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Synthesis, *In Vitro* α-Glucosidase Inhibitory Activity and Molecular Docking Studies of Novel Barbituric Acid Derivatives

Zhiyun PENG [1,2,3], Jie QIU 4, Fengjiao ZHOU [4], Anbai CAO [4] & Guangcheng WANG [1,2,3] *

[1] *Provincial Key Laboratory of Pharmaceutics in Guizhou Province, Guizhou Medical University, Beijing Road, Guiyang 550004, China*
[2] *School of Pharmacy, Guizhou Medical University, 4 Beijing Road, Guiyang 550004, China*
[3] *National Engineering Research Center of Miao's Medicines, 4 Beijing Road, Guiyang 550004, China*
[4] *College of Chemistry and Chemical Engineering, Hunan Engineering Laboratory for Analyse and Drugs Development of Ethnomedicine in Wuling Mountains Jishou University, Jishou 416000, China*

SUMMARY. A series of barbituric acid derivatives have been synthesized and evaluated for their *in vitro* α-glucosidase inhibitory activity. Biological studies revealed that compounds **5e** (IC_{50} = 40.83±0.31 μM), **5h** (IC_{50} = 48.20 ± 0.35 μM), **5j** (IC_{50} = 94.23 ± 0.46 μM), and **5k** (IC_{50} = 31.72 ± 0.23 μM) are the best α-glucosidase enzyme inhibitors in the series and showed greater activity than the standard drug acarbose (IC_{50} = 817.38 ± 6.27 μM). Among the series, **5k** containg chloro and barbituric acid groups at the *ortho*- and *para*-positions of the phenyl ring respectively, was found to be the most active compound, with IC_{50} value of 31.72±0.23 μM. Molecular docking study was carried out to illustrate the binding interactions of the most active analogs with α-glucosidase.

RESUMEN. Se han sintetizado y evaluado una serie de derivados de ácido barbitúrico para determinar su actividad inhibidora de α-glucosidase *in vitro*. Los estudios biológicos revelaron que los compuestos **5e** (IC_{50} = 40.83 ± 0.31 μM), **5h** (IC_{50} = 48.20 ± 0.35 μM), **5j** (IC_{50} = 94.23 ± 0.46 μM) y **5k** (IC_{50} = 31.72 ± 0.23 μM) son los mejores inhibidores de la enzima α-glucosidasa en la serie y mostraron una mayor actividad que el fármaco acarbosa estándar (IC_{50} = 817.38 ± 6.27 μM). Entre las series, se encontró que **5k** que contiene grupos de cloro y ácido barbitúrico en las posiciones *orto* y *para* del anillo de fenilo, respectivamente, es el compuesto más activo, con un valor de IC_{50} de 31,72 ± 0,23 μM. El estudio de acoplamiento molecular se llevó a cabo para ilustrar las interacciones de unión de los análogos más activos con α-glucosidasa.

KEY WORDS: barbituric acid, α-glucosidase inhibitor, Knoevenagel reaction, molecular docking.

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

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