Zagazig J. Pharm. Sci., June 1997
Vol.6 , No.1 , pp. 7-11

ISSN 1110-5089

EFFECTS OF NORFLOXACIN (NOROXIN)® AND OFLAXACIN (TARIVID)® ON LIVER AND KIDNEY FUNCTIONS AND SOME OTHER PARAMETERS OF ADULT MALE RATS

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ABSTRACT

The effect of noroxin and tarivid on liver and kideny functions, total lipids, blood glucose and some minerals was studied. After one week treatment tarivid significantly increasesd serum glutamic oxaloacetic transferase (SGOT), total bilirubin, alkaline phosphatase and creatinine but noticeably decreased the blood glucose level. On the contrary , noroxin showed no change. Both drugs significantly increased blood urea, uric acid, iron and phosphorous. After two weeks treatment both drugs significantly increased serum glutamic oxaloacetic transferase (SGOT) serum glutamic pyruvic transferase (SGPT), alkaline phosphatase, total bilirubin, direct bilirubin and blood glucose but total protein and albumin demonstrated no change.

INTRODUCTION

In recent years, several new quinolones have been developed as effective antibacterial agents and widely used to treat different varities of infections. Chemicaly[1], noroxin (norfloxacin) and tarivid (oflaxacin) are quinolone carboxylic acid derivatives ; 1-Ethyl-6-fluoro1-4-dihydro-4-oxo-7 (1-piperazinyl)-3-quinoline. They are used as antibacterial agents for oral administration[2,3] , rapidly absorbed from the gastrointestinal tract (GIT) and maximal plasma concentration have been observed within 1 to 2 hours after oral adminstration. The drugs are 10 - 15% bound to serum protein. Spectrama is widely distributed to most of the body fluids and tissues. About 30% of the given dose are excreted unchanged in the urine and thus producing high urinary concentration.

To our knowledge , litle is published about the toxicity of these drugs on the liver and kidney. Therefore, we decided to undertake the present investigation to uncover the dangerousness of repeated use of these agents among the treated patients .

MATERIALS AND METHODS

Aniamls : Adult male albino rats weighing 170g ± 20 were used in the present study. Animals were kept at constant environmental and nutritional conditions.

Antibiotics and chemicals : these chemicals and drugs were obtained from chemical drug companies in Egypt.

Experimental design:

The animals were divided into five groups each of 10 rats.

1-The first group was used as normal control.

2-The second group was given noroxin at a daily dose of 0.16 mg/kg orally for one week.

3-The third group was given noroxin at a dose of 0.16 mg/kg body weight orally for two weeks.

4-The fourth group was given tarivid at a dose of 0.06 mg/kg body weight orally for one week.

5-The fifth group was given tarivid at dose of 0.06 mg/kg for two weeks. Blood samples were taken and centrifuged. Serum was stored at -20°C and used for used for estimation of the chosen biochemical parameters.

Methods of estimations :

Estimation of **SGOT and SGPT** activities were carried out by using Randox kit (Ireland) according to the method described before [4,5] . **Serum alkaline phosphatase** activity was measured using Bio-Analytical Kits (Florida, USA) according to the method previously described by Roy [6].

Serum total and direct bilirubin levels were estimated according to the method described by Jendrassik [7] using Randox Kit (Ireland) ;while **serum total protein and albumin** were estimated by a colorimetric method of Gornall et al[8] using protein kit BioMerieus (France).

Estimation of **blood urea and uric acid** were done enzymatically according to the method of Patton and Crouch [9] using urea and uric acid kits (BioMerieux , Franc) . **Creatinine** was determined by a colorimetric method. **Total lipids** were determined according to the method described by Zollner and Kirsch [10] using lipid kits (BioMerieux, France). Estimation of **blood glucose** was carried out by a colorimetric method according to the method described by Hultman [11] using glucose kit (BioMerieux France).

Phosphorous was carried out according to the method described by El-Merzabani et al.,[12] using phosphorous kits (Egyptian American Co. for Laboratory Services);while **Iron** level was determined according to the method described by Dreux [13] using iron kits (Egyptian American Co. for Laboratory Services).

RESULTS

1-Effect on serum transaminases and alkaline phosphatase:

Oral administration of tarivid for one week induced a significant increase in SGOT and alkaline phosphatase but noroxin caused no change. Oral administration of both drugs for two weeks showed a significant increase in SGOT, SGPT and alkaline phosphatase (Fig. 1).

2- Effect on total and direct bilirubin:

Oral administration of tarivid for one week induced a significant increase in total bilirubin but direct bilirubin showed no change. Noroxin produced no change. Oral administration of both drug for two weeks induced a significant increase in total bilirubin but direct bilirubin was increased by noroxin only as shown in Fig. (2).

3- Effect on serum total protein and albumin:

The concentration of total protein and albumin showed non significant change after administration of both drugs (Fig. 3).

4- Effect on blood urea, uric acid and creatinine:

Administration of both drugs demonstrated a significant increase in uric acid level after one and two weeks but serum urea level was significantly increased after two weeks of drug administration. With respect to creatinin, tarivid only produced a significant increase in its level but noroxin showed non significant change (Fig. 4).

5- Effect on total lipid and blood glucose:

Oral administration of noroxin for one week induced significant increase in total lipid but tarivid produced no change. Administration of drugs for two weeks produced no significant change. With respect to blood glucose, oral administration of the two drugs for one week showed no change , while the there is significant decrease in blood glucose level after two weeks administration (Fig. 5).

6- Effect phosphorous and iron:

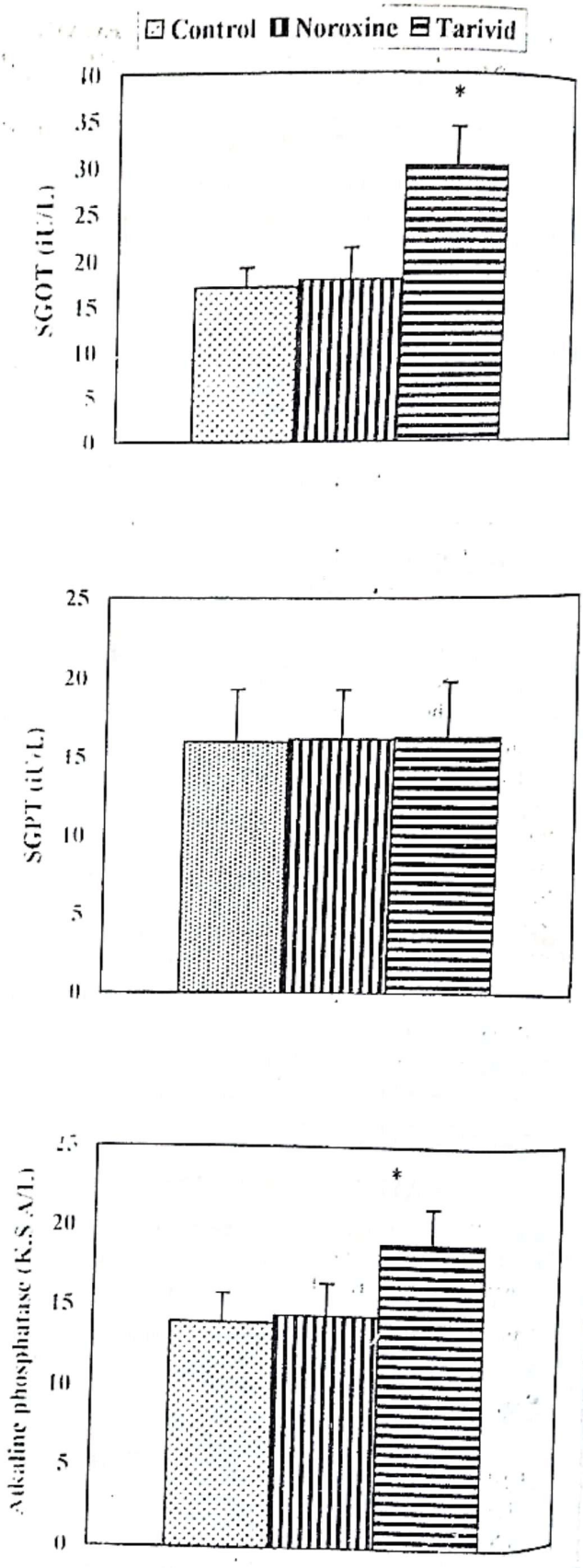
Oral administration of both drugs for one and two weeks induced a significant increase in their level (Fig. 6).

DISCUSSION

Obviously, quinolones are synthetic antibiotics with different potencies that cause inhibition of DNA-gyrase. All the members of this family are potent bactericidal at lower rather than higher concentration.

Results of the present study showed that oral administration of noroxin and tarivid individually in adult male rats increased SGOT which may result from the drug ability to induce marked impairment of ionic transport across the living membranes of the skeletal muscle fibers(14). The increase in SGOT may result from excessive enzymatic leakage from the toxic damage of the renal and hepatic structural consituents which normally serves as rich sources of SGPT(15,16).

The increase in alkaline phosphatase activity observed in this study could be interpreted on account that these drugs cause release of this enzyme by the effect of these drugs on the liver cell membrane.



* Significantly different from control value at $P < 0.01$

Fig. (1) : Effect of noroxine (0.16 mg/kg) and tarivid (0.06 mg/kg) on SGOT, SGPT of adult male rats after drug administration for one week.

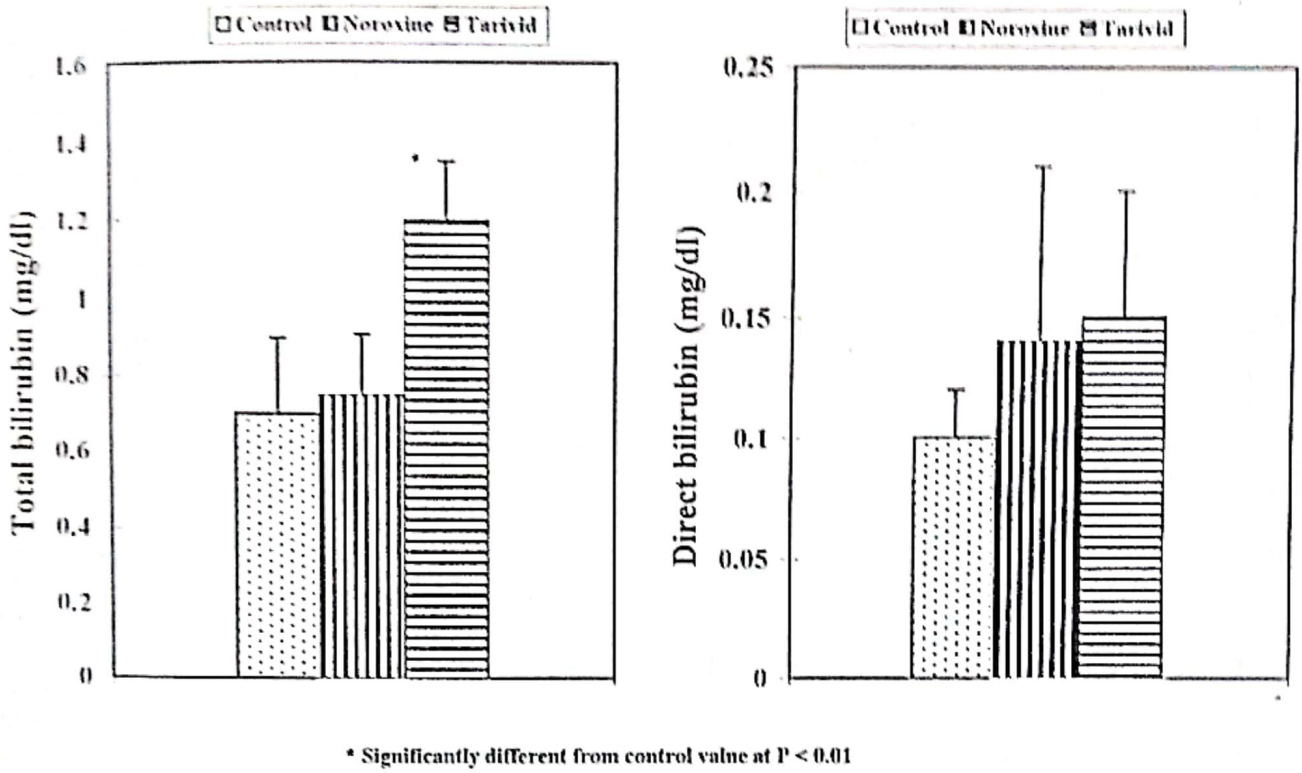


Fig. (2): Effect of noroxine (0.16 mg/kg) and tarivid (0.06 mg/kg) on total bilirubin (mg/dL) and direct bilirubin (mg/dL) of adult male rats after drug administration for one week.

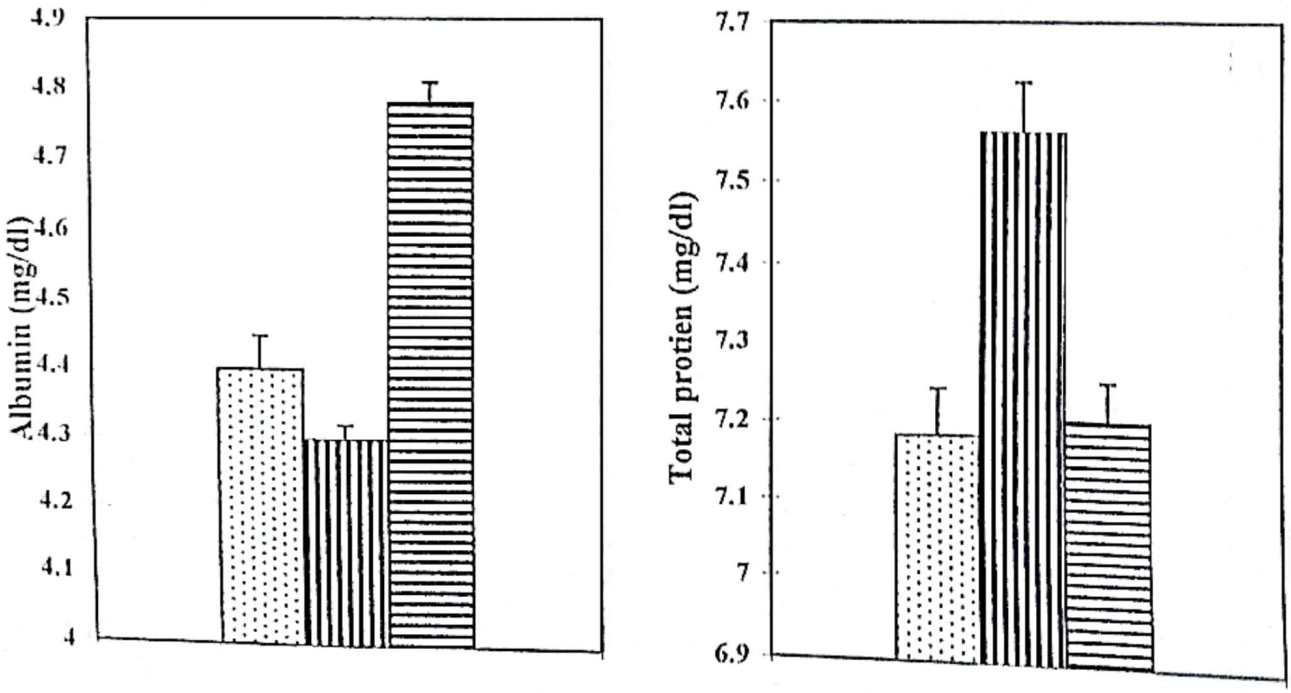


Fig. (3): Effect of noroxine (0.16 mg/kg) and tarivid (0.06 mg/kg) on total protein (mg/dL) and albunin (mg/dL) of adult male rats after drug administration for two weeks.

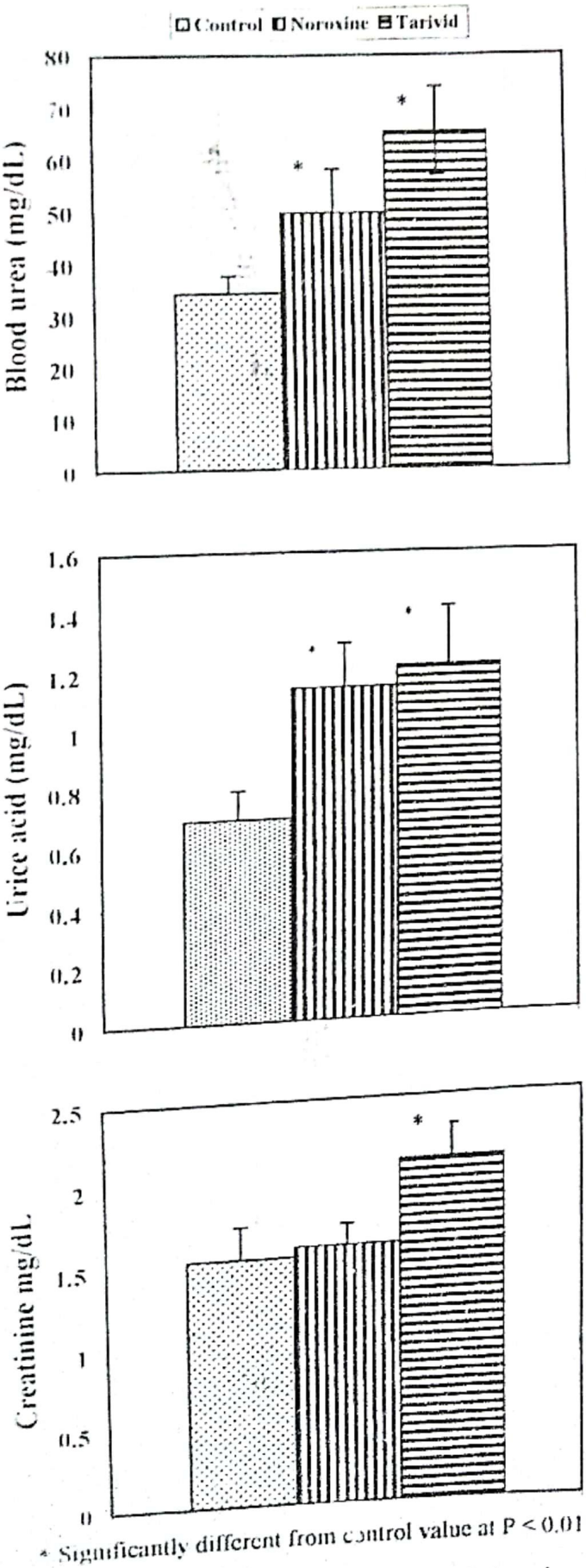


Fig. (4) : Effect of noroxin (0.16 mg/kg) and tarivid (0.06 mg/kg) on blood urea (mg/dL), uric acid (mg/dL) and creatinine mg/dL of adult male rats after drug administration for two weeks.

The elevation of bilirubin may reflect increasing the rate of bilirubin product which exceeds normal excretory capacity. Also it may explained according to that these drugs may complete for binding of bilirubin with (Y - protein) ligand enhancing its excretion[16].

The increase in urea, uric acid and creatinine in our experiments in adult male rats after administration of the drugs could be taken as a good index for impairement renal function. The increasing effect of noroxin in total lipid may be due to its lipid fractions where serum cholesterol, triacylglycerol and phospholipid increase significantly[17].

The decreasing effect of these drugs on blood glucose level may be attributed to the changes in cerebral glucose metabolism which occur as a consequence to the hyperexcitation caused by GABA receptor - blocking agents or antagonists in the central nervous system[18,19]. The effect in iron and phosphorous may be resulted from the drug effect on its excretion. From the data of the present work it could be concluded that noroxin and tarivid induce deterioration of both liver and kidney function in adult male rats.

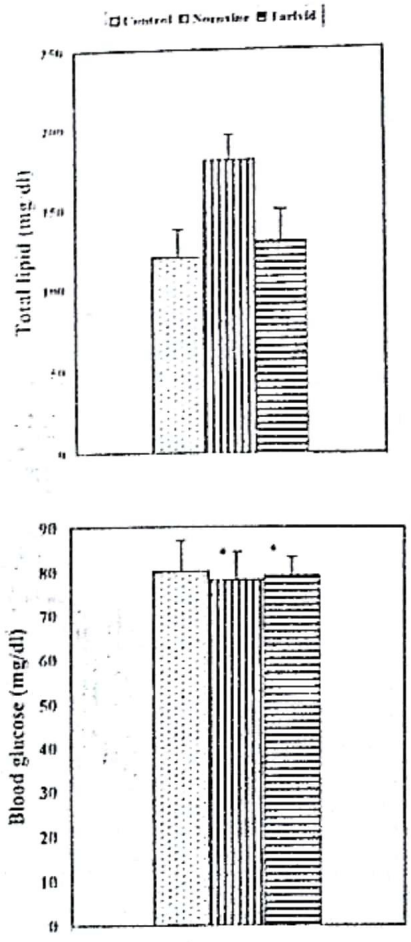


Fig. (5): Effect noroxin (0.16 mg/kg) and tarivid (0.6 mg/kg) on total lipid (mg/dL) and blood glucose (mg/dL) of adult male rats after drug administration for one week.

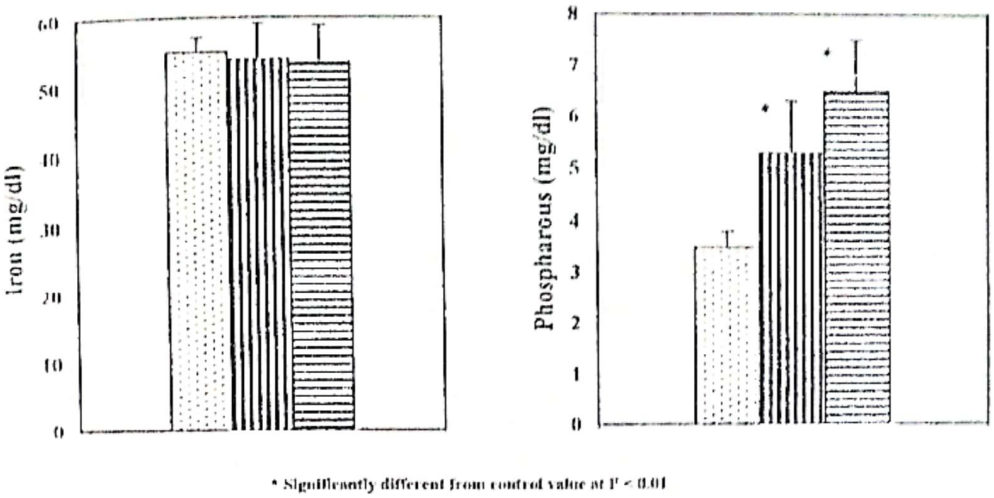


Fig. (6): Effect of noroxin (0.16 mg/kg) and tarivid (0.06 mg/kg) on iron (mg/dL) and phosphorous (mg/dL) of adult male rats after drug administration for one week.

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تأثير كل من نوركسين والتاريفيد على وظائف الكبد والكلى و بعض التغيرات الحيوية الاخرى فى ذكور الجرذان البالغة

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فى هذا البحث تمت دراسة تأثير كل من نوركسين والتاريفيد على وظائف الكبد متمثلة فى قياس نشاط ناقلات الامين فى مصل الدم (جلوتاميك ببروفيك ترانس أميناز - جلوتاميك أوكالو استيك ترانس اميناز) والفوسفاتاز القلوى والبيلوروبين الكى والمباشر وكذلك البروتين الكلى والزلال كما تمت دراسة التأثير على وظائف الكلى متمثلة فى قياس مستوى اليوريا وحامض اليوريك والكرياتنين فى الدم. وكذلك التأثير على الدهون الكلية ونسبة الجلوكوز فى الدم والفوسفوتر والحديد وذلك فى ذكور الجرذان البالغة بجرعة مقدارها ١٦ر٠ مجم / كجم نوركسين وجرعة قدرها ٠٦ر٠ مجم /كجم بالنسبة للتاريفيد لمدة أسبوع واسبوعين بعد تعاطى العقار عن طريق الفم وكان التأثير كما يلى :

أ- تعاطى العقار لمدة أسبوع :

احدث التاريفيد زيادة معنوية فى مستوى ناقلات الامين والبيلوروبين الكلى والفوسفاتاز القلوى كما احدث انخفاضاً معنوياً فى نسبة الجلوكوز بينما النوركسين لم يحدث اى تغير بينما احدث كل من العقارين زيادة معنوية فى نسبة كل من اليوريا وحامض اليوريك والحديد والفوسفور.

ب - تعاطى العقار لمدة اسبوعين :

احدث كل من النوركسين والتاريفيد زيادة معنوية فى نسبة كل من ناقلات الامين والفوسفاتاز القلوى والبيلوروبين الكلى والمباشر وكذلك الجلوكوز أما البروتين الكى والزلال لم يسجلوا اى تغير . من خلال نتائج البحث يمكن استنتاج أن كلا من النوركسين والتاريفيد يحدث اضطراباً فى وظائف الكبد والكلى فى ذكور الجرذان البالغة.

Received : Feb. 24, 1997
Accepted : May 26, 1997