Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **42** (8): 1693-9 (2023)

Received: May 14, 2023
Accepted: May 28, 2023

Synthesis and Biological Evaluation of 2-[(2-Hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione as an Anti-tuberculosis Agent

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SUMMARY. **In the present study synthesis of 2-[(2-Hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione was designed for investigation against *Mycobacterium tuberculosis* (H37R*v*) as an anti-tuberculosis agent. The 1,3-cycloheptandione was reacted with 2-hydroxy aniline and tri-ethylorthformate under sonication at 70 °C to deliver the desired 2-[(2-Hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione in 96% yield. Investigation of the synthesized compound against *M. tuberculosis* H37Ra revealed that it suppressed bacterial growth in dose-dependent manner. The MIC of 2-[(2-Hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione was found to be 1.25 µg/mL against *M. tuberculosis* H37Ra. Molecular docking study revealed that 2-(2-hydroxy-phenoxymethylene)-5,5-dimethyl-cyclohexane-1,3-dione interacts with enoyl acyl career protein reductase (InhA) enzyme, 6R9W with the bonding affinity ranging from -8.0 to -7.3 kcal/mol. The 2-(2-hydroxy-phenoxymethylene)-5,5-dimethyl-cyclohexane-1,3-dione interacts with InhA enzyme with the binding affinity of -8.0 kcal/mol at zero rmsd. In conclusion, in the present study 2-[(2-hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione was synthesized and identified as anti-tuberculosis agent with an MIC of 1.25 µg/mL. Therefore, 2-[(2-hydroxy-phenylamino)-methylene]-cycloheptane-1,3-dione may be developed as an effective anti-bacterial agent for treatment tuberculosis.**

RESUMEN. En el presente estudio, se diseñó la síntesis de 2-[(2-hidroxi-fenilamino)-metileno]-cicloheptano-1,3-diona para la investigación contra *Mycobacterium tuberculosis* (H37Rv) como agente antituberculoso. La 1,3-cicloheptanodiona se hizo reaccionar con 2-hidroxianilina y ortoformiato de trietilo bajo sonicación a 70 ºC para producir la 2-[(2-hidroxi-fenilamino)-metilen]-cicloheptano-1,3-diona deseada en una proporción del 96 %. La investigación del compuesto sintetizado contra *M. tuberculosis* H37Ra reveló que suprimía el crecimiento bacteriano de manera dependiente de la dosis. Se encontró que la MIC de 2-[(2-hidroxi-fenilamino)-metileno]-cicloheptano-1,3-diona era de 1,25 µg/mL frente a *M. tuberculosis* H37Ra. El estudio de acoplamiento molecular reveló que la 2-(2-hidroxi-fenoximetileno)-5,5-dimetil-ciclohexano-1,3-diona interactúa con la enzima enoil acil carrera proteína reductasa (InhA), 6R9W con una afinidad de enlace que va de -8,0 a -7,3 kcal/mol. La 2-(2-hidroxi-fenoximetileno)-5,5-dimetil-ciclohexano-1,3-diona interactúa con la enzima InhA con una afinidad de unión de -8,0 kcal/mol a cero rmsd. En conclusión, en el presente estudio se sintetizó e identificó 2-[(2-hidroxi-fenilamino)-metileno]-cicloheptano-1,3-diona como agente antituberculoso con una CIM de 1,25 µg/mL. Por lo tanto, la 2-[(2-hidroxi-fenilamino)-metileno]-cicloheptano-1,3-diona puede desarrollarse como un agente antibacteriano eficaz para el tratamiento de la tuberculosis.

KEY WORDS: anti-tuberculosis treatment, condensation, cycloheptane-1,3-dione, diones, minimum inhibitory concentration, *ortho*-hydroxy aniline, sonication,

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