Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **38** (11): 2287-94 (2019)

Received: June 13, 2019
Revised version: July 30, 2019
Accepted: August 1, 2019

Synthesis of Pyrrolidine-2,5-dione Based Anti-inflammatory Drug: *In Vitro* COX-2, 5-LOX Inhibition and *In Vivo* Anti-inflammatory Studies

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***SUMMARY*. This study was designed to evaluate the pyrrolidine-2,5-dione with a ketoester moiety for the *in vitro, in vivo,* and mechanism based anti-inflammatory potential. The compound ethyl 1-(1-cyclohexyl-2,5-dioxopyrrolidin-3-yl)-2-oxocyclohexane-1-carboxylate was synthesized by Michael addition of ethyl-2-oxy-cyclohexanecarboxylate with N-cyclohexylmaleimide. Initially, the compound was screened for *in vitro* anti-inflammatory potential followed by *in vivo* studies using experimental animals. The possible mechanism of inflammation was also investigated using various inflammatory mediators. The tested compound has marked activity in *in vitro* enzymes, *i.e.* COX-2 and 5-LOX with 78.08 and 71.66% inhibition at 1000 μg/mL, respectively, nearly as active as celecoxib and nordihydroguaiaretic acid (NDGA). In carrageenan-induced paw edema, the compound exhibited 54.77% inhibition at the highest dose and significant to standard drug. The compound produced dual inhibitory effect via the inflammatory effect of prostaglandin E2 and leukotriene with 76.08 and 59.11 μg/mL, respectively, which were significant and similar to standard drug celecoxib and montelukast.**

RESUMEN. Este estudio fue diseñado para evaluar la pirrolidina-2,5-diona con un resto cetoéster para el potencial antiinflamatorio *in vitro, in vivo* y sus mecanismos. El compuesto etil 1-(1-ciclohexil-2,5-dioxopirrolidin-3-il)-2-oxociclohexano-1-carboxilato se sintetizó mediante la adición de Michael de etil-2-oxiciclohexanocarboxilato con N-ciclohexilmaleimida. Inicialmente, el compuesto se seleccionó para determinar el potencial antiinflamatorio *in vitro* seguido de estudios *in vivo* utilizando animales experimentales. El posible mecanismo de inflamación también se investigó utilizando varios mediadores inflamatorios. El compuesto probado tiene una marcada actividad en enzimas *in vitro,* es decir, COX-2 y 5-LOX con 78.08 y 71.66% de inhibición a 1000 μg/mL, respectivamente, casi tan activo como el celecoxib y el ácido nordihidroguairético (NDGA). En el edema de la pata inducido por carragenano, el compuesto exhibió un 54,77% de inhibición a la dosis más alta y significativo para el fármaco estándar. El compuesto produjo doble efecto inhibitorio a través del efecto inflamatorio de prostaglandina E2 y leucotrienos con 76.08 y 59.11 μg/mL, respectivamente, que fueron significativos y similares al fármaco estándar celecoxib y montelukast.

KEY WORDS: bradykinin, COX-2, histamine, inflammation, leukotriene, 5-LOX, prostaglandin E2, succinimide.

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