

PROTECTIVE EFFECT OF NEEM *Azadirachta indica* A. JUSS, 1830 BARK EXTRACT AGAINST HEMORRHAGIC LESIONS AND HISTOPATHOLOGICAL DAMAGE CAUSED BY *Trimeresurus insularis* KRAMER, 1977 VENOM

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ABSTRACT

Snakebite envenoming is a global health issue, with an estimated 2.5 million cases per year and 85,000 deaths. The primary treatment available is the use of antiserum, which has limitations due to the high costs of production and time-consuming development. The use of alternative plants, such as Neem (*Azadirachta indica*), has become one approach in the development of first aid for snakebite cases. Observations on hemorrhagic lesions and histopathological tissue damage were conducted to assess the impact of Neem plant extract (*A. indica*) on the effects of envenomation from the snake species *Trimeresurus insularis*. The bark of the Neem tree was extracted using a freeze-drying method with distilled water as the test solution. Treatments included determining the Minimum Hemorrhagic Dose (MHD) and visual observations of hemorrhagic lesions and histopathological tissue damage through imaging using a camera, both macroscopically and microscopically. Data were analyzed using one-way ANOVA and Duncan's test, as well as the Kruskal-Wallis and Dunn tests for nonparametric data with a p -value < 0.05 . The *Minimum Hemorrhagic Dose* (MHD) of *T. insularis* venom was found to be 8.4 μ g. Macroscopic observations of hemorrhagic lesions showed a reduction in the size of hemorrhagic lesions after administration of Neem extract at a 100 MHD dose. Microscopic observations of hemorrhagic lesions revealed a decrease in the thickness of the epidermis and hypodermis layers, but an increase in the thickness of the dermis layer. Histopathological damage observations showed collagen degradation and infiltration of inflammatory cells caused by *T. insularis* venom, which was successfully minimized by the Neem extract at the 100 MHD dose. The results of this study indicate that Neem bark extract has the potential as a natural antihemorrhagic agent in countering the toxic effects of *T. insularis* venom..

Keywords: Snake venom, Trimeresurus insularis, Neem extract, Hemotoxin, Hemorrhagic lesions.

EFEK PROTEKTIF EKSTRAK KULIT BATANG MIMBA *Azadirachta indica* A. JUSS, 1830 TERHADAP LESI HEMORAGIK DAN KERUSAKAN HISTOPATOLOGIS AKIBAT BISA ULAR *Trimeresurus insularis* KRAMER, 1977

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INTISARI

Gigitan ular berbisa merupakan masalah kesehatan global dengan estimasi 2,5 juta kasus per tahun dan 85.000 kematian. Penanganan utama yang tersedia adalah penggunaan antiserum yang memiliki keterbatasan akibat biaya produksi dan pengembangan yang memakan waktu. Penggunaan alternatif tanaman seperti Mimba (*Azadirachta indica*) menjadi salah satu langkah dalam pengembangan pertolongan pertama dalam kasus gigitan ular berbisa. Pengamatan terhadap lesi hemoragik dan kerusakan histopatologis jaringan dilakukan untuk melihat dampak dari ekstrak tanaman Mimba (*A. indica*) terhadap efek gigitan berbisa ular *Trimeresurus insularis*. Kulit batang Mimba diekstrak menggunakan metode *freeze-dry* dengan pelarut akuades sebagai larutan uji. Perlakuan yang digunakan meliputi penentuan MHD (*Minimum Hemorrhagic Dose*) dan pengamatan visual terhadap lesi hemoragik serta kerusakan histopatologis jaringan melalui pengambilan gambar menggunakan kamera baik secara makroskopis maupun mikroskopis. Data dianalisis menggunakan ANOVA satu arah dan uji Duncan, serta Kruskal-Wallis dan uji Dunn untuk data nonparametric dengan nilai $p < 0,05$. *Minimum Haemorrhagic Dose* (MHD) bisa ular *T. insularis* diperoleh sebesar 8,4 µg. Pengamatan lesi hemoragik makroskopis menunjukkan penurunan luasan lesi hemoragik pemberian ekstrak Mimba dengan dosis 100MHD. Pada pengamatan lesi hemoragik mikroskopis menurunkan ketebalan lapisan epidermis dan hypodermis namun meningkatkan ketebalan lapisan dermis. Pengamatan kerusakan histopatologis menunjukkan adanya degradasi kolagen dan infiltrasi sel inflamasi akibat bisa ular *T. insularis* yang berhasil diminimalkan oleh ekstrak mimba pada dosis 100MHD. Hasil penelitian ini menunjukkan bahwa ekstrak kulit batang mimba memiliki potensi sebagai agen antihemoragik alami dalam mengatasi efek toksik bisa ular *T. insularis*.

Kata Kunci: Bisa ular, *Trimeresurus insularis*, ekstrak Mimba, Hemotoksin, Lesi hemoragik.