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## **The Absorption, Egg Hatchability Effects and Acute Toxicity of Nicarbazin**

Nicarbazin is a bimodal salt consisting of two molecules – DNC and HDP. DNC is the active component and extremely insoluble in water or other solvents. DNC is complexed with HDP to facilitate biological absorption. DNC remains in the bird for up to four days and is excreted through the liver in the feces whereas HDP is excreted rapidly through the kidneys in the urine. DNC alone is very poorly absorbed and requires the HDP component for absorption and to achieve a contraceptive blood level.

The representative parameter of nicarbazin bait absorption is the level of DNC in the blood plasma. Once absorbed, nicarbazin has the identical contraceptive action – depositing in the egg and interfering with hatchability – in all birds.

### **Absorption of Nicarbazin – DNC in the Blood**

Yoder<sup>1</sup> confirmed that different species absorb DNC at dissimilar rates but excrete the compound at similar rates. The chicken is the most efficient absorber of nicarbazin followed by ducks, geese and pigeons. Birds must absorb nicarbazin at an adequate and consistent rate in order to reach an effective contraceptive blood plasma level. In other words, a single or intermittent dose will not affect hatchability. The active ingredient must be consumed daily, consistently and in adequate quantity in order to achieve the contraceptive effect.

The dose rates in Table 1 illustrate the differences in mg/kg body weight/day, a common denominator,

**Table 1 – Comparative Absorption and Dose Rate in Four Species**

Species	mg/kg bw/day
Chicken	11.5
Duck	24.2
Goose	35.5
Pigeon	83.3

According to the Avery<sup>2</sup> studies, smaller birds have the most inefficient absorption of nicarbazin, requiring a higher bait concentration and dose. Smaller birds, including passerines, with shorter gut transit time, require an even higher dose. A pigeon requires a dose rate of 83mg/kg bw/day. Assuming similar values for pigeons and passerines, a 150g passerine would require 2.5g of OvoControl® G 0.5% to obtain the recommended dose. The effect, however, would only occur with daily and consistent exposure during their respective breeding season. Supervision by licensed pest control operators and periodic observations of the application sites helps ensure that non-target exposure is limited.

<sup>1</sup> Yoder, C. A., L. A. Miller, and K. S. Bynum. **Comparison of Nicarbazin Absorption in Chickens, Mallards and Canada Geese.** 2005 *Poultry Science* 84:1491-1494.

<sup>2</sup> Avery, M., K. Keacher, and E. Tillman. **Nicarbazin bait reduces reproduction by pigeons (*Columba livia*).** 2008. *Wildlife Research* 35(1) 80-85.

## Acute Toxicity of Nicarbazin in Birds

The non-toxic nature of nicarbazin has been studied and is well documented in the literature<sup>3</sup>. Following more than 50 years of research, the only consistent effect is the reduction of egg hatchability and production in birds following ingestion of nicarbazin. The phenomenon is a function of dose and time. The literature also reveals that nicarbazin does not bio-accumulate and that reproduction returns to normal again within 7-10 days once withdrawn<sup>4</sup>.

According to the EPA classification system, nicarbazin is considered “practically non-toxic”<sup>5</sup>. The acute toxicology values for nicarbazin in sensitive birds are provided in Table 2.

**Table 2 – Acute Toxicity Values of Sensitive Bird Species to Nicarbazin<sup>6</sup>**

Species	Toxicity Value
Mallard duck	LC <sub>50</sub> <sup>7</sup> = 3680 ppm in total diet
Northern Bobwhite	LC <sub>50</sub> > 5720 ppm in total diet LD <sub>50</sub> <sup>8</sup> > 2250 mg/kg bw

Nicarbazin is not only considered practically non-toxic in birds but also in mammals and other species. For example, the LD<sub>50</sub> in mice and rats is greater than 10,000mg/kg. Put in perspective, nicarbazin has similar acute toxicity values as table sugar. Overall, the published information for nicarbazin reflects an extremely non-toxic compound with no toxic effects when fed to mammals or other animals. Table 3 provides a summary of the acute and maximum tolerated dose data in other species<sup>9</sup>.

**Table 3 – Acute Toxicity of Nicarbazin**

Species	Single Dose LD <sub>50</sub> mg/kg	Single Dose LD <sub>50</sub> ppm	Maximum Tolerated Dose in Diet
Mouse	>10,000	>80,000	
Rat	>10,000	>80,000	1600 ppm for 177 days
Dog	>5,000	>40,000	5g/kg/day for 165 days (40,000 ppm)
Pig			10,000 ppm in diet for 49 days
Sheep			4,000 ppm in diet for 1 yr.
Calf			1600 ppm in milk for 42 days
Guinea Pig	>5,000	>40,000	
Rabbit	>5,000	>40,000	

The data included in the WHO-FAO Joint Expert Committee on Feed Additives (JECFA) established NOEL's for rat and dog 2 yr. studies, rat reproduction and teratology studies at values between 200 mg/kg and 400 mg/kg for the Codex Alimentarius food safety standard. These values translate to 1600 ppm to 3200 ppm in the diet, consistent with the Ott data.

### Summary

DNC, the active component of nicarbazin, circulates in the blood and interferes with hatchability when deposited in the egg. Nicarbazin must be dosed and absorbed in adequate quantity to achieve a contraceptive blood level. DNC alone is poorly absorbed and must be complexed with HDP to be biologically available and effective.

The only consistent effect for nicarbazin is the interference with egg hatchability and production in birds. According to EPA, nicarbazin is classified as “practically non-toxic”, the least toxic classification.

<sup>3</sup> Chapman, H.D. **A Review of the Biological Activity of the Anticoccidial Drug Nicarbazin and its Application for the Control of Coccidiosis in Poultry**. 1993. *Poultry Science Reviews*, v. 5 (4), p 231-243.

<sup>4</sup> Reinoso, V. 2008. **Contraceptive Action of Nicarbazin in White Pekin Ducks** (Master's thesis). Retrieved from <http://etda.libraries.psu.edu/theses/approved/WorldWideIndex/ETD-3193/index.html>

<sup>5</sup> EPA Fact Sheet, Nicarbazin Conditional Registration, Nov 2005.

<sup>6</sup> Wildlife International, Inc., Exton, MD. 2004.

<sup>7</sup> LC<sub>50</sub> (lethal concentration) -- 50% of the birds die within 5 days.

<sup>8</sup> LD<sub>50</sub> (lethal dose) – 50% of the birds die with a single dose.

<sup>9</sup> Ott, W.H., et. al. “**Biological Studies on Nicarbazin a New Anticoccidial Agent**”, *Poultry Science*, 1956, 35, 1355-1367