Abstract

Malaria is a dangerous endemic disease that infects millions of people every year. The Plasmodium falciparum species are responsible for most malaria deaths. Currently, most available antimalarial drugs are less effective due to the increased parasite's resistance to drugs. Hence, novel antimalarial agents with high efficiency to inhibit malaria are urgently needed. Falcipain enzyme is a promising target protein for developing new anti-malaria. However, conventional laboratory testing to design new drugs takes time and is very expensive. Therefore, the quantitative structure-activity relationship (QSAR) can be used to accelerate the drug design process. In this study, we developed a QSAR model using a genetic algorithm-support vector machine (GA-SVM) to predict the pIC50 values of falcipain inhibitors. The GA was utilized as a features selection method, while SVM with optimized hyperparameter was used to develop the prediction models. We performed three models with different SVM kernels, i.e., linear, radial basis function (RBF), and polynomial. The model performance was validated using both internal and external data. The validation results show that the RBF model produced the best result, with the R^2 values of the training and test sets of 0.98 and 0.84, respectively, while Q^2 of the leave-one-out cross-validation was 0.85.

Keywords: anti-malaria, falcipain, genetic algorithm (GA), quantitative structure-activity relationship (QSAR), support vector machine (SVM)