REPARTITIONING EFFECTS OF SOME O-ALKYL ANALOGUES OF CLENBUTEROL

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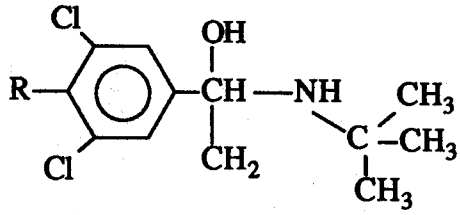
$ß_2$-Adrenergic agonists such as clenbuterol, cimaterol and ractopamine have been shown to have energy-repartitioning effects in a variety of species, resulting in carcasses with increased protein and reduced fat content (Hanrahan 1987). It has been found that physiological effects of hormones can be mimicked immunologically by anti-idiotypic antibodies (Langone 1989). As part of a study on developing an anti-idiotype mimicking clenbuterol, the production of anti-clenbuterol antibodies has led to the synthesis of four structural analogues of clenbuterol, two of which have been used as haptens (C2 and C6 acids) in antigen synthesis. In the present study we characterise the physiological effects of these analogues in comparison with clenbuterol in rodents.



R = NH_2 (Clenbuterol)
= OH (VUF $_{8303}$)
= OCH_3 (O-Methyl VUF $_{8303}$)
= OCH_2CO_2H (C_2 Acid)
= $O(CH_2)_5CO_2H$ (C_6 Acid)

Female Wistar rats (~200g), with free access to water and food ad libitum were given daily subcutaneous injections (in saline) of either clenbuterol, one of the four structural analogues (molar equivalent of 1mg/kg BW clenbuterol) or saline (n=6 per group). Animals were weighed daily. After 22 days, the rats were killed and carcass composition determined. Fat and protein are given on a dry matter (DM) basis. Results analysed by ANOVA.

Group	Δ BW (g)	% Water	% Fat (DM)	% Protein (DM)
Saline	44.6 ± 2.4	64.7 ± 0.6	33.6 ± 1.7	52.8 ± 1.5
Clenbuterol	60.8 ± 2.1*	69.3 ± 0.2*	23.5 ± 1.4*	63.5 ± 1.1*
VUF 8303	52.5 ± 2.7*	67.6 ± 0.9	31.5 ± 1.2	56.3 ± 1.4
O-Methyl VUF 8303	46.0 ± 3.6	66.6 ± 0.5	32.1 ± 1.4	56.9 ± 0.6
C2 Acid	43.5 ± 3.7	66.6 ± 0.4	34.2 ± 1.1	53.5 ± 1.1
C6 Acid	43.0 ±1.4	67.2 ± 0.5	31.0 ± 1.6	54.9 ± 1.2

All results given as mean ± SEM * P<0.05 versus saline (F-Test)

Clenbuterol and VUF 8303 showed significant change in the final bodyweight after 22 days of treatment, but only clenbuterol showed significant changes in carcass composition with respect to fat and protein content. The results of this study suggest that the substitution of the aromatic amine group of clenbuterol with either a hydroxy, methoxy, oxyacetic acid or 6-oxyhexanoic acid group significantly diminishes the energy-repartitioning action of clenbuterol. However, the structural features responsible for the growth promoting effects of ß-agonists are not entirely clear as VUF 8303 combines moieties common to both ractopamine and clenbuterol but still lacks the well-known energy-repartitioning effects of these two drugs.

HANRAHAN, J.P. (1987). 'Beta-agonists and their effects on animal growth and carcass quality' (Elsevier Applied Science: London).
LANGONE, J.J. (1989). 'Methods in Enzymology' Vol. 178 (Academic Press Inc.: San Diego).

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