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Letter to the Editor

Effect of Extract of *Agkistrodon blomhoffii* on Acute Gastric Mucosal Lesions Induced by Ischaemia-reperfusion in Rats

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Agkistrodon blomhoffii (mamushi snake) has been used for many years in Chinese folk medicine for nourishment, as a tonic and for the treatment of digestive disorders. Amino acids, such as taurine and cystathionine, and unsaturated fatty acids are reported to be the main components of the extract of *Agkistrodon blomhoffii* (Tomita 1956). Concentrations of cystathionine and taurine, in particular, are much higher in the aqueous extract of *Agkistrodon blomhoffii* than in tuna, eel, beef, ginseng radix and astragail radix (Noguchi et al 1985). Because the relationship between the high concentrations of sulphur-containing amino acids and many effective actions, especially the protective effect on the gastrointestinal tract, has not been elucidated, we have studied the protective effect of the extract of *Agkistrodon blomhoffii* on acute gastric mucosal injury induced by ischaemia-reperfusion in rats.

All animal experiments were performed in accordance with The Guidelines for Animal Experimentation of the Faculty of Medicine, Tottori University. Male Wistar rats, 250–280 g, from SLC (Shizuoka, Japan) were fasted for 18 h before the experiments, but were allowed free access to water. Gastric mucosal injury was produced by ischaemia-reperfusion (Wada et al 1995). Briefly, under pentobarbital (50 mg kg^{-1}) anaesthesia, the coeliac artery was clamped with a small clamp (Sugita standard aneurysm clip, holding force 145 g; Mizuho Ikakogyo, Tokyo, Japan) for 30 min and reperfused by removal of the clamp to obtain the ischaemia-reperfusion state. Sixty minutes after the reperfusion, the rats were killed and the stomach was removed. Macroscopic gastric erosional damage, expressed as total area (mm^2), was measured by computer imaging analysis.

Extract of *Agkistrodon blomhoffii* was a gift from Totosyu Seizou (Tokyo, Japan). Aqueous extract of *Agkistrodon blomhoffii* (1 g) was prepared from whole homogenized viper body (6 g). The extract was diluted with distilled water to 100, 330 and 1000 mg extract mL^{-1}. These extracts (100, 330 and 1000 mg kg^{-1}) were administered orally to rats 30 min before ischaemia. For investigation of the mechanism, cystathionine (2 and 5 mg kg^{-1}, p.o.) was administered 30 min before ischaemia. Control rats were given vehicle solution. Concentrations of various amino acids in the extract were measured by use of a Hitachi-835 automatic amino-acid analyser (Hitachi, Tokyo, Japan) according to the method described previously (Noguchi et al 1985).

After ischaemia-reperfusion, gastric mucosal lesions with haemorrhage were observed. The total area of erosions, as a morphological index of gastric injury, was reduced by pretreatment with the extract of *Agkistrodon blomhoffii* (Table 1). These protective effects were observed at extract doses of 330 to 1000 mg kg^{-1} when administered orally. Microscopic observation also showed the protective effect of the extract of *Agkistrodon blomhoffii* against the gastric mucosal lesions induced by ischaemia-reperfusion.

In our previous experiment, concentrations of cystathionine and taurine were higher in the aqueous extract of *Agkistrodon blomhoffii* than in tuna, eel, beef, ginseng radix and astragail radix (Noguchi et al 1985). We also reported that cystathionine has a protective effect against acute gastric mucosal injury induced by ischaemia-reperfusion in rats (Wada et al 1995). In addition, the protective effect of cystathionine was considered

Table 1. Effects of the extract of *Agkistrodon blomhoffii* and of cystathionine on the total area of erosion.

Treatment	Dose cystathionine (mg kg^{-1})	n	Area of erosion (mm^2)
Control	–	10	94·5 ± 9·7
Cystathione	2	6	80·4 ± 15·8
	5	6	34·0 ± 12·8*
Extract			
100 mg kg^{-1}	1·93	6	64·9 ± 16·9
330 mg kg^{-1}	6·37	8	18·6 ± 6·5*
1000 mg kg^{-1}	19·3	8	14·8 ± 4·1*

Gastric mucosal injury was produced by ischaemia-reperfusion resulting from clamping of the rat coeliac artery. The extract or cystathionine was administered orally 30 min before ischaemia. Values are mean ± s.e.m. *$P < 0.01$ compared with control.

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to be a result of the scavenging of superoxide radicals in the stomach (Wada et al 1995, 1996). Cystathionine might, therefore, be responsible for the protective effect of the extract of *Agkistrodon blomhoffii* on acute gastric mucosal injury. In this study the cystathionine content of the extract of *Agkistrodon blomhoffii* was 19·3 mg (g extract)$^{-1}$. The amounts of cystathionine included in the extract of *Agkistrodon blomhoffii* were calculated as 1·93, 6·37 and 19·3 mg kg^{-1}, respectively (Table 1). The same doses of cystathionine showed the same protective effect on acute gastric mucosal injury (Table 1).

Taurine is reported to have a protective effect against ammonia-induced gastric damage (Murakami et al 1989). This protective effect is, however, a result of scavenging of hypochlorous acid and monochloramine. Taurine did not show any protective effect on ischaemia-reperfusion injury (data not presented). Taurine is, therefore, probably not responsible for the protective effect in the present model. Further investigations are necessary to clarify the mechanism of the protective effect of the extract of *Agkistrodon blomhoffii*.

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