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Short communication

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Prediction of Metabolic Behaviour of Glioma Therapy Drug Noscapine Derivatives by CYP3A4

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***SUMMARY*. Great efforts have been made to synthesize the noscapine derivatives with stronger anti-glioma activities. Given that drug metabolic behaviour is another key factor limiting the research and development (R&D) of drugs, the present study aims to predict the metabolic behaviour of two noscapine derivatives (amino-noscapine and bromo-noscapine) with molecular docking. The results showed that the binding of amino-noscapine into the active sites of CYP3A4 has higher chemscoring value than the binding of bromo-noscapine, indicating easier biotransformation of amino-noscapine than bromo-noscapine by CYP3A4, which might be caused by more hydrogen bonds formation between amino-noscapine and CYP3A4. The most ranked binding orientation between noscapine derivatives and the active cavity of CYP3A4 indicated that the methoxyl groups in the phenyl group far from the the methylenedioxy group easily undergo the metabolic reaction. All these data will be helpful for development of noscapine derivatives as the promising anti-glioma drugs.**

RESUMEN. Se han hecho grandes esfuerzos para sintetizar derivados de noscapina con más potente actividad anti-glioma. Dado que el comportamiento metabólico de drogas es un factor clave que limita la investigación y desarrollo de las drogas, el presente estudio tiene como objetivo predecir el comportamiento metabólico de dos derivados de noscapina (amino-noscapina y bromo-noscapina) con acoplamiento molecular. Los resultados mostraron que la unión de amino-noscapina en los sitios activos de CYP3A4 tiene un mayor valor que la unión de bromo-noscapina, lo que indica una más fácil biotransformación de amino-noscapina que de bromo-noscapina por CYP3A4, que podría ser causada por la formación de más enlaces de hidrógeno entre amino-noscapina y CYP3A4. La orientación de unión más favorecida entre los derivados noscapina y la cavidad activa de CYP3A4 indicó que los grupos metoxilo en el grupo fenil lejano del grupo metilendioxilo fácilitan la reacción metabólica. Estos datos serán útiles para el desarrollo de derivados de noscapina como prometedoras drogas anti-glioma.

KEY WORDS: CYP3A4, Metabolism, Molecular docking, Noscapine derivatives.

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