

**IDENTIFIKASI PEPTIDA POTENSIAL ANTIKANKER DARI
HIDROLISAT TRIPSIN PROTEIN VENOM ULAR KOBRA MATA
TUNGGAL (*Naja kaouthia*)**

Garnis Putri Erlista
20/466461/PPA/06027

INTISARI

Telah dilakukan penelitian identifikasi peptida antikanker dari hidrolisat tripsin protein venom ular kobra mata tunggal *Naja kaouthia*. Urutan asam amino peptida dengan aktivitas antikanker diidentifikasi sebagai kandidat desain obat antikanker baru. Tujuan dari penelitian ini yaitu mendapatkan hidrolisat protein venom ular *Naja kaouthia* menggunakan hidrolisis enzim tripsin, mengetahui aktivitas antikanker hidrolisat dan fraksi peptida hidrolisat, memahami struktur peptida antikanker dari fraksi hidrolisat dengan LC-HRMS, dan mampu memprediksi mekanisme aksi peptida antikanker dengan teknik *in silico*.

Protein venom ular *Naja kaouthia* dihidrolisis secara enzimatis menggunakan tripsin. Hidrolisat protein difraksinasi menggunakan kolom RP-SPE HyperSep Retain PEP yang dielusi dengan variasi komposisi campuran metanol-air. Fraksi peptida masing-masing diuji antikanker terhadap garis sel kanker payudara MCF-7 dan sel Vero menggunakan metode MTT. Peptida yang terdapat dalam fraksi peptida yang paling aktif sebagai antikanker diidentifikasi menggunakan LC-HRMS. Struktur peptida-peptida teridentifikasi ditambatkan secara *in silico* ke protein reseptor EGFR.

Hidrolisis protein venom dengan tripsin menghasilkan nilai derajat hidrolisis sebesar 77,5%. Fraksi peptida hasil hidrolisat dengan aktivitas antikanker paling aktif ditunjukkan oleh fraksi 25% metanol pada sel kanker payudara MCF-7 dengan nilai IC_{50} sebesar 4,17 $\mu\text{g/mL}$ dan nilai indeks selektivitasnya sebesar 12,87. Urutan asam amino peptida yang berpotensi sebagai senyawa antikanker yaitu GDNLIQMPGAAMK, NSLLVK, SLLVK, GSGTVPDDLDR, GVGGTQLEVIK, IWDTIEK, WWSDHR, dan MFMVSNK. Hasil penambatan molekul menunjukkan bahwa peptida WWSDHR memberi interaksi spesifik terhadap asam amino Met769 dengan afinitas ikatan sebesar -9,3 kkal/mol, sedangkan peptida IWDTIEK memberi interaksi spesifik terhadap asam amino Lys721 dengan afinitas ikatan sebesar -8,4 kkal/mol.

Kata kunci: peptida, venom ular, hidrolisat, tripsin, antikanker

***IDENTIFICATION OF ANTICANCER POTENTIAL PEPTIDE FROM
TRYPSIN HYDROLYSATE PROTEIN VENOM OF MONOCLED COBRA
(*Naja kaouthia*)***

Garnis Putri Erlista
20/466461/PPA/06027

ABSTRACT

Research has been conducted to identify anticancer peptides from trypsin hydrolysate venom protein of the single-eyed cobra *Naja kaouthia*. The amino acid sequence of peptides with anticancer activity was identified as a candidate for the design of a new anticancer drug. The purpose of this study is to obtain protein tryptic hydrolysate from *Naja kaouthia* protein venom, find out the anticancer activity of the peptide fraction resulting from the hydrolysate, and understanding the structure of peptides which are active as anticancer using LC-HRMS, and predict the mechanism of action of anticancer peptides using in silico technique.

Naja kaouthia snake venom protein was hydrolyzed using trypsin. Protein hydrolysates were fractionated using the RP-SPE HyperSep Retain PEP column eluted with variations composition of methanol-water mixture. Peptide fractions were tested for anticancer against MCF-7 breast cancer cell lines and Vero cells respectively using the MTT method. Peptides present in the most active anticancer fractions were identified using LC-HRMS. The identified peptide structures were docked to the EGFR receptor protein.

Hydrolysis of venom protein with trypsin results in up to 77.5% degree of hydrolysis. The peptide fraction of the hydrolysate results with the most active anticancer activity is fraction eluted by 25% methanol with an IC_{50} value of 4.17 $\mu\text{g/mL}$ against MCF-7 breast cancer cells and a selectivity index value of 12.87. The amino acid sequence of peptides that have the potential to be anticancer compounds are GDNLIQMPGAAMK, NSLLVK, SLLVK, GSGTPVDDLDR, GVGGTQLEVIK, IWDTIEK, WWSHDR, and MFMVSNK. The results of molecular docking showed that WWSHDR peptides gave a specific interaction with amino acid Met769 of EGFR with binding affinity energy of -9.3 kcal/mol, while the IWDTIEK peptide gave a specific interaction with amino acid Lys721 of EGFR with binding affinity energy of -8.4 kcal/mol.

Keywords: peptide, snake venom, hydrolysate, trypsin, anticancer