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Synthesis, Biological Activity and Docking Study of Isatin Hydrazone Derivatives as Potential α-Glucosidase Inhibitors

Jing WANG, Guangcheng WANG *, Zhenzhen XIE, Yaping PENG, Luyao LI, Bing DENG, Ming CHEN, Shan CHEN & Wenbiao LI

College of Chemistry and Chemical Engineering, Hunan Engineering Laboratory for Analyse and Drugs Development of Ethnomedicine in Wuling Mountains, Jishou University, Jishou 416000, PR China

SUMMARY. α-Glucosidase is a key enzyme in carbohydrate digestion, which could be used as an important target for the treatment of type II diabetes mellitus. To discover potent α-glucosidase inhibitors, a series of isatin hydrazone derivatives (**6a-6p**) were synthesized and evaluated for their α-glucosidase inhibitory activity. Among the series, eight compounds displayed potent α-glucosidase inhibitory activity with IC_{50} values in the range of 10.82 ± 0.15 to 56.43 ± 0.32 μM, as compared to the standard drug acarbose. Compound **6p** (IC_{50} = 10.82 ± 0.15 μM) with 5,7-dimethyl substitution at phenyl part and 4-bromobenzyl at the N1-position of isatin ring was found to be the most active compound. Structure-activity relationship shows that substitution at N1 position of isatin ring is important for the inhibitory activity against α-glucosidase. Furthermore, the binding interaction of the most active compound **6p** with α-glucosidase was confirmed through molecular docking study.

RESUMEN. La α-glucosidasa es una enzima clave en la digestión de los carbohidratos, que podría utilizarse como un objetivo importante para el tratamiento de la diabetes mellitus tipo II. Para descubrir potentes inhibidores de α-glucosidasa, se sintetizaron una serie de derivados de isatina hidrazona (**6a-6p**) y se evaluó su actividad inhibidora de α-glucosidasa. Entre la serie, ocho compuestos mostraron potente actividad inhibidora de α-glucosidasa con valores de IC_{50} en el intervalo de 10,82 ± 0,15 a 56,43 ± 0,32 μM, en comparación con el fármaco estándar acarbosa. Se encontró que el compuesto **6p** (IC_{50} = 10,82 ± 0,15 μM) con sustitución 5,7-dimetilo en la parte fenilo y 4-bromobencilo en la posición N1 del anillo isatino era el compuesto más activo. La relación estructura-actividad muestra que la sustitución en la posición N1 del anillo isatino es importante para la actividad inhibidora contra la α-glucosidasa. Además, la interacción de unión del compuesto más activo **6p** con α-glucosidasa se confirmó mediante estudio de acoplamiento molecular.

KEY WORDS: diabetic, α-glucosidase inhibitor, hydrazine, isatin,molecular docking.

* Author to whom correspondence should be addressed. *E-mail:* wanggch123@163.com

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