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SHORT REPORT

Pharmacological effects on capillary permeability increasing activity of Russell's viper *(Daboia russelii siamensis)* venom

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Russell's viper bite is common in tropical countries. There is a geographical variation in clinical features of Russell's viper bites among countries and distinctive features of Russell's viper bite of Myanmar are pituitary haemorrhage and generalized increased capillary permeability evidenced by bilateral conjunctival oedema and facial oedema [1]. *In vitro* increased capillary permeability activity of Russell's viper (*Daboia russelii siamensis*) in Myanmar has been documented [2]. In order to find out the possible mechanism of this increased capillary permeability action of the venom, the following experiment was carried out in 1995.

Russell's viper(*D.r. siamensis*) venom used in the experiment was bought from Myanmar Pharmaceutical Factory. The minimum capillary permeability increasing dose was determined according to WHO recommended method on rodent [3]. A total of 150 male Wistar strain rats (200-230 gm body weight) from Laboratory Animal Services Division, Department of Medical Research (LM) were used. Five pharmacological agents (a) anti 5 hydroxy tryptinine (cyproheptadine, MSD, 4 mg/kg and promethazine hydrochloride, M&B, 10 mg/kg, (b) anti prostaglandin (indomethacin, MSD, 30 mg/kg), (c) antiphospholipase A_2 (hydrocortisone, UpJohn, 100 mg/kg, (d) anti H_1 receptor (diphenhydramine, Sigma, 10 mg/kg) and (e) anti-serotonin (methylsergide, Sandoz, 4 mg/kg) were used [4].

The pharmacological agents (0.1ml) dissolved in normal saline in varying concentrations (saline alone for the control) were injected intraperitoneally into the rats one hour before venom challenge. One minimum capillary permeability increasing dose (MCPID) (0.007 µg/ml) of the venom was dissolved in normal saline and then 0.1 ml/dose of the venom was injected intradermally into two marked sections on the depilated dorsal skin of the rat 20 minutes before 2 ml intravenous injection of 1% Evan's Blue dye (Sigma) in saline. Twenty minutes after the dye injection, the animal was sacrificed under light ether anaesthesia, then dorsal skin was removed and transverse diameter of the blue spots of the inner skin were measured in millimetre. Mean transverse diameters of four spots were recorded. The dose of the agent that gave 50% reduction of the diameter of the blue spot compared to the control (10x10 mm) was taken as end point. Three rats per dose were used and five doses with duplicate experiments were carried out for each pharmacological agent.

It was found that pretreatment of the animals with 2.5 µg/kg diphenhydramine, 125 µg/kg methyl sergide, 250 µg/kg indomethacin and promethazine hydrochloride, 500 µg/kg cyproheptadine and

1250 µg/kg of hydrocortisone resulted in 50% reduction of the size of the blue spot. It was evident that pretreatment of the rats with all pharmacological agents could inhibit the capillary permeability increasing activity of the venom. In other words, histamine, serotonin, 5HT, prostaglandin and PLA_2 play a role in causing increased capillary permeability of the venom.

Above all, diphenhydramine, anti H_1 receptor antagonist was the most potent agent. A similar finding was seen in *Trimeresurus mucroaquamatus* venom that histamine released from mast cells plays an important role in production of oedema and increased capillary permeability activity of the venom [5]. The proteases, phospho-lipases, membrane damaging polypeptides toxins and endogeneous autacoids released by the venom such as histamine, 5HT and kinins of the venom may induce increased vascular permeability [1]. It is concluded that histamine together with other agents namely serotonin, 5HT, prostaglandin and PLA_2 plays an important role in causing increased capillary permeability activity of Russell's viper venom.

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