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In Silico Molecular Design of 4-Benzylidene-6-aryl-2,4,5-trihydropyridazin-3-one Scaffolds as Antiproliferative Targets

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SUMMARY. **Two series of 4-benzylidene-6-(4-methyl-phenyl)-2,4,5-trihydropyridazin-3-ones (2a-e) and 4-benzylidene-6-(4-chlorophenyl)-2,4,5-trihydropyridazin-3-ones (2f-j) were designed to different *in silico* experimental methods to assess their prediction of biological characteristics by molinspiration, cell line cytotoxicities, ADMET-based toxicity like to hepatotoxicity, hERG (human Ether-à-go-go-Related Gene) blocking, acute toxicity (LD_{50}) and Ames toxicity, anatomical therapeutic chemical (ATC) classification and target predictions. In molecular docking studies, anti-proliferative activity was determined by using epidermal growth factor receptor (EGFR) kinase inhibitory effect of pyridazinone derivatives. Successive assays result showed that some compounds exhibited promising anti-proliferative effect when compared to Ceritinib as a reference drug. All the tested compounds (2a-j) showed significant kinase inhibitory activities.**

RESUMEN. Dos series de 4-benciliden-6-(4-metil-fenil)-2,4,5-trihidropiridazin-3-onas (2a-e) y 4-benciliden-6-(4-clorofenil)-2,4, Se diseñaron 5-trihidropiridazin-3-onas (2f-j) para diferentes métodos experimentales in silico para evaluar su predicción de características biológicas por molinspiración, citotoxicidades de líneas celulares, toxicidad basada en ADMET como hepatotoxicidad, hERG (éter-á-go humano -go-Related Gene), toxicidad aguda (LD50) y toxicidad de Ames, clasificación química terapéutica anatómica (ATC) y predicciones de objetivos. En los estudios de acoplamiento molecular, la actividad antiproliferativa se determinó utilizando el efecto inhibidor de la cinasa del receptor del factor de crecimiento epidérmico (EGFR) de los derivados de piridazinona. El resultado de ensayos sucesivos mostró que algunos compuestos mostraron un efecto antiproliferativo prometedor en comparación con Ceritinib como fármaco de referencia. Todos los compuestos probados (2a-j) mostraron actividades inhibidoras de quinasas significativas.

KEY WORDS: antiproliferative, Auto Dock, epidermal growth factor receptor kinase, *in silico* activity, pyridazinone.

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