IDENTIFIKASI TERPENOID KALUS *Gyrinops versteegii* (Gilg.) Domke DENGAN ELISITOR ASAM SALISILAT DAN PREDIKSI AKTIVITAS ANTIBAKTERI *Escherichia coli* DAN *Staphylococcus aureus* SECARA *IN-SILICO*

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INTISARI

Kasus resistensi antibiotik terhadap bakteri *Escherichia coli* dan *Staphylococcus aureus* di Indonesia terjadi sejak 2018. Hal ini meningkatkan urgensi eksplorasi antibiotik alternatif terhadap kedua bakteri tersebut, salah satunya dari terpenoid. Pemanfaatan daun *G. versteegii* sebagai teh herbal dikarenakan kandungan terpenoid yang diketahui memiliki efek farmakokinetik. Namun, produksi metabolit sekunder memiliki berbagai keterbatasan sehingga dibutuhkan elisitasi. Elisitasi dengan asam salisilat diketahui mampu meningkatkan kandungan terpenoid. Oleh karena itu, pada penelitian dilakukan identifikasi terpenoid kultur kalus *G. versteegii* yang dielisitasi asam salisilat dan pengkajian potensi aktivitas antibakteri terpenoid terhadap bakteri *E. coli* dan *S. aureus* secara *in-silico*. Penelitian diawali dengan induksi kalus *G. versteegii* dan dielisitasi dengan asam salisilat 15 μM selama 10 minggu. Kalus diekstraksi melalui sonikasi dan diidentifikasi profil terpenoid dengan GC-MS. Terpenoid dilanjutkan dengan prediksi potensi aktivitas antibakteri, *drug-likeness*, toksisitas, profil farmakokinetik, serta *molecular docking* terhadap enzim *DNA-gyrase* (PDB ID: 6F86) dan *penicillin-binding protein* (PDB ID: 3HUN). Berdasarkan hasil *profiling* terpenoid dengan GC-MS, diperoleh dua terpenoid dari ekstrak kalus *G. versteegii* dengan terelisitasi asam salisilat 15 μM, yaitu *caryophyllene oxide* dan *squalene*; dua senyawa dari ekstrak etanol kalus kontrol, yaitu *α-santalol* dan *β-santalol*; serta tiga senyawa dari ekstrak etanol daun *G. versteegii,* yakni *squalene, neophytadiene,* dan *α-gurjunene*. Berdasarkan skrining aktivitas antibakteri, *drug-likeness*, toksisitas dan profil farmakokinetik, dua dari enam senyawa terpenoid yaitu *caryophyllene oxide* dan *squalene* memenuhi persyaratan sebagai kandidat antibiotik dan dilanjutkan dengan uji *molecular docking*. *Caryophyllene oxide* dan *squalene* memiliki pengikatan yang sama terhadap enzim *DNA-gyrase* (-5,9 kcal/mol) dan *penicillin-binding protein* (-6,8 kcal/mol) pada *E. coli* dan *S. aureus*. Energi ikat pada kedua senyawa terpenoid dengan enzim *DNA-gyrase* dan *penicillin-binding protein* lebih lemah dibandingkan kontrol positif *amoxicillin.* Dengan demikian, *caryophyllene oxide* dan *squalene* diduga kurang efektif dalam menghambat aktivitas *DNA-gyrase* dan *penicillin-binding protein* secara *in-silico*.

Kata kunci: *Escherichia coli, Gyrinops versteegii, Staphylococcus aureus*, antibakteri, *in-silico*, terpenoid.

IDENTIFICATION OF TERPENOIDS FROM *Gyrinops versteegii* (Gilg.) Domke CALLUS ELICITED WITH SALICYLIC ACID AND IN-SILICO ANTIBACTERIAL ACTIVITY PREDICTION AGAINST *Escherichia coli* AND *Staphylococcus aureus*

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ABSTRACT

Cases of antibiotic resistance to *Escherichia coli* and *Staphylococcus aureus* bacteria in Indonesia have occurred since 2018. This increases the urgency of exploring alternative antibiotics against both bacteria, one of which is terpenoids. The use of *G. versteegii* leaves as herbal tea due to the content of terpenoids which are known to have pharmacokinetic effects. However, the production of secondary metabolites has various limitations so elicitation is needed. Elicitation with salicylic acid is known to increase the content of terpenoids. Therefore, the study is aimed to identify terpenoids from *G. versteegii* callus culture elicited with salicylic acid and assessed the potential antibacterial activity of terpenoids against *E. coli* and *S. aureus* through in-silico. The study began with callus induction of *G. versteegii* and elicited with 15 µM salicylic acid for 10 weeks. The callus were extracted via sonication and identified its terpenoid profiles with GC-MS. Terpenoids were followed by prediction of potential antibacterial activity, drug-likeness, toxicity, pharmacokinetic profile, and molecular docking with DNA-gyrase (PDB ID: 6F86) and penicillin-binding proteins (PDB ID: 3HUN). Based on the profiling results of terpenoids through GC-MS, two terpenoids were obtained from *G. versteegii* callus extract elicited with 15 µM salicylic acid, namely caryophyllene oxide and squalene; two compounds from the control callus ethanol extract, namely α-santalol and β-santalol*;* and three compounds from ethanol extract of *G. versteegii* leaves, namely squalene, neophytadiene, and α-gurjunene. Based on the screening of antibacterial activity, drug-likeness, toxicity and pharmacokinetic profile, two out of six terpenoid compounds namely caryophyllene oxide and squalene met the requirements as antibiotic candidates and continued with molecular docking assays. Caryophyllene oxide and squalene bind equally to DNA-gyrase enzymes (-5.9 kcal/mol) and penicillin-binding proteins (-6.8 kcal/mol) *in E. coli* and *S. aureus*. The binding energy in both terpenoid compounds with DNA-gyrase and penicillin-binding protein were weaker than the positive control *of* amoxicillin. Thus, caryophyllene oxide and squalene are thought to be less effective in inhibiting DNA-gyrase activity and penicillin-binding proteins through in-silico.

Keywords: *Escherichia coli*, *Gyrinops versteegii*, *Staphylococcus aureus*, antibacterial, in-silico, terpenoid.