



## Effect of capoten drug on different organs of rats embryos

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### Abstract

The purpose of this study was project effects capoten on weight human embryo with histological of heart embryos for 60 days with anatomical effects on stomach embryo rats . The 30 rats were divided into two groups (control and two treated groups), and animals were treated as follow: 1- Control group (n=20).2-Treatment group (n=10) treated every day with capoten for 50 days. At 60 days animals sacrificed next taken organs (kidney) for histopathological study. Results :present study showed that treatment with capoten cause a significant decrease in body weight of embryos .

**Keywords:** pregnant women , rats embryos , capoten , weight human newborn , kidney and stomach of embryos rats.

### Introduction

Capoten is an ACE inhibitor. ACE stands for angiotensin altering enzyme. Capoten is used to treat high blood pressure (hypertension), congestive heart failure, kidney problems caused by diabetes, and to improve survival after a heart attack (Castro *et al.*,2019) Beneficial for many patients at risk for heart disease; moderates risk of MI, stroke, diabetic nephropathy , microalbuminuria Good choice in hyperlipidemia patient (Markoulina *et al.*,2020)

Before you take Capoten for the first time, tell your doctor if you: • are pregnant or may become pregnant • are breastfeeding or intend to breastfeed • have any other medical problems, particularly diabetes, systemic lupus erythematosus, scleroderma, neutropenia (low white blood cell count), have had a heart attack, heart failure, ischaemic heart disease or cerebrovascular disease (Imre *et al.*,2018)

DESCRIPTION CAPOTEN: (captopril tablets, USP) is a specific competitive inhibitor of angiotensin I converting enzyme (ACE), the enzyme responsible for the change of angiotensin I to angiotensin II. CAPOTEN is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline [MW 217.29] and has the following structure: Captopril is a white to off-white crystalline powder that may have a slight

sulfurous odor; it is soluble in water (approx. 160 mg/mL), methanol, and ethanol and thinly soluble in chloroform and ethyl acetate. CAPOTEN is available in potencies of 12.5 mg, 25 mg, 50 mg, and 100 mg as scored tablets for oral administration. Inactive ingredients: microcrystalline cellulose, corn starch, lactose, and stearic acid (Geiger *et al.*, 2013 and Mulla *et al.*, 2007)

### **Metabolism and half-life**

Captopril is predominantly eliminated through renal excretion and has an approximate half-life of two hours. However, this half-life may be prolonged in patients suffering from congestive heart failure due to reduced renal clearance. Captopril is also formulated in several fixed-dose combinations with hydrochlorothiazide, such as Capozide and other similar preparations. The toxic or adverse effects commonly related with captopril and other angiotensin-converting enzyme (ACE) inhibitors include dizziness, fatigue, headache, persistent cough, gastrointestinal disturbances, and skin rash. ( Berger *et al.*, 2017 and Oktem *et al.*, 2014).

### **Contraindication of Captopril**

CAPTOPRIL (captopril) is contraindicated in patients with a history of hypersensitivity to the drug and in patients with a history of angioedema related to previous treatment with an Angiotensin Converting Enzyme inhibitor. ( Korbel *et al.*, 2014)

### **Warnings**

**Serious Warning** When used in pregnancy, angiotensin converting enzyme (ACE) inhibitors can cause injury or even death of the developing fetus. When pregnancy is detected, CAPTOPRIL should be discontinued as soon as possible.. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. See Warnings: Fetal Toxicity(Sacerdoti *et al.*, 2020)

### **Drug interactions**

ACE-inhibitors will increase the effect of diuretics. Combination of ACE inhibitor, diuretic and NSAID may precipitate acute renal failure. Potassium supplements or drugs which increase potassium level (eg spironolactone) – risk of hyperkalaemia Antihypertensive medications in combination with captopril will rise risk of hypotension( Iqbal *et al.*, 2016) .

## **Materials and Methods :**

Ten women and eight of newborn obtained from Al-Zahra teaching hospital .Cross section and histological study was conducted on embryos rats .Thirty adult rats were obtained from Kut Technical Institute / Middle Technical University Iraq between December in 2023 and March in 2024. Animals were placed at the animal house, College of science , Wasit University and fed with pellet through experimental periods ,temperature was 25C°.Female was left in a separate cage with one male for the each cage ratio 2:1. Male and female couple were kept together in mating cage for two weeks

The rats were divided into two groups ( one control and one treated groups), and the animals were treated as follow:

1- Treatment group. (n=10) treated daily with capoten /4mg for 50 days (Torries and Tazuma ,2012).The body weight of the embryos detect by electrical balance. At finish of experiment period pregnant rats sampling for anatomical section and embryo sampling kidney ,stomach preserved in 10% formalin buffer solution until groundwork of histopathological section. Tissue was cut at 7-8µm and embedded in paraffin and takes section intestine ,were stained with hematoxylin and Eiosin stain(H&E) for histopathological study(Mandel *et al.*, 2010).

**Statistical Analysis:**

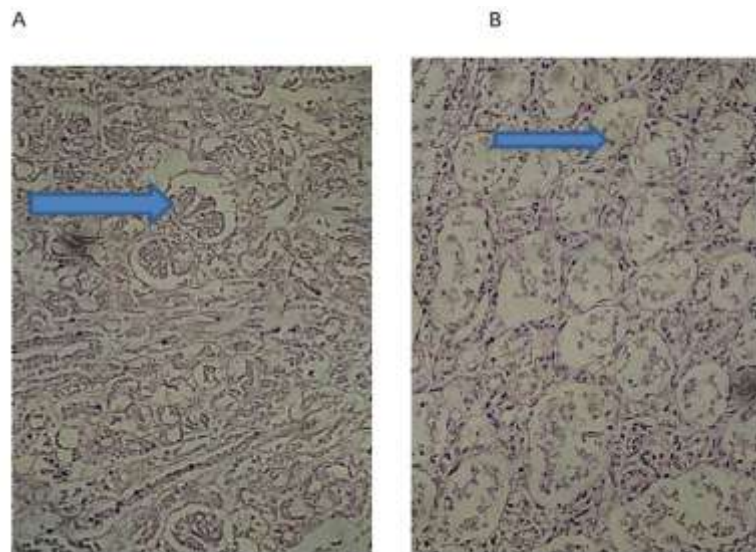
Data were expressed as mean ± standard error of mean and were compared by one way ANOVA followed by LSD. P value more than 0.05 was considered as statistically significant (Torries andTazuma ,2012 ).

**Result**

**Table(1): Effect of capoten on the body weight of the new born**

Time	Control weight Kg	Capoten weight Kg
1 day	2.6+0.097 A	1.52+0.056 B

The value represent Mean(gram) +Standard Error-The different small letters show significant effect while the same small letters show insignificant effect between different groups.



**Figure 1: Histopathological examination of Kidney embryos rats in (fig.1-A) control group normal glomerulus (fig. 1-B) abnormal treated group**

The slides of the embryo Kidney were examined via light microscopy in two stains: hematoxylin and eosin. (H&E).( 10\*0.25)



## Figure 2: cross examination of stomach embryo rat (A) control group. (B) treated group

### Discussion

Table (1) showed a significant decrease of body weight in capton compared with the control of the experimental periods. . pregnant women chronic administration of captopril for four weeks resulted in a reduction in body weight gain and adipose tissue mass, while simultaneously increasing plasma Ang-(1-7) levels. These effects were partially reversed when A-779 was administered. In addition, captopril treatment significantly improved the expression of the Mas receptor and the phosphorylation of hormone-sensitive lipase (p-HSL). However, no significant differences in adipocyte diameter were observed among the sham, captopril, and captopril + A-779 groups. Similar outcomes regarding body weight, Mas receptor expression, and p-HSL levels were also observed in rats treated with Ang-(1-7). Overall, these findings suggest that captopril diminishes body weight gain, potentially through mechanisms involving Ang-(1-7) and motivation of the Mas receptor pathway (Frithz *et al.*, 2010 and Chtterjee *et al.*, 2011).

Chronic oral toxicity studies were conducted in rats . Significant drug-related toxicity included effects on hematopoiesis, renal toxicity (Kovacevic *et al.*, 2003) Captopril caused hyperplasia of the juxtaglomerular apparatus of the kidneys Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function and associated with fetal and neonatal injury including hypotension, anuria, reversible or irreversible renal failure ( Heaton *et al.*, 1999 and Pomeranz *et al.*, 2015)

Cross examination of intestine embryos rats in (fig.1-A) control group normal without hemorrhages (fig. 1- B) treated group with hemorrhages

Chronic oral toxicity studies were conducted in pregnant rats Significant drug-related toxicity included effects on hematopoiesis (Rodecki *et al.*, 2000) toxicity, erosion/ulceration of the stomach Gastric erosions/ulcerations were increased in stomach embryos (Jones, 2003 and Rasanen, 2004).

### Conclusion

The use of Capoten (an ACE inhibitor) during pregnancy leads to a specific clinical condition known as ACE Inhibitor Fetopathy. It influence which on :

1. Renal System (The Primary Target) :The most significant effect is Fetal Renal Dysgenesis. Captopril reduces fetal glomerular filtration rates, leading to: Anuria: The fetus breaks producing urine.
2. Respiratory System :The lack of amniotic fluid results in Pulmonary Hypoplasia. Without the pressure and volume of amniotic fluid to enlarge the developing air sacs, the lungs fail to mature, making spontaneous breathing at birth nearly impossible.
3. Skeletal System: Captopril interferes with the ossification of membrane bones. This often results in Hypocalvaria (incomplete formation of the skull bones), sendoff the brain defenseless to mechanical pressure.
4. Cardiovascular & Growth Effects: Persistent Fetal Hypotension: Indications to ischemia and multi-organ hypoperfusion. Intrauterine Growth Restriction (IUGR): The fetus fails to meet its developmental weight and size milestones.

## References

1. Iqbal .J.; Dufendach ,K.;Wellons ,J.; Kuba, M.and Nickols, H. Gómez-Duarte OG, et al. Lethal neonatal meningoencephalitis caused by multi-drug resistant, highly virulent Escherichia coli. *Infect Dis (Lond)*. 48(6):461-466. (2016).
2. Frithz G., Morlin C. Comparison of captopril (SQ 14,225) with hydrochlorothiazide in the treatment of essential hypertension. *Int. J. Clin. Pharmacol. Ther. Toxicol*. 19:368-371, 2001.
3. Heaton PA, Smales O, Wong W. Congenital nephrotic syndrome responsive to captopril and indometacin. *Archives of disease in childhood*. (1999) Aug 1;81(2):174-5.
4. Pomeranz A, Wolach B, Bernheim J, Korzets Z. Successful treatment of Finnish congenital nephrotic syndrome with captopril and indomethacin. *The Journal of pediatrics*. Effect of cortisone on mucoprotein secretion by gastric antrum of rabbits . pathogenesis of xteroid ulcer. *Surgery*. (2015). 54. 19-27.
5. Jones,R. Intestinalabsorption and gastrointestinal digestion of protein during the normal and cortisone-induced post-closure. *Biochint. Biophys. Acta*. .(2003), 274: 4 12
6. Rasanen, T. Fluctuations in the mitotic frequency of the glandular stomach and intestine under the influence of ACTH, glucocorticoids, stress, and heparin. *Acta Physiol*. (2004). Scand., 58, 201-210
7. Berger-Gryllaki M, Podilsky G, Widmer N, Gloor S, Testa B et al. The development of a stable oral solution of captopril for paediatric patients. *EUR. J. HOSP. PHARM-S P*, 13(3):27-32. (2007)
8. Castro Díez C, Khalil F, Schwender H, Dalinghaus M, Jovanovic I *et al*. Pharmacotherapeutic management of paediatric heart failure and ACE-I use patterns: a European survey. *BMJ Paediatr Open.. Journal of Pharmacy Research*, 12(7): 924-928. (2019).
9. Chatterjee K., Ports T., Brundage B., Hiramatsu B., Parmley B. Immediate and sustained hemodynamic and clinical improvement in chronic heart failure by an oral angiotensin converting enzyme inhibitor. (2011) *Circulation* 61:931-937.
10. Geiger CM, Sorenson B,Whaley PA .Stability of Captopril in SyrSpend SF. *Int J Pharm Compd*, 17(4):336-338. (2013)
11. [Ilke Sipahi MD](#), [Sara M Debanne](#) , [Douglas Y Rowland](#) , [Daniel I Simon](#) , [James C Fang](#) . Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. [The Lancet Oncology](#).(2010). Vo.11 Issue.7, 627-636.
12. Imre S, Vancea S, Muntean DL, Sipos E, Cociş A et al .Stability of some medicinal solutions with captopril. *Rev Med Chir Soc. Med. Nat Iasi*, 112(3):848- 855. (2008)
13. Iqbal .J.; Dufendach ,K.;Wellons ,J.; Kuba, M.and Nickols, H. Gómez-Duarte OG, et al. Lethal neonatal meningoencephalitis caused by multi-drug resistant, highly virulent Escherichia coli. *Infect Dis (Lond)*. 48(6):461-466. (2016).
14. KorbelC,GuY,MengerMD,LaschkeMW.CombinedblockadeofangiotensinII type I receptor and activation of peroxisome proliferator-activated receptor-g by telmisartan effectively inhibits vascularization and growth of murine (2014);29(May (5)):011–24.
15. Kovacevic L, Reid CJ, Rigden SP. Management of congenital nephrotic syndrome. *Pediatric Nephrology*. 2003 May;18(5):426-30.
16. Mandell, L.; Wunderink ,R.and Anzueto A. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*.44 Suppl 2:S27–37. .(2010)

17. Markoulina B, Grégory P, Nicolas W, Stéphane G, Bernard T et al. The development of a stable oral solution of captopril for paediatric patients. *European Journal of Hospital Pharmacy Science*, 13(3):27-32. Vol. 12| Issue 06 |574-586. (2020)
18. Mesut Oktema, Pinar Ozcana, Ozlem Erdemb, Cengiz Karakayaa, Cahit Cenksoya, Haldun Gunera, Onur Karabacaka and Polat Dursunc ,*European Journal of Obstetrics & Gynecology and Reproductive Biology*. (2014). No. (180) :120-125
19. Mulla H, Tofeig M, Bu'Lock F, Samani N, Pandya H .Variations in captopril formulations used to treat children with heart failure: a survey in the United kingdom. *Archives of disease in childhood*, doi:10.1136/adc.2006.109389. (2007)
20. Rodecki T.; Brozowski ,T.; Grylewski ,R. and Gregory, H. Gastric cytoprotection by epidermal growth factor; role of endogenous prostaglandins and DNA synthesis. *Gastroenterology* (2000).81. 438-443
21. Sacerdoti F, De León R, Gentile T, Canellada A. Angiotensin II activates the calcineurin/NFAT signaling pathway and induces cyclooxygenase-2 expression in rat endometrial stromal cells. *PLOS ONE*( 2020) ;7(5):e37750.
22. Sun, D. The effect of corticotropin on gastric acid, pepsin, and mucus secretion in rabbits with fistulas. (1999). *Amer. J. dig. Dis.* 14. 107-112.
23. -Torries,J.andTazuma,S.Principlesand Procedures of Statistics. Biometrical approach, 2nd edition. McGraw-Hill Book Co. New York, USA.33:5-8.(2012).
24. Torries,J.andTazuma,S.Principlesand Procedures of Statistics. Biometrical approach, 2nd edition. McGraw-Hill Book Co. New York, USA.33:5-8.(2012).