SINTESIS TURUNAN EPOKSIDA OLEAT DARI MINYAK KELAPA SAWIT SEBAGAI AGEN ANTIKANKER BARU DAN PENAMBATAN MOLEKUL TERHADAP PROTEIN FASN

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INTISARI

Telah dilakukan isolasi *fatty acid methyl ester* (FAME) dari minyak kelapa sawit melalui reaksi transesterifikasi. Hasil isolasi FAME dimurnikan menggunakan metode inklusi dan dihidrolisis untuk mendapatkan asam oleat. Asam oleat direaksikan dengan 1,2-propanadiol dan gliserol menggunakan katalis asam sulfat sehingga berturut-turut menghasilkan senyawa turunan 1,2-propanadioleat dan 1,2,3-gliseril trioleat. Senyawa 1,2-propanadioleat dan 1,2,3-gliseril trioleat telah diepoksidasi berturut-turut menjadi epoksida dioleat dan epoksida trioleat dengan reagen asam performat pada suhu 28 °C selama 24 jam. Elusidasi struktur terhadap senyawa hasil sintesis dilakukan menggunakan FTIR, GC-MS atau LC-MS, ^{1}H-NMR, dan ^{13}C-NMR. Pengujian sitotoksisitas dilakukan secara *in vitro* terhadap sel kanker kolon (WiDr), payudara (T47D) dan sel normal Vero, sedangkan penambatan molekul dilakukan terhadap protein FASN pada subunit *thioesterase.*

FAME telah berhasil diperoleh dari minyak kelapa sawit dengan rendemen sebesar 96% dengan kandungan metil oleat sebesar 51%. Nilai rendemen FAME setelah proses inklusi diperoleh sebesar 89% dengan kandungan metil oleat sebesar 87%. Asam oleat, 1,2-propanadioleat, 1,2,3-gliseril trioleat, epoksida dioleat, dan epoksida trioleat diperoleh dengan rendemen berturut-turut 92%; 83%; 80%; 94%; dan 92%. Epoksida dioleat dan trioleat memiliki sifat sitotoksik sedang terhadap sel kanker namun bersifat aman untuk sel normal hal ini ditunjukkan dengan indeks selektivitasnya yang tinggi (SI > 6). Epoksida trioleat memiliki aktivitas antikanker terbaik terhadap sel T47D dan WiDr dengan nilai IC_{50} berturut-turut 27,40 dan 32,41 ppm. Epoksida dioleat memiliki aktivitas antikanker menengah terhadap sel T47D dan WiDr dengan nilai IC_{50} sebesar 35,66 dan 38,25 ppm. Hasil penambatan molekul mendukung hasil uji secara *in vitro* dimana senyawa epoksida trioleat memiliki interaksi yang lebih stabil terhadap FASN dibandingkan epoksida dioleat. Nilai afinitas ikatan epoksida dioleat dan epoksida trioleat berturut-turut -6,48 kkal/mol dan -6,60 kkal/mol.

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

SYNTHESIS OF OLEATE EPOXIDE DERIVATIVES FROM PALM OIL AS NOVEL ANTICANCER AGENTS AND MOLECULAR DOCKING TO FASN PROTEIN

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ABSTRACT

The isolation of fatty acid methyl ester (FAME) from palm oil was carried out through a transesterification reaction. The resulting FAME was purified using the inclusion method and hydrolyzed to yield oleic acid. Oleic acid was then reacted with 1,2-propanediol and glycerol to form 1,2-propanedioleate and 1,2,3-glyceryl trioleate derivatives, respectively. These derivatives were subjected to epoxidation using performic acid at 28 °C for 24 hours, resulting in dioleate epoxide and trioleate epoxide. The structures of the synthesized compounds were elucidated using FTIR, GC-MS or LC-MS, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. *In vitro* cytotoxicity assays were conducted on colon (WiDr), breast (T47D) cancer cell lines, and Vero normal cells. Molecular docking studies were performed against the FASN protein, targeting the thioesterase subunit.

FAME was successfully isolated from palm oil in 96% yield with methyl oleate content of 51%. After the inclusion process, purified FAME yielded 89%, with methyl oleate content increasing to 87% The subsequent syntheses of oleic acid, 1,2-propanedioleate, 1,2,3-glyceryl trioleate, dioleate epoxide, and trioleate epoxide achieved yields of 92%, 83%, 80.00%, 94%, and 92%, respectively. Dioleate and trioleate epoxides have moderate cytotoxic properties against cancer cells but are safe for normal cells as indicated by their high selectivity index (SI > 6). Trioleate epoxide showed the most potent anticancer activity, with IC_{50} values of 27.40 and 32.41 ppm against T47D and WiDr cells, respectively. Dioleate epoxide also exhibited anticancer activity against T47D and WiDr cells with IC_{50} values of 35.66 and 38.25 ppm, respectively. Molecular docking studies align with the *in vitro* results, showing that the trioleate epoxide forms more stable interactions with the FASN protein than the dioleate epoxide. The binding affinities were calculated as -6.48 kcal/mol for dioleate epoxide and -6.60 kcal/mol for trioleate epoxide.

Keywords: palm oil, epoxidation, oleic epoxide, anticancer, FASN