QSAR STUDIES OF ANTIBACTERIAL ACTIVITY OF SOME CURCUMIN DERIVATIVES

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Problematic: The serious problem of microorganisms increasing resistance to conventional chemicals and drugs has impelled scientists to search and discover new antimicrobial sources, such as plants derivatives [1]. These plants are likely to afford further new antibiotics in the future. However, the application of plant extracts or pure natural compounds combining with conventional antibiotics may hold good promise for providing affordable treatment options[2].Accordingly to this problem, the Quantitative Structure - Activity Relationship (QSAR) models-based tool is used to screen compounds databases for disclosing the relationship between structural features and their biological activities[3].

Objectif: Establish a reliable quantitative correlation of the antibacterial effects of curcumin derivatives molecules and their chemical structure used to obtain in silico models for predicting the activity of novel compounds that are profitable for screening promising molecules.

Methods: The QSAR methodology is applied to a set of 50 curcumin derivatives molecules, collected from different sources on account of their antibacterial activity against Gram-Positive Cocci (Streptococcus aureus) as well as Gram-Negative Bacilli (Escherichia coli) bacterial strains.

The biological activities were determined according to the Minimum Inhibitory Concentration sensitive cell growth (MIC) (in micromolar, μM) and were transduced into negative logarithmic values of MIC, where pMIC values ranged from 1 to 7.29.

These 2D structures are drawn by the ChemDraw program. Then, molecular fingerprints calculations are carried out using Canvas from the Schrodinger molecular modeling suite software. This study was submitted to the kernel-based Partial Least-Square (k-PLS) analysis, as a type of a non-linear regression method, using four non classical descriptors 2D binary fingerprints (linear, dendritic, radial, and MACCS) with four k-PLS factors, to explore the correlation between binary fingerprints and pMIC[4].

Results: In the presented workflow, QSAR models were obtained from the determined fingerprint descriptors and the antibacterial activities with a maximum of four latent k-PLS factors. Generally, these models present high statistical indicators for all the binary fingerprints: regression correlation coefficient $R2 > 0.9$ and t validation coefficient $Q2 > 0.8$.

Conclusion: By combining the k-PLS method and binary fingerprints, we developed a reliable and extendable QSAR modeling framework.

All the types of fingerprints reach the highest values of the correlation coefficients and the validation ones at four factors. Linear, dendritic, and radial fingerprints produced almost similar statistical results for the two sorts of bacteria. A comparison between all the studied

fingerprints KPLS models, in terms of correlation and validation, indicated that the dendritic fingerprint is selected as the best KPLS model.

References

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