SINTESIS TURUNAN SENYAWA XANTON, UJI AKTIVITAS BIOLOGIS, DAN MEKANISME AKSI MELALUI PENAMBATAN MOLEKUL SEBAGAI AGEN ANTIKANKER DAN ANTIMALARIA

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INTISARI

Telah dilakukan sintesis, uji antikanker, uji antimalaria, dan penambatan molekul terhadap senyawa xantenol dan xantena. Tujuan dari penelitian ini untuk mendapatkan senyawa turunan xanton dan mengetahui aktivitas biologisnya sebagai agen antikanker dan antimalaria secara *in vitro* dan *in silico*.

Senyawa xantenol diperoleh melalui reduksi senyawa xanton menggunakan pereduksi natrium triasetoksiborohidrida. Senyawa xantena diperoleh melalui metode reaksi asilasi menggunakan katalis $AlCl_3$, reaksi asilasi tanpa katalis dan reaksi esterifikasi. Spektrofotometer FT-IR, GC-MS, ^{1}H-NMR dan ^{13}C-NMR digunakan untuk karakterisasi senyawa produk. Uji sitotoksisitas dilakukan menggunakan metode MTT (3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazoinum bromida) terhadap *cell line* WiDr, HeLa dan T47D sebagai sel kanker dan *cell line* Vero sebagai sel normal. Aktivitas antimalaria diuji menggunakan metode penghambatan polimerisasi hem. Proses penambatan molekul dipelajari menggunakan perangkat lunak Autodock Vina.

Reaksi reduksi senyawa xanton menghasilkan senyawa xantenol yang berupa padatan putih kekuningan dengan persen hasil 30,50%. Reaksi asilasi menggunakan katalis $AlCl_3$, reaksi asilasi tanpa katalis dan reaksi esterifikasi menghasilkan produk yang sama yaitu senyawa xantena dan xanton. Ketiga reaksi tersebut menghasilkan senyawa xantena sebagai padatan berwarna putih kekuningan dengan persen hasil berturut-turut 75,48; 45,67 dan 39,35%. Uji antikanker menunjukkan jika senyawa hasil sintesis tidak bersifat selektif terhadap beberapa sel kanker yang digunakan. Senyawa xantena memiliki nilai IC_{50} paling kecil, yaitu 43,596 µg mL^{-1} (kategori lemah) terhadap *cell line* T47D. Uji antimalaria menunjukkan jika senyawa xantenol dapat menghambat polimerisasi hem dan memiliki nilai IC_{50} sebesar 35,957 µg mL^{-1}. Penambatan molekul menunjukkan jika aktivitas senyawa xantena sebagai agen antikanker terjadi melalui penghambatan kerja enzim siklooksigenase-2 dan topoisomerase II. Aktivitas senyawa xantenol sebagai antimalaria terjadi melalui penghambatan kerja enzim P*f*LDH.

Kata kunci: xantenol, xantena, xanton, antikanker, antimalaria

SYNTHESIS OF XANTHONE DERIVATIVES, BIOLOGICAL ACTIVITY TEST, AND MECHANISM OF ACTION THROUGH MOLECULAR DOCKING AS ANTICANCER AND ANTIMALARIAL AGENT

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ABSTRACT

Synthesis, anticancer tests, antimalarial tests, and molecular docking of xanthenol and xanthene compounds have been carried out. The purpose of this study was to obtain xanthone derivatives and to determine their biological activity as anticancer and antimalarial agents through *in vitro* and *in silico* methods.

Xanthenol compound was obtained through reduction of xanthone compound using sodium triacetoxyborohydride as a reducing agent. Xanthene compound was obtained by acylation reaction method using $AlCl_3$ catalyst, uncatalyzed acylation and esterification reaction. The FT-IR, GC-MS, ^{1}H-NMR and ^{13}C-NMR spectrophotometers were used to characterize the products. Cytotoxicity test was conducted using the MTT method (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoinum bromide) against WiDr, HeLa and T47D cell lines as cancer cells and Vero cell line as normal cells. The antimalarial activity was tested using the heme polymerization inhibition method. The molecular docking process was studied by Autodock Vina software.

Reduction of xanthone produced xanthenol compound as a yellowish-white solid in 30.50% yield. The acylation reaction using $AlCl_3$ catalyst, the uncatalyzed acylation reaction and the esterification reaction produce the same products, i.e., xanthene and xanthone compound. These three reactions produced xanthene compounds as a yellowish-white solid in 75.48, 45.67 and 39.35% yield, respectively. The anticancer test showed that the synthesized compound was not selective against some of the cancer cells used. Xanthene compound gave the smallest IC_{50} value of 43.596 µg mL^{-1} (weak category) against the T47D cell line. The antimalarial test showed that the xanthenol compound could inhibit heme polymerization and had an IC_{50} value of 35.957 µg mL^{-1}. Molecular docking showed that the activity of xanthene compound as the anticancer agent occurred through the inhibition of the cyclooxygenase-2 and topoisomerase II enzymes. The antimalarial activity of xanthenol compound occurred through the inhibition of the P*f*LDH enzyme.

Keywords: xanthenol, xanthene, xanthone, anticancer, antimalarial