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RESEARCH ARTICLE

TOPOLOGICAL MODELS FOR THE PREDICTION OF TYROSINE KINASE INHIBITORY ACTIVITY OF 4-ANILINOQUINAZOLINES

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The relationship of *Wiener's index* - a distance-based topological descriptor, *Zagreb group parameter* - M_1, an adjacency-based topological descriptor and *eccentric connectivity index* - an adjacency-cum-distance based topological descriptor with the tyrosine kinase inhibitory activity of 4-anilinoquinazolines has been investigated. A training set comprising of 30 analogues of substituted 4-anilinoquinazolines was selected for the present investigations. The values of the *Wiener's index, Zagreb group parameter, eccentric connectivity index* and each of 30 analogues comprising the data set, were computed. Resultant data was analyzed and suitable models developed after identification of active ranges. Subsequently, a biological activity was assigned to each analogue involved in the data set using these models, which was then compared with the reported tyrosine kinase inhibitory activity. Accuracy of prediction was found to vary from a minimum of ~82% for model based on *Zagreb group parameter* to a maximum of ~87% for model based on *Wiener's index* and *eccentric connectivity index.*

Key words: Wiener's index, Eccentric connectivity index, Zagreb group parameter, 4-Anilino-quinazolines, Tyrosine kinase inhibitory activity.

INTRODUCTION

An important area of research in computational and mathematical chemistry is the characterization of molecular structure using structural invariants (Basak *et al* 1990). The impetus for this research trend comes from various directions. Researchers in chemical documentation have searched for a set of invariants that will be more convenient than the adjacency matrix (or connection tables) for the storage and comparison of chemical structures (Randic, 1984). Invariants have been used to order sets of molecules (Wilkins and Randic, 1980).

Numerical graph invariants or topological indices are the molecular descriptors, which are produced directly from molecular structure (Basak and Grunwald, 1993). The interest in the influence of molecular topology on molecular properties has grown remarkably during the past few years. The objective of all such studies is to explore the role of connectedness of atoms in the expression of biological activities of molecules (Klopman and Raychaudhury, 1988). Thus molecular structures are translated into characteristic numerical descriptors known as topological indices, which may be used in structure activity/property relationship (SAR/SPR) studies (Sabljic and Trinajstic, 1981). The use of numerical graph invariants in structure activity/property relationship studies seems to play an important role in situations where the biological activity is determined predominantly by topological architecture of molecular structure where simple