Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **42** (7): 1362-8 (2023)

Received: March 9, 2023
Accepted: April 14, 2023

Neurotoxicity and Maximum Electroshock Induced Anticonvulsant Activity of GABA analogs of 6-Substituted Aryl-pyridazine derivatives

Mazen ALMEHMADI [1], Ahad Amer ALSAIARI [1],
Mamdouh ALLAHYANI [1], Abdulaziz ALSHARIF [1] & Mohammad ASIF [2] *

[1] *Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia*

[2] *Department of Pharmaceutical Chemistry, Era College of Pharmacy, Era University, Lucknow, 226003, Uttar Pradesh, India*

SUMMARY: **A series of 4-((6-phenylpyridazin-3-yl) amino)butanoic acid derivatives (3a-h) were synthesized by reaction of an appropriate aromatic hydrocarbon with maleic anhydride to yield 4-oxo-4-arylbut-2-enoic acid which was cyclized with hydrazine hydrate to gave 6-arylpyridazin-3(*2H*)-one (1a-h) or 6-arylpyridazin-3-ol (1a'-h'), which was reacted with phosphorous oxychloride ($POCl_3$) to yield 3-chloro-6-arylpyridazine (2a-h). These intermediate compounds reacted with gamma amino butyric acid (GABA) and were converted into title compounds 3a-h. Utilizing spectral data analysis, the structures of the synthesized compounds were ascertained. These title compounds were tested against maximum electroshock (MES) induced convulsions at 100mg/kg dose level for anticonvulsant activity in Swiss Albino mice. Phenytoin sodium (25mg/kg) was used as the standard drug. These synthetic substances have weak to strong anticonvulsant properties. As a result, the structure-activity relationship (SAR) revealed that aryl-pyridazine derivatives with hydrophobic substituents on the phenyl ring have stronger anticonvulsant action.**

RESUMEN: Se sintetizó una serie de derivados del ácido 4-((6-fenilpiridazin-3-il)amino)butanoico (3a-h) mediante la reacción de un hidrocarburo aromático apropiado con anhídrido maleico para producir 4-oxo-4-arilbut-2 -ácido enoico que se cicló con hidrato de hidrazina para dar 6-arilpiridazin-3(2H)-ona (1a-h) o 6-arilpiridazin-3-ol (1a'-h'), que se hizo reaccionar con oxicloruro de fósforo (POCl3) para producir 3-cloro-6-arilpiridazina (2a-h). Estos compuestos intermedios reaccionaron con ácido gamma amino butírico (GABA) y se convirtieron en los compuestos del título 3a-h. Utilizando análisis de datos espectrales, se determinaron las estructuras de los compuestos sintetizados. Estos compuestos del título se probaron frente a convulsiones inducidas por electrochoque máximo (MES) a un nivel de dosis de 100 mg/kg para la actividad anticonvulsiva en ratones albinos suizos. Se utilizó fenitoína sódica (25 mg/kg) como fármaco estándar. Estas sustancias sintéticas tienen propiedades anticonvulsivas de débiles a fuertes. Como resultado, la relación estructura-actividad (SAR) reveló que los derivados de aril-piridazina con sustituyentes hidrofóbicos en el anillo de fenilo tienen una acción anticonvulsiva más fuerte.

KEY WORDS: epilepsy, GABA, *in vivo* antiepileptic activity, maximal electroshock (MES) induced seizures, pyridazine

* Author to whom correspondence should be addressed. *E-mail:* aasif321@gmail.com

ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)