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Marimastat attenuates local tissue damage induced by Indonesian *Trimeresurus insularis* and *Calloselasma rhodostoma* venoms in a mouse skin model

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Abstract

Snakebite-induced local tissue damage remains a challenge in snakebite envenoming management because venom toxins rapidly disrupt vascular and extracellular matrix integrity at the bite site. This study evaluated the inhibitory effect of marimastat, an inhibitor of zinc-dependent metalloproteinases, against local tissue damage induced by Indonesian *Trimeresurus insularis* and *Calloselasma rhodostoma* venoms in a mouse skin model. The minimum hemorrhagic dose (MHD) of *C. rhodostoma* venom was determined in BALB/c mice and estimated to be 7.07 µg, while the MHD of *T. insularis* was adopted from a previous study. Mice received intradermal injections of venom at 2× MHD, either alone or pre-incubated with marimastat at venom:marimastat ratios of 1:1, 1:5, and

1:10 based on MHD equivalents. Macroscopic hemorrhage and histopathological changes, including erythrocyte extravasation, inflammatory cell infiltration, and collagen degradation, were assessed three hours after injection. Both venoms induced marked hemorrhagic lesions and tissue damage. Marimastat reduced venom-induced hemorrhage in both models, with near-complete inhibition in the *T. insularis* 1:10 group and complete inhibition in the *C. rhodostoma* 1:10 group. Marimastat also decreased erythrocyte extravasation, inflammatory infiltration, and collagen degradation, indicating preservation of microvascular and dermal matrix integrity. These findings support the central role of snake venom metalloproteinases in local viperid tissue damage and highlight marimastat as a promising adjunctive treatment for reducing venom-induced skin injury. ©2026 The Japanese Society of Veterinary Science This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License. (CC BY-NC-ND 4.0: <https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Author keywords

hemorrhage; marimastat; metalloproteinase; snakebite; venom

Indexed keywords

MeSH

Animals; Calloselasma rhodostoma; Crotalid Venoms; Crotalinae; Disease Models, Animal; Hemorrhage; Hydroxamic Acids; Male; Mice; Mice, Inbred BALB C; Skin; Snake Bites; Trimeresurus; Venomous Snakes

EMTREE drug terms

hydroxamic acid; marimastat; snake venom

EMTREE medical terms

animal; Bagg albino mouse; bleeding; Calloselasma rhodostoma; Crotalinae; disease model; drug effect; drug therapy; male; mouse; pathology; poisonous snake; skin; snakebite; Trimeresurus

Chemicals and CAS Registry Numbers

Unique identifiers assigned by the Chemical Abstracts Service (CAS) to ensure accurate identification and tracking of chemicals across scientific literature.

marimastat

154039-60-8

snake venom

55230-69-8

Crotalid Venoms

Hydroxamic Acids

marimastat

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