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ANNAI JKK SAMPOORANI AMMAL COLLEGE OF PHARMACY,

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One Day National Seminar on

"THE IMPACT OF AI ON DRUG DESIGN AND OPTIMIZATION OF EMERGING ANALYTICAL TECHNOLOGIES IN PHARMACY"

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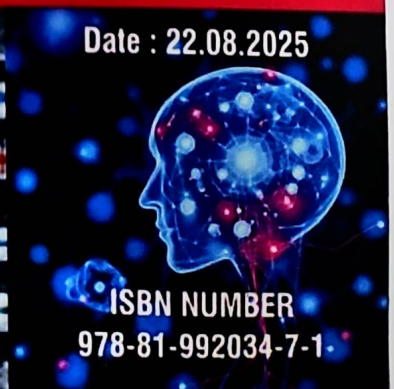
Date : 22.08.2025



ISBN NUMBER
978-81-992034-7-1

ISBN NO: 978-81-992034-7-1

Computational Design and Docking Evaluation of Novel Thiadiazole Derivatives with Anti-Cancer Activity

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ABSTRACT:- JKKM-ORAL 052

Melanoma, arising from uncontrolled melanocyte proliferation, is treatable in its early stages but poses significant challenges in advanced cases. This study aimed to design and evaluate novel thiadiazole derivatives as potential anti-cancer agents targeting the BRAF protein using 3D-QSAR modeling and molecular docking. A dataset of 51 reported BRAF inhibitors was analyzed using the Schrödinger suite, and the Gaussian-based QSAR model showed strong predictive reliability (r^2 = 0.93, r^2cv = 0.47, SE = 0.2, F ratio = 80.3), with field contributions of steric (0.29), hydrophobic (0.24), hydrogen bond donor (0.18), electrostatic (0.188), and hydrogen bond acceptor (0.08). Guided by these findings, 25 novel thiadiazole derivatives were designed and subjected to docking studies in PyRx. Among them, compound IA25 demonstrated the best binding affinity (−9.7 kcal/mol), comparable to the standard Dabrafenib, forming two hydrogen bonds with Asn221 and Phe209 residues. Other derivatives showed scores ranging from −8.0 to −9.6 kcal/mol, with 10 shortlisted for further study. These results highlight the critical role of hydrogen bond donor and acceptor substituents on the thiadiazole ring in BRAF inhibition and suggest IA25 as a promising anti-cancer lead.

KEYWORDS: Thiadiazole, BRAF enzyme, Quantitative structure–activity relationship, Docking studies.