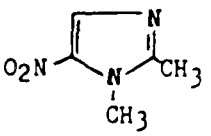
DIMETRIDAZOLE

IDENTITY

Chemical name: 1,2-dimethyl-5-nitroimidazole

Synonyms: Emtryl
Emtrymix
Emtrylvet
Unizole

Structural formula:



Molecular formula: $C_5H_7N_3O_2$

Molecular weight: 141.13

OTHER INFORMATION ON IDENTITY AND PROPERTIES

Pure active ingredient:

Appearance: needles from water

Melting point: 138-139°C

(Windholz, 1983)

RESIDUES IN ANIMALS AND THEIR EVALUATION

CONDITIONS OF USE

General

Dimetridazole is used in turkeys (1) for the prevention and treatment and as an aid in the control of blackhead (histomoniasis, infectious enterohepatitis), (2) for growth promotion, and (3) for improved feed efficiency. The drug is also effective in the prevention and treatment of swine dysentery.

Dosages

Dimetridazole is administered to poultry and swine primarily through feed or water in concentrations normally ranging from 0.01% to 0.06%. Dimetridazole, as the methane sulfonate, may also be administered to swine via injection in a dose that is similar to that delivered through feed or water.

RADIOLABELED RESIDUE DEPLETION STUDIES

Turkeys

Two turkeys weighing approximately 3 kg were administered a single dose of 32 mg/kg (equivalent to a daily dose of 0.05% in drinking water) dimetridazole labeled with 14C in

the 2-position of the ring and the 2-methyl group. The birds were sacrificed 72 hours after treatment and the residue in tissues was determined by both a radiochemical and polarographic method. For the samples analyzed, residue concentrations were below the limit of detection of the assays (polarographic method, <0.05 for muscle, liver and skin, <0.1 for kidney; radiochemical method, <0.03 for liver and <0.05 for kidney). It should be noted that the radiochemical determination for tissues was made on the benzene extract of tissue, not on the whole tissue. (Law, et al., 1962; Law, et. al., 1963)

Swine

Dimetridazole, labeled with 14C in the N-methyl group, was administered to two pigs in a single dose of 29.8 mg/kg or 16.6 mg/kg. The animals were sacrificed 6 or 17 hours after dosing, respectively. Concentrations of total residue in muscle (foreleg), liver, kidney and fat are given in Table I. (Mulcock and Unsworth, 1973a)

Table I. Total Residue in Tissues of Swine Treated With 14C-Labeled Dimetridazole (ppm)

Withdrawal Time	Muscle	Liver	Kidney	Fat
6 hours	8.59	15.40	36.05	3.60
17 hours	0.42	3.00	1.48	*

* not measured

Four pigs weighing 12 to 22 kg were treated with a single dose of approximately 25 mg/kg (actual range 19 to 37 mg/kg) of dimetridazole labeled with 14C in the N-methyl group. Muscle biopsies were taken from three pigs at 24 and 48 hours after treatment and from one pig at 72 hours after treatment. Animals were sacrificed 7 days after administration of labeled dimetridazole and samples of muscle, liver, kidney and fat were analyzed. The mean concentrations of total residue of dimetridazole measured in the biopsies and in the edible tissues at slaughter are given in Table II. (Unsworth, 1972)

Table II. Total Residue in Tissues of Swine Treated With 14C-Labeled Dimetridazole (ppm)

Withdrawal Time (hours)	Biopsy Muscle	Muscle	Liver	Kidney	Fat
24	0.67	---	---	---	---
48	0.27	---	---	---	---
72	0.40	---	---	---	---
168	---	0.32	0.91	0.81	0.37

RESIDUE DEPLETION STUDIES

Chickens

The concentrations of dimetridazole were determined in the edible tissues of chickens dosed at 0.025% or 0.05% through the feed or drinking water. Analyses were conducted with a polarographic method with a limit of detection of 0.1 ppm. Mean residue levels of dimetridazole in tissues at various withdrawal times are given in Table III. (Muggleton, 1963)

Table III. Mean Concentrations of Dimetridazole in Chicken Tissues (ppm)

Tissue	Withdrawal Time (days)								
	0			1			2		
	A	B	C	A	B	C	A	B	C
muscle	2.9	<0.1	0.4	<0.1	<0.1	*	<0.1	<0.1	*
liver	1.7	<0.1	0.5	<0.1	<0.1	*	<0.1	<0.1	*
kidney	0.5	<0.1	0.1	<0.1	<0.1	*	<0.1	<0.1	*
skin	1.8	<0.1	0.1	<0.1	<0.1	*	<0.1	<0.1	*

A = dosed for 6 days in drinking water at 0.05%
B = dosed for 14 days in the feed at 0.025%
C = dosed for 14 days in the feed at 0.05%

* no samples

Turkeys

Turkeys were treated with 0.025%, 0.05%, 0.1% or 0.2% dimetridazole in the feed until they were 24 weeks of age. For the 0.025% and the 0.05% groups, birds were sacrificed at 0, 3, 6, 12, 24 and 48 hours after withdrawal of medicated feed. For the 0.1% and 0.2% groups, the birds were sacrificed at 0, 3, 6, 12, 24, 48, 72 and 96 hours. Tissue samples of breast muscle, liver, kidney, fat and thigh skin were taken at sacrifice. The concentration of dimetridazole in tissues was determined using a polarographic method with a claimed limit of detection of 0.05 ppm. The results are given in Tables IV and V. (Condren, et al., 1963)

Table IV. Concentration of Dimetridazole in Turkeys (ppm)

Tissue	Drug Level(%)	Withdrawal Time (hours) 0	3	6	12	24	48
muscle	0.05	3.44	1.98	0.71	0.92	ND	<.05
	0.025	0.10	0.09	0.08	ND	<.05	ND
liver	0.05	6.67	1.17	2.34	0.10	<.05	ND
	0.025	0.12	<.05	0.12	<.05	<.05	ND
kidney	0.05	0.64	0.11	0.06	0.08	<.05	ND
	0.025	0.15	0.05	<.05	<.05	<.05	ND
fat	0.05	2.27	1.31	0.75	0.89	0.08	<.05
	0.025	0.12	<.05	0.05	<.05	0.05	<.05
skin	0.05	3.28	1.29	1.10	0.78	0.06	ND
	0.025	0.06	0.08	0.12	<.05	<.05	ND

ND = No detectable residue

Table V. Concentration of Dimetridazole in Turkeys (ppm)

Tissue	Drug Level (%)	Withdrawal time (hours) 0	3	6	12	24	48	72	96
muscle	0.1	11.56	5.75	5.24	3.31	0.22	0.08	0.05	0.06
	0.2	12.72	12.40	8.66	0.29	1.04	0.23	*	0.06
liver	0.1	15.20	6.52	6.96	4.75	0.48	<.05	<.05	0.06
	0.2	14.88	14.68	8.50	0.21	1.07	0.24	*	0.16
kidney	0.1	6.80	0.88	1.65	1.42	0.10	<.05	<.05	<.05
	0.2	17.76	12.44	6.75	0.90	0.14	0.14	*	0.08
fat	0.1	7.40	3.41	2.99	1.81	0.10	<.05	0.08	<.05
	0.2	*	0.03	2.69	*	0.69	0.29	*	0.11
skin	0.1	7.40	3.90	3.84	3.12	0.26	0.10	0.07	0.06
	0.2	15.68	6.60	6.67	0.27	0.75	0.22	*	0.10

* Insufficient sample or birds not available at this withdrawal time

Turkeys were given free access to medicated water (0.05%) for 6 days. Samples of tissues were assayed with a polarographic method with a level of sensitivity of 0.1 ppm. The results are given in Table VI. (Law, et al., 1962)

Table VI. Concentration of Dimetridazole (ppm) in Tissues of Turkeys Treated for 6 Days with 0.05% Dimetridazole in Drinking Water

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin
0	0.92	0.68	<0.1	0.38
1	0.04	0.22	<0.1	<0.1
2	<0.1	<0.1	<0.1	<0.1

A group of 20-week old turkeys was treated with 0.08% dimetridazole in the feed (therapeutic dose) for 7 days. Another group of 10-week old turkeys was treated with 0.02% dimetridazole in the feed (prophylactic dose) for 10 weeks. At the end of the dosing period for each group, six birds were sacrificed at each of the following withdrawal times: 0, 1, 2, 3, 5, 7, 10, and 14 days. Muscle, liver, kidney and skin were collected from each bird at the time of sacrifice. Tissue samples were assayed for dimetridazole using a gas chromatographic method with a limit of detection of 2 ppb. The results are presented in Tables VII and VIII. (DHHS, 1986)

Table VII. Dimetridazole in Tissues of Turkeys Treated With 0.08% Dimetridazole in the Feed (ppb)

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin
0	168	9.2	<2	170
1	<2	<2	<2	4.3
3	<2	<2	<2	<2
5	<2	<2	<2	<2

Table VIII. Dimetridazole in Tissues of Turkeys Treated With 0.02% Dimetridazole in the Feed (ppb)

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin
0	125	<2	<2	145
1	<2	<2	<2	2.5*
2	<2	<2	<2	3.7*
3	<2	<2	<2	3.0*
5	<2	<2	<2	2.5*
7	NS	NS	NS	2.6*

NS = not sampled
* samples thought to be contaminated

Swine

Numerous residue depletion studies have been conducted in swine. Many of these, however, report residue levels for parent dimetridazole determined with a dc polarographic assay with a limit of detection of 0.1 ppm. As discussed under the **Metabolism** section that follows, the metabolite 2-hydroxymethyl-1-methyl-5-nitroimidazole (HMMNI) was found to be the major identifiable component of the residue in muscle and kidney of pigs treated with dimetridazole. For this reason, analytical methods capable of monitoring for HMMNI as well as parent dimetridazole in the very low ppb range were developed. Therefore, only residue depletion studies relying on the improved analytical methodologies are noted.

Pigs approaching market weight were medicated with dimetridazole in the drinking water at 0.02% for 5 days. Groups of three pigs were sacrificed at various withdrawal times and samples of tissues were analyzed with a differential pulse polarographic assay with a limit of detection of 2 ppb. The results of this study are presented in Table IX. (Craine and Anderson, 1973a; Craine, et al., 1974)

Table IX. Residues in Tissues of Pigs Medicated With 0.02% Dimetridazole in Drinking Water (ppb)

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin	Fat
0	301	<2	235	123	25
3	<2	*	<2	*	*
5	<2	*	<2	*	*
6	<2	<2	<2	<2	<2
7	<2	*	<2	*	*

* not analyzed

Pigs were medicated with dimetridazole in the feed at 0.24% (approximately 20 times the proposed dosing level) for 14 days. Groups of three pigs were sacrificed at various withdrawal times and samples of tissues were analyzed with the differential pulse polarographic method noted above. The results are summarized in Table X. (Craine and Anderson, 1973b)

Table X. Residues in Tissues of Pigs Medicated With Dimetridazole at a Level of 0.24% in the Feed (ppb)

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin	Fat
0	4119	4	3137	2373	754
1	4	<2	4	12	<2
2	<2	<2	<2	4	<2
3	<2	*	<2	<2	*
4	<2	*	<2	<2	*

* not analyzed

Pigs were medicated with dimetridazole in the feed at 0.0125% for at least 30 days. Groups of three pigs were sacrificed at various withdrawal times and samples of tissues were assayed with the differential pulse polarographic method having a detection limit of 2 ppb. The results of this study are given in Table XI. (Craine and Anderson, 1973c)

Table XI. Residues in Tissues of Pigs Medicated With Dimetridazole at a Level of 0.0125% in Feed (ppb)

Withdrawal Time (days)	Muscle	Liver	Kidney	Skin	Fat
0	261	<2	168	147	53
1	<2	<2	<2	<2	<2
2	<2	<2	<2	<2	<2
3	<2	*	<2	*	*
4	<2	*	<2	*	*
5	<2	*	<2	*	*

* not analyzed

Five female piglets, 2-3 months of age, were medicated with dimetridazole at a level of 0.031% in the feed for 14 days. At 2, 6, 12, 25 and 49 hours post dosing one animal was sacrificed and samples of muscle, liver, kidney, fat and skin were collected. Tissues were analyzed for HMMNI and dimetridazole with an HPLC procedure with electrochemical detection. The method has a claimed limit of detection of 0.5 ppb. The results of this study are summarized in Table XII. (Sved and Carignan, 1987)

Table XII. Residues in Tissues of Piglets Medicated With Dimetridazole at a Level of 0.031% in the Feed (ppb) (ND = not detected)

Withdrawal	Muscle		Liver		Kidney	
Time (hrs)	HMMNI	DMZ	HMMNI	DMZ	HMMNI	DMZ
2	500	20	0.9	ND	92	1.7
6	100	1.3	0.2	0.2	6.7	ND
12	3.2	ND	ND	ND	0.7	ND
25	ND	ND	ND	ND	ND	ND
49	ND	ND	ND	ND	ND	ND

METABOLISM STUDIES

Turkeys

Three days after a single oral dose of labeled dimetridazole containing 14C in the 2-methyl group and the 2-position of the ring to turkeys at 32 mg/kg, an average of 79.4% of the radioactivity was recovered in the urine, 8% in the feces, and 1.2% in the expired air. Approximately 90% of the administered drug, therefore, can be accounted for in the three-day period after dosing. (Law, et al., 1962)

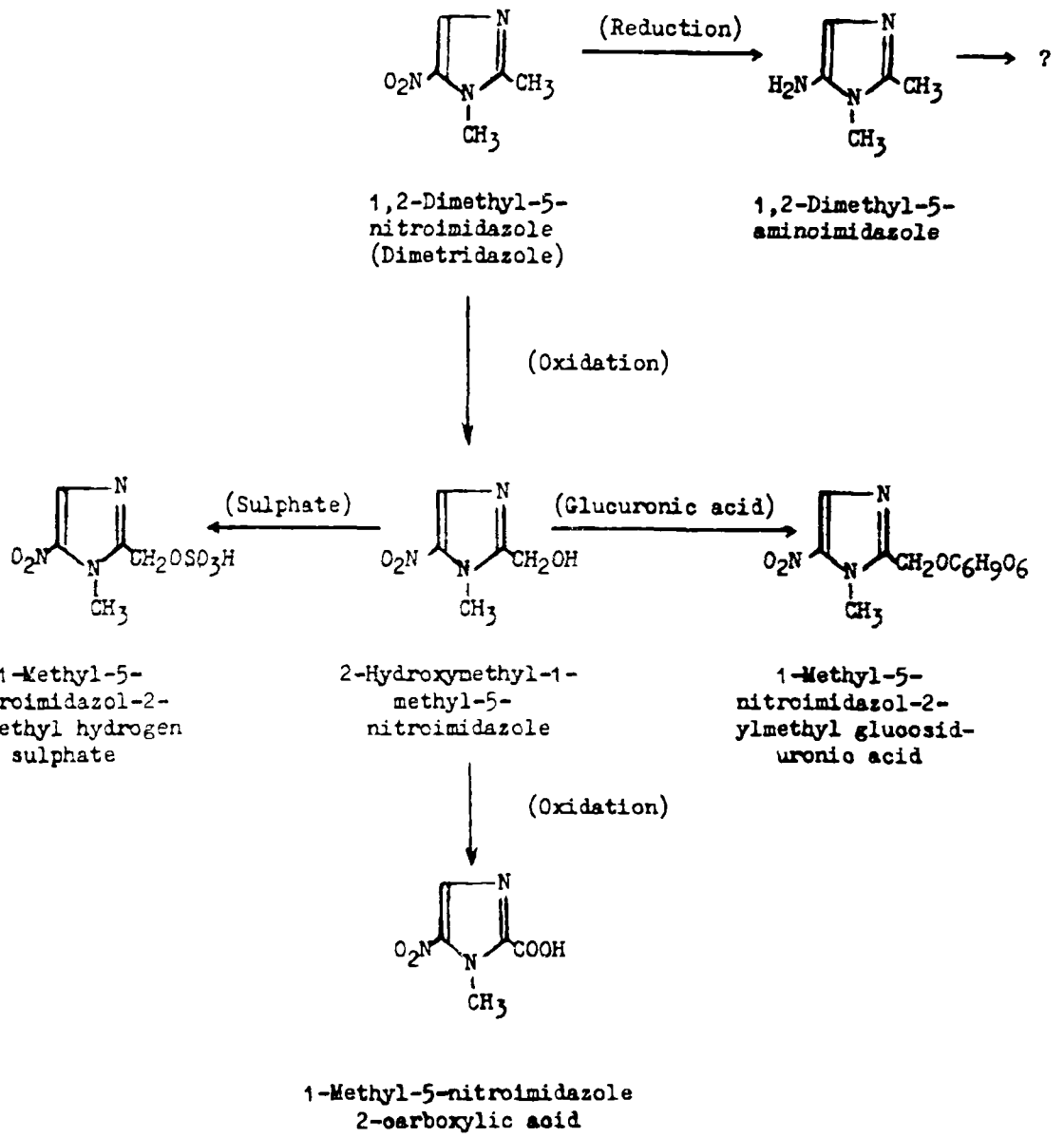
Following a single dose of 100 mg/kg or 300 mg/kg dimetridazole to turkeys, 66.1% and 63% of the dose could be recovered from urine and fecal extracts as determined with polarographic and colorimetric methods (methods that would detect nitro-containing compounds), respectively, over a three-day period. (Law, et al., 1962)

Turkeys were administered a single dose of dimetridazole, labeled as noted above, at a level of 32 mg/kg or unlabeled drug at 100 mg/kg or 300 mg/kg. Examination by ultraviolet light of a paper chromatogram of urine collected at 24 hours post dosing revealed six spots. In addition, a seventh spot was found with autoradiography in a urine sample from the birds treated with labeled drug. Four of the metabolites, comprising a total of 82.8% of the excreted dose, were identified by comparison to standards. Another metabolite, representing 8.8% of the excreted dose, was identified by color reactions as a conjugated glucuronide of a nitroimidazole, presumably HMMNI. The remaining two metabolites, comprising 10.9% of the excreted drug, were shown to be non-nitro containing compounds. One of these two compounds did not absorb uv light and was presumed to be a ring-degraded metabolite, because absorbing uv light is characteristic of ring-intact imidazoles. The metabolites and the percentage of the dose excreted in the urine that they represent are summarized in Table XIII. Most of the excreted drug, therefore, is metabolized via a pathway involving oxidation at the 2-methyl group. The proposed pathway for the metabolism of dimetridazole in turkeys is given in Figure 1. (Law, et al., 1962)

Table XIII. Metabolites Detected in Urine of Treated Turkeys and Their Percentages

Metabolite	% of dose excreted
dimetridazole	3.2
2-hydroxymethyl-1-methyl-5-nitroimidazole (HMMNI)	9.4
1-methyl-5-nitroimidazole-2-carboxylic acid (MNICA)	25.8
HMMNI sulfate	44.4
HMMNI glucuronide	8.8
unidentified non-nitro containing compound (uv sens)	6.2
unidentified non-nitro containing compound	4.7

Figure 1. Metabolism of Dimetridazole in Turkeys



Swine

Dimetridazole, labeled with 14C in the N-methyl group, was administered in a single oral dose to four pigs at a rate of 19-37 mg/kg. The pigs were maintained in enclosed cages permitting the collection of all labeled products. Mean recovery of radioactivity from the animals up to seven days post medication was determined to be 76.2%, broken down as follows: urine, 39.2%; feces, 33.1%; exhaled air, 3.9%. Chromatographic examination of the urine from dosed pigs collected during the first eight hours after dosing revealed the presence of parent dimetridazole at 0.2% of the urinary activity, HMMNI at 0.7% of the urinary activity and MNICA at 18.7% of the urinary activity. Conjugation of metabolites in swine was not observed to be a major pathway. Much of the radioactivity in urine was found to be associated with an abundance of isotopically labeled compounds, presumed to include purine and pyrimidine bases, proteins, fatty acids, choline, and lower molecular weight compounds such as amino acids and other simple naturally occurring molecules. (Mulcock and Unsworth, 1973a and 1973b)

Dimetridazole, labeled with 14C in the N-methyl group, was administered orally to a pig in a single dose of 29.8 mg/kg. The pig was sacrificed 6 hours after dosing. Samples of tissues were examined by several techniques, including paper and thin-layer chromatography, electrophoresis, and automatic amino acid analysis, for isotopically labeled products. The amounts of dimetridazole, HMMNI and MNICA in tissues are given in Table XIV. (Mulcock and Unsworth, 1973a)

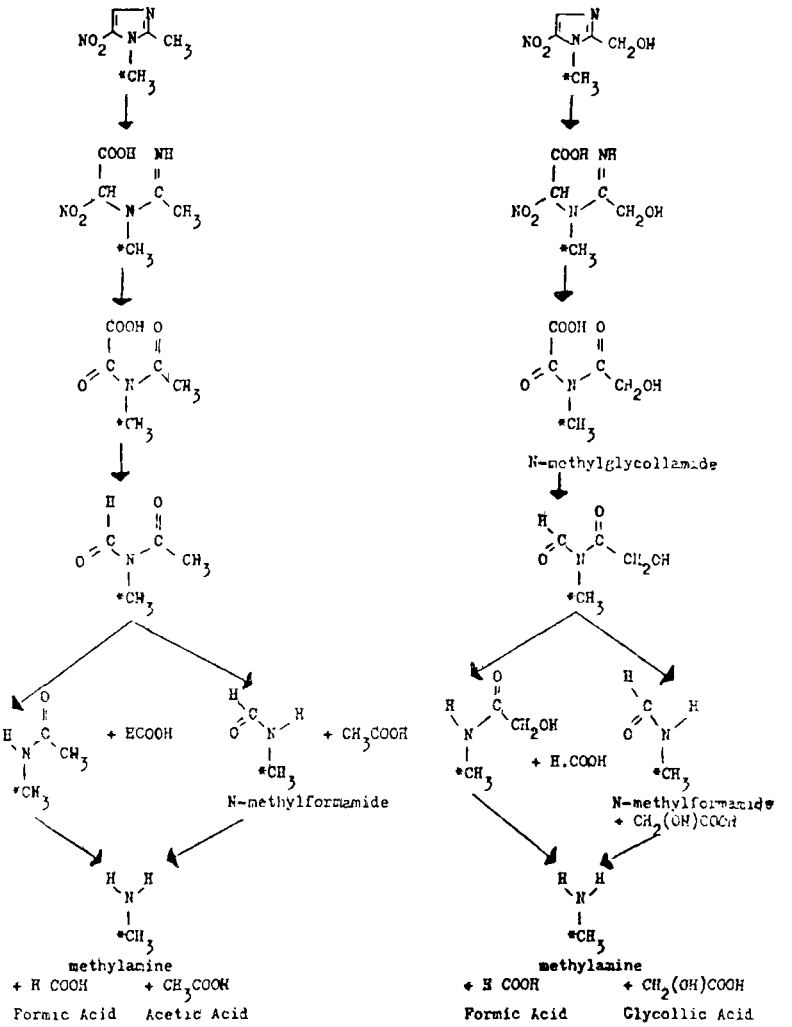
Table XIV. Tissue Residues of Metabolites in Swine Treated with 14C-Dimetridazole (6 hours post dosing)

	Amount of Compound Present					
	As % of Total 14C in specified tissue			In ppm		
Compound	Muscle	Kidney	Liver	Muscle	Kidney	Liver
dimetridazole	0.5	0.5	0.07	0.04	0.18	0.01
HMMNI	40.2	25.7	0.5	3.56	10.31	0.09
MNICA	13.8	3.6	ND	1.33	1.55	ND
Total	54.5	29.8	0.57	4.93	12.04	0.10

In a similar experiment, seventeen hours after dosing a pig with labeled dimetridazole at 16.6 mg/kg the only metabolite detectable was HMMNI in muscle. This metabolite represented about 10% of the tissue radioactivity or 0.04 ppm. (Mulcock and Unsworth, 1973a)

Based on the above work, the metabolism of dimetridazole in swine is believed to include: oxidation at the 2-methyl group to give the hydroxymethyl and carboxylic acid metabolites (see Figure 1); reduction at the 5-nitro group to give the 5-amino compound, which would undergo rapid degradation; and fission of the nitroimidazole ring (Figure 2). (Muggleton and Unsworth, 1974)

Figure 2. Metabolism of Dimetridazole via Fission of the Nitroimidazole Ring



Rats

Dimetridazole, labeled with 14C in the N-methyl group, was administered in a single oral dose to Sprague-Dawley rats at a rate of 25 mg/kg. The results of this study indicate qualitative similarity with those of the study in swine. That is, evidence has been provided for metabolism via oxidation at the 2-methyl group and degradation of the nitroimidazole ring. (Heijbroek, 1976)

METHODS OF RESIDUE ANALYSIS

The early methods of analysis for residues of dimetridazole in tissues of swine and turkeys relied on polarography. These assays had a level of sensitivity in the range of 0.05 to 0.1 ppm. The methods were designed for parent dimetridazole but would likely determine any nitroimidazoles that were extracted. Thus, although HMMNI would likely be measured by those early polarographic methods, the amount of HMMNI extracted would probably be low because of its water solubility. (Kane, 1961; Parnell, 1973)

A gas chromatographic procedure was also developed for parent dimetridazole in turkey tissues with a sensitivity of 2 ppb. (DHHS, 1986)

The finding that HMMNI was a major metabolite both in turkey and swine led to the development of assays that could measure the hydroxy metabolite. Improved assay methodology involving differential pulse polarography brought the limit of detection down to 1 to 2 ppb in swine tissue. The methods probably measure all nitroimidazole residues present in the extract. (Craine, et al., 1974; Ohst, 1987)

Recently, a HPLC procedure with electrochemical detection has been developed. The method has been applied to the simultaneous determination of both dimetridazole and HMMNI in swine tissue to concentrations of about 0.5 ppb. (Sved and Carignan, 1987)

APPRAISAL

The use of dimetridazole at permitted concentrations in the feed and drinking water of poultry and swine produces residues that deplete below detectable levels at 2 to 3 days postdosing. The most sensitive assays used in the depletion studies monitor for dimetridazole and/or HMMNI in the 0.5 to 2 ppb range.

The radiotracer work that was done in swine, however, shows that the total residue of dimetridazole in swine at 7 days postdosing ranges from 320 ppb in muscle to 910 ppb in liver (Table II). Unfortunately, because all residue values reported for dimetridazole or HMMNI are below the limit of detection at times beyond 2 days, it is impossible to establish any relationship between the total residue and a compound (or compounds) measured with a chemical assay.

The metabolism work that has been done supports the proposed pathways. In particular, oxidation at the 2-methyl group is the main route to ring intact metabolites and ring scission leads to fragmentation. It is possible that reduction of the 5-nitro group takes place, which in turn would lead to decomposition of the ring as well. Furthermore, it is likely that some radioactivity becomes incorporated into natural components via fragments from the ring scission of either dimetridazole or of the 2-methyl-oxidized products.

Although not discussed in the reports provided on dimetridazole, it is possible, based on work done for other nitroimidazoles, metronidazole, for example, that acetamide, a known carcinogen (IARC, 1974), can result from the fragmentation of dimetridazole. Moreover, the possibility of the formation of "bound" residues, residues that result from the reaction of a reactive metabolite or metabolic intermediate with natural tissue components, such as protein or nucleic acid, must be considered in view of the work done for ronidazole. At this time the total residue of dimetridazole in tissues of poultry and swine has not been fully characterized.

REFERENCES

Condren, H.B., Davies, R.E., Deyoe, C.W., Zavala, M.A., Creger, C.R. and Couch, J.R. (1963). Studies on the effect of 1,2-dimethyl-5-nitroimidazole on growth and reproduction in turkeys and its residual concentration in tissue. Poultry Science, 42, 585-594.

Craine, E.M. and Anderson, M.D. (1973a). Nitroimidazole residues in tissues of swine medicated with dimetridazole given in drinking water. Report EMC 73:32 from Hess and Clark, Ashland, Ohio. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Craine, E.M. and Anderson, M.D. (1973b). Nitroimidazole residues in tissues of swine fed a protein supplement containing 0.24% dimetridazole. Report EMC 73:50 from Hess and Clark, Ashland, Ohio. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Craine, E.M. and Anderson, M.D. (1973c). Nitroimidazole residues in tissues of swine medicated with 0.0125% dimetridazole in the feed. Report EMC 73:48 from Hess and Clark, Ashland, Ohio. Submitted to FAO by Rhone-Poulenc Sante, Paris

Craine, E.M., Parnell, M.J., and Stone, L.R. (1974). A method for analysis of swine tissue for the primary metabolite of dimetridazole at the 2 ppb level. J. Agric. Food Chem., 22, 877-881.

Department of Health and Human Services (1986). Dimetridazole; Opportunity for Hearing; Notice. Federal Register, 51, 45244-45262.

Heijbroek, W.M.H. (1976). Dimetridazole excretion and metabolism studies in rats. Report RES/2498 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

International Agency for Research on Cancer (1974). Some antithyroid and related substances, nitrofurans and industrial chemicals. WHO, Lyon, 7, 197-202.

Kane, P.O. (1961). Polarographic methods for the determination of two anti-protozoal nitroimidazole derivatives in materials of biological and non-biological origin. J. Polarogr. Soc., 8, 73-78.

Law, G.L., Mansfield, G.P., Muggleton, D.F. and Parnell, E.W. (1962). Dimetridazole (8595 R.P.): absorption, excretion and metabolism in turkeys. Report A.P.C.D./131 Biochem/246 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Law, G.L., Mansfield, G.P., Muggleton, D.F. and Parnell, E.W. (1963). Dimetridazole: absorption, excretion and metabolism in turkeys. Nature, 197, 1024-1025.

Muggleton, D.F. (1963). Dimetridazole residues in chicken tissues after oral administration in prophylactic and therapeutic amounts. Report A.P.C.D./136 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Muggleton, D.F. and Unsworth, J.B. (1974). Dimetridazole studies with the 14C-labelled compound in turkeys and pigs; a review. Report RG/2074 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Mulcock, P.A. and Unsworth, J.B. (1973a). Dimetridazole metabolism studies in pigs. Report RG/1612 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Mulcock, P.A. and Unsworth, J.B. (1973b). Dimetridazole excretion studies in pigs. Report RG/1613 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Ohst, E. (1987). Development of a method for detecting nitroimidazole residues in pig muscle. Report No. 1186. Submitted to FAO by BASF Aktiengesellschaft, Ludwigshafen.

Parnell, M.J. (1973). Determination of dimetridazole in pig tissue I. Method. Pestic. Sci., 4, 643-646.

Sved, S. and Carignan, G. (1987). The kinetics of elimination of dimetridazole and its hydroxylated metabolite in food animals. Presented at: AOAC Spring Workshop, Ottawa, Canada.

Unsworth, J.B. (1972). Dimetridazole absorption and excretion studies in the pig. Report RG/1502 from May and Baker Ltd., Dagenham, Essex. Submitted to FAO by Rhone-Poulenc Sante, Paris.

Windholz, M. ed. (1983). The Merck Index 10th Edition. Rahway, N.J., Merck and Co.