Table 2. *Effect of atropine on Ca-release induced by acetylcholine.* Each value (mean ±s.e. of 5 experiments) is expressed in %. The amount of Ca^{2+} in microsomes at 0 time has been considered as 100%.

Incubation time	0	30 s	90 s	240 s
Control	100	98 ± 1·0	93 ± 1·6	86 ± 1·0
Acetylcholine (5×10^{-5} M)	100	93 ± 0·8	86 ± 1·2	81 ± 1·4
Atropine (3×10^{-6} M)	100	99 ± 201	92 ± 1·8	87 ± 1·9
Acetylcholine (5×10^{-5} M) + atropine (3×40^{-6} M)	100	96 ± 1·5*	91 ± 1·3*	87 ± 2·0*

The paired *t*-test was performed.
* Significantly different from the value in the presence of acetylcholine alone ($P < 0{\cdot}05$).

vesicular structures. Most vesicles consisted of smooth muscle membranes. There were no intact mitochondria. The microsomal fraction used contained high concentrations of markers of plasma membrane, such as acetylcholinesterase, Na-, K-ATPase and 5′-nucleotidase.

The rate of Ca-release was significantly increased by acetylcholine (5×10^{-5} M) at all incubation times (Table 1). This increase was blocked by atropine (3×10^{-6} M) which had no significant effect on Ca-release in the absence of acetylcholine (Table 2). Thus release of Ca^{2+} induced by acetylcholine seems to be due specifically to acetylcholine receptors. However, histamine did not increase Ca-release significantly (Table 1). Baudouin, Meyer & others (1972) and Baudouin-Legros & Meyer (1973) demonstrated that angiotensin II increased the release of ^{45}Ca from the microsomes of rabbit aorta, while analogues of angiotensin II devoid of intrinsic activity failed to alter the release of ^{45}Ca. The present results concerned with the release of ^{45}Ca and the findings of Baudouin & others (1971) and Baudouin-Legros & Meyer (1973) suggest that the mechanical response induced by the drugs which affect the smooth muscle tone is, at least partially, initiated by a translocation of Ca^{2+} from the binding stores in cellular membranes. Furthermore the results in the present study suggest that the initial contraction of the rabbit taenia coli induced by acetylcholine is more dependent on the release of Ca from the cellular sites of storage than that induced by histamine, while the response to histamine is the more dependent on external Ca^{2+}.

July 19, 1977

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Mercury content of medicinal lithium preparations

FOLMER NIELSEN KUDSK, MOGENS SCHOU*, *Aarhus University Institute of Pharmacology, Aarhus, and The Psychopharmacology Research Unit, Aarhus University Institute of Psychiarty, Risskov, Denmark*

Lithium salts used prophylactically to attenuate or prevent recurrences of manic-depressive disease, are given to patients for long periods (Baastrup & Schou, 1967, Schou, 1976). Because of this the preparations should not contain impurities that might accumulate and exert toxic actions. Ordinary lithium hydroxide is bought for the extraction of ^{6}Li, and the residue is then made available for general use. Analysis of ^{6}Li depleted materials reveals that there is a significant increase of the content of mercury as a result of the ^{6}Li extraction procedure used (Lithium Corporation of America, private communication, 1976). For this reason some producers avoid using ^{6}Li-depleted material for lithium products intended for medicinal purposes. Other producers may not be equally cautious. We have therefore analysed 23 preparations from 14 countries using an unpublished method by Nielsen Kudsk for determination of total mercury. This is based upon a modification of the analytical principle described by Schütz (1969).

* Correspondence: Psychiatric Hospital, DK-8240 Risskov, Denmark.

Tablets or capsules were ashed by combustion at 1000° in a quartz tube in a stream of pure oxygen, and mercury liberated together with the combustion gas was trapped in an acid potassium permanganate solution. The amount of mercury collected was determined spectrophotometrically by atomic absorption, after reduction with stannous chloride and liberation from solution by shaking and aeration with an atmospheric air stream, using a Varian atomic absorption spectrophotometer AA-6, equipped with a 17 cm gas cuvette having quartz windows.

The detection limit is about 1·5 ng mercury per

Table 1. *Lithium preparations and their mercury content. Detection limit 1·5 ng per sample (1 tablet).*

Brand name	Drug company	Country	Lithium salt	Amount of salt per tablet (mg)	Lithium content per tablet (mmol)	Hg content per tablet mean (ng) ± s.d.	Number of tablets (n) analysed
Camcolit	Norgine	England	Carbonate	250	6·8	3·9 ± 1·5	(4)
Carbolith (ICN)	Winley-Morris	Canada	Carbonate	300	8·1	2·3 ± 0·9	(4)
Eskalith	S.K.F.	U.S.A.	Carbonate	300	8·1	<1·5	(6)
Limas	Taisho	Japan	Carbonate	200	8·1	<1·5	(4)
Litarex	Dumex	Denmark	Citrate	564	6·0	<1·5	(4)
Lithane	Roerig	U.S.A.	Carbonate	300	8·1	2·6 ± 1·5	(2)
Lithane	Pfizer	Canada	Carbonate	300	8·1	2·2 ± 0·7	(6)
Lithii Carbonas	DAK	Denmark	Carbonate	300	8·1	<1·5	(4)
Lithionit Duretter	Hässle	Sweden	Sulphate	330	6·0	<1·5	(4)
Lithium Negroni	Negroni	Italy	Glutamate	600	3·9	3·6 ± 1·2	(5)
Lithium Scharffenberg	Scharffenberg	East Germany	Adipate	630	8·0	34·8 ± 3·0	(14)
Lithium Carbonicum	Spofa	Czechoslovakia	Carbonate	300	8·1	6·5 ± 1·5	(9)
Lithium Carbonicum	Polfa	Poland	Carbonate	250	6·8	38·4 ± 2·1	(7)
Lithium-Orotat	Nadrol	West Germany	Orotate	150	0·9	21·5 ± 1·2	(5)
Lithium Phasal	Pharmax	England	Carbonate	300	8·1	<1·5	(4)
Lithizine	Paul Maney	Canada	Carbonate	300	8·1	<1·5	(4)
Lithonate	Rowell	U.S.A.	Carbonate	300	8·1	1·7 ± 0·9	(5)
Lithoduron	Orion	Finland	Carbonate	400	10·8	31·9 ± 1·9	(7)
Lithii Carbonas	Orion	Finland	Carbonate	50 mg powder		40·1 ± 3·2	(8)
Manialith	Muir & Neil	Australia	Carbonate	250	6·8	1448 ± 224	(22)
Plenur	Lasa	Spain	Carbonate	400	10·8	4·2 ± 1·5	(4)
Quilonorm	Dauelsberg	West Germany	Acetate	536	8·1	<1·5	(4)
Quilonorm Retard	Dauelsberg	West Germany	Carbonate	450	12·2	<1·5	(4)

sample (s.d. in duplicate determinations about 0·8 ng). Four or more analyses were made on each preparation.

In some cases the method of Magos & Clarkson (1972) was used to differentially determine the content of inorganic and organic mercury in the tablets.

The lithium preparations fell in three groups on their mercury content (Table 1): in 17 preparations this content was close to or below the detection limit; three preparations contained 20–40 ng per tablet; one contained about 1450 ng per tablet; and a lithium carbonate preparation in powder form had a mercury content of about 40 ng per 50 mg (the supplier having sent tablets with the highest mercury content later submitted a different batch of tablets which contained 27·6 ± 2·4ng Hg per tablet). As expected, differential analysis showed that the mercury in four of the preparations with the highest content was inorganic.

During maintenance treatment with lithium the dosage rarely exceeds 10 and never 15 tablets per day even when preparations with a low lithium content per tablet are used. This number of tablets would lead to mercury intakes with the three classes of preparations up to 0·05, 0·6 and 3–22 μg day^{-1}, respectively. This is well below the provisional tolerable weekly intake of 0·3 mg total mercury estimated by WHO (1972), especially since the mercury in the lithium preparations is inorganic, of which only about 10% is absorbed from the digestive tract.

Thus the amount of mercury administered with lithium tablets can probably be considered without direct toxicological significance. However, the ingestion of mercury with lithium preparations may occasionally give rise to allergic manifestations such as cutaneous eruptions in predisposed individuals.

We thank the psychiatrists and producers who sent us lithium preparations for analysis.

August 5, 1977

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