Journal of Animal and Feed Sciences, 13, Suppl. 1, 2004, 339–342

Polyethylene glycol increases intestinal absorption and hepatic uptake of indole and skatole in sheep fed sulla*

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ABSTRACT

Six lactating ewes were orally drenched each day with polyethylene glycol (PEG) to remove the effects of the condensed tannins in sulla (*Hedysarum coronarium*) and six other ewes (control) received a drench of water commencing 28 days prior to the measurement period according to a block design. At week 6 of lactation, portal absorption and hepatic uptake of indole and skatole were increased by PEG. Efficiency of hepatic extraction of indole and skatole was not different between the treatments. The splanchnic release of indole and skatole was higher in the PEG ewes compared with control.

KEY WORDS: sheep, condensed tannins, indole metabolism, skatole metabolism, intestine, liver

INTRODUCTION

The indole compounds, indole and skatole are amines that give a faecal taint to milk and dairy products and are perceived in Asian and European markets as undesirable flavours (Keen, 1998). Studies in Australia indicated that these compounds are not present in any significant quantity in forages (Conochie, 1953). The amines found in milk are most likely the result of rumen metabolism of the amino acid tryptophan (Keen, 1998).

Condensed tannins (CT) in the diet reduce the degradation of dietary protein in the rumen (McNabb et al., 1996) and the concentration of circulating indole and skatole in peripheral blood (Roy et al., 2002). Rumen microbial fermentation and

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liver metabolism of indole and skatole are two processes that potentially could modify their supply to the peripheral blood.

Our study tested the hypothesis that polyethylene glycol (PEG) increases the peripheral concentration of indole and skatole by reducing their absorption from the rumen into the portal vein and/or due to limited hepatic extraction. The aim was to measure their absorption into the mesenteric and portal veins and flux across the liver and total splanchnic tissue (TSP; PDV + liver) in lactating ewes.

MATERIAL AND METHODS

Animals, surgical procedures and dietary treatments

Twelve lactating ewes were prepared with catheters in the mesenteric, portal and hepatic veins, and in the mesenteric artery (Huntington et al., 1989). Three weeks postpartum, all ewes were offered fresh sulla (*Hedysarum coronarium*; 2000 g DM d^{-1}; 80 g CT d^{-1}) for 28 days. Six ewes were orally drenched daily with PEG (160 g d^{-1} in water) to remove the effects of the CT (CT inactive; PEG group) whilst six ewes were kept as controls (CT active).

Infusion and sampling protocols, measurement and statistics

Six weeks postpartum, para-aminohippurate was infused for 7 h into the mesenteric vein for measuring TSP plasma flows (Lobley et al., 1995). Plasma indole and skatole concentrations were measured in blood collected from the vessels previously mentioned (Roy et al., 2002). Splanchnic plasma flow and net flux of indole and skatole were calculated as described by Lobley et al. (1995). Data were subjected to the GLM procedure of SAS according to a completely randomized block design. One control ewe died during the experimental period for reasons not related to the treatment. Significant statistical differences between treatments were declared at a probability less than 0.05.

RESULTS

Plasma flows across the mesenteric-drained viscera (MDV), PDV, TSP and hepatic artery were not affected by PEG (Table 1). The concentration of indole and skatole in the mesenteric vein was similar between treatments. In the mesenteric artery, hepatic vein and portal vein, their concentration was higher in PEG ewes. Net appearance of indole and skatole in the mesenteric drainage was similar between the PEG and control groups and in the portal drainage, was higher in the PEG group. Net hepatic uptake of indole and skatole was higher in the PEG ewes, but their hepatic extraction ratio (net uptake/influx) was not affected by the treatments. The net release of these metabolites by the TSP was higher in the PEG group.

Table 1. Effect of polyethylene glycol (PEG) on net flux of skatole and indole across the mesenteric-drained viscera (MDV), portal-drained viscera (PDV), liver and total splanchnic tissue (TSP) in lactating ewes[1]

	Treatments		SED	Probability
	PEG, n=6	control, n=5		
Plasma flow, mL/min				
MDV	560.1	817.2	138.9	0.24
PDV	2270.8	2357.3	92.3	0.51
hepatic artery	195.3	164.1	61.1	0.71
TSP	2413.5	2455.2	112.6	0.79
Indole concentration, µg/mL				
mesenteric vein	24.3	20.3	5.4	0.62
portal vein	187.7	97.7	10.6	0.0004
hepatic vein	9.3	2.5	2.4	0.001
mesenteric artery	3.9	0.7	1.0	0.002
Skatole concentration, µg/Ml				
mesenteric vein	10.4	8.2	3.1	0.64
portal vein	135.1	47.4	23.6	0.03
hepatic vein	24.8	2.5	11.4	0.03
mesenteric artery	12.9	1.4	5.5	0.03
Indole arterious-venous concentration difference, µg/mL				
artery-mesenteric vein	-21.6	-19.5	5.5	0.79
artery-portal vein	-183.8	-97.0	11.2	0.0007
artery-hepatic vein	-5.3	-1.8	1.4	0.04
portal vein-hepatic vein	178.6	95.3	12.3	0.002
Skatole arterious-venous concentration difference, µg/mL				
artery-mesenteric vein	-3.9	-6.1	2.8	0.99
artery-portal vein	-122.2	-46.4	18.6	0.02
artery-hepatic vein	-11.7	-1.2	5.9	0.04
portal vein-hepatic vein	110.4	44.9	13.6	0.009
Net indole flux, µg/min				
MDV	-9.7	-17.8	7.0	0.45
PDV	-417.5	-226.4	28.2	0.002
liver	396.6	217.0	35.3	0.007
TSP	-13.0	-4.6	3.3	0.05
Net skatole flux, µg/min				
MDV	-2.4	-5.9	3.5	0.50
PDV	-278.3	-105.8	41.5	0.02
liver	238.6	102.1	21.3	0.002
TSP	-28.0	-3.2	14.0	0.04

[1] positive and negative values indicate net uptake and net production by the relevant organ

DISCUSSION

Our study shows that the intra-luminal addition of PEG to lactating ewes fed the CT-containing plant sulla increased the net portal flux of indole and skatole. Their mesenteric appearance represents less than 8% of their portal appearance. Although their gastric flux was not measured, the mesenteric data (small intestine only), suggest that these metabolites are primarily absorbed across the rumen epithelium, draining into the portal vein *via* the gastric vein. Our results also agree with a study where portal absorption of indole and skatole was correlated with their plasma concentration (Hammond et al., 1983). Our values (7.1 µg/min/kg) are within the range reported in Hammond's study (1 to 46 µg/min/kg). While the portal absorption and hepatic uptake of indole and skatole increased in the PEG ewes, their efficiency of removal by the liver did not and consequently, the splanchnic flux also increased.

CONCLUSIONS

These results establish that the intra-luminal addition of PEG to lactating ewes fed the CT-containing plant sulla increased the peripheral plasma concentration of indole and skatole most likely by altering their formation in the rumen and thereby increasing their absorption to the portal drainage.

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