SINTESIS EPOKSIDA OLEAT DARI MINYAK KELAPA SAWIT, UJI SITOTOKSIK TERHADAP SEL HeLa, T47D, WiDr, DAN Vero SERTA KAJIAN PENAMBATAN MOLEKULER PADA PROTEIN *FATTY ACID SYNTHASE* (FASN)

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INTISARI

Isolasi FAME dan FAEE dari minyak kelapa sawit telah dilakukan melalui reaksi transesterifikasi menghasilkan rendemen FAME dan FAEE berturut-turut 93,86 dan 92,12%. FAME dan FAEE mengandung metil oleat dan etil oleat sekitar 44%. Pemurnian FAME dan FAEE telah dilakukan dengan reaksi inklusi urea untuk meningkatkan konsentrasi metil atau etil oleat. Nilai perolehan kembali FAME dan FAEE setelah inklusi urea berturut-turut adalah 57 dan 42%. Metil oleat dalam FAME dan etil oleat dalam FAEE setelah diinklusi meningkat menjadi 89,36 dan 87,48%. FAME terinklusi, FAEE terinklusi, metil oleat, etil oleat, dan asam oleat murni telah diepoksidasi berturut-turut menjadi epoksida FAME terinklusi (EFAMEi), epoksida FAEE terinklusi (EFAEEi), epoksida metil oleat (EMO), epoksida etil oleat (EEO), dan epoksida asam oleat (EOA) dengan reagen asam performat pada suhu 28 ºC selama 24 jam. Rendemen (kemurnian) senyawa hasil sintesis epoksida yaitu EFAMEi 82,80% (84,26%); EMO 85,12% (90,28%); EFAEEi 85,80% (82,01%); EEO 82,80% (91,48%); dan EOA 95,21% (100%). Hasil elusidasi struktur telah berhasil membuktikan struktur senyawa target epoksida menunjukkan sintesis turunan epoksida oleat berhasil dilakukan. Epoksida oleat memiliki sifat sitotoksik kuat membunuh sel kanker dan bersifat aman bagi sel normal (SI > 6). Epoksida asam oleat memiliki aktivitas antikanker terbaik membunuh sel Hela dan T47D dengan IC_{50} berturut-turut 14,83 dan 7,33 ppm. Epoksida metil oleat memiliki aktivitas antikanker terbaik membunuh sel T47D dengan nilai IC_{50} 1,56 ppm. Secara umum dari semua sel kanker yang dievaluasi, semua senyawa epoksida oleat yang diuji memiliki potensi antikanker sangat baik membunuh sel WiDr dengan nilai IC_{50} kurang dari 15 ppm. Aktivitas antikanker epoksida oleat terjadi melalui inhibisi protein FASN pada subunit tioesterase berdasarkan hasil kajian penambatan molekuler. Hasil penelitian menunjukkan bahwa semakin banyak penambahan gugus alkil ester dapat mengurangi kemampuan sitotoksik epoksida oleat membunuh sel kanker.

Kata Kunci: sintesis, epoksida oleat, minyak kelapa sawit, antikanker, FASN

SYNTHESIS OF OLEATE EPOXIDES FROM PALM OIL, CYTOTOXIC EVALUATION ON HeLa, T47D, WiDr, AND Vero CELLS ALSO THE MOLECULAR DOCKING STUDY AT FATTY ACID SYNTHASE PROTEIN (FASN)

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ABSTRACT

The isolation of FAMEs and FAEEs from palm oil was carried out using the transesterification reaction to produce FAME and FAEE in 93.86 and 92.12% yield, respectively. FAMEs and FAEEs contain about 44% methyl oleate and ethyl oleate. FAMEs and FAEEs purification accomplished by the urea inclusion reaction to enhance concentration of methyl or ethyl oleate. Recovery value of FAMEs and FAEEs after purification was 57 and 42%, respectively. The content of methyl oleate and ethyl oleate in purified FAMEs and purified FAEEs were increased to 89.36 and 87.48%, respectively. The purified FAMEs, purified FAEEs, methyl oleate, ethyl oleate, and oleic acid were epoxidized into epoxide of purified FAME (EFAMEi), epoxide of purified FAEE (EFAEEi), epoxide of methyl oleate (EMO), epoxide of ethyl oleate (EEO), and epoxide of oleic acid (EOA), respectively using performic acid reagent at 28 ºC for 24 h. The yield (purity) of each synthesized epoxide was EFAMEi 82.80% (84.26%); EMO 85.12% (90.28%); EFAEEi 85.80% (82.01%); EEO 82.80% (91.48%); and EOA 95.21% (100%) successfully obtained. The results of the structure elucidation proved in confirming the structure of the epoxide target compound, which shows that the synthesis of oleate epoxide derivatives has occurred successfully. Oleate epoxides have potent cytotoxic properties against cancer cells and are safe for normal cells (SI > 6). Epoxide of oleic acid exhibited the best anticancer activity against Hela and T47D cells with IC_{50} values was 14.83 and 7.33 ppm, respectively. Epoxide of methyl oleate has potent anticancer activity against T47D cells with an IC_{50} value was 1.56 ppm. In general, among all evaluated cell lines, oleate epoxides that were examined gave strong anticancer activity against WiDr cells with the IC_{50} less than 15 ppm. The anticancer activity of oleate epoxides occurs through the inhibition of the FASN protein on the thioesterase subunit based on molecular docking results. The research results suggested that the addition of an alkyl ester group degrades cytotoxic activity against cancer cells.

Keywords: synthesis, oleate epoxide, palm oil, anticancer, FASN