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Docking Study of Noscapine into the Activity Cavity of Cytochrome P450 (CYP) 3A4

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***SUMMARY*. Herbal component noscapine has been drawing more and more attention due to its excellent anti-cancer activities. To improve the anti-tumor activities of noscapine, many noscapine derivatives have been chemically synthesized to increase the anti-cancer capabilities. The aim of the present study is to adopt the molecular docking method to predict the metabolic behaviour and possible inhibition mechanism of noscapine towards CYP3A4. The results showed that noscapine can be well docked into the catalytic cavity of CYP3A4, indicating the good substrate property of noscapine for CYP3A4. The most possible metabolic site in noscapine is its phenyl group far from the methylenedioxyphenyl group, indicating the higher metabolic rate for the phenyl group than the methylenedioxyphenyl group. Through well docking into the binding site of ketoconazole, we can know why noscapine is a strong competitive inhibitor of CYP3A4. All these data will be beneficial for the deeper elucidation of substrate and inhibitor properties of noscapine towards CYP3A4.**

RESUMEN. El compuesto vegetal noscapina ha atraído cada vez más atención debido a su excelente actividad anticancerígena. Muchos derivados se han sintetizado para mejorar las actividades antitumorales de noscapina. El objetivo del presente estudio consiste en adoptar el método de acoplamiento molecular para predecir el comportamiento metabólico y el posible mecanismo de inhibición de la noscapina hacia CYP3A4. Los resultados mostraron que noscapina puede ser bien acoplada en la cavidad catalítica de CYP3A4, indicando ser un buen sustrato para el CYP3A4. El sitio metabólico más adecuado en noscapina parece ser el grupo fenilo alejado del grupo metilendioxifenilo, siendo la tasa metabólica del grupo fenilo más alta que la del grupo metilendioxifenilo. Al acoplarse bien en el sitio de unión de ketoconazol se puede ver que noscapina es un fuerte inhibidor competitivo de CYP3A4. Todos estos datos serán beneficiosas para el esclarecimiento más profundo de la relación sustrato e inhibidor entre noscapina y CYP3A4.

KEY WORDS: CYP3A4, Herbs, Inhibitor, Molecular docking, Noscapine, Substrate.

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