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INVESTIGATING THE POTENTIAL OF CURCUMIN, DEMETHOXYCURCUMIN AND BISDEMETHOXYCURCUMIN AS WILD-TYPE AND MUTANT HER2 INHIBITORS AGAINST VARIOUS CANCER TYPES USING BIOINFORMATICS ANALYSIS

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ABSTRACT : HER2 is overexpressed and mutated in various types of cancer thus becoming prone to chemotherapy drug resistance. The purpose of this study was to investigate the potential of curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) as inhibitors of HER2 (wild type and mutant). Data for these three small molecules and HER2 protein were obtained from the PubChem and RCSB PDB databases. Analysis of pharmacokinetic, drug-likeness and toxicity of the compounds performed using SwissAdme and ProTox-II web server. Confirmation of HER2 overexpression in various cancer types performed using the UALCAN web portal. Specific docking using AutoDock Vina was performed to simulate the HER2-compound interaction. Curcumin, DMC and BDMC had drug-likeness properties based on five parameters and also had good bioavailability. HER2 was confirmed to be overexpressed in BLCA, BRCA, CESC, CHOL, ESCA, GBM, LIHC, LUAD, PAAD, SKCM, THCA, STAD and UCEC. The docking simulation showed that curcumin and BDMC bound to the ATP binding pocket of both wild-type and mutant HER2. Curcumin and BDMC also would constantly have a lower binding affinity value than ATP and produce many hydrogen bonds. Curcumin and BDMC are predicted to have high potential as alternative drugs for wild-type and mutant HER2 inhibitors.

Key words : Bisdemethoxycurcumin, curcumin, demethoxycurcumin, non-communicable disease, HER2, cancer.

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INTRODUCTION

Cancer is a major public health problem in almost all world countries with a high mortality rate (Ansori *et al*, 2020; Fadholly *et al*, 2019; Fadholly *et al*, 2020; Mathur *et al*, 2020; Proboningrat *et al*, 2021). In 2020, 19.3 million new cancer cases were found and almost 10 million died worldwide. The type of cancer that causes the most deaths is lung cancer, followed by colorectal, liver, stomach and breast cancer (Sung *et al*, 2021). In 2021, 1,898,160 new cancer cases and 608,570 deaths are projected in the United States (Siegel *et al*, 2021). Chemotherapy is