

Evaluating the risk of residues of the toxin indospicine in bovine muscle and liver from north-west Australia

M.T. Fletcher^{A,C}, G. Netzel^A, D.G. Palmer^B, A.M. Masters^B, S.Y. Tai^B and J.G. Allen^B

^AQueensland Alliance for Agriculture and Food Innovation, The University of Queensland, Brisbane QLD, 4108 Australia.

^BDepartment of Primary Industries and Regional Development, South Perth WA, Australia

^CEmail: mary.fletcher@uq.edu.au

The non-proteinogenic arginine analogue indospicine is a natural toxin found only in *Indigofera* plant species, including native *Indigofera linnaei* - a species prevalent in northern grazing regions of Western Australia. These legumes are palatable to cattle and residues of indospicine derived from these plants have been shown to accumulate as the free amino acid in cattle tissues (Fletcher *et al.* 2018). Dogs are particularly sensitive to indospicine toxicity and consumption of indospicine-contaminated horse and camel meat has caused hepatotoxicosis and mortalities in Australian domestic dogs (Hegarty *et al.* 1988; FitzGerald *et al.* 2011). Since the risk for human consumption was not known, a survey study was undertaken in Western Australia to assess the indospicine levels in bovine samples collected from abattoirs in Spring (August-November) and Autumn (March-July) of 2015-2017 and to predict the likelihood of significant residues being present (Netzel *et al.* 2019).

Muscle and liver paired samples from 776 cattle originating from the tropical Kimberley/Pilbara regions, where *I. linnaei* is prevalent, and 640 cattle from South West and South Coast regions, where the plant is not known to occur, were collected at abattoir and analysed by LC-MS/MS for indospicine. No indospicine residues were detected in any of the animals originating from southern regions, while indospicine content in tissues from northern regions ranged from below detection to 3.63 mg/kg. Indospicine residues in both muscle and liver collected from all Kimberley and Pilbara cattle in 'autumn' (March – July), were higher than in tissues collected in 'spring' (August – November) ($P < 0.001$) (Table 1). @Risk (Pallisade) best-fit probability distributions showed ninety-fifth percentile (P95) indospicine concentrations of 0.54 mg/kg in muscle and 0.77 mg/kg in liver during 2015-2017.

Table 1. Average indospicine residues in muscle and liver collected from all Kimberley and Pilbara cattle.

	Muscle (mg indospicine/kg)		Liver (mg indospicine/kg)	
	Autumn	Spring	Autumn	Spring
Average	0.156	0.043	0.221	0.076
SD	0.348	0.147	0.358	0.192
n	501	275	501	275

There is limited reported data available to estimate tolerable daily intake. The only published liver histopathological data relates to dogs (considered to be the most susceptible animal species) fed a diet of known indospicine content from naturally contaminated meat (Hegarty *et al.* 1988) and indospicine-dosed meat (Kelly *et al.* 1992), and this data was used to derive a provisional tolerable daily intake (PTDI) of 1.3 µg indospicine/kg body weight/day for both dogs and humans (Netzel *et al.* 2019). When considered with ABARES average Australian daily meat consumption data, the estimated consumer exposure was 0.32 µg indospicine/kg body weight/day from the P95 muscle, which compares favourably with our calculated PTDI. Canine exposure however compared less favourably, with active working dog exposure calculated to exceed this PTDI by a factor of 25 based on P95 indospicine concentrations of 0.54 mg/kg in muscle. Even allowing for the conservative nature of the PTDI calculation, this canine exposure risk is of potential concern.

References

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