

INTISARI

Penatalaksanaan luka masih menjadi tantangan besar di bidang kesehatan karena memerlukan waktu perawatan lama dengan pembiayaan tinggi. Gendola (*Basella rubra* L.) memiliki aktivitas antioksidan, antiinflamasi dan antibakteri yang berpotensi mendukung penyembuhan luka. Penelitian ini bertujuan mengkaji potensi ekstrak *B. rubra* dalam formulasi nanoemulsi dan nanoemulgel, mengidentifikasi senyawa serta protein target, dan mekanismenya pada penyembuhan luka eksisi.

Senyawa, protein target, serta jalur pensinyalan diprediksi menggunakan *network pharmacology* (NP), dilanjutkan dengan *molecular docking*. Konfirmasi keberadaan senyawa target dilakukan dengan LC-HRMS, sedangkan protein target dan mekanisme dilakukan secara *in vitro* menggunakan sel RAW 264.7 dan NIH 3T3 dengan metode ELISA. Formulasi nanoemulsi dan nanoemulgel dioptimalkan menggunakan *Design Expert 13*, kemudian diuji secara *in vivo* pada model luka eksisi *full-thickness*. Pengamatan dilakukan secara makroskopis dan histologis, kemudian dianalisis menggunakan *Image J* dan *Image Raster 3*.

Network pharmacology memprediksi 10 senyawa target, termasuk *linoleic acid*, *ferulic acid*, *luteolin* dan *quercetin*, dengan protein target seperti IL-1 β , TNF- α , EGFR, VEGFA, serta jalur pensinyalan PI3K-Akt, TNF, HIF-1, VEGF dan relaxin. Dua puluh lima senyawa dihasilkan dari identifikasi dengan LC-HRMS, dimana 10 senyawa prediksi terkonfirmasi didalamnya. Nanoemulsi yang dihasilkan memiliki ukuran droplet $96,340 \pm 0,586$ nm, PDI $0,284 \pm 0,008$, zeta potensial $-10,033 \pm 0,902$ mV dan *drug load* $47,516 \pm 1,250$ %. Sediaan nanoemulgel menghasilkan viskositas $3652,268 \pm 76,545$ cP, daya sebar $6,908 \pm 0,044$ cm, daya lekat $1,177 \pm 0,049$ detik, dan pH $6,175 \pm 0,034$. Formula nanoemulgel memenuhi kriteria yang dipersyaratkan. Secara *in vitro*, ekstrak dan nanoemulsi menurunkan kadar TNF- α , IL-1 β dan NO serta meningkatkan kadar EGFR, VEGFA, proliferasi dan migrasi fibroblas dibandingkan dengan kontrol negatif ($p < 0,001$). *B. rubra* berperan pada seluruh fase penyembuhan luka, dengan mekanisme penurunan infiltrasi sel radang serta peningkatan jumlah pembuluh darah, persentase reepitelisasi dan pembentukan kolagen pada uji *in vivo*. Korelasi antara hasil *network pharmacology*, uji *in vitro* dan *in vivo*, membuktikan kontribusi *B. rubra* secara signifikan terhadap peningkatan efikasi penyembuhan luka eksisi. Formulasi nanoemulsi dan nanoemulgel memberikan efikasi yang lebih tinggi dibandingkan ekstrak, kontrol positif dan kontrol negatif ($p < 0,001$).

Kata Kunci : ***Basella rubra*, senyawa target, protein target, mekanisme, luka eksisi**

ABSTRACT

Wound management remains a major challenge in the healthcare field because it requires a long treatment period and is costly. Gendola (*Basella rubra* L.) possesses antioxidant, anti-inflammatory, and antibacterial activities that have the potential to support wound healing. This study aims to investigate the potential of *B. rubra* extract in nanoemulsion and nanoemulgel formulations, identify target compounds and proteins, and elucidate the mechanisms involved in excision wound healing.

Target compounds, proteins, and signaling pathways were predicted using network pharmacology (NP), followed by molecular docking. The presence of target compounds was confirmed via LC-HRMS, while target proteins and mechanisms were confirmed in vitro using RAW 264.7 and NIH 3T3 cells via ELISA. The nanoemulsion and nanoemulgel formulations were optimized using Design Expert 13, then tested in vivo on a full-thickness excision wound model. Observations were made macroscopically and histologically, then analyzed using Image J and Image Raster 3.

Network pharmacology predicted 10 target compounds, including linoleic acid, ferulic acid, luteolin, and quercetin, with target proteins such as IL-1 β , TNF- α , EGFR, VEGF-A, as well as the PI3K-Akt, TNF, HIF-1, VEGF, and relaxin signaling pathways. Twenty-five compounds were identified via LC-HRMS, with 10 of the predicted compounds confirmed among them. The resulting nanoemulsion has a droplet size of 96.340 ± 0.586 nm, PDI 0.284 ± 0.008 , zeta potential -10.033 ± 0.902 mV, and a drug load of $47.516 \pm 1.250\%$. The nanoemulgel formulation exhibited a viscosity of 3652.268 ± 76.545 cP, spreadability of 6.908 ± 0.044 cm, adhesion time of 1.177 ± 0.049 seconds, and a pH of 6.175 ± 0.034 . Overall, the nanoemulgel met the required criteria. In vitro, the extract and nanoemulsion reduced levels of TNF- α , IL-1 β , and NO and increased levels of EGFR, VEGFA, fibroblast proliferation, and migration compared to the negative control ($p < 0.001$). *B. rubra* plays a role in all phases of wound healing. In vivo testing showed a reduction in inflammatory cell infiltration and an increase in the number of blood vessels, the percentage of re-epithelialization, and collagen formation. The correlation between the results of network pharmacology, in vitro, and in vivo tests demonstrates *B. rubra*'s significant contribution to enhancing the efficacy of excision wound healing. The nanoemulsion and nanoemulgel formulations provided higher efficacy compared to the extract, positive control, and negative control ($p < 0.001$).

Keywords: *Basella rubra*, active compounds, proteins target, mechanisms, full-thickness wound