Evaluation of Corn Furan Fatty Acid Putative Endocrine Disruptors on Reproductive Performance in Adult Female Chickens

K. W. Wilhelms  
*Iowa State University*

George A. Kraus  
*Iowa State University*, gakraus@iastate.edu

J. D. Schroeder  
*Iowa State University*

J. W. Kim  
*Iowa State University*

S. A. Cutler  
*Iowa State University*

*See next page for additional authors*

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Abstract
Based on evidence from rodent models, it was hypothesized that furan fatty acids found in corn would inhibit reproduction in the laying hen. An isomeric mixture of furan fatty acids [9, (12)-oxy-10,13-dihydroxystearic acid and 10, (13)-oxy-9,12-dihydroxystearic acid] was administered for a period of 3 wk via the diet (1 and 3 ppm) at levels greater than those in corn to 20-wk-old pullets. There were no overt indications of acute or chronic toxicity (no effects on mortality, feed intake, or average daily gain). Similarly, there was no dose-dependent effect on reproductive parameters [egg production, egg weight, shell thickness, ovarian weight, number or weight of large yolky preovulatory follicles, and number of small yellow follicles (4–8 mm in diameter)]. The present data do not suggest that furan fatty acids are a cause of concern to the poultry industry.

Keywords
corn furan fatty acid, endocrine disruptor, egg production, chicken

Disciplines
Organic Chemistry | Pharmacology, Toxicology and Environmental Health | Poultry or Avian Science

Comments

Authors
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K. W. Wilhelms,*† G. A. Kraus,*§ J. D. Schroeder,§ J. W. Kim,§ S. A. Cutler,† M. A. Rasmussen,|| L. L. Anderson,†‡1 and C. G. Scanes*†‡

*Interdepartmental Toxicology Program, †Department of Animal Science, ‡Department of Biomedical Sciences, and §Department of Chemistry, Iowa State University, Ames 50011; and ||National Animal Disease Center, USDA-ARS, Ames, IA 50010

ABSTRACT Based on evidence from rodent models, it was hypothesized that furan fatty acids found in corn would inhibit reproduction in the laying hen. An isomeric mixture of furan fatty acids [9, (12)-oxy-10,13-dihydroxy-stearic acid and 10, (13)-oxy-9,12-dihydroxy-stearic acid] was administered for a period of 3 wk via the diet (1 and 3 ppm) at levels greater than those in corn to 20-wk-old pullets. There were no overt indications of acute or chronic toxicity (no effects on mortality, feed intake, or average daily gain). Similarly, there was no dose-dependent effect on reproductive parameters [egg production, egg weight, shell thickness, ovarian weight, number or weight of large yolky preovulatory follicles, and number of small yellow follicles (4-8 mm in diameter)]. The present data do not suggest that furan fatty acids are a cause of concern to the poultry industry.

Key words: corn furan fatty acid, endocrine disruptor, egg production, chicken

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INTRODUCTION For over the past decade, there has been increasing attention focused on endocrine disruption. A wide range of chemicals has been classified as putative endocrine disruptors, natural or synthetic compounds that mimic, enhance, or inhibit endogenous hormones (Boorgeest et al., 2002). These include the soy isoflavones and other plant compounds (Kurzer and Xu, 1997), many pesticides (Cooper et al., 1999), and industrial plasticizers (Casajunga and Lacorte, 2004), among others.

For many years, there has been evidence that corn-based products possess compounds with the ability to alter growth and reproductive states (Dam et al., 1959; Booth et al., 1960). Recently, putative endocrine disruptors derived from linoleic acid were discovered in corn cob animal beddings (Markaverich et al., 2002a,b). These chemicals have been identified as an isomeric mixture of 9, (12)-oxy-10,13-dihydroxystearic acid and 10, (13)-oxy-9,12-dihydroxystearic acid furan fatty acids. These chemicals possess mitogenic activity in treated MCF-7 human breast cancer cells (Markaverich et al., 2002a). Furthermore, they have the ability to block progression of the estrous cycle (Markaverich et al., 2002a,b), to initiate persistent metestrus, and to reduce mating behavior in Sprague-Dawley rats (Schettler, 2003). However, they possess no detectable estrogenic or antiestrogenic activities (Markaverich et al., 2002a,b).

There is newfound concern about the putative endocrine disruptor effect of these compounds on reproduction, as corn-based products are a staple of many human, livestock, and experimental animal diets (Schettler, 2003). The present study examined the ability of furan fatty acids to inhibit reproductive development, egg production, and ovarian functioning in the hen.

MATERIALS AND METHODS

Birds All procedures were approved by the Iowa State University Committee on Animal Care (protocol 8-03-5498-G). White Leghorn pullets (19 wk old) from Sparboe Farms (Litchfield, MN) that had previously been on a short photoperiod of 10 h of light per day were used. The treatments were initiated 1 wk after the birds arrived at Iowa State University. At that time, they were on a light period of 14 h per day. By the beginning of the feeding trial, all birds were in lay. Birds were weighed and randomly placed individually into cages (30.5 × 40.5 × 44 cm) with a feeder supplying feed to 3 adjacent cages. The basal diet (ground corn, 566.7 g/kg; soybean meal (48% CP), 265.0 g/kg; animal and vegetable fat blend, 36.5 g/kg; DL-Met, 2.5 g/kg; dicalcium phosphate, 22.3 g/kg; limestone, 81.0 g/kg; oyster shell, ground 15.0 g/kg; NaCl (iodized), 5.0 g/kg; trace mineral premix, 3.0 g/kg; vita-
Experimental Design and Treatments

It was hypothesized that furan fatty acids would inhibit reproductive development in female poultry. There were 3 treatments of furan fatty acid in the diet added at the following concentrations: 0, 1, or 3 ppm. The highest dose was estimated to meet the concentration reported as having reproductive effects in rats (Casajuana and Lacorte, 2004). Blocks of 3 cages each containing 1 pullet were randomly assigned to 1 of 3 treatments, with 9 replicate cages/birds per treatment or 3 replicate blocks of cages/treatment. The furan fatty acid mixture was added directly into the basal diet using 0.12 mL/kg of ethanol as a vehicle. The diets were mixed for 20 min and then stored at room temperature throughout the experiment.

Fatty Acid Furan Synthesis

An isomeric mixture of furan fatty acids [9, (12)-oxy-10,13-dihydroxystearic acid and 10, (13)-oxy-9,12-dihydroxystearic acid] was prepared as follows (Moghaddam et al., 1996; Markaverich et al., 2002a). The purity of the synthesized compound was evidenced by proton NMR, by high-resolution mass spectrometry, and by thin-layer chromatography. Results of these analyses are NMR (CDC13) 0.87 (br t, J = 6 Hz, 3 H), 1.15 to 1.70 (m, 22 H), 1.78 to 2.21 (m, 2 H), 2.29 to 2.34 (m, 2 H), 3.32 to 3.48 (m, 1 H), 3.68 to 3.80 (m, 1 H), 3.95 to 4.12 (m, 1 H), and 4.20 to 4.32 (m, 1 H). The high-resolution mass spectrometry mass-to-charge ratio for C18H34O5, calculated 330.2406; found 330.2411. Bisepoxide linoleic acids were prepared directly from linoleic acid by epoxidation with chloric acid. The resulting mixture was used in the studies.

Experimental Protocol

At the start of the study, BW were recorded. The chickens were then fed the treatment diets ad libitum for 21 d. During this period, feed intake, number of eggs laid, egg weight, and any overt abnormalities were recorded. Shell thickness was also determined (measured at 4 sites on the egg and the mean used in analysis).

On d 21, the hens were weighed and killed by decapitation. Ovary and oviduct weights were determined, as were any reproductive overt abnormalities (atretic follicles, internal eggs). The ovarian follicles were collected. The weight of the F1 to F5 largest follicles were determined, as were the number of large yolky follicles (>8.0 mm in diameter) and the number of small yellow follicles (4 to 8 mm in diameter).

Statistics

The study was analyzed as a randomized design with subsampling. All data were analyzed using PROC MIXED in SAS Version 8.2 (SAS Institute Inc., Cary, NC), with the exception of egg lay. Egg lay was analyzed by binomial and multinomial logistic regression. Values found different were separated using Dunnett’s method. Significance was determined at P ≤ 0.05.

RESULTS AND DISCUSSION

The study examined the effect of furan fatty acids [an isomeric mixture of 9, (12)-oxy-10,13-dihydroxystearic acid and 10, (13)-oxy-9,12-dihydroxystearic acid present in corn] on reproduction in hens. The furan fatty acids exhibited no acute toxicity, as indicated by the absence of any mortality (0/9 in birds on 0, 1, and 3 ppm furan fatty acids). Similarly, there was no evidence for chronic toxicity, as neither feed intake nor BW gain were affected by the presence of furan fatty acids in the feed (Table 1).

These furan fatty acids exhibit marked inhibitory effects on reproduction in rodent models when exposed to concentrated extracts and synthesized compounds at a dose of ∼0.32 mg/kg per day (Markaverich et al., 2002a; Moghaddam et al., 1996). In contrast, the furan fatty acids had little effect on reproduction in the hen with daily doses of 0.096 and 0.28 mg/kg per day (at 1 and 3 ppm, respectively). For instance, treatment with either 1.0 or 3.0 ppm furan fatty acids did not influence (P > 0.05) any of the following parameters: weights of oviduct, ovary, or large yolky follicles (F1 to F5); number of large yellow follicles (>8.0 mm in diameter); and number of small yellow follicles (4 to 8 mm in diameter; Table 1). Moreover, furan fatty acids had no effect on egg production or quality (as indicated by number of yolks and shell thickness) in all weeks of treatment. There were, however, changes in 2 reproductive parameters. As might be expected, there was a decrease (P < 0.05) in shell thickness between the first and second and between the second and third week of lay, irrespective of furan fatty acid treatment.

In summary, furan fatty acids at concentrations above those found in corn (Markaverich et al., 2002a) have no overt toxicity and little acute effect on reproduction in the layer hen. It is unclear whether effects may be observed if administered over a longer period or at higher doses.

ACKNOWLEDGMENTS

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RESEARCH NOTE

Table 1. Effects of dietary furan fatty acids [an isomeric mixture of 9, (12)-oxy-10,13-dihydroxystearic acid and 10, (13)-oxy-9,12-dihydroxystearic acid] on growth and reproductive parameters in laying hens

<table>
<thead>
<tr>
<th>Parameter of growth, egg production, and quality</th>
<th>Furan fatty acids added to diet (^2) (ppm)</th>
<th>0</th>
<th>1.0</th>
<th>3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average daily gain (g)</td>
<td></td>
<td>3.5±0.60</td>
<td>3.1±0.65</td>
<td>3.3±1.15</td>
</tr>
<tr>
<td>Feed intake (g/hen)</td>
<td></td>
<td>92.0±4.82</td>
<td>96.3±1.01</td>
<td>94.0±2.64</td>
</tr>
<tr>
<td>Egg production (no./wk)</td>
<td></td>
<td>6.6±0.18</td>
<td>5.6±0.48</td>
<td>6.9±0.11</td>
</tr>
<tr>
<td>Week 1</td>
<td></td>
<td>6.8±0.15</td>
<td>6.9±0.11</td>
<td>6.9±0.11</td>
</tr>
<tr>
<td>Week 2</td>
<td></td>
<td>5.7±0.24</td>
<td>5.8±0.22</td>
<td>5.7±0.24</td>
</tr>
<tr>
<td>Egg weight (g)</td>
<td></td>
<td>49±1.1</td>
<td>48±0.4</td>
<td>49±0.8</td>
</tr>
<tr>
<td>Week 1</td>
<td></td>
<td>51±0.8</td>
<td>51±0.7</td>
<td>52±0.7</td>
</tr>
<tr>
<td>Week 2</td>
<td></td>
<td>53±1.0</td>
<td>53±0.8</td>
<td>53±0.6</td>
</tr>
<tr>
<td>Shell thickness ((\mu)m)</td>
<td></td>
<td>47±0.9</td>
<td>49±0.9</td>
<td>49±0.9</td>
</tr>
<tr>
<td>Week 1</td>
<td></td>
<td>44±0.6</td>
<td>44±0.6</td>
<td>45±0.6</td>
</tr>
<tr>
<td>Week 2</td>
<td></td>
<td>37±0.4</td>
<td>36±0.4</td>
<td>38±0.3</td>
</tr>
<tr>
<td>Ovary weight</td>
<td></td>
<td>42.6±3.03</td>
<td>48.1±2.92</td>
<td>45.6±1.86</td>
</tr>
<tr>
<td>Total weight of F1 to F5 follicles (g)</td>
<td></td>
<td>33.8±2.12</td>
<td>37.2±2.15</td>
<td>36.0±1.43</td>
</tr>
<tr>
<td>Number of yolks</td>
<td></td>
<td>6.0±0.41</td>
<td>6.4±0.29</td>
<td>6.0±0.24</td>
</tr>
<tr>
<td>Number of follicles &gt;8 mm in diameter</td>
<td></td>
<td>13.0±1.65</td>
<td>17.2±1.10</td>
<td>20.7±2.54</td>
</tr>
<tr>
<td>Oviduct weight (g)</td>
<td></td>
<td>52.4±1.89</td>
<td>54.3±2.02</td>
<td>56.6±1.46</td>
</tr>
</tbody>
</table>

\(^1\)From 20 to 23 wk of age with a long day length imposed to bring the pullets into lay.  
\(^2\)Values are mean ± SE.

the statistical advice from David F. Cox and Cory Heil- 
mann (Iowa State University, Department of Statistics).

REFERENCES


