

EFFECT OF PIROXICAM AND PIRPROFEN COMPOUNDS ON SERUM BIOCHEMICAL CONTENTS

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The effect of the anti-inflammatory drugs i.e. piroxicam and pirprofen compounds on serum biochemical contents was studied. Besides, an attempt was carried out to minimize their harmful side effects by using methyl androsthenolone as an anabolic steroid compound.

The obtained results indicated that glucose level, total protein, albumin, globulin and albumin to globulin ratios were not affected by the above mentioned anti-inflammatory drugs. Also, the obtained data illustrated that piroxicam (1.8 and 5.4 mg/kg) induced marked elevation after four weeks of treatment in serum bilirubin i.e. 71.25 and 82.5% over control values, respectively. On the other hand, the low dose pirprofen (8 mg/kg) did not cause any change in serum bilirubin, however, the high dose level of 24 mg/kg induced a significant increment i.e. 61.25% from the control values after eight weeks of treatment. This effect was abolished by the anabolic drug treatment.

Serum transaminase (GOT and GPT) activity was not pathologically affected by the anti-inflammatory drugs. Both the above mentioned drugs induced marked increment in serum alkaline phosphatase activity. The effect was pronounced in case of pirprofen (82.89%) than piroxicam. The anabolic compound was able to antagonize the effect of piroxicam than that of pirprofen. The increase of serum alkaline phosphatase along with the increment of serum bilirubin is an indicator of drug induced cholestatic jaundice.

The renal excretory function was not affected by the two anti-inflammatory drugs, since serum creatinine and urea were not elevated. However, serum urea was decreased to 60.46% in response to pirprofen. The effect was related to slight depression in liver function and was not corrected by the anabolic agent.

The estimation of serum prostaglandins confirmed that the anabolic compound may enhance the medical effects of the piroxicam and pirprofen drugs or at least shall not antagonize them. Also, the obtained results of determination of triglycerides showed that piroxicam (5.4 mg/kg) + anabolic compound (1.8 mg/kg), piroxicam (1.8 mg / kg), and anabolic compound alone caused a significant decrease in serum triglycerides i.e. 75.71, 73.52, and 64.2% below control values, respectively. However, pirprofen alone or with the anabolic compound showed no significant change in serum triglycerides.

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ABSTRACT

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The effect of the anti-inflammatory drugs i.e. piroxicam and pirprofen compounds on serum biochemical contents was studied . Besides , an attempt was carried out to minimize their harmful side effects by using methyl androsthenolone as an anabolic steroid compound .

The obtained results indicated that glucose level , total protein , albumin , globulin and albumin to globulin ratios were not affected by the above-mentioned anti-inflammatory drugs . Also , the obtained data illustrated that piroxicam (1.8 and 5.4 mg/kg) induced marked elevation after four weeks of treatment in serum bilirubin of rats i.e. 71.25 and 82.5 % over control values , respectively . On the other hand , the low dose of pirprofen (8mg/kg) did not cause any change in serum bilirubin . However , the high dose level of 24 mg / kg induced a significant increment i.e. 61.25 % from the control values after eight weeks of treatment . This effect was abolished by the anabolic drug treatment .

Serum transaminase (GOT and GPT) activity was not pathologically affected by the anti-inflammatory drugs . Both the above-mentioned drugs induced increment in serum alkaline phosphatase activity . The effect was pronounced in case of pirprofen (82.89 %) than piroxicam . The anabolic compound was able to antagonize the effect of piroxicam than that of pirprofen . The increase of serum alkaline phosphatase along with the increment of serum bilirubin is an indicator of drug induced cholestatic jaundice .

The renal excretory function was not affected by the two anti-inflammatory , since serum creatinine and urea were not elevated . However , serum urea level decreased to 60.46 % in response to pirprofen . The effect was related to slight depression in liver function and was not corrected by the anabolic agent .

The estimation of serum prostaglandin confirmed that the anabolic compound may enhance the medical effects of the piroxicam and pirprofen drugs or at least shall not antagonize them . Also , the obtained results of determination of triglycerides showed that piroxicam (5.4mg / kg) + anabolic compound (1.8 mg / kg) , piroxicam (1.8 mg / kg) and anabolic compound alone caused a significant decrease in serum triglycerides i.e. 75.71 , 73.52 and 64.2 % below control values , respectively . However , pirprofen alone or with the anabolic compound showed no significant change in serum triglycerides .

INTRODUCTION

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Anti-inflammatory drugs are one of the oldest medication used for pain

relief , treatment of rheumatic diseases and inflammatory syndromes (Flower et al., 1985) .

Alvart (1983) ; and Kummer and Nekora (1984) mentioned that piroxicam and piroprofen are anti-inflammatory drugs in common clinical use . Also , these compounds showed a surprising results in the treatment of rheumatic diseases and inflammatory syndromes .

Piroxicam [4 - hydroxy - 2 - methyl - N - (2- pyridyl) 2 - H - 1 , 2 , - benzothiazine - 1 ,1 , dioxide] is one of representative prototypes of the oxicam series of compounds distinguished from other non steroidal analgesic anti-inflammatory drugs " NSAIDS " by the possession of a novel structural entity conferring fairly high therapeutic efficacy (Lambardino et al., 1971; Lombardino and Wiseman , 1982 ; Zinnes et al., 1982) . Maier (1984) mentioned that piroprofen is a potent antirheumatic agent , combining excellent analgesic properties with anti-inflammatory and also antipyretic activity . Its chemical structure is 2 - [3 - chloro - 4 - (3- pyrrolin - 1 -yl) - phenyl] propionic acid. This compound acts as a strong inhibitor in the conversion of arachidonic acid into prostanoids , without interference with the formation of leucotrienes .

Flower et al. (1985) mentioned that in addition to the therapeutic activities of non-steroidal anti-inflammatory drugs , these compounds have some toxic effects as any other medication drugs . He added that these drugs have little effect on renal function in abnormal humans . Hartmann et al. (1984) found that prolonged cholestatic jaundice and leucopenia in response to piroxicam , histological examination of liver biopsy revealed pronounced canalicular and intracellular bile retention . After discontinuation of the drug serum bilirubin declined to normal values over a period of 10 weeks. Cooper and Malik (1984) observed that non-steroidal anti-inflammatory drugs act as inhibitor for prostaglandin synthesis .

According to Adams et al. (1986) patients presented to one unit with renal failure associated with piroxicam and other " NSAID" , all recovered when "NSAID" treatment was stopped .

Wise and Cockayne (1985) mentioned that the treatment with anti-inflammatory compounds caused bilirubin cholestasis and increased the synthesis of alkaline phosphatase . Also , Moss et al. (1987) stated that treatment with anti-inflammatory drugs induced increment in serum alkaline phosphatase . Aly et al. (1992) observed that there is an elevation in bilirubin of arthritic rats in response to piroxicam and piroprofen compounds.

Baulieu et al. (1971) stated that anabolic compounds may control the formation of an enzyme in specific tissues .

Kastrup et al. (1986) noticed that the anabolic steroids promote body tissue-building processes and reverse catabolic or depleting processes. The same author observed that methyl androstenedione acetate is a typical oral anabolic drug in common clinical use . It has an action similar to those of testosterone but its anabolic properties are more pronounced than its androgenic effects .

Casarett(1975) and Tietz(1976) mentioned that biochemical analysis may be utilized as markers or probs to demonstrate undesirable effects of drugs on internal organs and body systems . Also , it is an application of biochemical technology in the elucidation of toxicological aspects of medication .

The aim of this research is to elucidate the toxicological side effects of two commonly used non-steroidal anti-inflammatory drugs i.e. piroxicam and piroprofen on serum biochemical contents . Besides , an attempt was carried out to minimize their harmful side effect by using methyl androstenedione acetate as anabolic steroid compound .

MATERIALS AND METHODS

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Materials

I : Piroxicam drug :

This compound was supplied from Pfizer company in capsules form . Each capsule contained 20.0mg of piroxicam .

II: Piroprofen drug :

This compound was obtained from Ciba company in capsules form . Each capsule contained 400mg of piroprofen .

III: Primobolan compound

This compound was used as steroid anabolic drug . It was supplied from Schering company in tablets form . Each tablet contained 5.0mg of methyl androstenedione acetate (MAA) .

Animals

These studies were done on 100 adult normal male albino rats , weighing from 150 to 200 g . These rats were divided into 10 equal groups , each comprising 10 rats . The rats received daily the following treatments for 8 weeks

Group 1 :

This group received (1.0 ml / 100 g body weight) of the vehicle (water and 2 % Tween 80) and served as control .

Group 2 :

This group received orally methyl androsthenolone acetate (1.8mg/kg body weight)

Group 3 :

This group received piroxicam (1.8 mg / kg body weight) . This dose level is equivalent to human therapeutic dose (Paget and Barnes , 1964)

Group 4 :

This group received piroxicam (5.4 mg / kg body weight) . This dose level is equivalent to three times of therapeutic dose .

Group 5 :

This group received simultaneously both piroxicam (1.8 mg / kg) and methyl androsthenolone acetate (1.8 mg / kg) .

Group 6 :

This group received simultaneously both piroxicam (5.4 mg / kg) and methyl androsthenolone acetate (1.8 mg / kg) .

Group 7 :

This group received orally piroprofen (8.mg / kg body weight) , the effective dose in rats (Maier et al. , 1981) .

Group 8 :

This group received orally piroprofen (24.0 mg / kg body weight) , this dose level is three times of the effective dose in rats .

Group 9 :

This group received simultaneously both piroprofen (8 mg / kg) and methyl androsthenolone acetate (1.8 mg / kg) .

Group 10 :

This group received piroprofen 24 mg / kg body weight together with methyl androsthenolone (1.8mg / kg) .

All compounds were given orally as homogenous suspension in water by using Tween 80 (2 %) as a suspending agent . Animals were fed on the ingredients of ration (crushed wheat 46 % , shredded barley 40 % , fish meal powder 9% , dried milk 3% , yeast 1 % , and minerals , vitamins 1 %) , according to Ahmed (1976) . Animals were kept in air conditioned room housed 5 per cage. Food and drinking water were given ad-libitum . All treatments were given at 10.00 A.M. Animals were weighed weekly for monitoring body growth changes.

After 4 and 8 weeks of treatment , blood samples for biochemical investigations were taken from the retro-orbital plexus (Schermare , 1967) of 6

survivals of each group, 24 hr after the last dose . Blood samples were taken at 10.00 AM to avoid any variations arising from circadian rhythm.

Serum biochemical analysis

Determination of serum glucose was carried out by using the glucose oxidase method as described by Trinder (1969) . The reagents were obtained from Ames , Miles Ltd ; England .

Bilirubin was determined as described by Michaelsson (1961) . The chemicals were obtained from Egyptian American Company , Cairo , Egypt .

Glutamate oxaloacetate transaminase (GOT) and Glutamate pyruvate transaminase (GPT) were determined by the method of Reitman and Frankel (1957) . The reagents were obtained from the above-mentioned chemical company ,

Alkaline phosphatase was determined according to the method described by Belfield and Goldberg (1971) . The chemicals were obtained from the above-mentioned chemical company .

The biuret method was used for determination of total proteins in serum as described by Henry et al. (1974) . The chemicals were obtained from Ames , Miles Ltd. , England .

Serum albumin was determined as described by Dumas et al. (1971) . Serum creatinine was estimated according to Henry et al. (1974) method .

Determination of serum prostaglandin ($\text{PGF}_2\alpha$) was carried out by radioimmuno-assay (RIA) according to the method of Jaffe and Behrman (1974) .

Blood urea was determined according to Marsch et al. (1965) method . The chemicals were obtained from Egyptian - American Company , Cairo , Egypt.

Triglycerides were estimated according to the method described by Wieland (1974) . The reagents were obtained from Bio - analytic laboratories INC , U. S. A.

Statistical analysis :

Standard error (S.E.) was determined according to standard statistical methods (Bernstein and Weatherall, 1952) . Student (t) test described by Goldstein (1964) was used for testing significancy of differentiated between two samples means .

RESULTS AND DISCUSSIONS

I : The effect of piroxicam and pirprofen with or without methyl androsthenolone acetate on serum glucose and bilirubin levels of rats

Table (1) shows the effect of piroxicam and pirprofen drugs given alone and in the presence of methyl androsthenolone acetate (MAA) daily for 8 weeks during the experiment . The obtained results illustrate that the mean

Table (1) Serum glucose and bilirubin levels of rats receiving orally piroxicam (1.8 or 5.4 mg/kg), pirofen (8 or 24 mg/kg) given with or without methyl androsterone acetate, MAA (1.8 mg/kg), daily for 8 weeks.

Treatment	Mean (\pm SEM) serum glucose and bilirubin (mg %)			
	After 4 weeks of treatment n = 6		After 8 weeks of treatment n = 6	
	Glucose	Bilirubin	Glucose	Bilirubin
Vehicle control	75.27 \pm 6.8	0.80 \pm 0.11	68.3 \pm 8.2	0.89 \pm 0.13
MAA (1.8 mg/kg)	83.78 \pm 7.1	1.04 \pm 0.21	80.1 \pm 5.2	0.79 \pm 0.22
Piroxicam (1.8 mg/kg)	72.85 \pm 5.51	1.37 \pm 0.13**	69.0 \pm 6.3	0.95 \pm 0.11
Piroxicam (5.4 mg/kg)	83.8 \pm 5.8	1.46 \pm 0.14**	69.11 \pm 5.9	0.80 \pm 0.28
Piroxicam (1.8 mg/kg) + MAA (1.8 mg/kg)	76.18 \pm 4.93	1.15 \pm 0.18	83.2 \pm 8.1	0.86 \pm 0.14
Piroxicam (5.4 mg/kg) + MAA (1.8 mg/kg)	89.2 \pm 6.1	1.16 \pm 0.16	88.2 \pm 7.3	0.42 \pm 0.24
Pirprofen (8 mg/kg)	86.45 \pm 7.6	0.91 \pm 0.09	61.53 \pm 6.8	0.98 \pm 0.17
Pirprofen (24 mg/kg)	100.81 \pm 8.7	0.79 \pm 0.26	59.26 \pm 7.4 ^(a)	1.29 \pm 0.04 ^(a)
Pirprofen (8 mg/kg) + MAA (1.8 mg/kg)	75.79 \pm 6.58	1.07 \pm 0.23	73.46 \pm 5.4	0.89 \pm 0.23
Pirprofen (24 mg/kg) + MAA (1.8 mg/kg)	90.92 \pm 7.20	1.05 \pm 0.54	67.9 \pm 7.05	0.64 \pm 0.24

(a) n = 5

n = number of samples

* ** Denote significant differences from controls at P < 0.05 and P < 0.01.

(\pm SEM) initial serum glucose and bilirubin levels of rats before the treatment were 71.3 (\pm 7.6) and 0.85 (\pm 0.12) mg / dl , respectively . Control rats receiving the vehicle did not show any change in either serum glucose or bilirubin levels after 4 or 8 weeks of treatment from initial values . Neither the anabolic nor the anti-inflammatory drugs alone or together had no significant effect on serum glucose level during the experiment period .

Serum bilirubin was not significantly affected by the anabolic compound . The anti-inflammatory drug piroxicam (1.8 or 5.4 mg / kg) induced marked elevation in serum bilirubin after four weeks of treatment . The increment amounted to 71.25 % and 82.5 % from the control values , respectively . However , the effect was not observed at the end of treatment period . The results indicated that the presence of anabolic compound with piroxicam did not cause any change in serum bilirubin at 4 or 8 weeks of treatment .

The low dose of pirprofen did not cause any change in serum bilirubin . However , the high dose level of 24 mg / kg induced a marked increment in serum bilirubin i.e. 61.25 % over control values . This effect was observed after 8 weeks of treatment . The combined treatment of pirprofen with the anabolic showed normal serum bilirubin values over the experimental period.

The obtained results are in agreement with those reported by Aly et al. (1992) during their experiments on piroxicam and pirprofen .

II : The effect of piroxicam and pirprofen with or without methyl androst-
olone acetate on serum proteins level of rats

Table (2) elucidates the effect of piroxicam and pirprofen drugs given alone and in the presence of the anabolic (MAA) , daily for 8 weeks . The obtained results illustrate that all treatments , MAA (1.8mg / kg) , piroxicam (1.8 or 5.4 mg / kg) , pirprofen (8 or 24 mg / kg) , given alone or together with MAA showed no significant change in serum total protein , albumin , globulin or A / G ratio of control rats for 4 or 8 weeks . The lack of any changes in serum proteins indicates that the treatments had no effect on the biosynthesis of the protein function of the liver hepatocytes . This conclusion may be due to that the latter is the sole site of protein production (Grant et al. , 1987) . Also , the consistency of normal serum proteins levels over the 8 weeks period indicates that the dietary adequacy of the ratios employed in general retarded the growth rates but did not cause body weight loss . This observation is in agreement with that mentioned by Ross (1982) .

Table (2) Serum enzymes levels of rats receiving orally piroxicam (1.8 or 5.4 mg/kg), piroprofen (8 or 24 mg/kg) given with or without methyl androstenedione acetate; MAA (1.8 mg/kg) daily for 8 weeks.

Treatment	Mean (± SEM) serum enzymes (Iu/L)					
	After 4 weeks of treatment (n = 6)			After 8 weeks of treatment (n = 6)		
	GOT	GPT	ALP	GOT	GPT	ALP
Vehicle control	35.5±2.18	6.0±0.71	32.6±3.65	50.2±5.16	7.1±0.42	31.0±5.4
MAA (1.8 mg/kg)	41.0±0.45	6.6±1.36	34.4±4.01	44.3±3.26	5.8±0.46	28.3±0.34
Piroxicam (1.8 mg/kg)	33.1±1.19	4.9±0.83	58.5±5.7 ^{**}	39.2±3.18	4.8±0.36 ^{**}	30.9±0.97
Piroxicam (5.4 mg/kg)	35.8±1.92	7.0±0.65	45.0±10.78	44.2±9.04	3.13±0.13 ^{***}	30.7±2.32
Piroxicam (1.8 mg/kg) + MAA (1.8 mg/kg)	39.5±0.55	7.1±0.65	47.0±9.1	45.6±7.13	6.9±0.92	29.6±7.47
Piroxicam (5.4 mg/kg) + MAA (1.8 mg/kg)	39.5±1.79	9.5±0.82 ^{**}	38.6±6.95	50.2±8.16	4.8±0.46 ^{**}	30.5±3.01
Pirprofen (8 mg/kg)	31.6±0.24	7.8±0.64	45.5±87	52.8±4.31	8.8±0.91	50.3±5.4 [*]
Pirprofen (24 mg/kg)	36.7±3.71	6.7±0.59	59.7±6.78 ^{**}	58.2±4.25 ^(a)	8.0±2.0 ^(a)	52.6±4.3 ^(a)
Pirprofen (8 mg/kg) + MAA (1.8 mg/kg)	39.3±3.4	9.0±1.11	62.5±2.24 ^{***}	49.5±3.76	8.8±1.02	58.3±4.9 ^{**}
Pirprofen (24 mg/kg) + MAA (1.8 mg/kg)	36.1±2.09	6.8±1.11	70.2±7.0 ^{***}	47.1±3.55	9.4±0.93	64.2±6.1 ^{**}

(a) n = 5

n = number of samples

* ** *** Denote significant difference from controls at P < 0.05, P < 0.01 and P < 0.001.

III : The effect of piroxicam and pirprofen with or without methyl androsthenolone acetate on serum enzymes (GOT ,GPT and ALP) of rats:

The effect of piroxicam and pirprofen drugs in absence and presence of methyl androsthenolone acetate compound on serum enzymes i.e. transaminase (GOT , GPT) and alkaline phosphatase (ALP) is shown in table (3) . The obtained results illustrate that the mean (\pm SEM) initial serum transaminases (GOT and GPT) and alkaline phosphatase (ALP) levels of rats before the treatments were 40.01 (\pm 3.76) , 6.59 (\pm 0.83) and 39.4 (\pm 7.3) IU / L; respectively. Control rats receiving the vehicle did not show any change in their serum GOT , GPT or ALP levels from initial values . Treatment with the anabolic did not induce any change in GOT , GPT or ALP . It was also observed that thr serum transaminase GOT level was not modified over the 8 weeks experimentation period. Rats receiving piroxicam (1.8 or 5.4 mg / kg) for 4 weeks showed no change in GPT . However after 8 weeks of treatment they showed significant decrease in the activity of these enzymes . These values reached 33.15 % and 56.4 % below control values , respectively . Piroxicam (1.8 mg / kg) given with MAA (1.8 mg / kg) did not change GPT serum level. The higher dose of piroxicam (5.4 mg/ kg) given with the anabolic agent showed a significant elevation in serum GPT after 4 weeks but induced a significant decrease after 8 weeks . These fluctuations though significant statistically are within the range of normal values (Melby and Altman , 1974) . On the other hand pirprofen did not induce any change in serum GPT level .

The lack of any marked increment in serum GPT an GOT in response to the given treatments confirms , in particular , the lack of hepatocellular disorders (Johnson and Fody , 1985 ; Wise and Cockayne, 1985) .

Rats receiving piroxicam(1.8 mg / kg) showed a noticeable increment in serum level of alkaline phosphatase amounted to 79.06 % over control value after 4 weeks of treatment . This effect was not observed at the subsequent estimation or with the higher dose level of piroxicam or its combination with the anabolic compound . Rats receiving the low dose of pirprofen (8 mg / kg) showed non significant change in serum alkaline phosphatase after 4 weeks of treatment , but induced a marked increase i.e. 61.79 % after 8 weeks . The high dose level (24 mg / kg) induced marked increase at both examined periods i.e. 82.89 % and 69.4 % over control values , respectively . The administration of the anabolic MAA compound along with low or high doses of pirprofen induced a marked elevation in ALP at both 4 and 8 weeks observation periods .

The obtained data are in agreement with that obtained by Moss et al. (1987) and Hartmann et al. (1984) . Consequently , the chronic treatment with anti-inflammatory drugs , in particular , pirprofen may cause intrahepatic cholestasis (Johnson and Fody , 1985) . Increment levels of ALP may be

Table 3) Serum proteins levels of rats receiving orally piroxicam (1.8 or 5.4 mg/kg), piroprofen (8 or 24 mg/kg) given with or without methyl androstenedione acetate; MAA (1.8 mg/kg) daily for 8 weeks.

Treatment	Mean (\pm SEM) serum proteins (g/dL)							
	After 4 weeks of treatment				After 8 weeks of treatment			
	Total protein	Albumin	Globulin	A/G ratio	Total protein	Albumin	Globulin	A/G ratio
Vehicle control	7.5 \pm 1.15	3.1 \pm 0.57	4.3 \pm 0.75	0.7 \pm 0.11	7.4 \pm 1.02	3.2 \pm 0.61	4.2 \pm 0.58	0.7 \pm 0.08
MAA (1.8 mg/kg)	5.6 \pm 0.77	2.9 \pm 0.47	0.9 \pm 0.51	0.9 \pm 0.21	6.29 \pm 1.6	2.7 \pm 0.71	3.5 \pm 0.84	0.7 \pm 0.04
Piroxicam (1.8 mg/kg)	5.1 \pm 0.73	2.3 \pm 0.3	2.8 \pm 0.5	0.8 \pm 0.09	5.53 \pm 1.09	2.7 \pm 0.29	3.6 \pm 0.53	0.8 \pm 0.07
Piroxicam (5.4 mg/kg)	4.3 \pm 0.55	2.0 \pm 0.26	2.3 \pm 0.35	0.9 \pm 0.1	4.47 \pm 1.06	1.4 \pm 0.58	2.9 \pm 0.95	0.8 \pm 0.18
Piroxicam (1.8 mg/kg) + MAA (1.8 mg/kg)	5.8 \pm 0.55	2.8 \pm 0.32	3.0 \pm 0.38	1.0 \pm 0.15	7.15 \pm 0.52	3.3 \pm 0.43	3.7 \pm 0.36	0.9 \pm 0.14
Piroxicam (5.4 mg/kg) + MAA (1.8 mg/kg)	6.5 \pm 0.97	3.1 \pm 0.58	3.3 \pm 0.39	0.8 \pm 0.1	5.61 \pm 0.74	2.7 \pm 0.14	2.8 \pm 0.62	0.9 \pm 0.15
Piroprofen (8 mg/kg)	8.0 \pm 0.7	3.0 \pm 0.19	4.9 \pm 0.59	0.6 \pm 0.04	6.54 \pm 0.39	3.4 \pm 0.21	3.1 \pm 0.5	1.2 \pm 0.27
Piroprofen (24 mg/kg)	9.3 \pm 0.37	3.0 \pm 0.18	6.4 \pm 0.18	0.4 \pm 0.04	7.5 \pm 0.59	2.9 \pm 0.85	4.5 \pm 0.45	0.6 \pm 0.16
Piroprofen (8 mg/kg) + MAA (1.8 mg/kg)	7.8 \pm 0.69	2.8 \pm 0.05	4.9 \pm 0.55	0.6 \pm 0.07	7.57 \pm 0.48	3.5 \pm 0.74	4.0 \pm 0.44	1.0 \pm 0.22
Piroprofen (24 mg/kg) + MAA (1.8 mg/kg)	6.2 \pm 0.63	2.7 \pm 0.33	3.5 \pm 0.63	0.8 \pm 0.16	6.73 \pm 0.87	2.8 \pm 0.42	3.8 \pm 0.68	0.8 \pm 0.15

(a) n = 5

n = number of samples

arised from bone growth and healing (Wise and Cockayne, 1985). This interpretation may explain the synergistic increase in ALP after the combined treatment with pirofen and MAA . The anabolics are known to enhance bone ossification (Kastrup , 1986) .

IV : The effect of piroxicam and pirofen with or without methyl androstenedione acetate on serum non protein levels of rats

The results in table (4) illustrate the effect of piroxicam and pirofen drugs in absence and presence of anabolic agent on serum non protein , i.e. urea and creatinine levels of rats . The obtained results elucidate that the mean (\pm SEM) initial serum creatinine and urea levels of rats before the treatments were 0.56 (\pm 0.05) and 36.09 (\pm 4.75) mg / dl , respectively . Control rats receiving the vehicle did not show any change in serum creatinine or urea serum levels over 8 weeks period . Rats receiving MAA (1.8 mg / kg) or piroxicam (1.8 or 5.4 mg / kg) or their combination did not show any change in their creatinine or urea serum levels over the 8 weeks period .

Treatment with pirofen or its combination with the anabolic did not cause any increase in either creatinine or urea serum levels . On the contrary, a significant decrease in serum urea levels was observed after 4 weeks of treatment with the high dose of pirofen . The effect was not observed at the 8 week point of examination . The obtained results are in agreement with that opinion of Uthman (1985) , who mentioned that the anti-inflammatory drugs and the anabolic agent would not hinder the excretory function of the kidney . Also , the obtained data is in harmony with the finding of Aly et al. (1992) , who reported renormalization of elevated blood urea by piroxicam .

V : The effect of piroxicam and pirofen with or without methyl androstenedione acetate on triglycerides and prostaglandin serum levels of rats

The estimated serum levels of prostaglandin ($\text{PGF}_2\alpha$) at the end of treatment period i.e. 8 weeks , are shown in table (5) . The results indicate that the two different doses of piroxicam caused a great decrease in $\text{PGF}_2\alpha$ serum concentration i.e. 40 % . The effect was more pronounced when piroxicam was given along with the anabolic drug . By using the latter agent alone there is no change in $\text{PGF}_2\alpha$ level . On the other hand , pirofen did not induce any change by its higher dose level . However , the latter dose in the presence of MAA agent (1.8mg /kg) induced a 37 % decrease in $\text{PGF}_2\alpha$ serum level . The obtained results are in harmony with Tavares et al.(1985) .

Table (5) Serum triglycerides (TG) and prostaglandins (P₂α) levels of rats receiving orally piroxicam (1.8 or 5.4 mg/kg . , piroprofen (8 or 24 mg /kg) given with or without methyl androstenolone acetate ; MAA (1.8 mg/kg) , daily for 8 weeks .

Treatment	Mean (±SEM) TG in serum mg dl (n=6)	Mean PG (± SEM) PG (n=6)	Percent change from control (% PG)
Vehicle control	202.78±42.69	3867±328	-
MAA (1.8 mg/kg)	* 72.6±12.9	3750±320	-3.03
Piroxicam (1.8 mg/kg)	** 53.7±10.76	* 23 00±245	-40.52
Piroxicam (5.4 mg/kg)	134.3±13.5	* 2300±245	-40.52
Piroxicam (1.8 mg/kg) + MAA (1.8 mg/kg)	105.47±9.9	** 1535±465	-60.31
Piroxicam (5.4 mg/kg) + MAA (1.8 mg/kg)	** 49.26±5.52	** 1933±371	-50.01
Pirprofen (8 mg/kg)	151.57±32.99	3900±230	+0.85
Pirprofen (24 mg/kg)	183.13±18.2	(a) 2828±641	-26.87
Pirprofen (8 mg/kg) + MAA (1.8mg/kg)	144.15±17.8	3225±337	-16.61
Pirprofen (24 mg/kg) + MAA (1.8 mg/kg)	234.6±39.3	** 2425±249	-37.29

a n = 5

n = number of samples

** , *** Denote significant differences from controls at P < 0.05 and P < 0.01

Maier et al. (1981) mentioned that piroprofen was shown to be as a cyclo -oxygenase inhibitor and hence ,it is expected to reduce PG levels. Consequently , the use of anti-inflammatory e.g. piroxicam and piroprofen medication purpose is accompanied with lowering of prostaglandin level .

Administration of the anabolic potentiated the PG inhibiting effect on the ant-inflammatory (piroxicam) and unmasked the effect of the high dose of piroprofen . Several workers attributed the anti-inflammatory ,and other effects of these drugs to its cyclo-oxygenase or prostaglandin synthetase inhibition (Ward et al., 1984 ; and Tavares et al. ,1985) . It may be concluded that the anabolic drug will enhance the medical effects of the anti-inflammatory drugs or at least will not antagonise them .

The obtained results in table (5) illustrate the triglycerides (TG) levels in serum at the end of experiment periods . It is clearly from these results that rats receiving MAA (1.8 mg / kg) , piroxicam (1.8 mg / kg) and piroxicam (5.4 mg / kg) + anabolic compound (1.8 mg / kg) caused a significant decrease in serum triglycerides i.e. 64.2 , 73.52 and 75.71 % below control values . On the other hand , piroprofen given alone or with MAA showed no significant change in serum triglycerides . This effect may be due to suppression of pituitary hormones (Tietz ,1976) , The latter causes a decrease in serum T.G. (Kastrup , 1986) .

Finally,it may be recommended that estimation of serum biochemical contents should be done during prolonged therapy with piroxicam and piroprofen .The concurrent administration of anabolic steroid is also very much advisable .

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دراسات عن تأثير مركبات البيروكسيكام

والبيربروفين على بعض المكونات الكيماوية الحيوية فى مصل الفئران البيضاء

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** الهيئة القومية للرقابة الدوائية والبحوث - القاهرة .

تم فى هذا البحث دراسة تأثير عقارى البيروكسيكام والبيربروفين المضاديين لالتهابات على المكونات الحيوية بمصل الفئران البيضاء وكذلك أجريت محاوله باستخدام مركب خلاص الميثيل اندروستينولون كمادة بناءة لتقليل الاثار الجانبية السامه لهذين المركبين وقد اوضحت النتائج أنه لم يترتب على العلاج بهذين العقارين أى تغيير لمستوى الجلوكوز والبروتين الكلى أو نوعيهما (الالبيومين والجلوبولين) . وقد اظهرت النتائج أيضا أن تكرار اعطاء الجرعه البسيطة من البيروكسيكام (٨٨ ملليجرام/كجم) . كذلك الجرعه العاليه من هذه المادة (٤٤٠ ملليجرام/كجم) لمدة أربع أسابيع أدى الى ارتفاعا ملحوظا فى نسبة اليليسروبين (الصفراء) فى الدم بنسب ٧١٢٥ ، ٨٢٥٪ بالزيادة عن قيم الكونترول أما فى حالة البيربروفين فان الجرعة البسيطة (٨ ملليجرام/كجم) لم تؤثر على نسبة الصفراء فى الدم بينما الجرعات العاليه منه (٢٤ ملليجرام/كجم) أحدثت ارتفاعا معنويا بنسبة ٦١٢٥٪ من قيم الكونترول وذلك بعد فترة علاج لمدة ٨ أسابيع . وقد زال هذا الاثر باستخدام المادة البناءة .

اتضح من النتائج المتحصل عليه أنه لم يسبب أى من المركبين تغيير ملحوظ فى المستوى المصل للانزيمات الناقله لمجموعة الامين (جلوتاميك اكلواستيك وكذلك جلوتاميك بيروفات) بينما كل من المركبين أحدث ارتفاعا ملحوظا فى المستوى المصل لانزيم الفوسفاتير القلوى وكان هذا التأثير أكثر شدة فى حالة البيربروفين حيث وصل الى ٨٢٨٩٪ وقد أمكن ازالة هذا الارتفاع بواسطة المادة البناءة فى حالة البيروكسيكام فقط . وقد اوضحت النتائج أيضا أن المعالجة لكلا من المركبين لم تؤثر على الكفاءة الكلويه حيث لم يحدثا أى ارتفاع فى مستوى البولينا أو الكرياتينين فى السيرم بل على العكس أدى مركب البيربروفين الى نقص البولينا بسننه ٦٠٪ وقد أرجع هذا الى الضعف البسيط فى وظائف الكبد وهذا الاثر لم يتغير بواسطة المادة البناءة .

تبين من قياس مادة البروستاجلاندين أن المادة البناءة ربما تعزز الفاعليه الطبيه لكلا من المركبين أو على الاقل فانها لاتؤثر بطريقة عكسيه على فعلهم العلاجى .

وقد اظهرت النتائج أيضا أن اعطاء مركب البيروكسيكام (٨٨ مجم/كجم) منفردا وكذلك نفس الجرعه من هذا المركب ومع المركب البناءة وكذلك اطادة البناءة منفرده أدى الى انخفاض معنوى فى نسبة الجلوسريدات الثلاثيه فى المصل بنسب ٧٥٧١ ، ٧٣٥٢ ، ٦٤٢٢٪ منخفضة من قيمة الكونترول . بينما فى حالة المعالجه بالبيربروفين منفردا ومع المادة البناءة فان ذلك لم يؤدى الى أى تغيير معنوى فى نسب الجلوسريدات الثلاثيه بالسيرم .