THE INFLUENCE OF α-DIFLUOROMETHYLORNITHINE ON THE ACTIVITY OF WOOL FOLLICLES

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Introduction

The polyamines, spermidine and spermine, are involved in nucleic acid and protein synthesis, especially in actively dividing cells (Pegg and McCann, 1982), and are likely to be important in wool follicle bulb cells. Their synthesis requires the formation of putrescine from ornithine catalyzed by ornithine decarboxylase, and the addition of an aminopropyl group derived from methionine. α-Difluoromethylornithine (DFMO) is a specific and potent inhibitor of ornithine decarboxylase (Pegg and McCann, 1982). In order to ascertain whether DFMO influenced wool growth and follicle activity, sheep were given intravenous infusions of DFMO.

Materials and Methods

Four Merino sheep, body weight 38-44 kg, were given a daily ration of 800 g sheep pellets (Milling Industries, SA) which provided approx. 9 g nitrogen and 5.5 MJ metabolizable energy. DFMO (supplied by Merrell Dow Research Institute) was dissolved in sterile, isotonic saline and infused continuously via a jugular vein by means of a peristaltic pump for 4 days. Two sheep received DFMO at a rate of 75 mg/kg body weight/day and two at a rate of 100 mg/kg/day.

Tracer doses of L-[35S] cysteine were injected into a jugular vein at intervals of 4 days before, during and after the infusion of DFMO to enable measurement of length growth rate and diameter of wool fibres by the technique of autoradiography. Fibres were sampled from four sites along one side of each sheep; measurements were made on 120 fibres per sheep with approximately equal numbers from each site. Mitotic activity in wool follicle bulbs was estimated in mid-side skin biopsy samples following intradermal injections of colchicine to achieve metaphase arrest (Hynd et al., 1986; Hynd, 1989). At least 300 random bulb counts were made in skin taken 90 and 246 minutes after colchicine administration to give estimates of mitoses/hour, before DFMO infusion commenced and at the end of the 4-day infusion.

Results and Discussion

DFMO caused a reduction in fibre length growth rate (L) of 14-22% (mean 19.2%) in the 4 days after the infusion stopped; recovery was rapid thereafter (figure 1). The effect appeared to be slightly greater with the higher dose rate. Fibre diameter (D) increased by 1-2 μm during DFMO infusion and then declined to pre-treatment values or below (figure 1). These changes in L and D post-infusion caused a reduction in the volume of wool grown of 10-18% (mean 13.8%).

The differential effects of DFMO on L and D caused a considerable decrease in the ratio of mean length of fibre grown per day to mean fibre diameter (L/D ratio) during the 4-day period after the infusion (8-12 d, table 1). These effects are in contrast to the relative constancy of the L/D ratio for individual sheep over a wide range of wool growth rates induced by variations in nutrition (Downes and Sharry, 1971). However, similar changes in the L/D ratio have been observed with thyroid hormones and cold exposure (Downes and Sharry, 1971; Hynd, 1989).

In view of the effects of DFMO on wool growth, measurements were made of mitotic activity in follicle bulbs. Overall, there was little
Figure 1. Effect of intravenous infusion of DFMO on length growth (—) and diameter (●) of wool fibres. Values are means for two sheep.

TABLE 1. LENGTH/DIAMETER RATIO OF WOOL FIBRES AND MITOTIC RATE IN FOLLCLE BULB CELLS

<table>
<thead>
<tr>
<th>Sheep</th>
<th>Dose rate of DFMO(^a) (mg/kg/d)</th>
<th>Length/diameter ratio</th>
<th>Mitoses/hour</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0-4 d</td>
<td>4-8 d</td>
</tr>
<tr>
<td>1</td>
<td>75</td>
<td>13.8</td>
<td>13.9</td>
</tr>
<tr>
<td>2</td>
<td>75</td>
<td>16.6</td>
<td>15.2</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>15.4</td>
<td>14.1</td>
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<tr>
<td>4</td>
<td>100</td>
<td>18.6</td>
<td>17.2</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>16.1</td>
<td>15.1</td>
</tr>
</tbody>
</table>

\(^a\)DFMO was infused during days 4-8

(Key Words: α-Difluoromethylornithine, Mitotic Activity, Wool Growth)

Literature Cited


