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SYNTHESIS, CHARACTERIZATION AND MOLECULAR DOCKING OF CHLORO-SUBSTITUTED HYDROXYXANTHONE DERIVATIVES

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Abstract. Xanthone compounds are of great interest due to their wide range of biological applications. Xanthone compounds can be obtained by structural modification of the substituent on the xanthone rings through various reactions. In this study, the chloro-substituted hydroxyxanthones (**4a-c**) were prepared by cyclodehydration of acid derivatives and substituted phenol in the presence of Eaton reagent to afford **3a-c**, followed by halogenation step to electrophilic substitution of chlorine in a moderate yield. The *in vitro* anticancer activity study on various cell lines showed that there was an enhanced activity of compounds **4a-c** in comparison to **3a-c**. It has been shown that compounds **4a-c** have the best anticancer activity only toward P388 murine leukaemia cells with IC_{50} of 3.27, 1.809 and 0.18 µg/mL, respectively. The results revealed that the chloro functional group increases the anticancer activity of the hydroxyxanthone derivatives. As for the selectivity index, the number was increased from a range of 0.88-843 (**3a-c**) to 3.33-9199.67 (**4a-c**). This result indicates that the hydroxyxanthone derivatives (**4a-c**) have potential to be developed into chemotherapy agents due to their higher sensitivity and selectivity. Molecular docking studies showed that there was a binding interaction between **4c** and the amino acid residues such as Asp810, Cys809, Ile789, His790, and Leu644 of protein tyrosine kinase receptor (PDB ID: 1T46).

Keywords: chlorination, chloro-substituted hydroxyxanthone, derivative, anticancer, molecular docking.

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