**Ministry Of Higher Education and Scientific Research**

**University Of Al-Qadisiyah**

**College Of Pharmacy**

# Effect of Betamethasone on Oxidative Stress in Male Rats

**A graduation research submitted to the college of pharmacy in partial fulfillment of the requirements for the degree of B.Sc. in pharmacy**

By:

**Ahmad Nadhim Mahdi**

**Maitham Saad Hachim**

Supervised by

**Professor Dr.Ihsan Raisan Alrikabi**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

مَا كَانَ لِبَشَرٍ أَنْ يُؤْتِيَهُ اللَّهُ الْكِتَابَ وَالْحُكْمَ وَالنُّبُوَّةَ ثُمَّ يَقُولَ لِلنَّاسِ كُونُوا عِبَادًا لِي مِنْ دُونِ اللَّهِ وَلَكِنْ كُونُوا رَبَّانِيِّينَ بِمَا كُنْتُمْ تُعَلِّمُونَ الْكِتَابَ وَبِمَا كُنتُمْ تَدْرُسُونَ 79

صَدَقَ اللهُ العَظِيمُ

سورة آل عمران (79)

# *Supervisor Certificate*

I certify that this project

**(Effect Of Betamethasone On Oxidative Stress In Male Rats)**

Was prepared under my supervision at the College Of Pharmacy, University of Al-Qadisiyah as Graduation research

**Professor**

**Dr.Ihsan Raisan Al-Rikabi**

# Dedication

*To our…… families*

*To our ……supervisor*

*To our ……lecturers*

*To our…… friends*

**And to…….. all those who quench our homeland with their blood to make us live peacefully**

**Ahmad and Maitham**

# Acknowledgement

By the name of God most gracious, most merciful, the first who deserve all thanks and appreciation for granting us with well, strength patience and help with which this research has been accomplished.

We would like to express our deepest thanks to Dr.Ihsan , Raisan Al-Rikabi our supervisor for providing help and efforts in completion of this study.

We would like to express our deepest thanks and gratitude to all those who helped us during the preparation of this project.

**Ahmad and Maitham**

## Summary:

Current study was carried to evaluate effect of betamethasone on some oxidative stress indicators.

Ten male rats were divided into two groups.

First group was given normal saline for 10 days and was considered as control group while the second group was given betamethasone orally at dose 0.5mg/kg for 10 days.

At the beginning of the experiment, body weight was recorded, as well as at the end of the experiment. Blood samples were collected for measurement malondialdehyde (MDA), catalase (CT), Alanine transaminase (ALT) and Aspartate transaminase (AST).

Results of the current study showed significant increase in levels of malondialdehyde, Alanine transaminase (ALT) in the group treated with betamethasone compared with the control group. While aspartate transaminase (AST) increased non significantly in the group treated with betamethasone in comparison with the control group.

Catalase was decreased non-significantly in rats treated with betamethasone compared with the control group.

It was concluded that Betamethasone induce oxidative stress in male rats.

## List of contents:

# *Chapter one*

# Introduction

## 1-1 Introduction

Betamethasone is in a class of drugs called steroids.
A glucocorticoid given orally, parenterally, by local injection, by inhalation, or applied topically in the management of various disorders in which corticosteroids are indicated. Its lack of mineralocorticoid properties makes betamethasone particularly suitable for treating cerebral edema and congenital adrenal hyperplasia. [1]

Betamethasone is used to treat many different conditions such as allergic disorders, skin conditions, ulcerative colitis, arthritis, lupus, psoriasis, or breathing disorders.

Maternal administration of betamethasone to enhance fetal lung maturation for women who threaten preterm labor is common clinical practice. [2]

Betamethasone and its derivatives, betamethasone sodium phosphate and betamethasone acetate, are synthetic glucocorticoids. Used for its anti-inflammatory or immunosuppressive properties, betamethasone is combined with a mineralocorticoid to manage adrenal insufficiency and is used in the form of betamethasone benzoate, betamethasone dipropionate, or betamethasone valerate for the treatment of inflammation due to corticosteroid-responsive dermatoses. Betamethasone and clotrimazole are used together to treat cutaneous tinea infections. [3]

Betamethasone is a glucocorticoid receptor agonist. This leads to changes in genetic expression once this complex binds to the GRE. The anti-inflammatory actions of corticosteroids are thought to involve lipocortins, phospholipase A2 inhibitory proteins which, through inhibition arachidonic acid, control the biosynthesis of prostaglandins and leukotrienes. The immune system is suppressed by corticosteroids due to a decrease in the function of the lymphatic system, a reduction in immunoglobulin and complement concentrations, the precipitation of lymphocytopenia, and interference with antigen-antibody binding. Betamethasone binds to plasma transcortin, and it becomes active when it is not bound to transcortin. [3]

Symptoms of overdose include burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. [1]

## Aim of study

Current study was carried to evaluate the effect of betamethasone ( an anti-inflammatory drug ) in oxidative stress through study the following :

1- measurement of the product of lipid peroxidation , malondialdehyde (MDA) in serum of rats.

2- Catalase (CT) as antioxidant enzyme.

3- Measurement of enzymes Alanine transaminase (ALT) and Aspartate transaminase (AST).

# *Chapter Two*

# Review of literatures

## 2-1 Betamethasone:

Betamethasone is a steroid medication. It is used for a number of diseases including rheumatic disorders such as rheumatoid arthritis and systemic lupus erythematosus, skin diseases such as dermatitis and psoriasis, allergic conditions such as asthma and angioedema, preterm labor to speed the development of the baby's lungs, Crohn's disease, cancers such as leukemia, and along with fludrocortisone for adrenocortical insufficiency, among others.

Synthetic corticosteroids such as dexamethasone and betamethasone are widely used in clinical practice of the perinatal period to enhance lung maturation. However, indications emerged both on the basis of investigations in humans and in experimental animals that such treatment leads to abnormal brain development. [4]

Corticosteroids are potent anti-inflammatory drugs and have been used clinically to treat septic shock and other inflammatory diseases for half a century. Antenatal corticosteroid therapy has also been used to reduce the incidence of respiratory distress syndrome and other complications of preterm birth. [5]

## 2-2 Uses of Betamethasone:

Betamethasone is a corticosteroid that is available as pill, by injection, and as a cream. It is used as a topical cream to relieve skin irritation, such as itching and flaking from eczema. It is used as a treatment for local psoriasis, as betamethasone dipropionate and salicylic acid, or as the combination calcipotriol/betamethasone dipropionate. Betamethasone sodium phosphate is used orally and via injection with the same indications as other steroids. Many betamethasone-based pharmaceuticals include the steroid as the valerate ester. In a randomized controlled trial betamethasone was shown to reduce some of the ataxia symptoms associated with ataxia telangiectasia (A-T) by 28-31%.[6]

Results showed that prenatal betamethasone exposure provoked a significant reduction in body weight at PND 01 and, at adulthood,

decrease in FSH levels, sperm motility and production. Furthermore, seminal vesicle weight was decreased while testicular and ventral prostate weights were increased. [7]

Pelvic nerve crush (PNC) causes autonomic neuropraxia and functional and morphologic changes of isolated bladder tissue that can be recorded as bladder dysfunction during awake cytometry in female rats. Perioperative systemic Betamethasone treatment reduced macrophage contents of pelvic plexus and bladder, partially counteracted changes in bladder tissue, and had protective effects on micturition function. [8]

In addition, steroidal anti-inflammatory drugs such as dexamethasone can inhibit COX-2 gene expression. The glucocorticoids have widespread effects because they influence the function of most cells in the body. Glucocorticoids dramatically reduce the manifestations of inflammation. This is due to their profound effects on the concentration, distribution and function of peripheral leukocytes and their suppressive effects on the inflammatory cytokines, such as TNF-α or interleukin-6 (IL-6) and chemokines or other lipid and glucolipid mediators of inflammation. In addition to these effects, glucocorticoids influence the inflammatory response by reducing the prostaglandin synthesis that results from activation of phospholipase $A_2$. [9]

Decreased body weight in betamethasone-exposed rats confirmed long-lasting effects of prenatal exposure. Thus, prenatal betamethasone treatment consistently increases hippocampal NPY, with decreases in anxiety-related behaviors and hippocampal role in anxiety in rats. Animal models may assist in differentiation between pathways of the desired main effect of the antenatal corticosteroid treatment and pathways of unwanted side effects. This differentiation can lead to specific therapeutic interventions directed against the side effects without eliminating the beneficial main effect of the corticosteroid treatment. [10]

Administration of corticosteroids to mothers before preterm delivery significantly reduces perinatal morbidity and mortality. In 1994, the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes consensus conference sponsored by the National Institutes of Health (NIH) concluded that giving a single course of corticosteroids to pregnant women at risk for preterm delivery reduces the risk of death, respiratory

distress syndrome, and intraventricular hemorrhage in their preterm infants. [11]

Pregnant rats received 0.1 mg kg (-1) betamethasone on Days 12, 13, 18 and 19 of pregnancy. This treatment impaired sperm quality, sperm production, fertility and plasma testosterone levels in adult male offspring compared to the control group. Thus, the results of the present study indicate that the long-term effects of prenatal betamethasone exposure may be deleterious to offspring. The consequent decrease in testosterone production during adulthood, in association with damaged semen parameters, may explain for the observed decrease in the capacity of adult male offspring to themselves generate viable descendants. [12] Topical betamethasone inhibits inflammatory stimuli in a different manner from systemic betamethasone. The broad spectrum of inhibition suggests that topical betamethasone acts by affecting a fundamental feature of the inflammatory response common to all of the stimuli. [13]

Cytokine levels in P1 rat lungs were increased by intrauterine infection, and these increases were attenuated by antenatal betamethasone. Hyperoxic lung injuries, indicated by morphometric changes and an inflammatory response in the lung and BAL fluid, were aggravated by intrauterine infection at P14. This aggravation was significantly attenuated by antenatal betamethasone. Antenatal betamethasone attenuated aggravated hyperoxic lung injuries induced by intrauterine infection in neonatal rats via its anti-inflammatory actions. [14]

## 2-3 Side effects of Betamethasone:

Subacromial injections of methylprednisolone or betamethasone repeated frequently can cause deleterious changes in the normal structure of the rat rotator cuff. In light of these findings, therapy for subacromial impingement syndrome of the shoulder with frequent, repeated steroid injections is potentially harmful. [15]

In other clinical trials, Animals that were prenatally treated with a single course of betamethasone exhibited long-lasting behavioral changes consistent with anxiety-like behavior in the open-field test, together

with (1) reduced cerebellar weight and volume, (2) Purkinje cell dendritic atrophy, and (3) an overexpression of calbindin-D28k. The current results indicate that an experimental single course of betamethasone in pregnant rats produces long-lasting anxiety-like behaviors, together with macroscopic and microscopic cerebellar alterations. [16]

Randomized clinical trials of postnatal steroid therapy have raised concerns regarding an increase in the rates of cerebral palsy and adverse neuromotor and cognitive outcomes [14]. Experimental studies in neonatal animals have demonstrated adverse effects of potent glucocorticoids, such as dexamethasone on brain growth, cell division, differentiation, myelination, apoptosis, and neurogenesis. [17]

The use of this drug may carry some risk of fetal death in pregnancies complicated by severe hypertension-edema-proteinuria syndromes. [18]

Another contentious issue is to what extent antenatal glucocorticoids (GC) affect fetal well-being and neurological development. It is well known that betamethasone and dexamethasone reduce fetal movements and cause an altered heart rate pattern for 1 or 2 days after administration. [19]

## 2-4 chronic use of betamethasone:

Corticosteroid treatment effects in the central nervous system depend on genetic background [20] . A study results showed that a multidose of antenatal betamethasone accelerated fetal lung maturation more than after a single dose but was accompanied with a decrease in lung weight that persisted into adulthood. [21]

Betamethasone-exposed subjects gained less weight during pregnancy and were delivered of fewer live pups, with fewer male survivors and lower birth weights. [22]

Patients with chronic severe asthma, having previously shown an FEV1 increase of less than 20% of the predicted value with prednisolone treatment (20-60 mg daily for 10 days), took part in a double blind

crossover comparison of equipotent anti-inflammatory doses of betamethasone and prednisolone. Betamethasone (8 mg) and prednisolone (40 mg) were administered daily for 10 days with a washout period of 10 days between. In this first part of the study betamethasone was administered intramuscularly and prednisolone orally. Placebo injections and tablets were used. Mean FEV1 was not significantly different before each period. There was a significant increase in FEV1 while they were taking betamethasone but not prednisolone. Individual analysis of the data showed that FEV1 increased with betamethasone in nine patients and remained stable or decreased in three [23]

A dose of 0.5mg of betamethasone for children under 5 years of age and a dose of 1.0mg was prescribed for children >5, were effective for prompt resolution of PFAPA flares. We believe that as long as there is an effective lowest dose for treating PFAPA episodes, a great reduction of corticosteroid consumption will be exercisable globally. [24]

## 2.5 Oxidative stress

Free radicals and other reactive oxygen species (ROS) are constantly formed in the human body. Free-radical mechanisms have been implicated in the pathology of several human diseases, including cancer, atherosclerosis, malaria, and rheumatoid arthritis and neurodegenerative diseases. For example, the superoxide radical and hydrogen peroxide are known to be generated in the brain and nervous system *in vivo*, and several areas of the human brain are rich in iron, which appears to be easily mobilizable in a form that can stimulate free-radical reactions. Antioxidant defenses to remove superoxide radical and hydrogen peroxide exist.

Superoxide dismutases (SOD) remove superoxide by greatly accelerating its conversion to H2O2. Catalases in peroxisomes convert H2O2 into water and O2 and help to dispose of H2O2 generated by the action of the oxidase enzymes that are located in these organelles. Other

important H2O2-removing enzymes in human cells are the glutathione peroxidases. When produced in excess, ROS can cause tissue injury. However, tissue injury can itself cause ROS generation (e.g., by causing activation of phagocytes or releasing transition metal ions from damaged cells), which may (or may not, depending on the situation) contribute to a worsening of the injury. Assessment of oxidative damage to biomolecules by means of emerging technologies based on products of oxidative damage to DNA (e.g., 8-hydroxydeoxyguanosine), lipids (e.g., isoprostanes), and proteins[25]
Increases in the intracellular levels of reactive oxygen species (ROS), frequently referred to as oxidative stress, respresents a potentially toxic insult which if not counteracted will lead to membrane dysfunction, DNA damage and inactivation of proteins. Chronic oxidative stress has numerous pathological consequences including cancer, arthritis and neurodegenerative disease. Glutathione-associated metabolism is a major mechanism for cellular protection against agents which generate oxidative stress.

Thus, glutathione provides the cell with multiple defenses not only against ROS but also against their toxic products. This article discusses how glutathione biosynthesis, glutathione peroxidases, glutathione *S*-transferases and glutathione *S*-conjugate efflux pumps function in an integrated fashion to allow cellular adaption to oxidative stress. Co-ordination of this response is achieved, at least in part, through the antioxidant responsive element (ARE) which is found in the promoters of many of the genes that are inducible by oxidative and chemical stress. Transcriptional activation through this enhancer appears to be mediated by basic leucine zipper transcription factors such as Nrf and small Maf proteins. The nature of the intracellular sensor(s) for ROS and thiol-active chemicals which induce genes through the ARE is described. Gene activation through the ARE appears to account for the enhanced antioxidant and detoxification capacity of normal cells effected by many cancer chemopreventive agents. In certain instances it may also account for acquired resistance of tumours to cancer chemotherapeutic drugs. It is therefore clear that determining the mechanisms involved in regulation of ARE-driven gene expression has enormous medical implications. [26]

Malondialdehyde (MDA) is one of the most frequently used indicators of lipid peroxidation. To generate reliable reference intervals for plasma malondialdehyde (P-MDA), a reference sample group was established in Funen, Denmark. Daily smokers had a slightly higher average concentration of P-MDA than nonsmokers (P = 0.05), and P-MDA correlated with daily exposure to cigarette smoke (r = 0.162; P = 0.03). A positive correlation was also demonstrated between P-MDA and weekly alcohol consumption (r = 0.153; P = 0.03). However, on a group basis, the present data support that P-MDA may be a potential biomarker for oxidative stress. [25]

In premature infants, glucocorticoids ameliorate chronic lung disease, but have adverse effects on long-term neurological function. Glucocorticoid excess promotes free radical overproduction. This hypothesized that the adverse effects of postnatal glucocorticoid therapy on the developing brain are secondary to oxidative stress and that antioxidant treatment would diminish unwanted effects. [27]

# Chapter Three
# Materials and method

## 3.1 Laboratory animals:

Male rats weighing (70-96)g housed under environmental conditions such as (12:12) hr. light to dark cycle, and at 23±2 C˚. Rats were given food and water

Ten male rats were divided into:

1- control group (C): five male rats were given normal saline by oral gavage for ten days.

2- Treatment group (T): five male rats were given betamethasone sodium phosphate at dose (0.5 mg/kg/day) once daily orally for 10 days.

## 3.2 Betamethasone Preparation:

The type of betamethasone that was used in this study was (betamethasone sodium phosphate) produced by dissolving 3.5 mg of betamethasone (Furason Furat pharma®) in 10 ml of normal saline, to obtain the dose of (0.5 mg/kg)

## 3.3 Collection of samples:

Blood samples were collected at the end of the experiment. After the male rats were anesthetized, blood was collected by cardiac puncture and placed in non-anticoagulant tubes and then centrifuged at 3000 rpm for 15 min.

Sera, then, were isolated and placed in tubes for measurements of the parameters involved in the current study.

## 3.4 Measurement of malondialdehyde MDA:

Malondialdehyde (MDA) was measurent according to method followed by Guidet and Shah, (1989)

This method depends on the reaction between lipid peroxidase and Thiobarbituric acid in acidic medium.

## 3.5 Determination of catalase:

Catalase activity was determined according to measurement of the absorbance at 240 nanometer by spectrophotom

## 3.6 Estimation of AST and ALT:

Activity of Alanine Transaminase (ALT) and Aspartate Transaminase were estimated according to the method which is followed by (Duncan etal, 1997) by using kit produced by (Biomerieux, France).

## 3.7 Statistical analysis:

Results undergo statistical analysis know significant differences between groups in the current study. T test was used for examine the differences in means between the control group and treatment group.

# *Chapter four*

# *Results*

# Results

Figure (4-1) revealed non-significant decrease ( $p < 0.05$ ) in weight gain rate in rats treated with betamethasone in comparison with a control group. Results also showed significant increase in malondialdehyde in the group treated with betamethasone compared with the control group.

Catalase enzyme activity decreased non-significantly in rats treated with betamethasone compared with a control group, also betamethasone caused a significant increase in level of, Alanine transaminase (ALT) compared with a control group, while there is non-significant increase in Aspartate transaminase (AST) compared with the control group

**Figure (4-1) effect of betamethasone on weight gain rate in male rats**

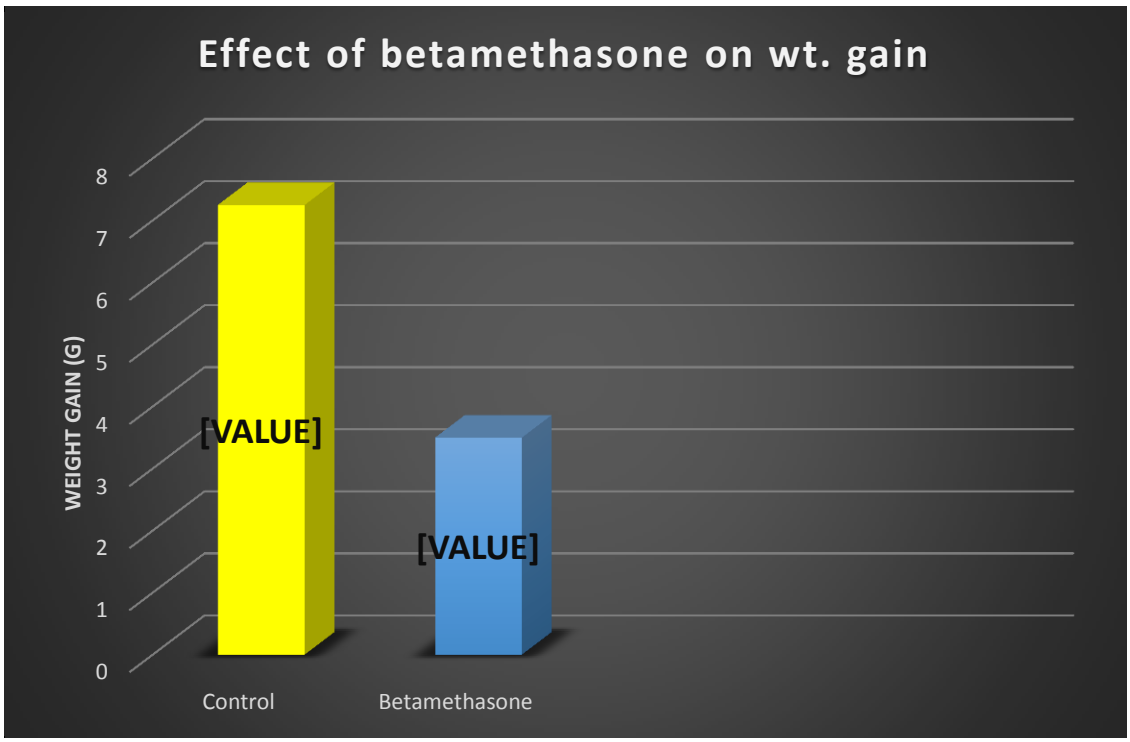

**Table (4-2) effect of betamethasone on (MDA, CAT, ALT, AST) in male rats**

| Parameters | Control group | Group treated with betamethasone |
|---|---|---|
| MDA (µmol/L) | 0.16 ± 0.08 | 0.36 ± 0.06 * |
| CAT (µmol/L) | 1.15 ± 0.15 | 0.73 ± 0.09 |
| ALT (µmol/L) | 44.33 ± 6.25 | 59.66 ± 3.53 * |
| AST (µmol/L) | 142 ± 9.75 | 168.3 ± 11.33 |

- Numbers refer to mean ± SD
- *Significant difference

# *Chapter five*

# *Discussion*

# Discussion

Results of current study revealed non-significant decrease in body weight gain in rats which administered with betamethasone, this result agreed with previous study that indicated that long term administration of betamethasone induced significant reduction on body weight of male rats. [8]

This effect may be to the influence of glucocorticoids in protein catabolism in process pf gluconeogenesis. And this cause in decrease of protein content that results in reduction in body weight.

Betamethasone elevated malondialdehyde concentration in male rats compared with control group. In some studies was reported that glucocorticoids increase oxidative damage via effect on mitochondria level. [28]

Also betamethasone induce oxidative stress by increasing the level of malondialdehyde which is produced by lipid peroxidation in cells.

Betamethasone (as glucocorticoid) administration cause elevation in malodialdehyde also reduction in glutathione peroxidase in newborn who administrated betamethasone before birth. And these effects may be to increase level of glucose and free fatty acids. [29]

And this increase the formation of free radicals that induce lipid peroxidation, which in turn increase the malodialdehyde as the final product of lipid peroxidation. And decrease the level of antioxidants such as catalase. And this agreed with our results

This oxidative damage may cause deleterious effect on liver resulting in release of Alanine Transaminase and Aspartate Transaminase from hepatocytes, and this agreed with current result which showed significant increase in ALT and non-significant increase in AST. And these effects may be caused by oxidative damage to liver and other organs, ALT represent main indicator for liver dysfunction and damage.

# Conclusions and Recommendations:

## Conclusions:

1- Use continuous treatment with betamethasone has negative effects on health.
2- Continuous administration of betamethasone may cause oxidative damage in most tissue

## Recommendation:

1- Decreasing of continues use of betamethasone as possible
2- Study other effects of betamethasone on other functions of other systems such as reproductive system and nervous system

**References :**


[1] - Martindale, The Extra Pharmacopoeia, ,(1993) 30th ed,pharmaceutical press.London p724.

[2] - European Pharmacopoeia (EP) Reference Standard (2017). ).9th ed.EDQM

[3] - Tanigawa K, Nagase H, Ohmori K, Tanaka K, Miyake H, Kiniwa M, Ikizawa K: 2002 **"Species-specific differences in the glucocorticoid receptor transactivation function upon binding with betamethasone-esters".** Int Immunopharmacol. : 941-50.

[4] – Albert Gramsbergen and Edu J H Mulder. (1998) **"The influence of betamethasone and dexamethasone on motor development in young rats".** Pediatric research, 44:105-110.

[5] - Cavalieri RL, and Cohen WR**.** (2006) **"Antenatal steroid therapy: have we undervalued the risks?**" J Matern Fetal Neonatal Med. 19:265–269.

[6] - Zannolli, R; Buoni, S; Betti, G; Salvucci, S; Plebani, A; Soresina, A; Pietrogrande, MC; Martino, S; Leuzzi, V; Finocchi, A; Micheli, R; Rossi, LN; Brusco, A; Misiani, F; Fois, A; Hayek, J; Kelly, and C; Chessa, L (Sep, 2012). **"A randomized trial of oral betamethasone to reduce ataxia symptoms in ataxia telangiectasia"**. Movement disorders: official journal of the Movement Disorder Society. 27 (10): 1312–1314.

[7] – Cibele dos S. Borges , Ana Dias , Patricia Silva , Josiane Rosa , Marina T. Guerra , Raquel Silva , Luiz Ricardo Kiguti , Andre S. Pupo , and Wilma G. Kempinas . (2017) "**Long-term adverse effect on reproductive function in male rats exposed prenatally to glucocorticoid betamethasone".** Toxicology, 376:15-22.

[8] – Fabio Castigleione , Alice Bergamini , Arianna Bettiga , Trinity J. Bivalacqla , Fabio Benigni , Frank Strittmater , Giorgio Gandaglia , Patrizo Regatti , Francseco Montorsi , and Petter Hedlund . (2012) **"Perioperative Betamethasone treatment reduces signs of bladder dysfunction in a rat model for neuropraxia in female urogenital surgery".** EUROPEAN UROLOGY, 62:1076-1085.

[9] - Katzung BG. (2004) **"Basic and clinical pharmacology".** Appleton and Lange: New York; 98-311, 577, 643-6.

[10] – Libor Velísek. (2006) "**Prenatal exposure to betamethasone decreases anxiety in developing rats: hippocampal neuropeptide y as a target molecule".** Neuropsychopharmacology, 31:2140-2149.

[11]- NIH Consensus Development Panel on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. (1995) **"Effect of corticosteroids for fetal maturation on perinatal outcomes".** JAMA; 273:413-418

[12] – Renata Piffer, Patricia C. Garcia, Daniela C. Gerardin, Wilma G. Kempinas, and Oduvaldo C. M. Pereira.(2009) "**Semen parameters, fertility and testosterone levels in male rats exposed prenatally to betamethasone" .** Reproduction, Fertility and Development, 21:634-639.

[13] - A. Ahluwalia, S. H. Peers, and R. J. Flower. (1992) **"Steroid inhibition of oedema formation in the rat skin".** Br J Pharmacol. 106(3): 628–631.

[14] - Yoo HS, Chang YS, Kim JK, Ahn SY, Kim ES, Sung DK, Jeon GW, Hwang JH, Shim JW, and Park WS.(2013) "**Antenatal betamethasone attenuates intrauterine infection-aggravated hyperoxia-induced lung injury in neonatal rats".** Pediatr Res. 73(6):726-733.

[15] – Secan Akpinar, Murat Hersekli , Huseyin Demirors , Reha N. Tandogan, and Fazilet Kayaselcuk .(2002) **"Effects of methylprednisolone and betamethasone injections on the rotator cuff: an experimental study in rats" .** Advances in Therapy, 19: 194-201.

[16] - Rodrigo Pascual, Martina Valencia, Sebastián Larrea, and Carlos Bustamante. (2014) **"Single course of antenatal betamethasone produces delayed changes in morphology and calbindin-D28k expression in a rat's cerebellar Purkinje cells".** Acta Neurobiol Exp 2014, 74: 415–423

[17] - Shinwell ES, Karplus M, Reich D, Weintraub Z, and Blazer S, et al. (2000) "**Early postnatal dexamethasone treatment and increased incidence of cerebral palsy**". Arch Dis Child Fetal Neonatal Ed 83: F177–181.

[18] - Liggins GC, Howie RN. (1972) **A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants**. *Pediatrics*.50: 515–525.

[19] - Magee LA, Dawes GS,Moulden M, RedmanCW.( 1997) **A randomized controlled comparison of betamethasone with dexamethasone: effects on the antenatal fetal heart rate.** Br J Obstet Gynaecol; 104:1233–8.)

[20] – Rossana Aielloa Rosalia Crupib AntonioLeo Serafina Chimirria Vincenzo Rispolic Rosario Marrad Rita Citraroa Salvatore Cuzzocreab Giovambattista De Sarroa Emilio Russoa (2014) "**Long-term betamethasone 21-phosphate disodium treatment has distinct effects in CD1 and DBA/2 mice on animal behavior accompanied by opposite effects on neurogenesis**" Behavioural Brain Research: 278, 155-166

[21] – American Journal of Obstetrics & Gynecology **"Placebo-controlled comparison between a single dose and a multidose of betamethasone in accelerating lung maturation of mice offspring".** (1998); 179:1241-7

[22] – Jeffrey D., Stewart MD, Christina L. Gonzalez BS, H.Dix Christensen PhD, William F.Rayburn MD, (1997) **"Impact of multiple antenatal doses of betamethasone on growth and development of mice offspring"** American Journal of Obstetrics and Gynecology; 177, 1138-1144

[23] - B GRANDORDY, N BELMATOUG, A MORELLE, D DE LAUTURE, and J MARSAC. (1987) "**Effect of betamethasone on airway obstruction and bronchial response to salbutamol in prednisolone resistant asthma**". Thorax; 42:65-71

[24] - Nadim H Nasser, Nadir N Nasir, Mona G Habib, and Nadra G Samra. (2017) "**The lowest dose of corticosteroids, which stops the episodes of PFAPA syndrome"**. Australian medical journal AMJ; 10(4):322–328

[25] - John D. Hayes &Lesley I. McLellan. (2009) "**Glutathione and glutathione-dependent enzymes represent a co-ordinately regulated defence against oxidative stress**" Talyor & francis, Pages 273-300

[26] - Nielsen F, Mikkelsen BB, Nielsen JB, Andersen HR, and Grandjean P**,** 1997**,"Plasma malondialdehyde as biomarker for oxidative stress: reference interval and effects of life-style factors."** Clin Chem. ; 1209-14.

[27] - Camm EJ, Tijsseling D, Richter HG, Adler A, and Hansell JA, 2011, "**Oxidative Stress in the Developing Brain: Effects of Postnatal Glucocorticoid Therapy and Antioxidants in the Rat".** Plos one, p1

[28] – JohanVerhaeghe, Ritavan Bree, ErikVan Herck (2009) **"Oxidative stress after antenatal betamethasone: Acute downregulation of glutathione peroxidase-3."** Early Human Development; 85; 767-771

[29] – Tang M.V. (2012) "**Glucocorticoid effects on oxidative stress and mitochondrial dysfunction**." Master thesis the University of British. Colombia

وزارة التعليم العالي والبحث العلمي

جامعة القادسية

كلية الصيدلة

# تأثير البيتاميثازون على الإجهاد التأكسدي في ذكور الجرذان

## بحث تخرج

مقدم إلى كلية الصيدلة , جامعة القادسية كجزء من متطلبات نيل درجة البكالوريوس في علوم الصيدلة

تقدم به كل من :

احمد ناظم مهدي

ميثم سعد حاجم

بأشراف

الاستاذ الدكتور

د.أحسان ريسان الركابي

1439 ه

2018 م

الخلاصة :

**أجريت الدراسة الحالية لتقييم تأثير بيتاميثازون على بعض مؤشرات الإجهاد التأكسدي.**

**تم تقسيم عشرة ذكور من الجرذان إلى مجموعتين. اعتبرت المجموعة الأولى كمجموعة سيطرة واعطيت المحلول الفسيولوجي في حين أعطيت المجموعة الثانية بيتاميثازون عن طريق الفم بجرعة 0.5 ملغ / كغ لمدة 10 أيام.**

**في بداية التجربة ، تم تسجيل وزن الجسم ، وكذلك في نهاية التجربة. تم جمع عينات الدم لقياس المالون ثنائي الالديهايد MDA وانزيمات (CAT)، (ALT) و (AST)..**

**أظهرت نتائج الدراسة الحالية زيادة معنوية في مستويات MDA، (ALT) في حين كانت الزيادة غير معنوية في انزيم (AST) في المجموعة المعالجة بالبيتاميثازون مقارنة بمجموعة السيطرة . انخفض مستوىCAT)) بشكل غير معنوي في الجرذان المعالجة بالبيتاميثازون مقارنة بمجموعة السيطرة.**

**و قد استنتج من الدراسة الحالية أن مادة البيتاميثازون تحفز الإجهاد التأكسدي في ذكور الجرذان.**