pan-2-one) was more effective than AY-14,948 and was the most potent of the series in blocking the basal gastric secretion. The level of antigastric secretory activity of AY-18,672 is moreover similar to that observed with imipramine. Also, as with imipramine the stimulation of gastric secretion induced by reserpine is blocked by AY-18,672. It is of interest that AY-18,672 blocks the uptake of noradrenaline and is also more potent in this activity than AY-14,948[7]. Further, in studies utilizing the same compounds examined in the present studies AY-18,672 was the most active of the series in interfering in the uptake of noradrenaline[7]. Other drugs which prevent the uptake of noradrenaline, such as chlorpromazine and cocaine in addition to imipramine, are effective as inhibitors of the basal gastric secretion in the pylorus-ligated rat[6,11].

Zusammenfassung. AY-14,948 [4-Chlor-α,α-Dimethylphenethylaminopropan-2-on] setzt die basale Ausscheidung von Magensäure in der Ratte herab. Die Prüfung der strukturverwandten Verbindungen ergab, dass AY-18,672 [α,α-Dimethylphenethylaminopropan-2-on] in dieser Hinsicht wirksamer ist als AY-14,948, indem es auch die reserpinbedingte Erregung der Magensäureausscheidung blockiert.

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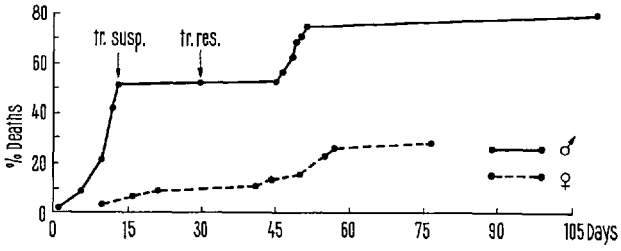
A Sex Difference in Some Toxic Effects of Lithium-Carbonate

Lithium carbonate is widely used in clinical trials against manic phases of the manic-depressive phychosis[1,2] and as prophylactic agent against recurrent depressions[3]. There is, therefore, a considerable interest in toxic effects after chronic treatment, using different ways of administration and different animal species[4-6].

Using lithium carbonate by gastric intubation in rats, consistently more pronounced toxic effects have been observed for male than for female animals under our experimental conditions. Male and female rats from Sprague Dawley strain weighing 180–210 g were kept on a standard diet (containing 5 g/kg of sodium chloride). The male rats were kept separated from the female animals, in a constant room temperature of 27 °C.

Lithium carbonate (Merck Co.) dissolved in water, (10 mg/ml) was administered daily by gastric intubation in a dose of 15 mg/100 g body weight.

Animals were allowed diet and tap water ad libitum. The parameters measured were body weight, survival time and blood non-proteic nitrogen. In all these parameters, in male rats more toxic effects than in the corresponding females have been observed.



Toxicity in rats receiving lithium carbonate (15 mg/100 g body weight per day).

Non-proteic nitrogen from blood of male and female rats after 15 days of treatment with lithium carbonate.

Control animals	Males	Females
0.33 ± 0.05	0.49 ± 0.02	0.35 ± 0.04

The results represent the average of 6 animals ± S.E.

In the Figure the survival time in both male and female animals is recorded. The toxic effect is higher in male rats. In this group the administration was interrupted after 15 days of treatment. During the days of interval no further deaths were observed while the animals rapidly died shortly after resumption of lithium carbonate.

The body weight decreased in both animal groups, but in male rats the decrease was about 30% more than in female rats.

The Table shows the changes in blood non-proteic nitrogen after 15 days of treatment in the 2 groups, again showing marked increase in male rats. The sex difference of lithium carbonate toxicity has not been reported in any of the reviews on the subject[7-10], and it is of interest to clinical investigators for the possibility that lithium carbonate may be more toxic in male human subjects during treatment of psychotic diseases.

Riassunto. Abbiamo notato una netta diversità di risposta tra ratti maschi e femmine durante il trattamento cronico con 15 mg/100 g di peso corporeo di carbonato di Litio, somministrato per sonda gastrica. La tossicità era molto più spiccata nei maschi che nelle femmine. Nei maschi la mortalità cessava con l'interruzione della somministrazione e riprendeva con il trattamento. L'azotemia determinata dopo 15 giorni di trattamento nei due gruppi, testimoniava pure valori significativamente più elevati negli animali maschi.

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