Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **41** (10): 1998-2003 (2022)

Received: June 21, 2022
Accepted: July 23, 2022

Analysis of the Therapeutics Effects of Tamoxifen in Ovarian Cancer Induced by Dimethylbenzene Anthracene: Animal Model Studies

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SUMMARY. **The aim of this study was to evaluate the therapeutic effects of tamoxifen (TAM) in dimethyltetraphene Or DMBA induced breast tumors using animal model. 100mg/kg of DMBA was administered to female rats to induce ovarian cancer and treated with tamoxifen (3 mg/kg) starting the day right after DMBA administration and lasting for 16 weeks served as a positive control treatment. Untreated DMBA group was considered as control. Tumor incidence, tumor multiplicity, tumor weight, tumor volume were monitored. Detection of the apoptosis of tumor tissue cells was performed by the TUNEL assay and the expression of Caspase-3 and Bcl-2 was evaluated by immunohistochemistry. Bcl-2 and Bax were detected by Western blotting. The cumulative incidence of tumors in the DMBA group and the DMBA+Tamox group were 80% and 50%, respectively which was statistically significantly different among the groups. Average tumor weight and average tumor numbers per rat were also significantly decreased in tamoxifen treatment group. TAM group regulated the expression levels of apoptosis-related proteins such as Caspase-3, Bax and Bcl-2. The expression level of anti-apoptotic protein Bcl-2 was down-regulated and the ratio of Bcl-2/Bax was increased. This study indicated that that TAM can inhibit DMBA induced ovarian tumor in rats.**

RESUMEN. El objetivo de este estudio fue evaluar los efectos terapéuticos del tamoxifeno (TAM) en tumores de mama inducidos por dimetiltetrafeno o DMBA utilizando un modelo animal. Se administraron 100 mg/kg de DMBA a ratas hembra para inducir cáncer de ovario y se trataron con tamoxifeno (3 mg/kg) comenzando el día inmediatamente posterior a la administración de DMBA y durante 16 semanas que sirvió como tratamiento de control positivo. El grupo de DMBA no tratado se consideró como control. Se controlaron la incidencia del tumor, la multiplicidad del tumor, el peso del tumor y el volumen del tumor. La detección de la apoptosis de las células del tejido tumoral se realizó mediante el ensayo TUNEL y la expresión de Caspasa-3 y Bcl-2 se evaluó mediante inmunohistoquímica. Bcl-2 y Bax se detectaron mediante transferencia de Western. La incidencia acumulada de tumores en el grupo de DMBA y el grupo de DMBA + Tamox fue del 80 % y el 50 %, respectivamente, que fue estadísticamente significativamente diferente entre los grupos. El peso medio del tumor y el número medio de tumores por rata también se redujeron significativamente en el grupo de tratamiento con tamoxifeno. El grupo TAM reguló los niveles de expresión de proteínas relacionadas con la apoptosis, como caspasa-3, Bax y Bcl-2. El nivel de expresión de la proteína antiapoptótica Bcl-2 se reguló a la baja y se incrementó la proporción de Bcl-2/Bax. Este estudio indicó que TAM puede inhibir el tumor de ovario inducido por DMBA en ratas.

KEY WORDS: apoptosis, ovarian cancers, tamoxifen.

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