

Uncovering Natural CARM1 Inhibitors for Breast Cancer from *Hibiscus* Species - A Multistep Computational Approach Integrating Docking, Pharmacophore Modeling and MD Simulations

Soundar Rajan Kulandhaivel¹, Antony Stalin², Balasubramanian Sivaprakasam¹, Vidhyavathi Ramasamy¹, Jesudass Joseph Sahayarayan^{1*}



¹Department of Bioinformatics, Science Campus, Alagappa University, Karaikudi - 630003, Tamilnadu, India.

²Institute of Fundamental and Frontier Sciences, University of Electronic Science and Technology of China, Chengdu, 610 054 China.

*Corresponding Authors:

Jesudass Joseph Sahayarayan (josephj@alagappauniversity.ac.in)

Abstract

Breast cancer is the most prevalent cancer among women, with a rising incidence, second only to lung cancer. *CARM1* receptor promotes metastasis and estrogen receptor alpha (ER α)-mediated cell proliferation. Its high expression underscores its clinical significance, as gene knockdown inhibits cancer growth. Traditionally, extracts from *Hibiscus* species such as *H. rosa-sinensis*, *H. cannabinus*, *H. syriacus*, *H. sabdariffa*, and *H. taiwanensis* have been used to treat breast cancer. In this study, compounds from these species were investigated as potential inhibitors of the *CARM1* receptor in breast cancer. The 207 phytochemicals from five *Hibiscus* species were selected and docked against the *CARM1* receptor. The pharmacophore mapping was performed for the lead compound after ADME studies, and pharmacophore-based virtual screening was performed against ten databases to identify *CARM1* inhibitors for the protein. The electrostatic nature of the compounds was studied by DFT, and dynamic simulation studies were performed to check the stability of complexes. The compound 12046471 from *H. rosasinensis* showed better binding affinity of -10.681kcal/mol and the pharmacophore-based virtual screening of compound 12046471 has

shown Asinex_204526 better binding with the target protein with poor ADME properties. The molecular dynamics simulation studies showed that the *CARMI* complexed with lead phytocompounds from each Hibiscus species and lead virtual screened compounds remained stable throughout the 100ns simulation period. This study concludes that compound 12046471 from *H. rosasinensis* is a potent inhibitor for *CARMI* receptor based on docking, MMGBSA, ADME, and DFT studies compared to pharmacophore based screened compounds from ten different databases.

Keywords: Breast cancer, Coactivator-Associated Arginine Methyltransferase 1 (*CARMI*), *Hibiscus* genus, Pharmacophore modeling, virtual screening, Molecular dynamics