Faculty of Education
Department of Biological and Geological Sciences

THE EFFECT OF AN ANTI-INFLAMMATORY DRUG ON PREGNANT MICE AND THEIR FETUSES

A THESIS
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BY

Sahar Ahmed Sabry Sobhy

General Diploma for Teacher Preparation in Science (Zoology) - 2003
Special Diploma for Teacher Preparation in Science (Zoology) – 2004
Master Degree for Teacher Preparation in Science (Zoology)-2008

SUPERVISED BY

Prof. Dr. Mohamed Abd El Hamid Shahin
Professor of Experimental Embryology,
Department of Biological and Geological Sciences,
Faculty of Education, Ain Shams University

Prof. Dr. Ramadan Abd El Sadek Ramadan
Professor of Histology and Cytology,
Department of Biological and Geological Sciences,
Faculty of Education, Ain Shams University

.

Dr. Samia Mohamed sakr
Assistant Professor of Histology and Cytology,
Department of Biological and Geological Sciences,
Faculty of Education, Ain Shams University

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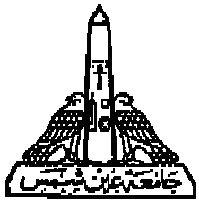

كلية التربية
قسم العلوم البيولوجية والجيولوجية

تأثير عقار مضاد للإلتهابات على الفئران الحوامل وأجنتها

رسالة مقدمة من

سحر أحمد صبري صبحى

للحصول على درجة دكتوراه الفلسفة لإعداد المعلم في العلوم
(تخصص علم الحيوان)

تحت إشراف

أ.د./ محمد عبد الحميد شاهين
أستاذ علم الأجنه التجريبى - قسم العلوم البيولوجية والجيولوجية
كلية التربية - جامعة عين شمس

أ.د./ رمضان عبد الصادق رمضان
أستاذ علم الأنسجة والخلية- قسم العلوم البيولوجية والجيولوجية
كلية التربية- جامعة عين شمس

د./سامية محمد صقر
أستاذ علم الأنسجة والخلية المساعد- قسم العلوم البيولوجية والجيولوجية
كلية التربية- جامعة عين شمس

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ABSTRACT

The non-steroidal anti-inflammatory drug (NSAID) **Diclofenac sodium** with the trade name **"Declophen**" is considered one of the most important and widely used drug in the medical area in Egypt. It is used for treatment of many cases of rheumatoid arthritis, osteoarthritis, acute gout and soft tissue rheumatism as well as cases of ankloysing spondilitis. In spite of such beneficial role of this drug, yet some medical reports incriminating it in producing certain adverse toxic and pathogenic consequences in the body organs following its medical use.

Hence, the present investigation was carried out to evaluate the effect of the therapeutic and double the therapeutic doses (1.5 & 3mg/kg body weight, respectively) of the non-steroidal anti-inflammatory drug **diclofenac sodium (DS**) on the pregnant females of albino mice and their fetuses from the morphological and skeletal points of view and also to assess any expected evoked consequences following the usage of such drug doses on the liver and stomach of the fetuses of albino mice from the histological and ultrastructural points of view.

In order to achieve these intended goals, the experimental design was carried out in the following manner:

Sixty adult pregnant female mice were used in the present investigation. They were allocated into 6 groups (10 mice each). The first two groups served as control and were injected intraperitoneally (i.p.) with the solvent of the drug. Pregnant mice of the third and fourth groups were treated with 1.5 & 3mg/kg body weight, of DS for 6 days (gestation days 1-6), respectively; those of the fifth and sixth groups were treated with1.5 & 3mg/kg body weight, of DS for 8 days (gestation days 7-14), respectively.

The morphological result: The mean body weight of pregnant females was less in all the treated groups, while morphological examination of the fetuses of treated groups showed conspicuous decrease in the average body weight and body length in all treated groups. The fetuses maternally treated with the drug showed noticeable external morphological malformations and their skeletons exhibited mild retardation in skeletal growth.

The histopathological examination of the liver sections of the fetuses of diclofenac-treated groups showed vacuolar and fatty degenerations in the cytoplasm of the hepatocytes with conspicuous devastations in the hepatic vasculatures, inflammatory lymphocytic infiltration and proliferation of Kupffer cells.

The electron microscopical examination of the hepatocytes of fetuses maternally treated with DS revealed conspicuous alterations, represented by gradual devastations of mitochondria that displayed apparent loss of their cristae and their internal matrices materials and contained tiny flocculent densities. The cisternae of rough endoplasmic reticulum displayed dilation and fragmentation into smaller stacks. Lysosomes and lipid droplets were apparent in such cases.

The histopathological examination of the wall of the stomach of the fetuses of the treated groups showed features of vacuolar degeneration of the epithelial and glandular cells. In addition marked coagulative cell necrosis with conspicuous damage and bleeding in the micro-vessels of the supporting lamina propria and in the sub-mucosal connective tissue were also observed.

The electron microscopical examination of the gastric mucosal cells of fetuses maternally treated with DS, revealed conspicuous alterations, in the cytoplasmic organelles of all gastric mucosal cells (surface epithelial, peptic and parietal cells). The cisternae of RER were dilated and fragmented into smaller stacks. The mitochondria displayed gradual devastations; being in the form of swelling or hypertrophy as well as condensation and gradual loss of their matrices materials as well as loss of their internal ridges. The nuclei of the gastric mucosal cells showed certain degrees of pathological changes appeared in the form of irregular nuclear envelope and condensation of their chromatin materials.

Conclusion: The use of such doses of the NSAID diclofenac sodium manifested serious teratogenic and morphological deterioration in mice fetuses and their mothers, as well as conspicuous histological and ultrastructural alterations of the liver and gastric wall of maternally treated fetuses. The severity of such changes are correlated with the drug doses and the gestation period during which treatment was performed.

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