

SITOTOKSISITAS DAN INDUKSI APOPTOSIS *VENOM KOBRA JAWA Naja sputatrix* Boie, 1827 TERHADAP SEL KANKER PARU-PARU A549

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INTISARI

Kanker paru-paru merupakan jenis kanker yang paling umum didiagnosis dan menjadi penyebab utama kematian akibat kanker. Keterbatasan terapi konvensional, seperti operasi, radiasi, dan kemoterapi mendorong pencarian agen antikanker baru yang lebih efektif dan memiliki efek samping lebih rendah. *Venom* ular diketahui mengandung berbagai komponen bioaktif yang berpotensi dimanfaatkan sebagai terapi kanker. Penelitian ini bertujuan untuk mengevaluasi efek sitotoksitas dan kemampuan induksi apoptosis *venom* kobra jawa *Naja sputatrix* terhadap sel kanker paru-paru A549, serta menilai selektivitasnya menggunakan sel normal Vero. Metode yang digunakan meliputi uji sitotoksitas menggunakan MTT *assay* dan nilai IC_{50} melalui metode interpolasi linear. Uji apoptosis dilakukan menggunakan *flow cytometry* dengan pewarnaan Annexin V-FITC dan *propidium iodide* (PI) pada berbagai konsentrasi *venom* ular kobra jawa. Data sitotoksitas dianalisis menggunakan *one-way* ANOVA ($p \leq 0,05$), dilanjutkan dengan uji *post hoc* Duncan dan Games-Howell, sedangkan data apoptosis dianalisis menggunakan uji Kruskal-Wallis ($p \leq 0,05$) dan dilanjutkan uji Mann-Whitney untuk melihat perbedaan antar kelompok perlakuan. Hasil uji sitotoksitas menunjukkan bahwa *venom* kobra jawa menurunkan viabilitas sel A549 secara *dose-dependent* dengan nilai IC_{50} sebesar 36,7 $\mu\text{g/mL}$ dan sel Vero sebesar 22,9 $\mu\text{g/mL}$ sehingga menghasilkan indeks selektivitas (SI) 0,62. Hasil uji apoptosis menunjukkan bahwa *venom* kobra jawa mampu menginduksi apoptosis pada sel A549. Pada konsentrasi 19 $\mu\text{g/mL}$ ($\frac{1}{2} IC_{50}$), apoptosis awal tercatat sebesar $28,17 \pm 2,41\%$ dan apoptosis akhir sebesar $7,33 \pm 0,41\%$. Pada konsentrasi 38 $\mu\text{g/mL}$ (IC_{50}), apoptosis awal meningkat menjadi $36,63 \pm 0,50\%$, sedangkan apoptosis akhir sebesar $4,90 \pm 0,70\%$. Meskipun demikian, apoptosis akhir yang dihasilkan masih jauh lebih rendah dibandingkan *doxorubicin*, dan persentase nekrosis relatif rendah pada semua perlakuan. Secara keseluruhan, *venom* kobra jawa menunjukkan aktivitas sitotoksik dan dapat menginduksi apoptosis pada sel A549, tetapi selektivitasnya terhadap sel kanker masih rendah.

Kata kunci: apoptosis, sel A549, sel Vero, sitotoksitas, *venom* kobra jawa.

CYTOTOXICITY AND APOPTOTIC INDUCTION OF JAVANESE COBRA VENOM *Naja sputatrix* Boie, 1827 ON A549 LUNG CANCER CELLS

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ABSTRACT

*Lung cancer is the most commonly diagnosed type of cancer and a leading cause of cancer deaths. The limitations of conventional therapies, such as surgery, radiation, and chemotherapy, encourage the search for new anticancer agents that are more effective and have fewer side effects. Snake venom is known to contain various bioactive components that have the potential to be used as cancer therapy. This study aims to evaluate the cytotoxicity effect and apoptosis induction ability of Javanese cobra *Naja sputatrix* venom on A549 lung cancer cells, as well as assess its selectivity using normal Vero cells. The methods used include cytotoxicity testing using the MTT assay and IC_{50} values using the linear interpolation method. Apoptosis testing was carried out using flow cytometry with Annexin V-FITC and propidium iodide (PI) staining at various concentrations of Javanese cobra venom. Cytotoxicity data were analyzed using one-way ANOVA ($p \leq 0.05$), followed by Duncan and Games-Howell post hoc tests, while apoptosis data were analyzed using the Kruskal-Wallis test ($p \leq 0.05$) and continued with the Mann-Whitney test to see the differences between treatment groups. The results of the cytotoxicity test showed that Javanese cobra venom decreased the viability of A549 cells in a dose-dependent manner with an IC_{50} value of 36.7 $\mu\text{g/mL}$ in Vero cells and 22.9 $\mu\text{g/mL}$ in Vero cells, resulting in a selectivity index (SI) of 0.62. The results of the apoptosis test showed that Javanese cobra venom was able to induce apoptosis in A549 cells. At a concentration of 19 $\mu\text{g/mL}$ ($\frac{1}{2} IC_{50}$), early apoptosis was recorded at $28.17 \pm 2.41\%$ and late apoptosis at $7.33 \pm 0.41\%$. At a concentration of 38 $\mu\text{g/mL}$ (IC_{50}), early apoptosis increased to $36.63 \pm 0.50\%$, while late apoptosis was $4.90 \pm 0.70\%$. However, the resulting late apoptosis was still much lower than doxorubicin, and the percentage of necrosis was relatively low in all treatments. Overall, Javanese cobra venom exhibited cytotoxic activity and could induce apoptosis in A549 cells, but its selectivity towards cancer cells was still low.*

Keywords: apoptotic, A549 cells, cytotoxicity, javanese cobra venom, Vero cell.