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学 位 論 文 要 旨
Dissertation Abstract

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学位論文題目：
Title of Dissertation　Biochemical Utilization of Indonesian Forest Biomass as Antioxidant, Antidiabetic, and Antihyperlipidemic Agents
（インドネシアの森林バイオマスの生化学的利用，特に抗酸化剤，抗糖尿病薬および抗高脂血症薬として）

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Indonesia has about 60% of its territory covered with the rain forest. In order to reduce deforestation as well as to generate forest based economic development, it is important to optimize the use of non-timber forest products and forest waste biomass. Therefore, this research has been conducted to explore the bioactivity of eight Indonesian species, including *Albizia falcataria* wastewood and bark, *Baccaurea racemosa* (Reinw. Ex. Blume) Mull. Arg. fruit, *Graptophyllum pictum* (L.) Grif leaf, *Mangifera caesia* Jack fruit, *Pouteria campechiana* (Kunth) Baehni fruit, *Phyllanthus acidus* (L.) Skeel fruit, *Sandoricum koetjape* (Burm. F.) Merr. fruit, and *Syzigium cumini* (L.) Skeel fruit.

G. pictum is a shrub that used as medicine in Indonesia. The present study was undertaken to provide detailed mechanism on antidiabetes and antioxidant activities of *G. pictum* leaf extract in diabetic animal model as well as to determine the responsible compounds for their bioactivity.

Rats were divided into 7 groups. A normal group was injected with a sterile isotonic solution, while diabetic groups were injected with alloxan to induce diabetic condition. A positive control group was given oral administration of glibenclamide 3 mg/kg body weight, while a negative control group was untreated. The treatment groups were given oral administration of 70% ethanol extract of *G. pictum* leaves with the dose of 25, 50, 100, and 200 mg/kg bw. Separation was done by successive extraction with acetone and methanol followed by successive fractionation using dichloromethane, ethyl acetate, and water. Fraction with the highest activity was separated using silica gel 60 F_{254} thin layer chromatography (TLC). Antioxidant activity was evaluated using a 1,1-diphenyl-2-picrylhydrazil (DPPH) radical scavenging activity.

Intraperitoneal Glucose Tolerance Test showed that the best *G. pictum* extract dose used as antidiabetic was 50 mg/kg bw. It was found that the concentration of liver lipid peroxide in the extract-treated groups was lower than that of the negative control group. Based on the immunohistochemical findings, treating the rats with the extract of *G. pictum* leaves would restore pancreas β-cell function in expressing insulin. The

acetone extract showed low antihyperlipidemic activity (inhibition 9.29%) without antioxidant activity. The methanol extract and its dichloromethane fraction showed strong antioxidant activity (IC_{50} 1.81 and 3.05 µg/mL). TLC separation of the dichloromethane fraction with a mixture of ethyl acetate and *n*-hexane (1:1) as a mobile phase gave eleven bands with the highest activity given by band 11 (brown color Rf 0, IC_{50} 5 µg/mL) and band 1 (brown color Rf 0.81, IC_{50} 20 µg/mL).

Antioxidant and antihyperlipidemic effect of the six tropical Indonesian fruits (*B. racemosa*, *M. caesia*, *P. campechiana*, *P. acidus*, *S. koetjape*, and *S. cumini*) were analyzed. Separation was done by successive extraction with acetone and methanol followed by successive fractionation using dichloromethane, ethyl acetate, and water. The fraction with the highest activity was separated using TLC. Antioxidant assay was done based on scavenging activity of DPPH radicals and antihyperlipidemic activity was based on inhibition of 3-hydroxy-3-methyl-glutaryl (HMG) CoA reductase.

The results showed that all parts of *S. cumini* fruits exhibited antioxidant activity with the strongest in its raw seed acetone extract (IC_{50} 4.49 µg/mL). The ethyl acetate fraction from the acetone extract was the best fraction (IC_{50} 3.63 µg/mL). Further separation by TLC with ethyl acetate as a mobile phase gave five bands with the band 5 (brown color Rf 0, IC_{50} 3.69 µg/mL) and band 3 (yellow color Rf 0.30, IC_{50} 3.72 µg/mL) given high activity. The band 5 was separated using high performance liquid chromatography (HPLC) to afford 6 fractions, and the highest antioxidant activity was given by fraction 5-3 (IC_{50} 4.21 µg/mL).

The highest antihyperlipidemic activity was exhibited by *P. acidus* acetone extract (inhibition 80.0%) of the forty four extracts. The ethyl acetate fraction from the acetone extract gave strongest activity (inhibition 87.3%).

Screening of antioxidant and antihyperlipidemic activities from *A. falcataria* waste wood and bark showed that the methanol extract from the bark gave the highest activity for antioxidant (IC_{50} 7.52 µg/mL) as well as for antihyperlipidemic (inhibition 50.5%) of the *A. falcataria* samples. The ethyl acetate fraction from the bark acetone extract gave the strongest antioxidant activity (IC_{50} 2.48 µg/mL), while its methanol extract gave slightly weaker activity (IC_{50} 4.73 µg/mL). However, considering its antihyperlipidemic activity, the methanol-ethyl acetate fraction was chosen to be purified. Further separation of the fraction by TLC with ethyl acetate as a mobile phase gave four bands, of which band 4 gave the highest activity (dark brown color Rf 0, IC_{50} 5.36 µg/mL).

In conclusion, some extracts showed very significant results for the treatment of oxidation-related diseases, especially diabetes and hyperlipidemia. *In vivo* study of the *G. pictum* extract on treated animal showed that the extract was effective to treat diabetes. It was found that *S. cumini* raw seeds and *A. falcataria* bark were potential candidates for antioxidant sources and *P. acidus* fruit was to be a potential candidate for antihyperlipidemic agent.