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Semisynthetic Theophylline Analogues as Potent Diuretics: An Integrated *in vivo* and Molecular Docking Study

Abdulaziz S. SAEEDAN [1], Menshawy A. MOHAMED [2,3], Gamal A. SOLIMAN [1,4], Khaled M. ALASIRI [5], Maged S. ABDEL-KADER [5,6] * & Mai H. ELNAGGAR [7]

[1] *Department of Pharmacology, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia.*

[2] *Department of Pharmaceutical Chemistry, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia.*

[3] *Department of Organic Chemistry, Faculty of Pharmacy, Al-Azhar University, Cairo- 11884, Egypt.*

[4] *Department of Pharmacology, College of Veterinary Medicine, Cairo University, Giza, Egypt.*

[5] *Department of Pharmacognosy, College of Pharmacy, Prince Sattam bin Abdulaziz University, Al kharj 11942, Saudi Arabia.*

[6] *Department of Pharmacognosy, Faculty of Pharmacy, Alexandria University, Alexandria University, Alexandria 21215, Egypt.*

[7] *Department of Pharmacognosy, Faculty of Pharmacy, Kafrelsheikh University, 33516, Kafrelsheikh, Egypt.*

SUMMARY. **Ten 7-substituted theophylline derivatives were synthesized by the reactions with aryalkyl compounds substituents in acetone in the presence of anhydrous potassium carbonate under reflux. The prepared compounds were identified by various spectroscopic methods. The Evaluated of the diuretic effect in comparison with theophylline was conducted using mice as experimental animal model. Compounds 1-4, 7 and 9 showed little diuretic activities (0.72–1.00). However, compounds 5, 6 and 8 showed moderate diuretic activities (>1.00–1.5) in mice. Compound 10 showed a stronger diuretic activity (1.68) than theophylline (1.00). Molecular docking study against three human targets namely AR-A1, CA-II, and UT-B indicated that 10 showed the highest binding affinity to the three investigated targets which explain its high diuretic activity obtained from the *in vivo* study.**

RESUMEN. Diez derivados de teofilina sustituidos en 7 fueron sintetizados por reacciones con sustituyentes de compuestos arilalquilo en acetona en presencia de carbonato de potasio anhidro bajo reflujo. Los compuestos preparados fueron identificados por varios métodos espectroscópicos. La evaluación del efecto diurético en comparación con la teofilina se realizó utilizando ratones como modelo animal de experimentación. Los compuestos 1-4, 7 y 9 mostraron poca actividad diurética (0,72-1,00). Sin embargo, los compuestos 5, 6 y 8 mostraron actividades diuréticas moderadas (>1,00-1,5) en ratones. El compuesto 10 mostró una actividad diurética más fuerte (1,68) que la teofilina (1,00). El estudio de acoplamiento molecular contra tres objetivos humanos, a saber, AR-A1, CA-II y UT-B, indicó que 10 mostró la mayor afinidad de unión a los tres objetivos investigados, lo que explica su alta actividad diurética obtenida del estudio *in vivo*.

KEY WORDS: Synthesis; 7-substituted theophylline; diuretic, *in vivo*; molecular docking.

* Author to whom correspondence should be addressed. *E-mail:* mpharm101@hotmail.com

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