INTISARI

Pentagamavunon-1 (PGV-1) merupakan senyawa analog kurkumin yang memiliki aktivitas antiproliferasi sel, antiinflamasi, antibakteri, analgesik, dan antioksidan. Potensi PGV-1 dan senyawa induknya, kurkumin, sebagai obat dengan target aksi di sistem saraf pusat (SSP) belum pernah digali karena keduanya memiliki kelarutan dan bioavailabilitas yang buruk dalam cairan biologis, serta tidak dapat menembus sawar darah otak. Untuk meningkatkan kelarutan dan bioavailabilitas kurkumin dan PGV-1, dikembangkan formulasi nanopartikel kurkumin dan PGV-1 dengan metode *self nano-emulsifying drug delivery system* (SNEDDS). Nanopartikel kurkumin dan PGV-1 diketahui dapat menembus sawar darah otak sehingga berpotensi menjadi kandidat obat bagi *brain disorder* yang target aksinya di SSP. Uji perilaku dilakukan dengan pemberian nanoemulsi kurkumin dan nanoemulsi PGV-1 terhadap fenotip yang muncul pada gejala *brain disorder* yaitu: *open field test* mewakili aspek perilaku kecemasan dan *passive avoidance test* mewakili aspek fungsi kognitif memori.

Mencit diadaptasikan terlebih dahulu selama seminggu dan diberi makan dan minum secukupnya serta dipuasakan selama 18-24 jam. Untuk menginduksi terjadinya kerusakan otak, mencit diberi etanol 10% v/v selama 7 hari secara per oral. Pada hari ke-8, senyawa uji nanoemulsi kurkumin dan nanoemulsi PGV-1 dosis 5; 10; 20; dan 40 mg/kgBB (per oral), kontrol positif natrium butirat 1,2 g/kgBB (intraperitoneal), dan kontrol pelarut berupa campuran mygliol, tween 20, tween 80, dan PEG 400 (per oral) diberikan kepada mencit selama 21 hari. Selanjutnya, pada hari ke-29 dilakukan uji perilaku *open field test* dan *passive avoidance test* dihubungkan dengan *phenotype* yang muncul pada *brain disorder*. Data masing-masing parameter antarkelompok dibandingkan secara statistika dengan *one-way* ANOVA taraf kepercayaan 95%. Data tersaji dalam tabel dan histogram efek *vs* kelompok hewan uji.

Hasil penelitian menunjukkan pemberian nanoemulsi kurkumin dosis 20 mg/kgBB dan nanoemulsi PGV-1 dosis 40 mg/kgBB menurunkan kecemasan pada mencit yang diinduksi etanol yang ditunjukkan dengan peningkatan frekuensi *line crossing*, penurunan frekuensi *stretch attend posture*, dan penurunan durasi *grooming* dan *freezing* melalui *open field test*. Nanoemulsi kurkumin dosis 40 mg/kgBB dapat meningkatkan fungsi kognitif memori yang ditunjukkan oleh peningkatan waktu latensi 1 yang menggambarkan ingatan jangka panjang dan waktu latensi 2 yang menggambarkan ingatan jangka pendek melalui *passive avoidance test*.

Kata kunci: kurkumin, PGV-1, *open field test*, *passive avoidance test*, etanol

ABSTRACT

Pentagamavunon-1 (PGV-1) is an analogue of curcumin which have been proved as anti-proliferation to cell, anti-inflammation, anti-bacteria, analgetic, and anti-oxidant. The potency of PGV-1 and its lead compound, curcumin, as a medicine on central nervous system (CNS) have not yet studied because their poor solubility and bioavailability in biological fluid, also they can not penetrate blood-brain barrier. Nanoparticle formulation of curcumin and PGV-1 has been developed with self nano-emulsifying drug delivery system (SNEDDS) method to improve its solubility and bioavailability. Nanoparticle of curcumin and nanoparticle of PGV-1 are known to be able to penetrate blood-brain barrier, so those could be potential medicine candidates for brain disorder which targeting on CNS. Behavior test which related to phenotype from brain disorder is conducted in this research by giving nanoemulsion of curcumin and nanoemulsion of PGV-1 to ethanol-induced mice, which are: open field test represent anxiety behavior and passive avoidance test represent cognitive memory function.

Mice are adapted for a week with sufficient food and drink supply then refrained not to consume anything for 18-24 hours. Ethanol 10% v/v is given for 7 days to mice to induce brain damage. On the 8th day, nanoemulsion of curcumin and nanoemulsion of PGV-1 dose 5; 10; 20; and 40 mg/kg (per oral), positive control sodium butyrate 1,2 mg/kg (intraperitoneal), and solvent control which is a mixture of mygliol, tween 20, tween 80, and PEG 400 (per oral) are given to mice for 21 days. On the 29th day, behavior tests, open field test and passive avoidance test, are conducted to observe phenotype occured in brain disorder. The parameters of each group is statistically analyzed with one-way ANOVA, significancy level 95%. The result is presented with table and histogram effect vs group of mice tested.

The result shows that nanoemulsion of curcumin dose 20 mg/kg and nanoemulsion of PGV-1 dose 40 mg/kg reduce the anxiety in ethanol-induced mice which is shown by increasing frequency of line crossing, decreasing frequency of stretch attend posture, and decreasing duration of grooming and freezing in open field test. Nanoemulsion of curcumin dose 40 mg/kg improves cognitive memory function which is shown by increasing of latency time 1 represent long term memory and latency time 2 represent short term memory in passive avoidance test.

Keyword: curcumin, PGV-1, open field test, passive avoidance test, ethanol