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Halogenated Anthrapyrazolone derivatives regulate JNK signals in inflammation

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Design of inhibitors for signal proteins has been targeted with a view to supress inflammatory chemokine expression and in this context Anthrapyrazolone and its derivatives have been explored extensively. Extensive studies among small molecules to evaluate quantitative features of halogen bonding have paved the way for the classification of Type I and Type II interactions and theoretical studies invoke the concept of σ-holes to understand the interaction potential. Importantly, halogen derivatives are often preferred as enzyme inhibitors. Halogens improve the protein-ligand binding affinity, specificity and also tune ADME/T property of the inhibitor. Similar to hydrogen bonding, halogen bonding is also specific,directional, where halogen acts as an electron acceptor. Studies on anthrapyrazolone and its derivatives indicate that halogen substitution on 1-chloroethylene-4-chloro-1,9-pyrazoloanthrone significantly augments the binding ability of inhibitor precisely towards JNKs activity and thereby expression of chemokines in LPS-activated macrophages. Importantly, several diseases are associated with disproportionate expression of chemokines wherein c-Jun N-terminal Kinases (JNKs)-mediated signalling play a significant role in regulating the chemokines expression. Indeed, several halogenated derivatives have been tested in this context and the quantitative evaluation of halogen bonding in terms of strength and directionality is essential for futuristic drug design.

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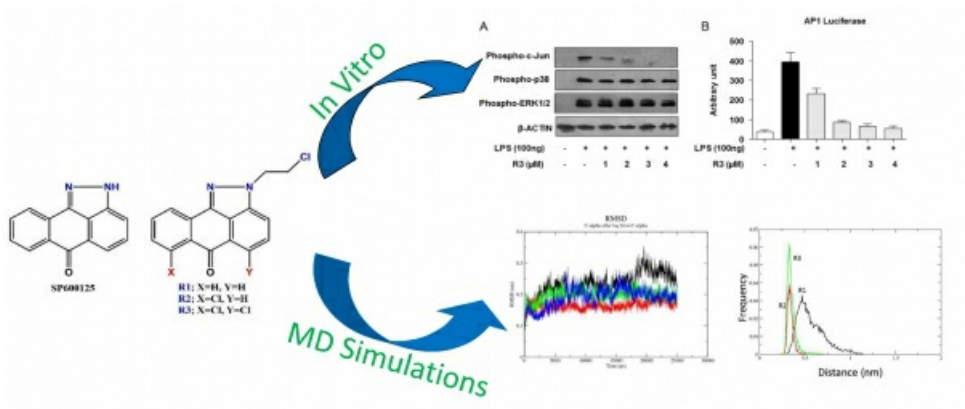

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