

초두구로부터 glycerol-3-phosphate acyltransferase 저해제의 분리 및 그  
생리활성

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Glycerol-3-phosphate acyltransferase Inhibitors from *Alpinia katsumadai*

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### Objectives

The regulation of triacylglycerol synthesis and metabolism plays an important role in whole body energy homeostasis in mammals, and dysregulation of triglyceride synthesis and oxidation pathways have been implicated in the pathogenesis of obesity, lipodystrophy, cardiovascular disease, insulin resistance and type 2 diabetes. Inhibition of glycerol-3-phosphate acyltransferase (GPAT), which catalyze the first step in de novo triacylglycerol synthesis, has been proposed as one of the drug targets for insulin resistance and type 2 diabetes. The present study was to isolate a series of sesquiterpenes from The seed of *Alpinia katsumadai* Hayata (Zingiberaceae) and to examine their inhibitory activity on GPAT and triglyceride synthesis in cells.

### Materials and Methods

Bioassay-guided fractionation and isolation of bio-active substances from ethanol extracts of *Alpinia katsumadai* were carried out by using chromatographic techniques and in vitro GPAT enzyme assay. The GPAT inhibitory effect of the isolates was evaluated by measuring the GPAT activity of mitochondrial protein prepared from rat liver and the effects of compound 2 and 3 on cellular triglyceride synthesis were investigated by incubating human hepatocellular carcinoma, HepG2 with [<sup>14</sup>C]acetate for 6 h or [<sup>14</sup>C]glycerol for 18 h.

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## Results

The ethanol extract of *A. katsumadai* inhibited GPAT enzyme activity of mitochondrial protein prepared from rat liver in dose-responsive manner. Three terpenoids (1-3) were isolated and identified by physical and spectral properties, and IC<sub>50</sub> values of these compounds were 25.3 (1), 27.5 (2), and 43.5 (3) µg/ml, respectively (Figure 1). When the cells were incubated in the presence of compound 2 with radio-labeled acetate or glycerol, compound 2 showed 38 and 48% (for radio-labeled acetate) and 42 and 61% (for radio-labeled glycerol) inhibition against cellular triglyceride synthesis at concentrations of 5 and 10 µg/ml, respectively. compound 2 was confirmed to be the main active component and may be useful for the design of GPAT inhibitors.

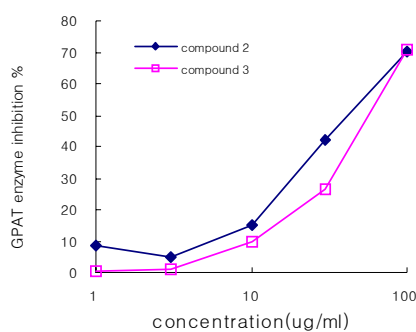


Fig. 1. Inhibitory effects of 2(■) and 3(□) on activities of rat liver mitochondrial GPAT

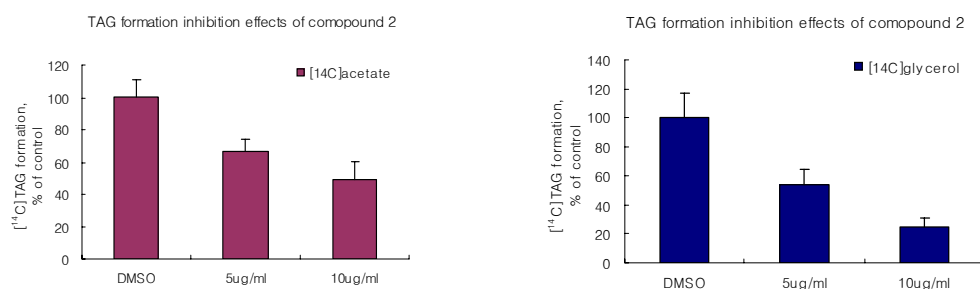


Figure 2. Inhibition of triglyceride synthesis by compound 2 in HepG2 cells. Values are expressed as percentages of control and are means ± SD(n=3). A; [<sup>14</sup>C]acetate, B; [<sup>14</sup>C]glycerol