

ABSTRAK

Latar Belakang: Stroke merupakan salah satu penyebab utama kematian di seluruh dunia. Keterbatasan model hewan dalam merepresentasikan patologi stroke pada manusia secara akurat menjadi tantangan bagi kedokteran translasional di bidang stroke. Ikan zebra (*Danio rerio*) yang diinduksi dengan ponatinib dapat menjadi model alternatif untuk stroke iskemik. *Graptophyllum pictum* (daun ungu) menunjukkan potensi sebagai terapi stroke berkat kandungan senyawa bioaktif yang dapat menghambat agregasi trombosit.

Metode: Uji toksisitas akut ekstrak etanol daun ungu dilakukan pada embrio zebrafish usia 6 hours post-fertilization (hpf) dengan protokol OECD No. 236 untuk menentukan nilai LC50 dan LC10. Larva zebrafish 2 days post-fertilization (dpf) dibagi menjadi 8 kelompok. Larva diinduksi ponatinib 1 µg/mL dan diberikan perlakuan ekstrak etanol daun ungu (dosis ¼ LC10, ½ LC10, dan LC10). Larva diberikan edaravone 12,5 µg/mL dan DMSO 0.1% sebagai kontrol positif dan kontrol pelarut. Evaluasi dilakukan terhadap motilitas larva, edema otak, apoptosis sel, dan area trombus.

Hasil: Uji toksisitas ekstrak etanol daun *Graptophyllum pictum* menunjukkan nilai LC50 sebesar 77,37 µg/mL (kategori sedikit toksik) dan nilai LC10 sebesar 38,107 µg/mL. Induksi ponatinib 1 µg/mL terbukti memicu stroke iskemik yang ditandai dengan penurunan motilitas, peningkatan edema otak, pembentukan area trombus, serta peningkatan apoptosis sel otak. Pemberian ekstrak etanol daun ungu dosis 38,107 µg/mL secara signifikan memulihkan motilitas larva, mengurangi edema otak, dan menurunkan tingkat apoptosis sel dengan efektivitas yang sebanding dengan edaravone 12,5 µg/mL ($p < 0,05$). Dosis ekstrak etanol daun ungu 9,52 µg/mL merupakan dosis terendah yang aman dan efektif secara signifikan menurunkan area trombus otak.

Kesimpulan: Ekstrak etanol daun ungu berpotensi memperbaiki stroke iskemik yang diinduksi ponatinib pada larva zebrafish melalui pengurangan area trombus, penurunan edema otak, pencegahan apoptosis sel, dan pemulihan fungsi motilitas larva.

Kata Kunci: *Graptophyllum pictum*, Daun Ungu, Zebrafish, Stroke Iskemik, Ponatinib.

ABSTRACT

Background: Stroke remains a leading cause of death worldwide. The limitations of animal models in representing human pathology pose a significant challenge for translational stroke medicine. Ponatinib-induced zebrafish (*Danio rerio*) offer a potential alternative model for ischemic stroke. Purple leaves (*Graptophyllum pictum*) show promise as a stroke therapy due to bioactive compounds with anti-platelet aggregation properties.

Methods: An acute toxicity test of the *Graptophyllum pictum* ethanol extract was conducted on zebrafish embryos at 6 hours post-fertilization (hpf) following OECD Guideline No. 236 to determine LC50 and LC10 values. Zebrafish larvae at 2 days post-fertilization (dpf) were divided into eight groups. The larvae were induced with 1 µg/mL ponatinib and treated with *Graptophyllum pictum* ethanol extract at doses of ¼ LC10, ½ LC10, and LC10. Larvae were also treated with 12.5 µg/mL edaravone as a positive control and 0.1% DMSO as a vehicle control. Evaluations were performed regarding larval motility, cerebral edema, cell apoptosis, and thrombus area.

Results: The toxicity test showed an LC50 value of 77.37 µg/mL (slightly toxic category) and an LC10 value of 38.107 µg/mL for the *Graptophyllum pictum* ethanol extract. Induction with 1 µg/mL ponatinib successfully triggered ischemic stroke, characterized by decreased motility, increased brain edema, thrombus formation, and increased brain cell apoptosis. Treatment with *Graptophyllum pictum* ethanol extract at a dose of 38.107 µg/mL significantly restored larval motility, reduced brain edema, and decreased cellular apoptosis, showing comparable effectiveness to 12.5 µg/mL edaravone ($p < 0.05$). The dose of 9.52 µg/mL was identified as the lowest safe and effective dose to significantly reduce the brain thrombus area.

Conclusion: The ethanol extract of *Graptophyllum pictum* has the potential to treat ponatinib-induced ischemic stroke in zebrafish larvae by reducing thrombus area, alleviating cerebral edema, preventing cell apoptosis, and restoring larval motility.

Keywords: *Graptophyllum pictum*, Purple Leaves, Zebrafish, Ischemic Stroke, Ponatinib.