EFFECT OF COMBINED LITHIUM AND CADMIUM ADMINISTRATION ON WATER, ELECTROLYTES, AND TRACE ELEMENTS EXCRETION AND ACCUMULATION OF CADMIUM IN RAT.

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ABSTRACT.

Adminstration of a combined Lithium and Cadmium suppiemented in diet to male Wistar albino rats for 28 days were associated with alter metabolism of water. Electrolytes and trace elements in liver , kidney and muscle tissue. Asignificant increased of urinary excretion of K. Cl, Fe, and Cu, and a significant reduction in tissues content of Cl, Zn, & Cu, in liver, kidney and muscle, also occurred. An increases in water intake and urine production was also observed which was less severe than Li- treatment alone. A reduction in Cd accumulation in tissues was obsered by 42.24 % in liver, kidney and muscles compaired with Cd- treatment alone. This might be suggest ghat there is antagonistic action between Li & Cd in both kidney tubules, liver and muscle, Aproteinuria has been observed also during the first 4 days and the last 28 days of treatment .

Introduction :

Lithium is extensively used in psychiatric praetice . But, this drug has an disturbing side effect often induces polyuria and polydipisia. Experimental studies have shown that , this effect is due to a nephrogenic diabetes insipidus (NDI) which caused by a Li - induced inhibition of the action of antidiuretic hormone (Singer, 1981; Khudhair, 1982; Christensen, 1983; Christensen et al , 1985 ; Ottosen et al., 1987; Marcussen et al., 1989; Yamaki et al., 1991) . The mechanism of the pathogensis of NDI due to chronic Li - treatment has been gradually clarifeid , but is still only party understood. Most previous studies have been aimed at the pathogensis of Li -0 induced NDI have been made use of mammalian kidney and amphibian epithelia (Abramow and Cogan, 1984, Cogan, et al. 1990) to examine the effect of acute exposure to Li in vitro or acute Li -infusion in vivo on the AVP- dependent adenosine 3,5 Cyclic Monophosphate (cAMP) mediated tansport process. Such studies have suggest that ionic Li - inhibits the increase in water permeability induced by AVP mainly at the step of AVP dependent cAMP generation (Abramow and Cogan , 1984) Christensen . et al. (1985) examined the effect of Li on renal components of urinary concentration mechanism and suggesting that oral administration of Li impairs AVP dependent cAMP metabolism in the collecting tubule system at step of AVP - sensitive adenylate cyclase, reducing the corticopapillary gradient of solutes in renal tissue (Cogan, et al. 1987) ; Goldberg et al , 1988; Yamaki et al., 1991) .

Cadmium has been recognized as one of the most toxic industrial and environmental element. Cadmium toxicity in human and animals resulted from its accumulation almost in all the organs, mainly in liver and kidney and its ability to produce morphological and functional changes after long term low level exposure by food and air (Friberg et al., 1974; Hoffmann et al., 1975;Friberg et al,. 1986; Groten et al. 1990) . Most of the Cd studies have been shown that Cd caused hepatotoxicity ; but with chronic administration , the target organ of toxicity altered from liver to kidney by release of CdMT in blood such hepatotoxicity was anaemia (Groten et al., 1990) .

Chonic exposure to Cd cause renal tubular cell injury and dysfunction which may progress to chronic interstitial nephropathy, These changes are associated with low molecular weight proteinuria, amino acid phosphatouria, Calciuria, Glycosuria, Polyuria (Friberg, et al. 1974; ;Nordberg, et al., 1975; Pu- Wang, et al., 1993 Jin, et al., 1992; Groten, et al., 1992). Little information are avaliable on urinary excretion of

water, electrolytes such as Na,K,Cl, following Cd- induced renal disorder (Leffler, et al, 1990; Kido, et al., 1992) as well as the urinary excretion of trace elements such Fe, Zn and Cu (Pu-Wange. et al., 1993).

The objective of the present study was to investigate renal handling of water , electrolytes and trace elements Fe, Zn and Cu following the combined Li and Cd administration in addition to determine the accumulation of Cd and trace elements in tissues in presence of both Li and Cd as new model of reducing toxicity of cadmium.

Materials and Methods:

A twenty four male rats of Wistar albino strain were obtainen from general laboratory of general public health -Baghdad, of 350-410 g. body weight, and after conditioning for one week were divided into 4 groups. Group I (6 animals) was considered as ccontrol group which was receved normal diet and distal water and Lithium during the period of experiment . Group II (6 animals) were housed individually in metabolism cage (Jecons Metabowl, Hemel Hempsted) the animals were left for 10-14 days adaptation in new environment metabolism cages. An another 3 days of collecting samples , the animals were receved normal diet which was served as control period. On day three the normal diet was replaced by Cd & Li supplemented diet for 28 days. A daily measurement of body weight, food intake, water drink, urine production were recording during the whole period of experiment. At the end of experimental time, the animals were killed, blood sample, kidney, liver and muscle tissues were taken. Group III (6 animals) were held in colony cages and were fed Li & Cd incorporated diet for 4- days. On day four the animals were killed under ether anaesthesia, blood sample, liver, kidney and muscle tissues were taken. Group 4 (6 animals) were also held in acolony cages for 14- days fed Li & Cd diet. On day 14, the animals were killed, blood sample, liver, kidney and muscle tissues were taken for assayed the parameters. All samples collecting were kept at- 20 C till assay. In other studies a similar groups were treated in the same regime but were receved either Cd-supplemented diet alone or Li-supplemented diet..

Preparation of incorporated diet (Li & Cd).

An important aspect pertinent, the influence of Cd and Li on the rat was the methods of administration of the Li & Cd. Lithium and Cadmium are toxic elements, Li is as a therputic drug and Cd is apolutent element. In this study both Li & Cd were added to the normal diet which has provided a relatively constant rate of up take. Li & Cd supplemented diet was prepared by incorporating 1.1g of LiCl and 10 mg Cd in each kg. (Khudhair, 1982;Groten, et al. 1991).

Chemiccal analysis

Sodium, Potasium, Iron, Zinc, Lithium and Copper in urine, plasma and muscle sample were determined via and atomic flame emission absorption spectrophotometric using Atomic Absorption Spectrophotometer (PYE Unicam) . Cadmium in all samples was determined using flameless atomic absorption AAS (SP9 Aatomic Absorption Furnace Graphate equiped with data Graphics system and Vedio Furnace Programer) . The chloride in urine and plasma was determined using Chloride Analyzer 925 (Coring Medical and Scientific Ltd)) . Detailes of all procedure are given in the manuals of the equipments have been used. The total protein in urine was estimated by method of Lowery, et al. (1951).

Statistical analysis:

The various parameters of metabolism studies were standerised relatively to the body weight and time expressed per 100 g B.W./ 24h (Khudhair, 1982). The manipulation and statitical analysis of the data from metabolism studies were achieved by a specially designed computer program (Khudhair, 1982). All values are expressed as mean + SE. for each of the parameters measured, the average value for each rat was calculated for the control period,using a paired " t" test the changes in the experimental period compared with the control values. Other unpaired data were compared by Students "t" test. Differences were considered statistically significant at the 5% confidence limit.

Results:

The 10 days period of adaptation for animals in the metabolism cages was found to be sufficient to ensure stability of the parameters measured in the subsequent control period. Measurements of water, electrolytes, trace elements turnover in rats before and after Li & Cd administration are shown in figures 1-7. Food intake was significantly reduced ($P < 0.001$) during

the first 24 h, compared to the control period (Fig. 1) which was returned to the pretreatment level during the period of experiment, except that on 5, 11, 12, and 24 days of treatment was reduced ($P < 0.05$). Body weight wasnt changed during the whole period of time. Water intake was not changed during the period of treatment, except that on days 4, 14, 15 and 18 of treatment was increased ($P < 0.05$)(Fig.1). The urine production showed a stable increases from the 1st 24h of treatment until day 16, though only was statistically significant ($P < 0.05$) on days 5, 14, and 15; which was returned to the pretreatment level from day 17 to 28 days (Fig.2). Water balance (water intake - urine production) was not changed throughout he experimental period in animals treated with Li & Cd compared with untreated animals (Tables 2-4).

The urinary excretion of Na and Na balance has not been artected by Li & Cd administration for 28 days . Plasma Na concentration was significantly reduced ($P < 0.05$) on day 4 Li treated animals compared with untreated animals (Table 1). On the other hand, plasma Na concentration was not changed in animals treated for 14 and 28 days Table 1. Tissue Na content (table 2) was reduced on day 4 in liver tissue and on day 14 in kidney tissue only (Table 3), while it was not affieted during the experimental period in muscle tissue.

Urinary excretion of Potassium was significantly increased ($P < 0.05$) from day 2 to day 14 which was returned to the pretreatment level from day 20 to day 28 (Fig.3). Potassium balance (Fig. 3) was not chnged except that on days 7,14 and 19 of treatment was reduced ($P < 0.05$). Plasma K concentration was not change by Li & Cd administration throughout the experimental period (Table 1) . Potassium content in liver and kidney tissues was reduced in all animals recieved Li & Cd compared with untreated animals during the periods of experiment, while K content in muscle tissue was significantly reduced ($P < 0.05$) in treated animals only atfer 14 and 28 days of treatment (Tables 2-4).

The urinary excretion of anion chloride was significantly reduced on day 4 ($P < 0.05$) and on days 14 & 28 ($p < 0.01$) of Li & Cd treatment (Fig. 5). Accordingly Cl balance was reduced by 4 & 14 days ($P < 0.05$) and 28 days ($P < 0.01$) of treatment . The plasma chloride concentration was significantly reduced in treated animals by 4, 14 , 28 days of treatment (Table 1) .

The renal handling of trace elements following Li & Cd administration was shown in Fig 4. The urinary excretion of Fe was significantly increased ($P < 0.01$) on day 4 of treatment, while it was not changed after 14 & 28 days of treatment compared with pretreatment period. The plasma Fe concentration was not changed in animals recieved Li & Cd compared with untreated animals (Table 1) . The tissue content of Fe was not affected by Li & Cd during the whole period of treatment only that in liver tissue, the Fe content was significantly reduced in animals treated for 4 and 14 days (Table 2). The urinary excretion of Zn was significantly increased ($P < 0.01$) after 4, 14 and 28 days of Li & Cd treatment zinc balance was not altred during the time course of experiment . The plasma concentration of Zn was significantly reduced after 4, 14 and 28 days of treatment period (Table 1). On the other hand tissue content of Zn in liver , kidney and muscle was not affected in treated animals compared with untreated animal .

The urinary excretion of Cu was not changed after 4 days of Li & Cd treatment, while it was increased in urine after 14 and 28 days of experimental period ($P < 0.05$). Copper balance was increased ($P < 0.05$) during the first 4 days of treatment, then it was returned to the pretreated level after 14 & 28 days of treatment (Fig.4). The plasma concentration of Cu (Table 1) was inceased in animals treated for 4- days , while it was not changed in animals treated for 14 days and 28 days compared with untreated animals . The Cu content in liver tissue was reduced in treated animals compared with untreated animals for 28 days of exposure (Table 2). On the other hand, Cu content in kidney tissue reduced in animals treated for 4 - days only compared with control animals, while it was not altred in animals treated for 14 - and 28 days (Table 3).

The urinary excretion of Li was reduced ($P < 0.05$) after 28 days of treatment compared with urinary excretion after 4 and 14 days of treatment with Li & Cd diet (Fig. 6). Plasma Li concentration was not changed during the whole experimental period. The Li content in liver and kidney tissue was not differed in animals treated

with Li & Cd during the period of exposure, while Li content in muscle tissue was reduced in animals recieved Li & Cd ($P < 0.05$) after 28 days of treatment compared with 4 & 14 days of treatment (Tables 4). The highest content of Li was found in muscle tissue after 4 days of treatment compared with treated period of 14 & 28 days (Table 2-4).

The urinary excretion of Cd was not detected during the whole priod of experiment in this study. The plasma concentration of Cd was higher in animals treated with Li & Cd for 4 - days ($P < 0.01$). compared with animals treated for 14 & 28 days . Also, the tissue content of Cd was increased with increased period of treatment. Though, it was higher in liver and kidney tissue ($P < 0.05$) compared with muscle tissue content (Tables 2-4).

A combined treatment of Li & Cd caused a decreased in the accumulation of Cd in all tissue (Table 5) ($P < 0.05$) compared with Cd- treatment alone, thuogh , it was the highest Cd in tissue content as a mean of accumulation in animals recieved Cd only . On the other hand , the accumulation of Cd in tissue was reduced in animals recieved Li & Cd ($P < 0.05$) (Table 6). In contrast, the higher content of Cd in tissue for the two treatments with Cd & Li and Cd - alone was appeared in kidney tissue (table 7). ($p < 0.05$) compared with liver and muscle tissues. Also this study showed that the higher concentration of Cd in kidney tissue in animals treated with Cd only. and the lowest concentration of Cd found in the muscle tissue in animals recieved Cd & Li diet (Table 5).

Urinary excretion of total protein following Li & Cd treatment was significantly increased ($P < 0.001$) on 4 and 28 days compared with untreated period (Fig 7)

Discussion:

The adminstration of Li & Cd supplemented diet was associated with reduced food intake compared with pretreatment period. This reduction might be related to the effect of both Li & Cd on the central appetite in brain or may be due to the presence of Li & Cd in diet changed the taste of food, which inturned not well accepted by animals. This observation might be confirmed by other studies which has been shown that Li - treated animals caused a reduction in food intake (Balment, et al., 1997, Khudhair, 1982). Also, Cd administration showed a decreased in food intake (Doyle, et al., 1974; Al Mamoom, 1995).

Lithium and Cadmium treatment was also associated with slight increased in body weight, which may be due to the presnce of Li, where

Li- treatment was showed increases in body weight by other studies (Vendsberg,1980; Vestergaard, et al., 1988; Schou, 1993).

The clear changes in the pattern of water intake and urine production following Li & Cd treatment, the Fluctuate increase in water drink may reflect the effect of both Li & Cd on water metabolism in kidney. The percentage of increament of water intake following Li & Cd -

treatment was only 15.8% while in other studies the percentage of increament of water drink, when only Li was given to the animals was 33.4%. On the other hand, Cd administration only caused a reduction in water intake by 28.4%. The increases of the pattern of water intake was reflected by the increase of urine output by 25.6% following the Li & Cd administration. In contrast, Li- treatment alone caused an increase in urine production by 58.3% while Cd-treatment alone caused a reduction in urine production by 26.64%. The reduced in urine production in compared with Li - treatment alone suggest that there is an effect of Cd on Li-produced polydipisia and polyuria which have been reported by other studies (Cox and Singer, 1975; Schou and Veestergaard, 1988; Qureshi, et al., 1990; Schou, 1993). One of the possible explanation that Cd might be reduced the inhibitory effect of Li at level of distal and collecting duct (Jenner and Eastwood, 1978; Camey et al., 1976. Khudhair, 1982, Ottosen, et al., 1987, Cogan, et al., 1990).

The unchanged in urinary excretion of Na when animals given acombined Li & Cd might be related to the presence of both Li & Cd which abolished their effect on renal handling of Na and the unchanged in tissues content of Na in this study might be confirm this concept. Pervious studies have shown that Li- treatment alone and Cd- treatment alone caused an increases in urinary excretion of Na, both in human and ani mals (Forrest, et al., 1976; Balment et al., 1977; Jin, et al., 1987: Leffler , et al., 1990: Kido, et al., 1992;).

Also a combined Li & Cd treatment showed

an increases in urinary excretion of K by 32 %. This increasment might be due to the presence of Li in diet which might exert its inhibitory action at the level of proximal tubule (Carney et al., 1980). or might be Li substitute the K ion itracellularly, the reduced K ion in tissue content may support this notion.

The increases in urinary excretion of Cl anion was a case have been reported by other studies (Galla, et al., 1975; Fleisher. et al., 1975) but the percentage of increases in urinary Cl excretion was only 25.24% ; when was Li & Cd - treated (unpublished) showed an increases of Cl excretion by 36.44 % and 27.14% respectively. This means that the presence of both Li & Cd their effect on renal metabolism might be reduced at level of active transport either at proximal or distal parts or both part of kidney tubule, which needs further investigation.

The combined Li & Cd administration was not affect the renal handling of water and electrolytes turnover , but it was included renal handling of trace elements. The increases of urinary excretion of Fe following Li & Cd treatment might be related to the effect of both Li & Cd on Fe metabolism especially at the level of liver, because the reduction in Fe content of liver tissue was more affected than other tissues studies. Other studies in our laboratory (unpublished)Li - treatment was associated with an increased in tissue content of Fe especially in kidney tissue. In contrast, it has been reported that Cd have an antigonistic effect with Fe (Richardson, et al, 1974; Wegel, et al., 1984; Friel. et al. 1987) . Though the presence of Cd may be causes a reduction of Fe in tissues content especially the liver. This means that, the Cd may either inhibits the Fe absorption form intestinal mucosa (Hailton and Valberg, 1974; Shukla, et al , 1992) or may be affected on the Fe metabolism in liver or in other tissues (Groten, et al., 1992)

The increase in urinary excretion of Zn by Li & Cd treatment might be due to both inhibitory effect of these ions on the metabolism of Zn particularly in liver tissue, the reduced ion of Zn content in liver and plasma concentration after treatment confirm this concept. There was no changed appeared in Zn excretion in animals recieve Li only (unpublished) while the excretion of Zn in animals given Cd only was reduced. On the other hand, it was found that Li .increased renal tubular flow (Carney, et al., 1980) , while Cd was found to be inhibits the competative reabsorption of Zn by a mechanism that Cd- inhibit the transport of Na- amino acid taht linked with Zn which caused the increases of Zn exeretion (Gachot , et al., 1991).

The copper metabolism has also been affected by Li & Cd administration to the normal rats This effect was appeared as increased in urinary excretion of Cu in a manner similar to that of Zn, where it was not affected when Li or Cd has given separately (unpublished). It a ppears that when both Li & Cd present in time have an unknown effect on Cu either at renal level or in tissue which needs further investigation.

Lithium and Cadmium administration reduced the accumulation of Cd in tissue by 42.24% compared with animals recieved Cd only , and this may mainly related to the presence of Li. The changes appeard in renal handling of water and electrolytes in this study compared with observed changes in renal handling of water and electrolytes following either Li- treatment or Cd-treatment support this concept. The reduced Cd content in tissues might be due to the inhibitory effect of Li to the obsorptive mechanism of Cd in intestine or may be there is a competative in transport mechanism of Cd through the cell membrane of tissues , or may be effected the formation of CdMT at liver or kidney level, which needs more studies.

The appearance of proteinuria following Li & Cd treatment was related to the effect of both Li & Cd on kidney handling of protein. In other studies, it was found that Li- caused proteinuria as transient proteinuria during the early Li- administration (Singer, et al., 1979; Chritensen and Ottosen, 1983; Schou and Vestergaard, 1988). On the other hand, Cd also caused a proteinuria in both human and experimental animals (Bernard, et al., 1981; Lauwerys, et al., 1984; Jin, et al., 1987). This indicate that the presence of Li & Cd have an addative effect on renal handling of protein either at glomerular level or at proximal tubules level. The high proteinuia 35.12 % compared with proteinuria following Li - treatment was 17.4% or 31.1% following Cd-treatment confirmed this concept, which needs further studies .

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Index. Effect of dietary Cd & Li and Cd alone on Cd concentration of various tissues followin varoius period of treatment in rat.

Diet	Period(day)	Liver	Kidney	Muscle	Means of treat. period
Cadmium	4	1.30	1.47	0.06	0.94
	14	4.11	6.52	0.11	3.58
	28	9.62	12.46	0.20	7.43
	Composit average	5.01	6.82	0.12	
Lithium and Cadmium	4	0.26	0.48	0.04	0.26
	14	1.94	2.91	0.05	1.63
	28	6.64	8.27	0.08	4.99
	Composite average	2.95	3.88	0.06	LSD 0.05

Table 1: Effect of Li & Cd on plasma concentration of some electrolytes and trace elements after 4, 14 and 28- days of treatment. (Values are mean ± SE. n= 6).

Cont.		4-days	14-days	28-days
Na Meq/1	142.70±2.42	137.23±106.3 p<0.05	145.11±1.65 Ns	142.69±2.07 Ns
K. Meq/1.	3.74±0.26	3.37±0.19 Ns	40.3±0.26 Ns	4.11±0.29 Ns
Cl Meq/L	11.5.50±5.67	94.50±5.08 P<0.01	98.67±1.71 P<0.01	98.50±3.31 p<0.01
Fe mg/L	2.97±0.40	4.05±1.05 Ns	2.81±0.31 Ns	2.58±0.42 Ns
Zn mg/L	0.44±0.03	0.09±0.02 P<0.01	0.20±0.08 P<0.01	0.15±0.02 P<0.01
Cu mg/L.	0.33±0.03	0.30±0.04 Ns	0.54±0.08 p<0.05	0.33±0.07 Ns
Li meq/L.		0.48±0.03	0.50±0.04 Ns	0.50±0.05 Ns
Cd mg/L		0.02±0.004	0.01±0.002 P <0.01	0.01±0.005 P<0.01

Table 2. Effect of Li & Cd on water, electrolytes and trace element in liver following 4, 14, 28 days of treatment . (Values are mean ± SE N = 6).

	cont.	4-days	14-days	28-days
Na mg/g D.W.	5.24±0.30	2.88±0.74 Ns	4.36±0.84 Ns	4.34±0.76 Ns
K mg/gD.W.	25.00±0.97	11.82±4.61 P<0.05	15.46±5.38 P<0.05	14.05±4.20 P<0.05
Fe ug/g D.W.	339.23±1786	203.33±54.83 P<0.05	266.76±64.48 p<0.05	333.75±42.99 Ns
Zn µg/g.D.W.	84.81±1.11	84.81±9.44 Ns	81.84±12.71 Ns	90.41±7.98 Ns
Cu µg/gD.W	10.54±1.11	8.20±2.69 Ns	10.30±2.76 Ns	7.30±1.10 P<0.05
Li µg/g D.W.		53.49±7.09	50.47±2.27 Ns	49.53±5.32 Ns
Cd µg/g.D.W.		0.26±0.02	1.94±0.13 P<0.001	6.64±0.21 P< 0.001
Water Con. t.	70.28±0.21	69.98±0.24 Ns	68.95±3.96 Ns	70.14±0.25 Ns

Table.3 Effect of Li & Cd on water electrolytes and trace elements in kidney tissue following 4, 14, 28 days of treatment N= 6 (Values are mean + SE.)

	Cont.	4-days	14-days	28-days
Na mg/g.D.W.	14.23±2.88	9.36±2.55 Ns	8.03±1.3 P<0.05	9.11±2.08 Ns
K.mg/g.D.W.	24.08±1.53	15.38±3.92 P<0.05	14.96±3.11 P<0.05	15.82±4.35 P<0.05
Fe. µg/g.D.W.	274.42±61.60	298.38±45.30 Ns	232.62±41.90 Ns	314.59±13.46 Ns
Zn. µg/g.D.W.	131.37±25.99	129.65±45.30 Ns	94.50±16.31 Ns	99.91±12.27 Ns
Cu. µg/g.D.W.	26.44±421	12.96±4.09 P<0.05	20.68±5.63 Ns	15.40±4.28 P<0.05
Li µg/g.D.W.		79.11±5.90	79.02±0.16 Ns	69.54±7.74 Ns
Cd µg/g.D.W.		0.48±0.02 P<0.001	2.19±0.16 P<0.001	8.27±0.19 P< 0.001
Wat. Cont.	76.25±2.76	76.58±0.40 Ns	75.02±0.31 Ns	76.49±0.60 Ns

Table 4 Effect of Li & Cd - treatment on water electrolytes and trace elements in muscle tissue following 4, 14, and 28 days (All value are mean ± SE), N = 6.

	Cnt.	4-days	14-days	28-days
Na, mg/g D.W.	7.39±3.32	5.38±0.97 Ns	4.53±1.2 Ns	9.35±5.37 Ns
K,mg/g.D.W.	33.56±2.58	24.76±6.39 Ns	20.75±6.69 P<0.05	18.42±3.96 P<0.05
Fe, µg/g.D.W.	147.37±56.19	144.10±26.31 Ns	205.15±44.41 Ns	105.14±18.25 Ns
Zn, µg/g.D.W.	159.47±62.80	203.22±82.64 Ns	211.42±77.48 Ns	98.75±13.89 Ns
Cu, µg/g.D.W.	22.25±7.48	8.28±1.94 P<0.05	15.89±3.50 Ns	10.24±2.47 Ns
Li, µg/g.D.W.		125.25±26.56	130.54±40.15 Ins	74.07±5.04 P<0.001
Cd, µg/g.D.W.		0.04±0.004	0.05±0.003 Ns	0.08±0.005P < 0.001
Wat.Cont.	76.05±0.22	74.71±0.56 Ns	75.50±3.80 Ns	74.66±0.4 Ns

Table. 5 :Composit average of treatment for various period on Cd concentration in tissues(µg/g. dry wt.) in rats fed for dietary Cd & Li and Cd alone.

Tissue/ Diet	Liver	Kidney	Muscle	Composite average
Cadmium	5.01	6.82	0.12	a 3.98
Li & Cd	2.94	3.89	0.06	b 2.29
Composite	b	a	c	LSD 0.03
average	3.98	5.35	0.09	
a,b,c.Significantly at 5%				

Table. 6: Composite average of Cd concentration in the tissues (Ug/g. drywt) of rats fed Cd & Li and Cd alone following 4,14 and 28 days.

period of treat/ diet	4-days	14-days	28-days	Composit average
Cademium	0.95	3.58	7.42	a 398
Li & Cd	0.26	1.63	5.00	b 2.29
Composit average	c 0.60	b 2.61	a 6.21	LSD 0.30
a,b,c. Significantly differece at 5%				

Table 7: Composite average of dietary Cd & Li and Cd alone on the Cd concentration in the varios tissue in rats following 4,14 and 28 days.

Tissues/ period of treat.	4- days	14-days	28- days	Composite average
Liver	0.78	3.00	8.13	a 3.98
kidney	0.97	4.72	10.36	b 5.35
muscle	0.05	0.08	0.14	c 0.09
Composite average	c 0.60	b 2.60	a 6.21	LSD 0.36

a,b,c. Significant differece at 5%

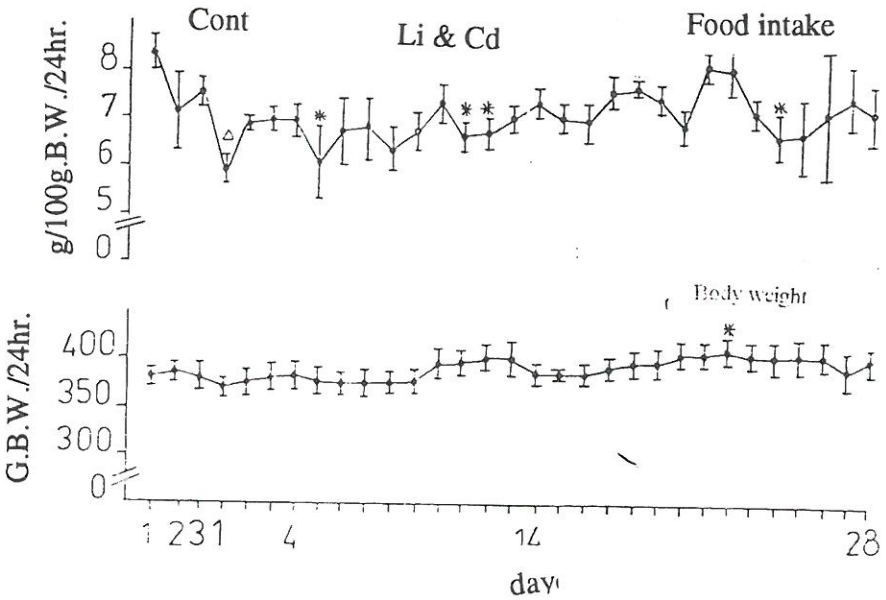

Fig. 1. Effect of Li & Cd diet on body weight and food intake 24hr. in rats. (Values are mean + SE.) n = 6.* P.<0.05.

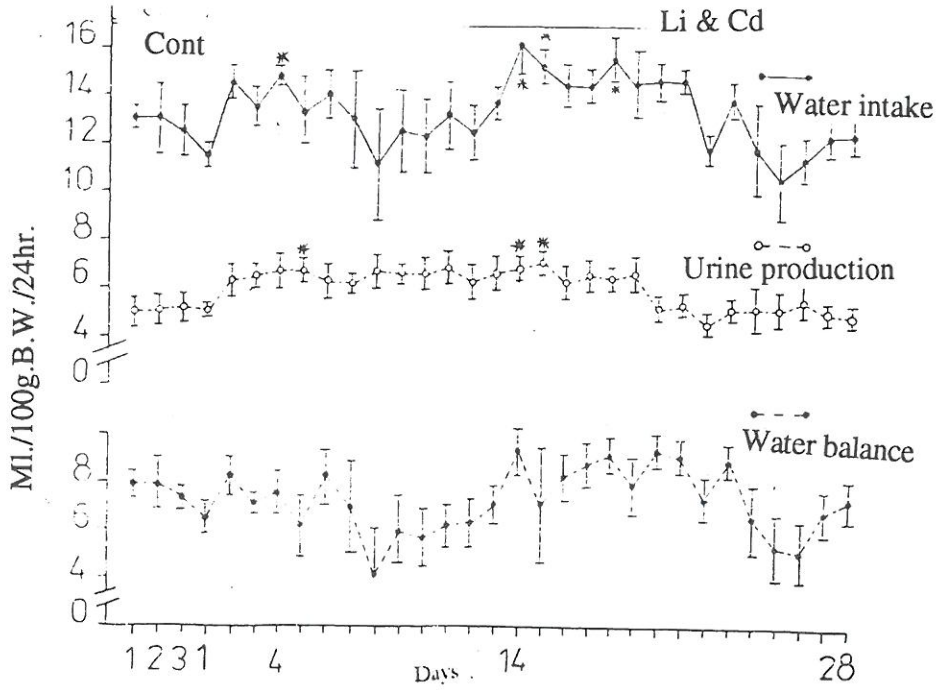

Fig 2: Effect of Li & Cd diet on water drink and urine production and water balance/ 24hr. in rats. (Value are mean + SE. n=6.* P< 0.05).

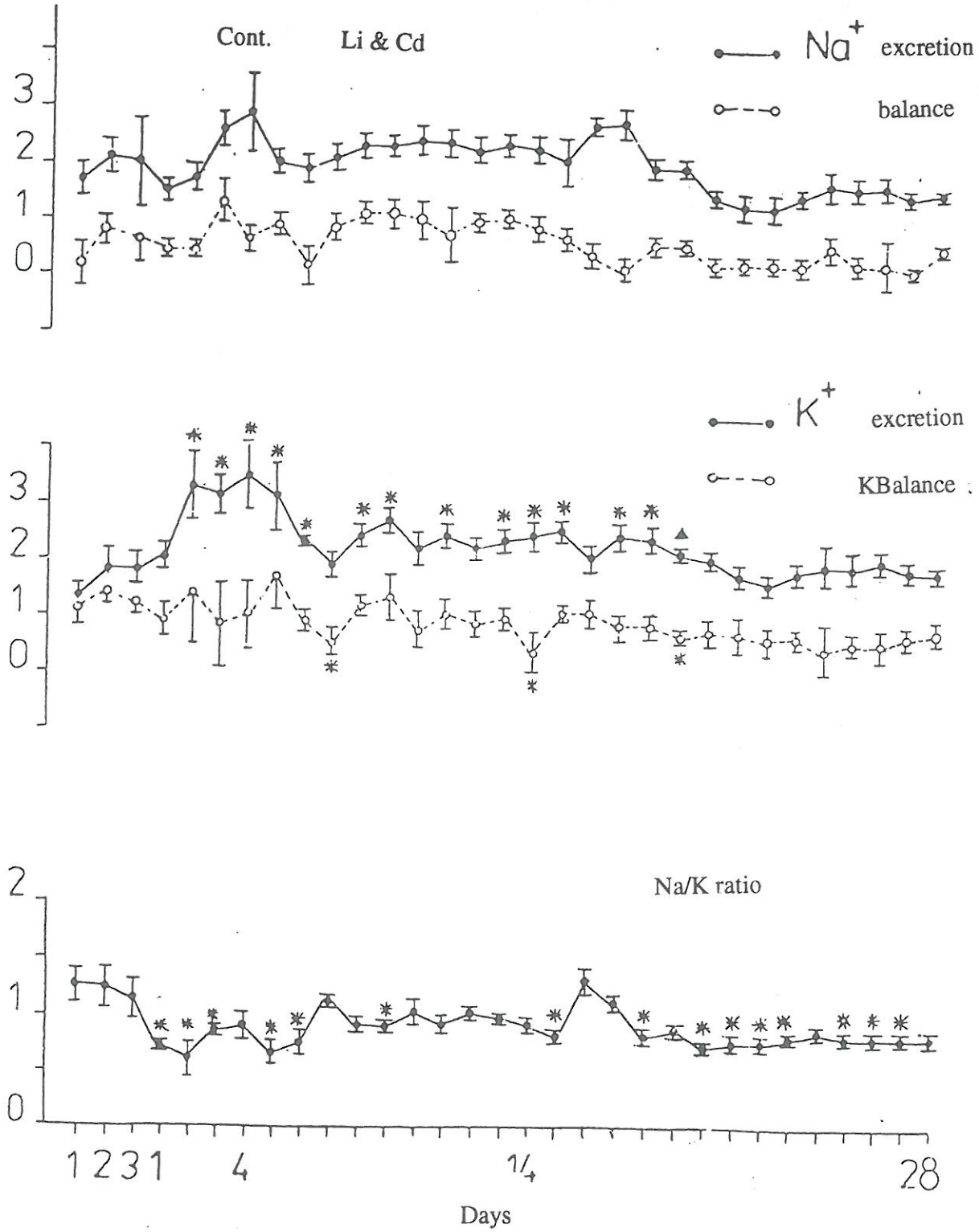

Fig 3. Effect of Li & Cd diet on urinary excretion and balance of Na and K in the rats. (Values are mean = SE. n= 6.* P< 0.05, ^P< 0.01.

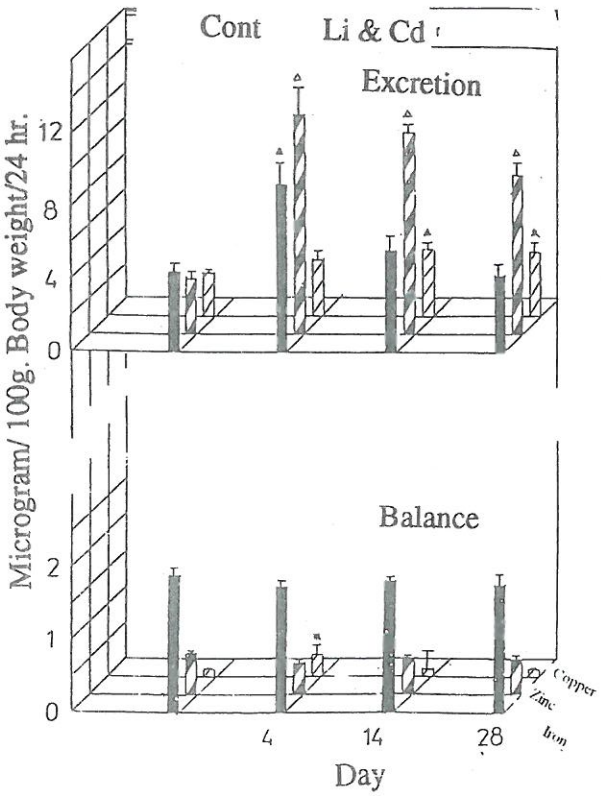

Fig.4: Effect of Li & Cd diet on urinary excretion and balance of Zn, Fe and Cu after 4.14 and 28 days of treatment/ Values are mean ± SE. n = 6. *P<0.05.

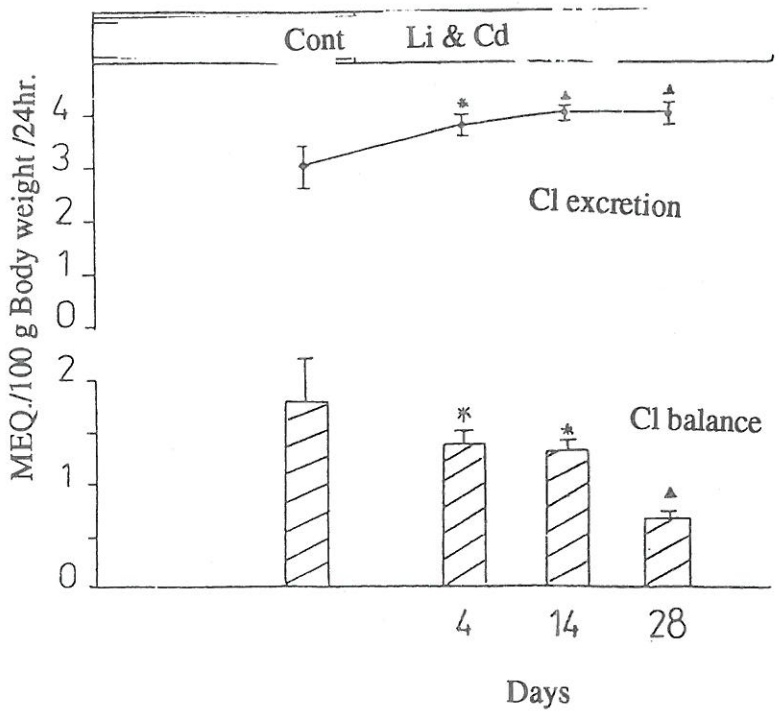

Fig. 5: Effect of Li & Cd diet on urinary excretion and balance of chloride following 4,14 and 28 days of treatment. (Values are mean ± SE. n=6 *P<0.05

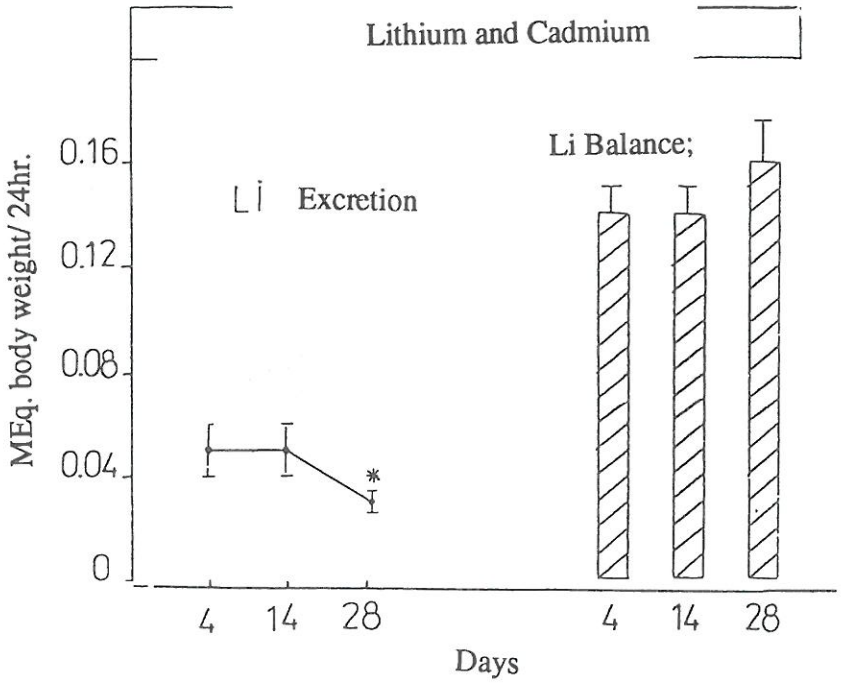

Fig6: Effect of Li & Cd diet on urinary excretion of and balance of Li following 4,14 and 28 - days of treatment in rats. (Values are mean ±SE) n=6. *P<0.05.

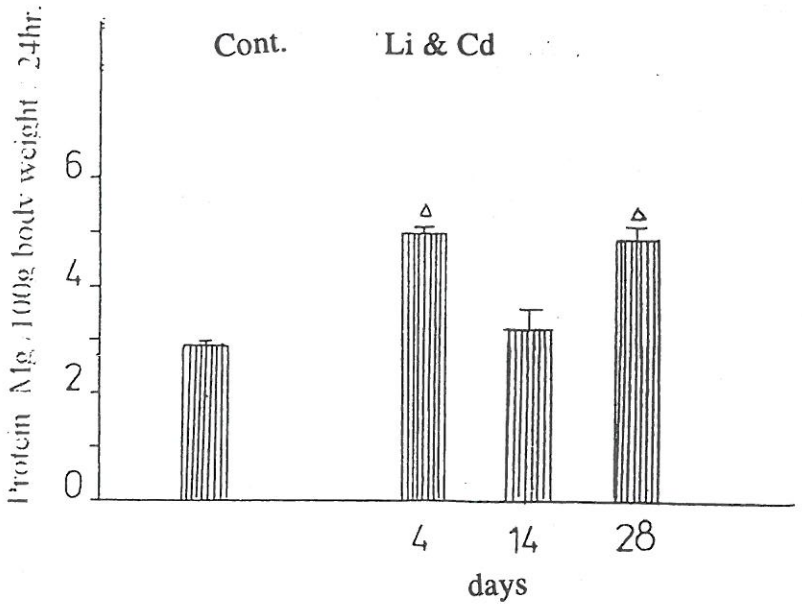

Fig7: Effect of Li & Cd diet onurinary excretion of protein following 4.14 and 28-days of treatment (Values are mean ± SE) n=6. * P<0·001.