EKSPLORASI POTENSI KALINCUANG (*Gambier Liquid Byproduct*) UNTUK MENGATASI DIABETES MELALUI PENDEKATAN *IN SILICO*, *IN VITRO*, DAN *IN VIVO*

TESIS

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ABSTRAK

Diabetes mellitus dapat memicu stres oksidasi, yang ditandai dengan tingginya kadar malondialdehid (MDA) dan jumlah trombosit total, sehingga dapat menimbulkan komplikasi. Kalincuang dengan kandungan antioksidan yang tinggi, memiliki potensi untuk menekan stres oksidasi tersebut. Penelitian ini bertujuan mengevaluasi efektivitas kalincuang dalam mengatasi dan mencegah komplikasi diabetes melalui pendekatan *in silico*, *in vitro*, dan *in vivo*. Kalincuang kering yang diperoleh melalui pengeringan beku dan senyawa metabolit sekundernya diidentifikasi menggunakan LC-MS/MS. Selanjutnya, dilakukan evaluasi *in silico* terhadap protein target alfa-glukosidase (5ZCD) dan alfa-amilase (3BAI). Uji *in vitro* dilakukan menggunakan metode *alpha-glucosidase inhibition assay* dan *alpha-amylase inhibition assay*, sedangkan uji *in vivo* dilakukan pada tikus putih jantan diabetes yang diinduksi dengan streptozotocin 50 mg/kgBB, dengan pembagian lima kelompok perlakuan: kontrol negatif (NaCMC 0,5%), kontrol positif (glibenklamid 0,45 mg/kgBB), dan tiga kelompok lainnya diberi kalincuang dengan dosis 10, 20, dan 40 mg/kgBB. Perlakuan diberikan selama 14 hari dan kadar glukosa darah diukur pada hari ke-0, ke-1, ke-3, ke-7, dan ke-14. Analisis rasio pankreas, histopatologi pankreas, rasio hati, kadar malondialdehid (MDA) dan jumlah trombosit total dilakukan pada hari ke-14. Hasil *in silico* menunjukkan bahwa dua senyawa dalam kalincuang dapat menghambat enzim alfa-glukosidase, dan enam senyawa dapat menghambat enzim alfa-amilase. Uji *in vitro* menunjukkan nilai IC_{50} kalincuang terhadap alfa-glukosidase dan alfa amilase berturut-turut 91,28 dan 24.185 µg/mL, dibandingkan akarbose yang IC_{50} untuk kedua enzim berturut-turut 3,73 dan 10.912,02 µg/mL. Uji *in vivo* menunjukkan bahwa kalincuang secara signifikan menurunkan kadar glukosa darah ($p<0,01$), skor kerusakan histopatologi pankreas, kadar MDA, dan jumlah trombosit total ($p<0,01$), serta memperkesil rasio hati ($p<0,1$)) tikus diabetes tanpa memengaruhi rasio pankreas ($p>0,05$). Dengan demikian, penelitian ini menyimpulkan bahwa kalincuang efektif dalam mengelola dan mencegah komplikasi diabetes melalui efek antioksidannya.

Kata kunci : kalincuang, alfa amilase, alfa glukosidase, malondialdehid (MDA), trombosit total.

EXPLORATION OF KALINCUANG (*Gambir Liquid Byproduct*) POTENTIAL FOR TREATING DIABETES THROUGH IN SILICO, IN VITRO, AND IN VIVO APPROACHES

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ABSTRACT

Diabetes mellitus can trigger oxidative stress, characterized by high levels of malondialdehyde (MDA) and total platelet count, which can lead to complications. Kalincuang, with its high antioxidant content, has the potential to suppress that oxidative stress. This study aims to evaluate the effectiveness of kalincuang in addressing and preventing diabetes complications through in silico, in vitro, and in vivo approaches. Dried kalincuang obtained through freeze-drying and its secondary metabolite compounds were identified using LC-MS/MS. Next, an in silico evaluation of the target proteins alpha-glucosidase (5ZCD) and alpha-amylase (3BAI) was conducted. In vitro tests were conducted using the alpha-glucosidase inhibition assay and the alpha-amylase inhibition assay, while in vivo tests were performed on male diabetic white rats induced with streptozotocin 50 mg/kgBW, divided into five treatment groups: negative control (NaCMC 0.5%), positive control (glibenclamide 0.45 mg/kgBW), and three other groups given kalincuang at doses of 10, 20, and 40 mg/kgBW. The treatment was administered for 14 days, and blood glucose levels were measured on days 0, 1, 3, 7, and 14. Analysis of the pancreatic ratio, pancreatic histopathology, liver ratio, malondialdehyde (MDA) levels, and total platelet count was conducted on day 14. In silico results show that two compounds in kalincuang can inhibit the enzyme alpha-glucosidase, and six compounds can inhibit the enzyme alpha-amylase. In vitro tests showed that the IC_{50} of kalincuang against alpha-glucosidase and alpha-amylase were 91.28 and 24.185 µg/mL, respectively, compared to acarbose which had IC_{50} values of 3.73 and 10.912.02 µg/mL for the two enzymes, respectively. In vivo tests showed that kalincuang significantly reduced blood glucose levels ($p<0.01$), pancreatic histopathological damage scores, MDA levels, and total platelet counts ($p<0.01$), as well as decreased liver ratios ($p<0.1$) in diabetic rats without affecting pancreatic ratios ($p>0.05$). Thus, this study concludes that kalincuang is effective in managing and preventing diabetes complications through its antioxidant effects.

Keywords: kalincuang, alpha amylase, alpha glucosidase, malondialdehyde (MDA), total platelets.