

## **EFFECT OF MARBOFLOXACINE AND CEFTIOFUR SODIUM ON HEPATORENAL FUNCTION AND IMMUNOLOGICAL STATUS IN FATTENING CALVES**

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### **SUMMARY**

The objective of this study is designed to clarify the effect of marbofloxacin and ceftiofur sodium on the hepatorenal, cellular and humoral immune responses in fattening cattle calves. Twenty five baldy fattening cattle calves were divided into five equal groups (5 each). 1<sup>st</sup> group served as control, 2<sup>nd</sup> and 3<sup>rd</sup> groups were injected with therapeutic dose (5mg/kg bwt) and double therapeutic dose (10 mg/kg bwt) of marbofloxacin for three consecutive days respectively, 4<sup>th</sup> and 5<sup>th</sup> groups were injected with therapeutic dose (10 mg/kg bwt) and double therapeutic dose (20 mg/kg bwt) of Ceftiofur sodium for three consecutive days respectively. At 3<sup>rd</sup> day 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> week post injection, blood samples were collected in two portions, 1<sup>st</sup> one was collected on heparinized tube for determination of total and differential leucocytic count, phagocytic and killing %. 2<sup>nd</sup>

one was centrifuged at 3000 r.p.m. for 15 min. to separate clear serum, for determination of humoral immune response and some biochemical parameters.

Both marbofloxacin and Ceftiofur sodium in both therapeutic and double therapeutic doses elucidated significant reduction of phagocytosis and bacterial killing efficiency of blood polymorphonuclear leucocytes at the 1<sup>st</sup> and 2<sup>nd</sup> week post injection. Also both drugs evoked a significant increase in total leucocytic count and neutrophil and decrease in lymphocytes at the 3<sup>rd</sup> day 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> week post injection.

Marbofloxacin in therapeutic and double therapeutic doses in fattening calves evoked a significant decline of total protein, albumin, gamma globulin, total globulin and A/G ratio, meanwhile alpha and beta globulin levels demonstrated a

Fluoroquinolones are a class of synthetic antimicrobial agents. Structurally, all fluoro-quinolones contain a fluorine molecule at the 6-position of the basic quinolone nucleus. It is a series of synthetic antimicrobial agents that are used in the treatment of a variety of bacterial infections. Marbofloxacin (3rd generation) is a synthetic bactericidal antimicrobial fluoroquinolone carboxylic acid derivatives with a broad spectrum activity against both G-ve, and G+ve bacteria and Mycoplasma spp Spreng et al. (1995), recently introduced for use in veterinary medicine as they have a wide spectrum of antimicrobial activity, a large volume of distribution and are effective at very low concentrations Eytell (1997).

Cephalosporins are a group of antibiotics derived from mould of cephalo-sporium species and are based on 7-aminocephalosporic acid which cross-ponds to 6-penicillanic acid in penicillins. Ceftriaxone sodium is a third generation of cephalosporin antibiotics. It is a broad spectrum antibacterial activity against G+ve and G-ve bacteria and remain safety of the first and second generation products Brander, et al. (1982). It is a broad spectrum beta-lactamase resistant cephalosporin. It is bactericidal destroying bacteria by preventing the synthesis of the cell wall Yancey et al. (1987). This antibacterial activity due to ability of beta-lactamase ring to bind bacterial enzymes transpeptidase which is important for proper cell wall synthesis (Thomson, et al. 1984).

Immunosuppression properties of some antibiotics are effective in inhibition of both cellular and humoral immune responses to a variety of vaccines Shalaby (1989). Several antibiotics suppress the immune response by their ability to interfere with protein or immunoglobulin synthesis Richard and Merle (1984).

### INTRODUCTION

It was concluded that marbofloxacin and ceftriaxone sodium in both therapeutic and double therapeutic dose may provoke a remark hepatorenal change and immunosuppressive effect in calves.

significant increased at the 3rd day, 1st and 2nd week post injection. Ceftriaxone sodium in a therapeutic or double therapeutic dose resulted in a significant decrease in total protein, gamma globulin, total globulin levels and insignificantly decrease in albumin but alpha and beta globulin levels insignificantly increased as compared with control calves at the 3rd day, 1st, 2nd week post injection of ceftriaxone sodium.

The obtained results showed that marbofloxacin and ceftriaxone sodium in therapeutic and double therapeutic doses elicited significant elevation in serum AST, ALT, ALP urea and creatinine at the 3rd day, 1st, 2nd week post injection.

**MATERIALS AND METHODS**

The present work was planned to investigate the capability of marbofloxacin and ceftriaxone sodium in inducing hepatorenal and change immunosuppressive effect on fattening cattle calves.

**1-Drug :**

1-Marbofloxacin:(Marbocyl)<sup>®</sup> injectable sterile solution from Vétocin, Lure, (France) available as 50ml vial each one milliliter contain 100mg marbofloxacin.

2-Ceftriaxone sodium(excel)<sup>®</sup> a vial containing 1-4 gm.Obtained from Upjohn Co. kalamazoo, U.S.A.

**2-Animals :**

Twenty five baldy fattening cattle calves aged 8-12 months from a private farm El-Ebrahima, Sharkia province were divided into five equal groups (5 each).The 1<sup>st</sup> group served as control,2<sup>nd</sup> and 3<sup>rd</sup> groups were injected with therapeutic dose (5mg/kg bw) and double therapeutic dose (10 mg/kg b.wt.) dose of marbofloxacin (LM) for three consecutive days respectively, 4<sup>th</sup> and 5<sup>th</sup> groups were injected with therapeutic dose (10 mg/kg b.wt ) and double therapeutic dose (20 mg/kg b.wt.)of Ceftriaxone sodium (LM) for three consecutive days respectively.

**3 - Sampling :**

Jugular vein puncture was used to collect two blood samples at the 3<sup>rd</sup> day,1<sup>st</sup>, 2<sup>nd</sup> and 4<sup>th</sup>

**1- Cellular immune response**

**A-Determination of phagocytic and killing percentage.**

Heparinized blood samples were used to obtain polymorphonuclear cells according to Rouse et al. (1980). Mixtures of Staphylococcus aureus and polymorphonuclear cell were incubated at 37°C for 2 hours with regular stirring and then the mixtures were centrifugated for 5 min at 4 °C. The supernatant were used to estimate the percentage of bacteria phagocytosed.The mixture of bacteria and polymorphonuclear cell were treated with one cycle of freezing and thawing and the percentage of bacteria killed was estimated according to the formula described by Woldewit and Rowan (1990).

**B-Total and differential leucocytic count**

count were performed on collected heparinized blood samples using the method described by Jain (1986).

immune response receptively.

serum, for determination of cellular and humoral

left for about 2hour inroom temperature then centrifuged at 3000rpm for 15 min to separate clear

injection with therapeutic or double therapeutic dose of marbofloxacin or ceftriaxone sodium. Our results were supported by the results obtained by Zahra and Abd-El-Azem (2003) who noticed that the therapeutic dose of marbofloxacin results in depressed phagocytic and natural killer cell activities. Also, Ahmad, (1999) Confirmed that decrease in phagocytic activity and killing percent in calves after parental administration with therapeutic dose of ceftriaxone sodium. These results may be attributed to that the prolonged exposure of leukocyte membrane to the marbofloxacin of leukocyte membrane for the possible alteration in phagocytosis. Pullin, et al. (1991). Pions and Hawley (1972) mentioned that marbofloxacin might depress the synthesis of cytochrome oxidase inhibiting metabolic process of phagocytic cells.

It is clear evident from table (1&2) revealed that the injection of fattening calves with therapeutic or double therapeutic doses of marbofloxacin or ceftriaxone sodium resulted a significant increase in total leucocytic count, neutrophils, eosinophils and decrease in lymphocyte at the 3rd day, 1st and 2nd week post injection. Our results were in complete harmony with those reported by Zahra and Abd-El-Azem (2003) stated that marbofloxacin induce significant increase in total white blood cell count, neutrophils and eosinophils. Jayakumar, et al. (2002) reported that, Ciprofloxacin (10 mg/bw.) induce significant increase in total leukocytes count. Also Helal and Abdel Fattah (2003) reported that enrofloxacin induced significant decrease

**2-Humoral immune response**  
**Determination of total serum protein and protein fractions :**  
 Total protein was estimated according to Doumas, et al (1981), quantitative estimation of serum protein fractions were performed using cellulose acetate electrophoresis test according to Henry et al. (1974).

**3- Biochemical examination :-**

Aspartate aminotransferase (AST), alanine aminotransferase (ALT) were estimated according to Reitman and Frankel (1957), alkaline phosphatase according to (John 1982). Serum urea was estimated according to Fawcett and Scott (1960) and serum creatinine (Husdan and Rapoport 1968).

The obtained data was statistically analyzed (T-test) according to Petrie and Watson (1999).

**RESULTS AND DISCUSSION**

In veterinary practice antibiotics are involved in the treatment of bacterial infection, many of these antibiotics are capable of depressing the immune system even at therapeutic levels Shalaby (1989).

Statistical analysis of the obtained data showed that there was a highly significant decrease in the phagocytic activity and killing percent than in control calves at the 3rd day, 1st and 2nd week post



in lymphocytes percentage in sheep. Similar effects on the nuclear DNA of lymphocytes by several quinolones had been reported by De Simone et al. (1986) who revealed that, all studied quinolones induced inhibition of DNA synthesis of human lymphocytes. Our results are in accordance with Ahmad, (1999) who found ceftifure sodium induce significant increase in total leucocytic count and neutrophils in chickens after 3<sup>rd</sup> day, 1<sup>st</sup> and 2<sup>nd</sup> week post injection. In same line Bogert and Kroon (1982) recorded that the ceftifure sodium could be able to penetrate lymphocytes and thereby inhibit the protein and DNA synthesis and eventually suppress the cellular function.

Our results revealed that calves injected with therapeutic dose of marbofloxacin or ceftifure sodium exerts a significant decrease in serum total proteins, and albumin at 3<sup>rd</sup> day, 1<sup>st</sup> and 2<sup>nd</sup> week post injection if compared with non injected control group and these results parallel with those obtained by Zahra and Abd-El-Azem (2003) Who found that significant decrease in the level of serum total proteins and albumin in calves after administration of marbofloxacin. These results might be attributed to generalized inhibition of protein synthesis and B-cells activity in mammalian cells by marbofloxacin, Stroev (1986). Significant hypalbuminemia produced by marbofloxacin might be related to liver dysfunction, as liver a source for albumin biosynthesis Stroev (1986). Furthermore the obtained data coincide with re-

sults of Abd-Latif and Gamal El-Din (1998)). Who found that treatment healthy chickens with ceftiofur sodium improved adverse effects represented by significant decrease in total protein, significant decrease value of globuline and insignificant decrease serum albumine levels. Emam and Abd El Azem (2001) mentioned that Healthy buffalo-calve given ceftiofur sodium showed significant decrease in total proteins, albumine and globuline.

Electrophoretic separation of serum proteins in this work revealed a decrease in gamma globulin and total globulin levels in calves at 3<sup>rd</sup> day, 1<sup>st</sup> and 2<sup>nd</sup> week post injection with therapeutic dose of marbofloxacin or ceftifure sodium. This results are in agreement with those of Zahra and Abd-El-Azem (2003) who reported a significant decrease in gamma globulin and total globulin levels after marbofloxacin injected in calves. The reduction of parameters serum globulin might be attribute to reconstruction, activation and hyperplasia of lymphoreticular cells at the beginning of immunogenesis as mentioned by (Danielova and Humbartsumian 1976), Helal and Abdel Fatah (2003) reported that enrofloxacin induced significant decrease in gamma globulins in sheep. In keeping with this line, danofloxacin had immunosuppressive effect on the sheep (Zaghawa and Khalil, 1997). Our results was previously recorded by Ahmad, (1999) in chicken.

Measurement of serum transaminases (AST and

ALT) activities are a standard tests for hepatocellular damage. It is well known that the enzymes are intracellular, being located in the mitochondria. The cytoplasm or both, consequently, circulating levels increase following liver cell damage (Doxey 1971).

Concerning the effect on liver function parameters, the obtained results showed that marbofloxacin in therapeutic and double therapeutic doses elicited significant elevation in serum AST, ALT and ALP activities of normal cattle-calves. These findings might be attributed to alteration of membrane permeability or damage of the hepatic cells by direct effect of the drug resulting in escape of these enzymes to the plasma (Coles 1986 and Hanafy 1993). The present findings are supported by the results previously recorded by Gellert (1981) and Hanafy (1993) who noted that norfloxacin at therapeutic dose resulted in elevated liver enzymes. The rise in serum alkaline phosphatase activity is concomitantly recorded with liver damage leading to escape of this enzyme into serum in abnormal high concentration (Joan and Pannall 1981).

There were no significant difference in the liver enzymes (AST, ALT and Alkaline phosphatase) between the normal calves given therapeutic or double therapeutic doses of ceftriaxone sodium and the normal ones that were given no medication which agree with Abd-Latif and Gamal El-Din (1998). Who found that the normal chickens given (1998).

en ceftriaxone sodium showed no significant difference in the liver enzymes. Same results were reported by Emam and Abd El Azem (2001) mentioned that Healthy buffalo-calves given ceftriaxone sodium showed non significant effect on liver enzymes (AST, ALT and Alkaline phosphatase). Nouguchi, et al. (1984) found also that sulphazon at a doses of 1200 mg/kg for rats produced slight increase in hepatic weight, but no effect on SGOT or SGPT. A similar result was recorded in rabbits by Hassan (1996) who found that cefoperazone in therapeutic or double therapeutic doses (140 or 280 mg/kg h.wt) revealed non significant effect in the level of ALP in rabbit. Our results were in complete harmony with those reported by Mawry, (2000).

The results of this study indicated that urea and creatinine levels were significantly elevated in both healthy calves treated with marbofloxacin in both therapeutic or double therapeutic dose of ceftriaxone sodium. These result agree with reported by Abd-Latif and Gamal El-Din (1998), where they mentioned that therapeutic dose of ceftriaxone sodium induce non significance change in urea and creatinine in chicken. Same results were reported by Emam and Abd El Azem (2001) in calves given therapeutic dose of ceftriaxone sodium. Treatment with norfloxacin (10mg/kg B.W.) for 5 days resulted in an increase in the levels of creatinine and urea (Eisa (1998). Our findings coordinated with the finding of Roushdy, (2007) who found that pefloxacin resulted in elevated urea and creatinine.

**Table(1)Effect of therapeutic and double therapeutic dose of Marbofloxacin and Ceftifur sodium on phagocytosis % and killing % of treated calves compared with control calves (n=5).**

Parameter	Contr ol	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
therape	Phagocytosis %	86.67± 2.80	78.8± 1.08*	76.33± 1.05**	75.29± 1.98*	85.25± 2.97	76.48± 1.01**	77.07± 1.11**	80.97± 0.62*	83.3± 1.43
	Killing %	84.50± 1.11	77.9± 0.92**	79.83± 0.87**	81.60± 0.77*	83.83± 1.86	75.17± 2.31**	78.6± 1.61*	80.6± 1.21*	82.65± 1.65
Doubl	Phagocytosis %	86.67± 1.80	77.09± 1.23**	76.13± 1.15**	78.03± 1.92*	83.15± 1.38	75.14± 1.18**	78.20± 1.11**	79.52± 1.36*	83.20± 1.94
	Killing %	84.50± 1.71	74.03± 1.84**	77.41± 1.39**	79.37± 0.91*	84.25± 1.91	76.52± 1.12**	77.21± 1.01**	79.51± 0.89*	83.83± 1.73

\* P<0.05

\*\* P< 0.01

**Table(2)Effect of therapeutic dose of Marbofloxacin and Ceftifur sodium on total and differential leucocytic count of treated calves compared with control calves (n=5).**

Parameter	Contr ol	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
Total leukocytic 103/ul	9.5± 0.96	12.5± 0.33*	11.80± 0.18*	11.62 ± 0.17*	10.7± 0.62	13.5± 0.44**	12.2± 0.48*	10.5± 0.13	9.89± 0.42	
Differential count (103/ul)	Neutrophil %	26.14± 0.70	28.5± 0.21**	27.80± 0.16*	27.63± 0.13*	26.67± 0.37	29.67± 0.32*	29.09± 0.66*	28.5± 0.34*	27.12± 0.93
	Esinophil %	5.17± 0.69	7.67± 0.41*	7.43± 0.27*	7.34± 0.76*	5.13± 0.31	8.13± 0.51**	8.00± 0.22**	7.33± 0.33*	6.01± 0.96
	Lymphocyt e%	64.5± 1.18	61.3± 0.21*	59.2± 0.12**	61.17± 0.31*	62.83± 0.65	59.87± 1.22*	60.6± 0.33*	61.1± 0.14*	62.95± 0.51
	Monocyte %	4.16± 0.61	2.53± 0.26*	2.17± 0.48*	3.86± 0.43	4.67± 0.33	1.63± 0.43**	1.74± 0.61*	3.07± 0.17*	3.91± 0.29

\* P<0.05

\*\* P< 0.01

**Table(3)Effect of double therapeutic dose of Marbofloxacin and Ceftifur sodium on total and differential leucocytic count of treated calves compared with control calves (n=5).**

Parameter	Cont rol	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd day	1st week	2nd week	3rd week	
Total leukocytic 103/ul	9.5± 1.26	14.02± 0.25**	13.95± 0.43**	13.48± 0.41**	11.06± 0.95	14.38± 0.22**	13.12± 0.31*	12.28± 0.23*	12.07± 0.75	
Differential count (103/ul)	Neutrophil %	26.14± 0.78	31.81± 0.42**	30.94± 0.21**	29.12± 0.43*	28.09± 0.84	31.09± 0.36**	30.13± 0.31**	29.13± 0.22*	28.66± 0.89
	Esinophil %	5.17± 0.17	6.98± 1.06	5.97± 1.23	5.48± 1.13	5.31± 0.97	6.71± 1.21	5.62± 1.41	5.45± 1.09	5.01± 1.48
	Lymphocyt e%	64.5± 1.48	58.29± 0.14**	59.14± 0.22**	61.21± 0.48*	62.46± 0.83	59.60± 0.22**	60.04± 0.28*	61.06± 0.13*	62.10± 0.52
	Monocyte %	4.16± 0.31	2.92± 0.12*	3.95± 0.33	4.19± 0.13	4.14± 0.19	2.60± 0.23*	4.21± 0.13	4.36± 0.14	4.23± 0.19

\* P<0.05

\*\* P< 0.01

**Table(4)Effect of therapeutic dose of Marbofloxacin and Ceftifur sodium on serum total protein and protein fractions of treated fattening calves compared with control calves (n=5).**

Parameter	Control	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
T. protein (gm/dl)	7.18± 0.43	5.44± 0.43*	5.12± 0.35*	5.15± 0.48*	6.10± 0.46	4.76± 0.53**	5.50± 0.43*	5.30± 0.90*	6.30± 0.36	
Albumin (gm/dl)	2.40± 0.33	1.48± 0.25*	1.68± 0.13**	1.85± 0.20*	2.17± 0.30	1.12± 0.12*	1.75± 0.19	1.83± 0.26	2.05± 0.18	
Globulin (gm/dl)	Alpha	1.19± 0.08	1.49± 0.10*	1.34± 0.18	1.31± 0.09	1.29± 0.07	1.52± 0.06	1.38± 0.21	1.29± 0.19	1.16± 0.14
	Beta	1.22± 0.09	1.57± 0.09*	1.40± 0.02	1.37± 0.04	1.27± 0.08	1.40± 0.16	1.35± 0.18	1.30± 0.07	1.28± 0.09
	Gamma	2.37± 0.31	0.90± 0.09**	0.99± 0.07**	1.17± 0.08**	1.97± 0.17	0.72± 0.16**	1.02± 0.11**	1.28± 0.07*	1.81± 0.17
	Total	4.78± 0.17	3.96± 0.07*	3.44± 0.14*	3.30± 0.12*	3.93± 0.32	3.64± 0.09*	3.75± 0.08*	3.47± 0.05*	4.25± 0.24
A/G Ratio	0.50± 0.07	0.35± 0.06	0.40± 0.05	0.56± 0.04	0.45± 0.05	0.31± 0.03	0.47± 0.05	0.47± 0.11	0.48± 0.05	

\* P<0.05

\*\* P<0.01

**Table (5) Effect of double therapeutic dose of Marbofloxacin and Ceftifur sodium on serum total protein and protein fractions of treated calves compared with control calves (n=5).**

Parameter	Control	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
T. protein (gm/dl)	7.18± 0.43	5.46± 0.39*	6.09± 0.35*	6.33± 0.38*	6.56± 0.53	4.94± 0.35**	5.58± 0.43*	5.53± 0.50*	6.11± 0.81	
Albumin (gm/dl)	2.40± 0.33	1.40± 0.25*	1.58± 0.13*	1.85± 0.17*	1.97± 0.20	1.38± 0.47	1.35± 0.39	1.63± 0.247	2.22± 0.38	
Globulin (gm/dl)	Alpha	1.19± 0.08	1.46± 0.09*	1.37± 0.02*	1.29± 0.13	1.20± 0.09	1.31± 0.12	1.27± 0.14	1.25± 0.12	1.30± 0.21
	Beta	1.22± 0.09	1.63± 0.08*	1.54± 0.04*	1.47± 0.06*	1.31± 0.06	1.53± 0.17	1.32± 0.13	1.33± 0.11	1.23± 0.06
	Gamma	2.37± 0.31	0.97± 0.12*	1.60± 0.05*	1.72± 0.09*	2.08± 0.07	0.72± 0.05**	1.53± 0.04*	1.32± 0.19	1.36± 0.37
	Total	4.78± 0.17	4.06± 0.13*	4.51± 0.07*	4.48± 0.03**	4.59± 0.12	3.56± 0.09*	4.23± 0.04*	3.90± 0.10*	3.89± 0.4
A/G Ratio	0.50± 0.07	0.34± 0.04	0.35± 0.05	0.41± 0.04	0.43± 0.05	0.39± 0.03	0.43± 0.05	0.42± 0.11	0.57± 0.05	

\* P<0.05

\*\* P<0.01

**Table(6)Effect of therapeutic dose of Marbofloxacin and Ceftifur sodium on liver enzymes ,urea and creatinine of treated calves compared with controls (n=6).**

Parameter	Control	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
Liver enzymes	AST U/L	32.18 ± 1.002	39.52± 1.84**	36.11 ± 1.42*	34.31± 1.43	33.32± 1.74	33.40± 1.90	33.08 ± 1.51	32.47± 0.92	32.25± 1.02
	ALT U/L	11.42 ± 1.08	25.40± 2.84**	19.21 ± 1.3**	15.19± 1.63	12.21± 1.34	12.40± 1.90	12.08 ± 1.51	11.87± 0.92	11.58± 1.02
	AIK.Ph. I.U/ml	12.92 ± 0.77	19.31± 1.34**	14.97 ± 0.84*	13.43± 1.99	11.53± 1.23	14.70± 1.65	14.21 ± 1.52	13.47± 1.07	12.18± 1.37
Kidney function	Urea mg/dl	37.25± 1.32	43.57 ± 1.33**	42.18± 0.9*	38.14± 3.81	36.22± 1.78	39.92± 1.94	39.24± 1.78	37.60± 1.90	37.42± 1.61
	Creatini mg/dl	1.13± 0.22	1.93± 0.11*	1.86± 0.10*	1.33± 0.11	1.34± 0.11	1.23± 0.32	1.29± 0.10	1.21± 0.12	1.19± 0.21

\* P<0.05

\*\* P<0.01



Table (7) Effect of double therapeutic dose of Marbofloxacin and Ceftifur sodium on liver enzymes ,urea and creatinine of treated calves compared with controls (n=6).

Parameter	Control	Marbofloxacin				Ceftifur sodium				
		3rd days	1st week	2nd week	3rd week	3rd days	1st week	2nd week	3rd week	
Liver enzymes	AST (U/L)	32.18 ± 1.002	43.21± 2.63**	39.17 ± 1.5**	35.31± 1.87	33.34± 1.49	35.40± 1.90	34.08 ± 1.51	33.47± 0.92	32.18± 1.002
	ALT (U/L)	11.42 ± 1.08	27.39± 3.35**	25.83 ± 3.89*	21.59± 2.74*	17.48± 2.94	13.42± 1.40	12.26± 1.25	13.26± 1.32	12.30± 1.13
	Alk.Ph. (I.U/ml)	12.92 ± 0.77	20.21± 1.68**	16.24 ± 1.73*	14.09± 1.39	12.31± 1.84	13.29± 1.52	13.24± 1.751	13.49± 2.73	12.30± 1.32
Kidney function	Urea mg/dl	37.25± 1.32	44.67± 2.42*	41.18± 1.08*	38.13± 2.94	37.54± 1.94	39.92± 2.61	38.24± 3.78	37.60± 2.90	36.92± 3.61
	creatinin mg/dl	1.13± 0.22	1.98± 0.21*	1.76± 0.110*	1.59± 0.15	1.56± 0.27	1.23± 0.53	1.26± 0.15	1.24± 0.22	1.10± 0.12

\*\* P<0.05

\* P< 0.01

It was concluded that marbofloxacin and ceftiofur sodium in both therapeutic and double therapeutic dose provoked a remarkable immunosuppressive effect in calves.

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