UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 10 1994

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Karen R. Blundell
Senior Registration Specialist
BASF Corporation
P.O. Box 13528
Research Triangle Park, NC 27709-3528

SUBJECT: Review of nature of the residue in goats for reregistration of sodium acifluorfen, chemical 114402

Dear Ms. Blundell:

We have reviewed the residue chemistry data you have submitted in support of the reregistration of sodium acifluorfen. Our conclusions are described below.

GDLN 171-4(b) Nature of the residue - livestock MRID 428156-01

These data, MRID 428156-01, were reviewed and are considered acceptable. Conclusions on the qualitative nature of the sodium acifluorfen residue in ruminants are deferred pending submission of the goat metabolism study being conducted with a radiolabelled nitrophenyl ring, due January 25, 1995. A copy of our review is enclosed.

If you have any questions regarding this letter, please call the Chemical Review Manager, Tom Luminello, of the Accelerated Reregistration Branch at (703) 308-8075.

Sincerely yours,

Kathy Davis

Kathy Davis, Section Chief
Reregistration Section II
Accelerated Reregistration Branch
Special Review and
Reregistration Division

Enclosure

cc: Joanne Miller, PM-23
Leung Cheng, HED

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 12 1994

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Sodium Acifluorfen. Case No. 2605. Nature of Residue in Goats. MRID No. 42815601. CBRS No. 12130. DP Barcode: D192655.

FROM: Leung Cheng, Chemist
Special Review Section II
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

THROUGH: Andrew R. Rathman, Section Head
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

TO: Thomas Luminello, Jr, CRM 52
Accelerated Reregistration Branch
Special Review/Reregistration Division (7508W)

Attached is a review of a goat metabolism study for sodium acifluorfen submitted by the registrant for reregistration. This information was reviewed by Dynamac Corporation under the supervision of CBRS, HED. The data assessment has undergone secondary review in the branch and has been revised to reflect branch policies.

The submitted goat metabolism study in which the chlorophenyl ring is radiolabeled with carbon-14 is adequate. The registrant has also committed to conduct a similar study in which the nitrophenyl ring is labeled with carbon-14. The due date for this study was revised to early 1994 (Greybeard meeting minutes). Thus, conclusions on the qualitative nature of the residue in ruminants are deferred pending review of the second study.

If you need additional information, please advise.

Attachment: Dynamac review of metabolism of sodium acifluorfen in goats
cc(without Attachment):RF
cc(with Attachment):Circ, SF, List B File, Cheng, Dynamac
RDI:ARRathman:5/10/94:MSMetzger:5/10/94:EZager:5/11/94
7509C:CBRS:LCheng:CM#2:RM804D:5/11/94:03:a\ACIFLUORFEN\GOAT1.DYN

DYNAMAC
CORPORATION
Environmental Services

Final Report

SODIUM ACIFLUORFEN
Shaughnessy No. 114402
(DP Barcode D192655;
CBRS No. 12130; Case No. 2605)

TASK 4
Registrant's Response to Residue Chemistry Data Requirements

November 1, 1993

Contract No. 68-D2-0053

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

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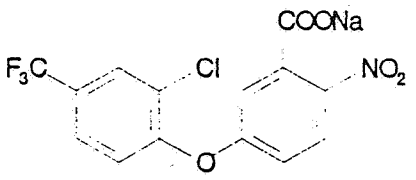
SODIUM ACIFLUORFEN



Shaughnessy No. 114402; Case 2605

(CBRS No. 12130; DP Barcode D192655)

Task 4

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

In response to the Sodium Acifluorfen Phase 4 Reviews (S. Funk, 2/14/91), BASF Corporation submitted a study (1993; MRID 42815601) pertaining to the metabolism of sodium acifluorfen in lactating goats. These data are reviewed here for adequacy in fulfilling the outstanding data requirements. The Conclusions and Recommendations stated in this document pertain only to ruminant metabolism; all other data requirements specified in the Phase 4 Reviews are not addressed herein.

The qualitative nature of sodium acifluorfen residues in plants is not adequately understood. A new soybean metabolism study is required. Additional data to upgrade the rice metabolism study are required and a new peanuts study is underway (J. Abbotts, 11/3/93, CBRS No. 12380, DP Barcode D194099). In addition, data pertaining to the qualitative nature of the residue in hens are currently under review (DP Barcode D192899).

Tolerances for residues of sodium acifluorfen are currently expressed as the combined residues of the sodium salt of acifluorfen [sodium 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid] and its metabolites (the corresponding acid, methyl ester, and amino analogs) in/on plant and animal commodities [40 CFR §180.383]. No Codex MRLs have been established for sodium acifluorfen; therefore, there are no questions with respect to compatibility with the U.S. tolerances.

Adequate methodology is available for the enforcement of tolerances for sodium acifluorfen and its amine and methyl ester metabolites in/on soybeans, milk, and beef liver. A GC/electron capture detection (ECD) method and a GC/MS method are listed in Pesticide Analytical Manual (PAM) Vol. II as Methods I and A, respectively (Pesticide Reg. Sec. 180.383). It should be noted that in Methods I and A, diazomethane is used to derivatize acifluorfen residues to the corresponding methyl esters prior to GC/ECD analysis.

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CONCLUSIONS AND RECOMMENDATIONS

Qualitative Nature of the Residue in Lactating Goats

1. Conclusions on the qualitative nature of the sodium acifluorfen residue in ruminants are deferred pending the submission of a goat study in which the radiolabel is introduced in the nitrophenyl ring.

2. The study indicates that following dosing of a lactating goat with uniformly chlorophenyl ring labeled [^{14}C]sodium acifluorfen at 10.1 ppm/day in the diet (150x the maximum theoretical dietary burden) for four consecutive days, the levels of radioactive residues reached maximums of 0.0078 ppm in milk, 0.0138 ppm in muscle, 0.0147 ppm in fat, 0.353 ppm in liver, and 0.396 ppm in kidney. The registrant presented data indicating that ca. 82% of the administered dose was excreted in the urine and feces.

3. The following levels of radioactivity were successfully characterized/identified in the milk and tissues: milk (94.8% of TRR), fat (94.7% of TRR), kidney (93.7% of TRR), liver (80.4% of TRR), and muscle (79.3% of TRR). Acifluorfen was a minor metabolite in milk and all tissues (1.0-5.2% of TRR). The major metabolite was acifluorfen amino which accounted for ca. 15% of TRR in milk, 52% of TRR in fat, 65% of TRR in kidney, 41% of TRR in liver, and 33% of TRR in muscle. Acifluorfen amino glucuronide accounted for ca. 16% of the TRR in milk, 6% in fat, 10% in kidney, 24% in liver, and 19% in muscle. Acifluorfen acetamide was a major metabolite in milk (ca. 17% of TRR) but a minor metabolite in fat (4% of TRR), kidney (8% of TRR), liver (4% of TRR), and muscle (3% of TRR). Acifluorfen amino methyl ester was identified in milk (ca. 3% of TRR), fat (5% of TRR), and muscle (1% of TRR).

4. Based on the evidence presented, the registrant proposed that sodium acifluorfen is metabolized by reduction of the nitro group to form acifluorfen amino, which is conjugated or acylated to produce acifluorfen amino glucuronide or acifluorfen acetamide, respectively. Methylation of the carboxy moiety of acifluorfen amino metabolite also takes place to produce acifluorfen amino methyl ester. There was no evidence of any ring cleavage of acifluorfen in goats.

5. The requirement for the radiovalidation of the enforcement analytical method(s) is reserved until the HED Metabolism Committee determines the residues to be regulated.

The molecular structures of sodium acifluorfen and its metabolites that were identified in goat matrices are presented in Table 1.

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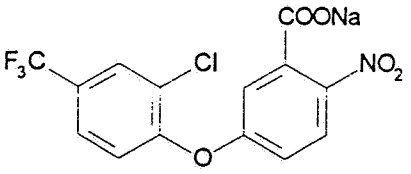
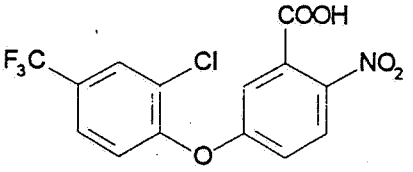
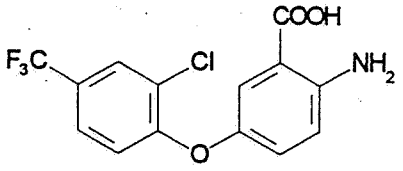
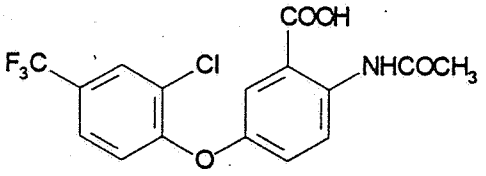
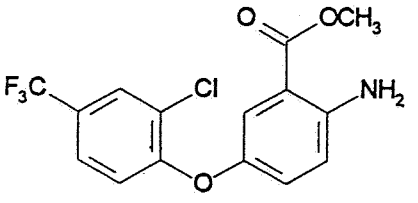
Table 1. Sodium acifluorfen and its metabolites in a lactating goat (MRID 42815601).

Code	Chemical Name Structure	Substrate Common Name
I.	Sodium 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate	
		**Sodium acifluorfen**
II.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-nitrobenzoic acid	
		goat milk, fat, kidney, liver, and muscle **Acifluorfen**
III.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-aminobenzoic acid	
		goat milk, fat, kidney, liver, and muscle **Acifluorfen amino**
IV.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-acetamidobenzoic acid	
		goat milk, fat, kidney, liver, and muscle **Acifluorfen acetamide**
V.	Methyl 5-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-aminobenzoate	
		goat milk, fat, and muscle **Acifluorfen amino methyl ester**

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DETAILED CONSIDERATIONS

Qualitative Nature of the Residue in Lactating Goats

BASF Corporation submitted data (1993; MRID 42815601) depicting metabolism of uniformly [^{14}C] chlorophenyl ring-labeled sodium acifluorfen in a lactating goat. The biological and analytical phases of the study were conducted by Battelle (Columbus, OH). A test goat and a control goat were used. The test goat was orally dosed once a day for four consecutive days with 19.7 mg of [^{14}C]sodium acifluorfen, prepared by neutralizing uniformly chlorophenyl ring-labeled [^{14}C]acifluorfen (radiochemical purity 95.3%; specific activity 18.03 mCi/mmole), with sodium hydroxide and diluting with technical grade sodium acifluorfen to give a final specific activity of 8.67 mCi/mmole (22.6 μCi/mg or 50172 dpm/μg). The test substance was prepared in deionized water and transferred into gelatin capsules containing feed which were then placed inside Torpac No. 12 capsules containing feed. The control capsules were prepared in the same manner, except that no test substance was used. The daily dose was formulated in two separate capsules and both capsules were administered within five minutes of each other using a balling gun. The dose of [^{14}C]sodium acifluorfen used in the study was equivalent to 10.1 ppm at a feed consumption of 1.95 kg/goat/day. Based on a diet consisting of 10% soybean soapstock, 25% peanut meal (85% dry matter), 25% rice grain (88% dry matter), and 50% alfalfa forage, with tolerances of 0.1 ppm for peanuts, rice, and soybeans, and 0 ppm for alfalfa, the theoretical maximum dietary burden of sodium acifluorfen is estimated to be 0.068 ppm. Therefore, the dosing level of 10.1 ppm is ca. 150x the maximum dietary burden.

During the study, the animals were fed a base diet consisting of Rumilab Chow supplemented with alfalfa cubes and hay; water was provided *ad libitum*. The registrant submitted calculations deriving the daily dose of sodium acifluorfen as well as information pertaining to feed consumption, milk production, urine and feces, and general health of the test animals. Urine, feces and cage washings were collected prior to dosing and once daily from the day of treatment. Milk was collected twice daily and the two collections/day were pooled. The goats were sacrificed ca. 22 hours following the final dose. Blood, muscle, intestine and intestine contents, liver, kidney, fat, bile, rumen, rumen contents, stomach, and bladder contents were collected at the time of sacrifice. All samples were frozen immediately after collection and stored frozen at -20 C until analysis.

Total radioactive residues (TRR)

Aliquots of milk samples were analyzed in triplicate directly by liquid scintillation spectrometry (LSS). Samples of liver, kidney, muscle, and fat tissues were cut into small pieces, mixed, and subsamples were analyzed by LSS following combustion. The reported limits of detection (LOD) were: 0.0054 ppm (muscle), 0.0060 ppm (milk), 0.0062 ppm (fat), 0.0064 ppm (kidney), and 0.0102 ppm (liver). The radioactivity in control samples was not reported. The registrant provided sample calculations and raw data. The TRR in milk and tissues, expressed as ppm [^{14}C]sodium acifluorfen equivalents, is presented in Table 2.

Table 2. Total radioactive residues (TRR) in milk and tissues from a lactating goat orally dosed with [^{14}C]sodium acifluorfen for four consecutive days at 150x.

Matrix	TRR, ppm (sodium acifluorfen equivalents) [a]
Milk, Day 1	<0.0060
Milk, Day 2	0.0074
Milk, Day 3	0.0075
Milk, Day 4	0.0078
Fat	0.0147
Kidney	0.3960
Liver	0.3530
Muscle	0.0138

[a] TRR from bulk samples.

The registrant presented data from two TRR determinations; an initial TRR from a small sample of each tissue and a bulk TRR from a representative sample of the matrices used for the extraction and analysis procedures. Both TRR determinations were made by combustion and were comparable; therefore, only the TRR from bulk samples are included in this review. The TRR data indicate that radioactive residues were found in the milk and all tissues of the test goat. ^{14}C-Residues reached a maximum of 0.0078 ppm in milk during the four day test period. The radioactivity was relatively low in muscle (0.0138 ppm) and fat (0.0147 ppm) and was higher in liver (0.353 ppm) and kidney (0.396 ppm). The registrant also presented data indicating that 82.4% of the administered radioactivity was excreted in the urine and feces.

Extraction of ^{14}C-residues

The registrant provided descriptions and flow charts of the fractionation schemes used in the study. During each step of the extraction and partitioning procedures, aliquots were analyzed for radioactivity by LSS or combustion/LSS. Subsamples of goat milk and tissues were extracted as described below.

Fat, kidney, liver, and muscle: Subsamples of fat, kidney, liver, and muscle were blended three times in acetonitrile (ACN):water (9:1; v:v) and filtered. The three ACN:water extracts were combined, concentrated, and analyzed by HPLC. The non-extractable fraction of fat tissue was extracted twice with hexane, and the hexane extracts were pooled and concentrated. The remaining non-extractable fraction of fat and the non-extractable fractions of kidney, liver, and muscle were dried and analyzed by combustion/LSS.

Milk: A subsample of day-4 milk was blended three times with ACN and filtered. The supernatant fractions were pooled, concentrated, and analyzed by HPLC. The non-extractable fraction was dried and analyzed by combustion/LSS.

The registrant noted that precipitates formed during the concentration of the ACN extract of milk and ACN:water extracts of kidney, liver, muscle, and fat. This precipitate was not analyzed; therefore, no information on levels of radioactivity in the precipitates was provided.

The registrant evaluated the suitability of the extraction and analytical procedures by studying a sample of liver tissue from the control goat fortified with [^{14}C]sodium acifluorfen. Approximately

93% of the added radioactivity was recovered in the ACN:water extract and ca. 94% of the radioactivity was recovered by HPLC analysis, indicating that the test substance was stable through the extraction and analysis.

Characterization and identification of residues

The ACN extracts of milk and goat tissues were analyzed by reversed-phase HPLC using a Partisphere C-18 column with a mobile phase gradient of 0.25% glacial acetic acid in water and 0.25% glacial acetic acid in ACN changing from 80:20 to 5:95 (v:v) over 45 minutes in a series of step and linear gradients. Non-labeled reference compounds and radioactive metabolites in the HPLC fractions were detected by UV (254 nm) and by a radioflow analyzer, respectively. Radioactive peaks from the tissue extracts were identified by cochromatography or comparison of retention with those of the following reference standards: acifluorfen, acifluorfen amino, acifluorfen acetamide, acifluorfen amino methyl ester, acifluorfen methyl ester, descarboxy acifluorfen, desnitro acifluorfen, and acetamide acifluorfen methyl ester.

The metabolites identified by HPLC were confirmed by cochromatography with reference standards on 2-D TLC using silica gel 60 F_{254} coated plates and a solvent system of hexane:ethyl acetate:glacial acetic acid (10:4:1; v:v:v) in one direction and methylene chloride:hexane (5:1; v:v) in the other. The reference standards were visualized with a hand held shortwave UV lamp and the radioactive areas were detected by a radioanalytical imaging system.

Acid/base hydrolyses of extracts: One metabolite, eluting at 26.0-27.5 minutes in HPLC chromatograms of milk, fat, kidney, liver, and muscle ACN or ACN:water extracts, did not cochromatograph with any of the reference standards. In bile, this metabolite was found at high levels (78.2% TRR, 1.69 ppm). To further characterize this component, subsamples of the ACN:water extract from bile, kidney, and liver were incubated with 1 N hydrochloric acid at 100 C. After 30 minutes, the hydrolysate was neutralized with 6 N sodium hydroxide and centrifuged. Additional subsamples of the ACN:water extracts of bile, kidney, and liver were incubated with 0.5 N sodium hydroxide at 100 C. After 1 hour, the dry residue was dissolved in 250 μL of buffer, neutralized with 6 N hydrochloric acid or with 6 N sodium hydroxide (depending upon the pH) and centrifuged. The acid and base hydrolysates were analyzed by HPLC and 2-D TLC, which indicated the presence of acifluorfen amino. To confirm the identity of the 26.0-27.5 minute peak, it was isolated and concentrated from bile by preparative solid-phase extraction. The integrity of the metabolite fraction was verified by HPLC and the fraction was then analyzed by liquid chromatography/thermospray mass spectroscopy (LC/TSMS) operating in the positive ion mode. Representative sample chromatograms and scans were submitted. The registrant then concluded that the unknown metabolite eluting at 26.0-27.5 was acifluorfen amino glucuronide. The presence of acifluorfen amino glucuronide in liver and kidney was confirmed by cochromatography of the metabolite isolated from bile.

The distribution of radioactivity in goat milk and tissues is presented in Table 3 and a summary of the characterized and identified metabolites is presented in Table 4.

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Table 3. Distribution of TRR in the milk and tissues of a lactating goat dosed with [^{14}C]sodium acifluorfen at 150x for four consecutive days.

Fraction	% TRR	ppm	Characterization/Identification [a,b]
Milk (0.007 ppm)			
ACN	94.8	0.0069	Acifluorfen (5.2% TRR, 0.0004 ppm), acifluorfen amino glucuronide (15.9% TRR, 0.0011 ppm), acifluorfen acetamide (16.9% TRR, 0.0012 ppm), acifluorfen amino (14.7% TRR, 0.001 ppm), and acifluorfen amino methyl ester (2.6% TRR, 0.0002 ppm) were identified. Unknown metabolites eluting at retention times of 3.5 (2.2% TRR, 0.0002 ppm), 4.5 (3.3% TRR, 0.0003 ppm), 9.0-10.0 (1.9% TRR, 0.0002 ppm), 19.5-20.5 (1.9% TRR, 0.0002 ppm), 20.5 (2.3% TRR, 0.0002 ppm), 21.5-22.5 (3.7% TRR, 0.0003 ppm), and 46.0 (1.6% TRR, 0.0001 ppm) minutes, and others (>21 peaks each <2% TRR, 0.0001 ppm; collectively 22.6% TRR, 0.0015 ppm) were resolved.
Non-extractable	18.8	0.0013	N/A
Goat fat (0.0147 ppm)			
ACN:water	90.4	0.0136	Acifluorfen (1.0% TRR, 0.0002 ppm), acifluorfen amino glucuronide (5.5% TRR, 0.0009 ppm), acifluorfen acetamide (3.7% TRR, 0.0006 ppm), acifluorfen amino (51.7% TRR, 0.0078 ppm), and acifluorfen amino methyl ester (4.7% TRR, 0.0007 ppm) were identified. Unknown metabolites eluting at retention times of 3.5 (2.2% TRR, 0.0003 ppm), 7.0-7.5 (1.1% TRR, 0.0002 ppm), 30.5-31.0 (1.4% TRR, 0.0002 ppm), 39.0-39.5 (1.6% TRR, 0.0003 ppm), 41.0 (1.4% TRR, 0.0002 ppm), 46.0-46.5 (1.5% TRR, 0.0002 ppm), and 58.5-59.5 (0.9% TRR, 0.0001 ppm) minutes, and others (>21 peaks each <2% TRR, <0.0003 ppm; collectively 13.7% TRR, 0.0018 ppm) were resolved.
Hexane	3.3	0.0005	N/A
Non-extractable	17.3	0.0026	N/A
Goat kidney (0.396 ppm)			
ACN:water	93.7	0.371	Acifluorfen (1.9% TRR, 0.0075 ppm), acifluorfen amino glucuronide (10.3% TRR, 0.0409 ppm), acifluorfen acetamide (8.1% TRR, 0.0319 ppm), and acifluorfen amino (64.5% TRR, 0.2555 ppm) were identified. An unknown metabolite eluting at a retention time of 31.0 minutes (1.6% TRR, 0.0064 ppm) and other unknown metabolites (26 peaks each <2% TRR, <0.008 ppm; collectively 7.3% TRR, 0.0288 ppm) were resolved.
Non-extractable	11.3	0.0446	N/A

(continued; footnotes follow)

Table 3 *(continued)*.

Fraction	% TRR	ppm	Characterization/Identification [a,b]
Goat liver (0.353 ppm)			
ACN:water	80.4	0.2838	Acifluorfen (1.7% TRR, 0.0061 ppm), acifluorfen amino glucuronide (24.1% TRR, 0.085 ppm), acifluorfen acetamide (3.5% TRR, 0.0125 ppm), and acifluorfen amino (41.2% TRR, 0.1453 ppm) were identified. Other unknown metabolites (29 peaks each <2% TRR, <0.0071 ppm; collectively 9.9% TRR, 0.0349 ppm) were resolved.
Non-extractable	15.0	0.0528	N/A
Goat muscle (0.0138 ppm)			
ACN:water	79.3	0.0114	Acifluorfen (3.2% TRR, 0.0005 ppm), acifluorfen amino glucuronide (18.7% TRR, 0.0027 ppm), acifluorfen acetamide (3.1% TRR, 0.0005 ppm), acifluorfen amino (33.2% TRR, 0.0047 ppm), and methyl ester amino acifluorfen (1.3% TRR, 0.0002 ppm) were identified. An unknown metabolite eluting at a retention time of 3.5 minutes (2.5% TRR, 0.0004 ppm) and other unknown metabolites (>27 peaks, each <2% TRR, <0.0003 ppm; collectively 17.3% TRR, 0.0024 ppm) were resolved.
Non-extractable	22.8	0.0032	N/A

[a] Metabolites were identified by HPLC and confirmed by 2-D TLC.

[b] Acifluorfen amino glucuronide was identified by acid/base hydrolysis of kidney, liver, and bile extracts followed by HPLC/2-D TLC, and by LC/TSMS analysis of the metabolite isolated from bile.

Table 4. Summary of identification/characterization of [^{14}C]sodium acifluorfen residues from a lactating goat.

Metabolite	Milk		Fat		Kidney		Liver		Muscle	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified										
Acifluorfen	5.2	0.0004	1.0	0.0002	1.9	0.0075	1.7	0.0061	3.2	0.0005
Acifluorfen amino glucuronide	15.9	0.0011	5.5	0.0009	10.3	0.0409	24.1	0.0850	18.7	0.0027
Acifluorfen acetamide	16.9	0.0012	3.7	0.0006	8.1	0.0319	3.5	0.0125	3.1	0.0005
Acifluorfen amino	14.7	0.0010	51.7	0.0078	64.5	0.2555	41.2	0.1453	33.2	0.0047
Acifluorfen amino methyl ester	2.6	0.0002	4.7	0.0007	--	--	--	--	1.3	0.0002
Subtotal	**55.3**	**0.0039**	**67.6**	**0.0102**	**84.8**	**0.3358**	**70.5**	**0.2489**	**59.5**	**0.0086**
Characterized										
Unknown metabolite; RT = 3.5[a]	2.2	0.0002	2.2	0.0003	--	--	--	--	2.5	0.0004
Unknown metabolite; RT = 4.5	3.3	0.0003	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 7.0-7.5	--	--	1.1	0.0002	--	--	--	--	--	--
Unknown metabolite; RT = 9.0-10.0	1.9	0.0002	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 19.0-19.5	1.9	0.0002	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 20.5	2.3	0.0002	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 21.5-22.5	3.7	0.0003	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 30.5-31.0	--	--	1.4	0.0002	--	--	--	--	--	--
Unknown metabolite; RT = 31.0	--	--	--	--	1.6	0.0064	--	--	--	--
Unknown metabolite; RT = 39.0-39.5	--	--	1.6	0.0003	--	--	--	--	--	--
Unknown metabolite; RT = 41.0	--	--	1.4	0.0002	--	--	--	--	--	--
Unknown metabolite; RT = 46.0	1.6	0.0001	--	--	--	--	--	--	--	--
Unknown metabolite; RT = 46.0-46.5	--	--	1.5	0.0002	--	--	--	--	--	--
Unknown metabolite; RT = 58.5-59.5	--	--	0.9	0.0001	--	--	--	--	--	--
All other unknown metabolites[b]	22.6	0.0015	13.7	0.0018	7.3	0.0288	9.9	0.0349	17.3	0.0024
Hexane extract	--	--	3.3	0.0005	--	--	--	--	--	--
Total identified/characterized	**94.8**	**0.0069**	**94.7**	**0.0140**	**93.7**	**0.3710**	**80.4**	**0.2838**	**79.3**	**0.0114**
Non-extractable	18.8	0.0013	17.3	0.0026	11.3	0.0446	15.0	0.0528	22.8	0.0032
Total Recovery	113.6	0.0082	112.0	0.0166	105.0	0.4156	95.4	0.3366	102.1	0.0146

[a] RT = HPLC retention time in minutes.

[b] Consists of 21 or more HPLC peaks, each <2.0% TRR (<0.0001-<0.0080 ppm).

Storage Stability

Goat milk and tissue samples were frozen immediately following collection and were stored frozen at -20 C until extraction. The registrant stated that samples were stored frozen for approximately 12 months prior to final analysis. To support this storage interval the registrant presented data from aliquots of ACN:water extracts of liver tissue that were analyzed by HPLC at the beginning of the study, after approximately 3 months of frozen storage, and at the end of the study, after approximately 12 months of frozen storage. The registrant submitted sample chromatograms and quantitative data indicating comparable levels of metabolite residues at the beginning and end of the study. These data are adequate to support this metabolism study.

Radiolabeled validation of analytical methods

Samples from this metabolism study were not analyzed using any of the current enforcement methods. The requirement for the radiovalidation of the enforcement analytical method(s) is reserved until the HED Metabolism Committee determines the residues to be regulated.

In summary, the qualitative nature of the residue in ruminants is adequately understood. Acifluorfen was a minor metabolite in milk and all tissues (1.0-5.2% of TRR). The major metabolite was acifluorfen amino which accounted for ca. 15% of TRR in milk, 52% of TRR in fat, 65% of TRR in kidney, 41% of TRR in liver, and 33% of TRR in muscle. Acifluorfen amino glucuronide accounted for ca. 16% of the TRR in milk, 6% in fat, 10% in kidney, 24% in liver, and 19% in muscle. Acifluorfen acetamide was a major metabolite in milk (ca. 17% of TRR) but a minor metabolite in fat (4% of TRR), kidney (8% of TRR), liver (4% of TRR), and muscle (3% of TRR). Acifluorfen amino methyl ester was identified in milk (ca. 3% of TRR), fat (5% of TRR), and muscle (1% of TRR).

The following levels of radioactivity were successfully characterized/identified in the milk and tissues of a lactating goat orally dosed with [^{14}C-chlorophenyl-ring-labeled] sodium acifluorfen: milk (94.8% of TRR), fat (94.7% of TRR), kidney (93.7% of TRR), liver (80.4% of TRR), and muscle (79.3% of TRR). Non-extractable residues were ca. $\leq$0.05 ppm in all matrices. No additional characterization/identification of non-extractable residues is required.

MASTER RECORD IDENTIFICATION NUMBERS

The citation for the MRID document referred to in this review is presented below.

42815601 Steginsky, C.A., Powell, J., Veley, K., and Nelsen, J. (1993) Nature of the Residue Study of ^{14}C-Radiolabeled Sodium Acifluorfen Using Lactating Goats. Battelle Study Reference No. SC910215, BASF Study No. 91116, BASF Report No. M9310. Unpublished study conducted by Battelle, Columbus, OH and submitted by BASF Corporation, Research Triangle Park, NC. 208 p.

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