Potensi ekstrak tertarget lunasin (ET-Lun) dari biji kedelai pada penghambatan karsinogenesis kanker payudara : studi in silico dan in vivo = Antimammary tumor effect of soybean extract with targeted lunasin (ET-Lun) : in silico and in vivo studies

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Abstrak

Latar belakang: Kedelai (Glycine max (L.) Merr.) merupakan tanaman yang sedang dikembangkan aktivitasnya sebagai antikanker. Salah satu senyawa aktifnya adalah Lunasin. Permasalahannya harga lunasin komersial sangat mahal karena biaya sintesis lunasin yang besar dan lama. Pada penelitian ini akan dikembangkan sediaan ekstrak tertarget Lunasin (ET-Lun) dengan tujuan untuk membuktikan aktivitas antikanker payudara ET-Lun secara in silico dan in vivo.
Metode: Uji In silico, senyawa aktif pada kedelai sebagai ligan dilihat ikatannya terhadap protein ER, ER, HER2, dan EGFR. Pengujian in vivo dibagi menjadi 2 kelompok besar yaitu kelompok kuratif dan preventif. Pada kelompok kuratif, tikus SD diinduksi dengan DMBA 20 mg/kg BB sebanyak 11 kali, 2 kali dalam seminggu kecuali kontrol normal (NOR). Setelah terbentuk nodul dengan volume 1-2 cm3, tikus diberikan perlakuan selama 8 minggu dengan tamoksifen 10 mg/kg BB (TAM), ET-Lun 500 mg/kg BB (ET- Lun), kombinasi ET-Lun dan tamoksifen (ADJ). Pada kelompok kontrol negatif (DMBA) pertumbuhan tumor diamati selama 8 minggu. Kelompok preventif (PREV), diberikan ET-Lun 1 minggu sebelum, selama, dan setelah induksi DMBA selama 24 minggu. Setelah perlakuan, tikus diterminasi, dan diambil tumornya. Volume tumor diukur, dan dilakukan pemeriksaan eskpresi ER, ER, HER2, dan EGFR secara imunohistokimia dan qPCR.
Hasil: Uji in silico menunjukkan Genistein dan Lunasin mempunyai afinitas terbesar terhadap ER, ER, dan EGFR. Uji in vivo menunjukkan ET-Lun kelompok preventif dapat menekan pertumbuhan tumor sebesar 80%, sedangkan kelompok kuratif, terjadi perlambatan pertumbuhan tumor dibandingkan kelompok DMBA yaitu 0,31 kali pada kelompok ET-Lun; 0,37 kali pada tamoksifen; dan 0,15 kali pada kelompok adjuvan selama 8 minggu perlakuan. Secara molekuler, ET-Lun kelompok preventif dan kuratif dapat menurunkan ekspresi protein dan mRNA ER, serta ekspresi protein EGFR jika dibandingkan kelompok DMBA.
Kesimpulan: ET-Lun berpotensi sebagai kandidat antikanker pada pencegahan dan perlambatan karsinogenesis payudara tikus SD yang diinduksi DMBA.
.....Background: Soybean (Glycine max (L.) Merr.) is a plant that is being developed for its anticancer activity. One of the active compounds is Lunasin. The problem is that the price of commercial lunasin is very expensive because of the high cost of synthesizing lunasin and it takes a long time. In this study, the soybean extract with targeted lunasin (ET-Lun) will be developed with the aim of proving the anti-breast cancer activity of ET-Lun in silico and in vivo.
Method: In silico study, the active compounds in soybean as a ligand was seen for their binding to ER, ER, HER2, and EGFR. In vivo assay, the rat was randomized into 2 major groups, namely curative and preventive groups. In the curative group, the SD rats were induced with DMBA 20 mg/kg BW 11 times, 2 times a week, except for normal controls (NOR). After forming nodules with a volume of 1-2 cm3, the rats were treated with tamoxifen 10 mg/kg BW (TAM), ET-Lun 500 mg/kg BW (ET-Lun), a combination of ET-

Lun and tamoxifen (ADJ), for 8 weeks. For negative controls (DMBA), tumor growth in rats was observed in 8 weeks. In the preventive group (PREV), was given ET- Lun 1 week before, during, and after DMBA induction for 24 weeks. After treatment, all the rats were terminated, and the tumors were taken. Tumor volume was measured, and ER, ER, HER2, and EGFR expression were examined by immunohistochemistry and qPCR.
Results: In silico study showed the Genistein and Lunasin had the greatest affinity for ER, ER, and EGFR. In vivo study showed ET-Lun in the preventive group could suppress tumor growth by 80%, while in the curative group, ET-Lun could delay tumor growth by 0,31 times DMBA, tamoxifen 0,37 times DMBA, and adjuvant group 0,15 times DMBA, in 8 weeks of treatment. Molecularly, ET-Lun in the preventive and curative group, could decrease the expression of ER protein and mRNA, as well as the expression of EGFR protein when compared to the DMBA group. Conclusion: ET-Lun has potential as an anticancer candidate for the prevention and delays of tumor growth in the DMBA-induced breast cancer rat model.