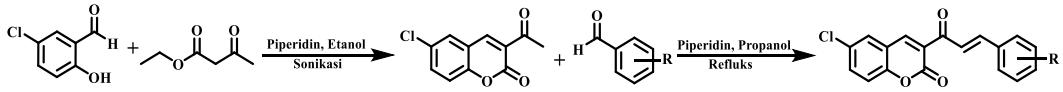
SINTESIS DAN UJI SITOTOKSISITAS KLOROKUMARIN DAN KLOROKUMARIN-KALKON SEBAGAI AGEN ANTIKANKER

Aditya Eko Saputra
21/477713/PA/20692

INTISARI

Senyawa turunan kumarin dan kumarin-kalkon memiliki potensi sebagai senyawa antikanker. Pada penelitian ini dilakukan sintesis senyawa turunan kumarin tersubstitusi kloro dan turunan kalkonnya, kemudian semua hasil sintesis diuji sitotoksisitasnya terhadap beberapa sel kanker. Senyawa klorokumarin disintesis melalui reaksi *Knoevenagel* antara 5-kloro-2-hidroksibenzaldehida dan etil asetoasetat dengan metode sonikasi menggunakan pelarut etanol dan katalis piperidin. Senyawa kalkon **1** dan **2** disintesis melalui reaksi kondensasi *Claisen-Schmidt* antara senyawa klorokumarin dengan 2-metoksibenzaldehida dan 2,4-dimetoksibenzaldehida. Reaksi dilakukan dengan metode refluks dalam pelarut 1-propanol dan katalis piperidin. Semua produk dielusidasi menggunakan spektroskopi GC-MS, ATR-IR, ^{1}H-NMR, dan ^{13}C-NMR. Senyawa hasil sintesis kemudian diuji sitotoksisitasnya dengan metode MTT terhadap sel kanker payudara (T47D dan MCF-7), serviks (HeLa), dan sel normal (Vero).

Sintesis klorokumarin menghasilkan padatan kuning dengan titik leleh 206,7-208,5 °C dan persen hasil 92%. Kalkon **1** diperoleh berupa padatan kuning dengan persen hasil 62% dan titik leleh 180,0-181,0 °C, sedangkan kalkon **2** dihasilkan berupa padatan kuning pucat dengan persen hasil 63% dan titik leleh 216,7-217,9 °C. Seluruh hasil sintesis memiliki kemurnian yang tinggi. Hasil uji sitotoksisitas menunjukkan bahwa senyawa kalkon **1** memiliki aktivitas sitotoksik paling tinggi terhadap sel kanker payudara (T74D) dengan nilai IC_{50} sebesar 0,64 $\mu g.mL^{-1}$ dan indeks selektivitas sebesar 190,60. Hasil ini menunjukkan bahwa kalkon **1** merupakan senyawa yang paling potensial untuk diuji lebih lanjut sebagai senyawa antikanker.



5-kloro-2-hidroksi benzaldehida | Etil Asetoasetat | 6-kloro-3-asetilkumarin | Benzaldehida Tersubstitusi

Kalkon **1**: R= **2-OMe**
Kalkon **2**: R= **2,4-diOMe**

Kata kunci: 3-asetil-6-klorokumarin, antikanker, kumarin-kalkon, uji MTT.

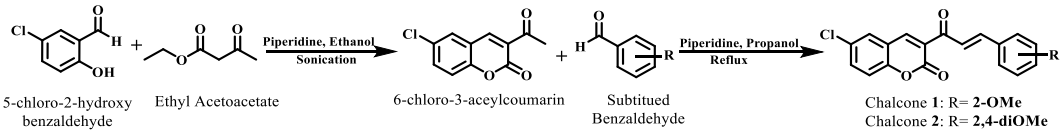
SYNTHESIS AND CYTOTOXIC ASSAY OF CHLOROCOUMARIN AND CHLOROCOUMARIN-BASED CHALCONES AS ANTICANCER AGENTS

ADITYA EKO SAPUTRA
21/477713/PA/20692

ABSTRACT

Coumarin and coumarin–chalcone derivatives have potential as anticancer agents. In this study, chlorinated coumarin derivatives and their corresponding chalcone analogs were synthesized, and all resulting compounds were subsequently evaluated for their cytotoxic activity against various cancer cell lines. Chlorinated coumarin was synthesized *via* Knoevenagel condensation between 5-chloro-2-hydroxybenzaldehyde and ethyl acetoacetate, carried out under sonication in ethanol with piperidine as a catalyst. Next, chalcones **1** and **2** were obtained through Claisen–Schmidt condensation of the synthesized coumarin with either 2-methoxybenzaldehyde or 2,4-dimethoxybenzaldehyde, under reflux in 1-propanol with piperidine. The structures of all synthesized compounds were confirmed by GC-MS, ATR-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. The synthesized compound was then evaluated for cytotoxicity using the MTT assay against breast cancer (T47D and MCF-7), cervical cancer (HeLa), and normal (Vero) cell lines.

The chlorinated coumarin was obtained as a yellow solid in 92% yield with a melting point of 206.7-208.5 °C. Chalcone derivatives **1** and **2** were yielded in 62% and 63% with melting points of 180.0-181.0 °C and 216.7-217.9 °C, respectively. All compounds showed high levels of purity. The cytotoxicity assay revealed that chalcone **1** exhibits the most potent cytotoxic activity against T47D cells, with an IC_{50} of 0.64 µg/mL and a selectivity index (SI) of 190.60. These findings highlight chalcone **1** as the most promising selective anticancer candidate for further investigation



Keywords: 3-acetyl-6-chlorocoumarin, anticancer, coumarin-chalcone, MTT assay.