2-hydroxy-4,6-dimethylpyrimidine ("HDP"). DNC is the biologically active component and, for effective absorption, must be complexed with HDP[1,2]. Due to its hydrophobic nature, DNC without HDP has very limited biological availability and will simply pass through birds unabsorbed.

Following digestion and absorption by the bird, DNC and HDP follow separate excretion pathways. DNC is unable to re-complex with HDP, and therefore, once digested, there is no potential for any secondary effect.

The metabolism of the compound has been well characterized in residue depletion studies with Carbon-14 labeled nicarbazin[3]. Both components are absorbed through the intestines into the blood. HDP is excreted rapidly, predominately through the kidneys and in urine, whereas DNC is excreted through the feces via the liver. No detectible residues of either component remain in any tissue after 7 days. DNC does accumulate in the egg and the accumulated egg DNC concentration is typically less than 5 ppm.

DNC can enter the environment either through the bird consuming the bait, as fecal matter, or directly as unconsumed bait. Both routes have the same outcome since nicarbazin will break down into its components and DNC becomes irreversibly bound to soil or fecal material[4].

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[1] Ott, W.H., S. Kuna, C.C. Porter, and A.C. Cuckler. 1956. **Biological studies on nicarbazin, a new anticoccidial agent.** Poultry Science 35:1355-1367.
[2] Burnett, T.J. Elanco Animal Health, 2010. "**Relative Bioavailability of DNC in Rats Administered Alone, Mixed with HDP and as Nicarbazin**. HVDRA Conference, Ghent, Belgium. June 1-4, 2010.
[3] World Health Organization (WHO), FAO Food and Nutrition Paper #41/11. **Residues of Some Veterinary Drugs in Animals and Foods** (1999).
[4] EPA Nicarbazin Fact Sheet

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The Solubility of DNC

DNC is highly insoluble in water with maximum solubility of just 46 ppb (pH7)[5]. In laboratory experiments, DNC at this concentration has no biological effect even on the most sensitive species of fish.

Based on Carbon-14 labeled DNC soil studies[3], the sorptive properties of the molecule are well documented. DNC binds irreversibly to feces or soil particles and does not translocate[6].

OvoControl is typically not applied to water although may enter water through runoff or bird feces. In either scenario, the compound enters water as DNC and HDP and not as the nicarbazin complex.

If left on the ground, dissociated DNC binds irreversibly to soil and there is a very limited risk of water contamination. In the inadvertent application to water, OvoControl baits will disassociate and the DNC would bind irreversibly to sediment.

The Persistence of DNC in the Environment

Carbon 14-labeled nicarbazin studies have shown that the half-life of DNC in soil is between 18 and 49 weeks in greenhouse or field soil, respectively[7]. The range can be attributed to a variety of environmental factors including weather conditions and soil characteristics. Studies of radio-labeled nicarbazin in field soil plots have shown that when the compound is incorporated into the upper 3 inches of soil it does not leach beyond 6 inches in depth and slowly degrades over time.

Nicarbazin has been used in the poultry industry for more than 50 years and hundreds of tons of nicarbazin and DNC in spent litter are spread on agricultural fields every year as fertilizer amendment. Nevertheless, DNC residues are not found in adjacent rivers, lakes or ponds further demonstrating that the material is irreversibly bound to soil and feces.

In the same manner, non-target species are not affected by previously ingested nicarbazin or runoff since bound DNC is not biologically available.

Summary

The environmental fate of nicarbazin and DNC is well documented. Once excreted by the animal, DNC is irreversibly bound to soil particles or fecal matter. Nicarbazin is an ecologically benign compound which has little or no impact on the environment.

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[5] Exygen Research, Inc., State College, PA (2005)
[6] A. MacDonald, et. al, **Nicarbazin Residue in Chicken Tissue: The Effect of Litter Recycle in Three Studies** EuroResidue IV, Proceedings pp.. 733-737, Veldhoven, The Netherlands, 8-10 May 2000.
[7] **A greenhouse study to determine the rate of decline of soil incorporated narasin and ^{14}C nicarbazin singly and in combination**, Lilly Research Laboratories, 1984.