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

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Abstract. 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 halogenations step to electrophilic substitution of chlorine in a moderate yield. An *in vitro* anticancer activity to various cell line showed that there was an increased activity of compounds **4a-c** in comparison to **3a-c**. It has been shown that compound **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 chloro functional group could increase the anticancer activity of the hydroxyxanthone derivatives. As for the selectivity index (*SI*), 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 a chemotherapy agent due to their higher sensitivity and selectivity. Molecular docking studies showed there was a binding interaction between 4c and the amino acid residues such as Asp810, Cys809, Ile789, His790, and Leu644 of 1T46.pdb protein tyrosine kinase

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