

BRIEF COMMUNICATION

Plasma Lithium as a Marker of Lithium Chloride in Wild Norway Rats (*R. norvegicus*)

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STERNER, R. T. *Plasma lithium as a marker of lithium chloride in wild Norway rats* (*R. norvegicus*). *PHYSIOL BEHAV* **47**(5) 1013–1015, 1990.—A parametric study was conducted to determine the efficacy of plasma lithium as a marker of lithium chloride ingestion and dose in conditioned taste aversion research with rats. Separate groups of male wild Norway rats were given 60, 120 and 240 mg/kg doses of a lithium chloride solution by gavage. At 0.5, 1, 2, 24, 48 and 72 hr after dosing, 2–3 cc samples of blood were taken from each rat; these were centrifuged and 0.5–1.0 cc specimens of plasma were frozen for later analysis. Flameless atomic absorption spectroscopy was then used to determine quantities (ppm) of lithium in these specimens. Analyses of the data revealed that plasma lithium was both dose and time dependent; however, uptake and elimination of the lithium was rapid (≤ 48 hr for 60 and 120 mg/kg-dosed rats). Results showed that measurements of plasma lithium has some utility as a marker of lithium chloride ingestion in laboratory studies, but limited potential in field studies, of conditioned taste aversion with rats.

Conditioned taste aversion Lithium chloride Plasma lithium Biomarker

NUMEROUS attempts to control unwanted foraging of crops and predation of livestock by wildlife via use of conditioned taste aversion (CTA) have been reported (2, 3, 5, 7). Nevertheless, few articles have addressed the potential application of CTA in reducing rodent damage of field crops and stored commodities [see (9)]. This is noteworthy because: (a) most laboratory studies of CTA use the rat as the animal model and (b) alteration of rat consummatory behaviors with CTA is well documented [see (9)].

One difficulty in developing CTA techniques for agriculture is the lack of a reliable method for estimating either the dose of aversive drug ingested by wild rodents or the number of dosed animals in wild populations (11). Lithium chloride (LiCl) is by far the most frequently used emetic [see (9)]. Although prior reports have described the pharmacokinetics of lithium in humans and pigs (1,6), the plasma lithium (Li) response of rats administered single doses of LiCl commonly associated with CTA is lacking.

The present study examined the timecourse of Li uptake and elimination in the blood of wild Norway rats. If Li reflects LiCl ingestion and dose for prolonged periods (i.e., 5–10 days), it would offer a distinct advantage over supplemental-type markers for CTA research—no adulteration of the novel tastant used to induce CTA.

METHOD

Rats

One hundred and five male wild Norway rats, weighing

between 300–482 g at the time of LiCl gavage, were used. All rats were obtained from a wild rat colony (10.5-m dia. breeding pit) maintained at the Center. Throughout the study (7–14 days acclimation plus a maximum of 3 days postdosage), rats were housed in individual stainless steel cages (25 × 20 × 18 cm) located in a temperature-controlled room (25 ± 2°C), with a 12:12-hr light/dark schedule (0600–1800 and 1800–0600 hr, respectively). Except for a 24-hr fast prior to gavage, the rats were maintained on ad lib Purina Rat Chow (Ralston Purina Co., St. Louis, MO) and water.

LiCl

Three solutions of technical grade LiCl (Lithium Corp. of America, Bessemer City, NC) and deionized water were prepared. These 4.68, 8.75 and 18.75 percent solutions (w/v) allowed for rats to be gavaged with 60, 120 and 240 mg/kg LiCl using approximately equivalent volumes of fluid.

Design and Procedures

The study was accomplished in 5 replications that encompassed a 44-day period. In each replication, 6 rats received a dose of 60 mg/kg LiCl, 6 received 120 mg/kg, 6 received 240 mg/kg, and 1 rat received a dose of deionized water equal to the largest volume of LiCl given. This latter rat was included as a monitor of specimen contamination.

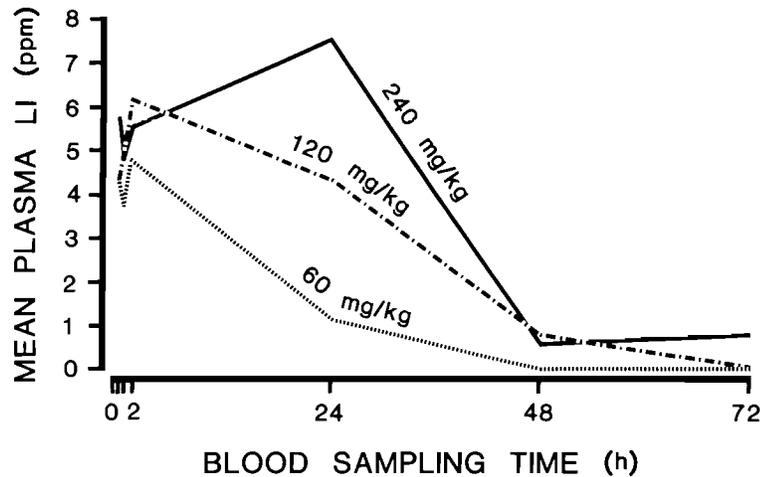


FIG. 1. Mean plasma Li (ppm) values for rats in the 60, 120 and 240 mg/kg LiCl groups at each of the 0.5, 1, 2, 24, 48 and 72 hr sampling times—the dose \times sampling time interaction.

For the collection of blood samples, rats were anesthetized using ether (bell jar) and immediately decapitated with a small animal guillotine (Harvard Instrument Co., Ayer, MA). About 2–3 cc of blood were collected from each rat in a 5-cc sodium heparin Vacutainer Tube (Baxter Healthcare Corp., McGaw Park, IL). The blood was then centrifuged (International Equipment Co., Needham, MA) for 15 min at 4,000 rpm, and 1–2 cc of plasma was frozen for later analysis.

Flameless atomic absorption spectroscopy was used to determine the quantities (ppm) of Li in these specimens (10). A single-blind procedure was followed during the analyses. Specifically, specimens were coded and blinded from the chemist. Duplicate analyses were run on 10 split specimens; computation of correlation coefficient between the 10 duplicate pairs yielded excellent agreement ($r = .98$; $p < 0.005$).

Plasma Li values (nondetected = 0 ppm) were analyzed as a 3 (dose) \times 6 (sampling time) analysis of variance (ANOVA), with sampling time nested in dose (12). Significant sources of variance were further assessed using Duncan's New Multiple Range Test (4).

RESULTS AND DISCUSSION

All ANOVA effects were significant: dose, $F(2,72) = 8.32$, $p < 0.0006$; sampling time, $F(5,72) = 26.86$, $p < 0.0001$; and dose \times sampling time, $F(10,72) = 2.37$, $p < 0.02$. Thus, uptake and elimination of Li from the blood of rats was both dose and time dependent. The 120 and 240 mg/kg doses produced greater Li uptake than the 60 mg/kg dose, with elimination of Li for the 60 and 120 mg/kg doses completed within 72 hr.

The main effect of dose reflected a significant monotonic increase of about 1 ppm mean Li among groups. Mean Li values for rats in the 60, 120 and 240 mg/kg groups were 2.3, 3.4 and 4.1 ppm, respectively. Duncan Range Tests showed that the mean Li value for the 60 mg/kg group was significantly less than the means for the 120 and 240 mg/kg groups.

The main effect of sampling time was straightforward. Mean Li values for the 0.5, 1, 2, 24, 48 and 72 hr blood collections were 4.8, 4.4, 5.5, 4.3, 0.4 and 0.2 ppm, respectively. Duncan Range

Tests revealed that the 48 and 72 hr means were significantly less than all other means.

Figure 1 shows the dose \times sampling time interaction effect. This interaction is attributed to the divergence of ppm Li values found for the 3 LiCl groups within the first 24 hr. The highest mean Li value (7.5 ppm) occurred for the 240 mg/kg group 24 hr postgavage; this was significantly greater than all other cell means. Additionally, the 1.1 ppm Li mean for the 60 mg/kg group 24 hr postgavage, as well as all 48 and 72 hr means for the 3 groups, were less than other cell means. This indicates that a dose of 240 mg/kg LiCl drastically increased the plasma Li level in rats within 24 hr of dosing relative to levels observed for the 60 and 120 mg/kg groups. Differences in plasma Li among groups were nonexistent by 48 hr, and only 240 mg/kg-dosed rats remained marked for 72 hr.

The effective LiCl dose linked with reliable CTA in rats is 120 mg/kg (8). Although significant ANOVA effects characterized the current data, rapid (<72 hr) elimination of Li from blood severely limits the practicality of Li as a marker of CTA. Such elimination would require that rats be treated and caught within 2 days of LiCl ingestion to ensure estimation of either the sufficiency of LiCl dose or proportion of a colony that had ingested the emetic. This is a prohibitive constraint. Neophobic behaviors and irregular dosings of rats would necessitate at least several days for bait (LiCl) consumption and Li monitoring. This, coupled with variable bait-ingestion patterns and dominance hierarchies affecting bait pickup by rats, suggests some potential for Li as a marker of CTA in laboratory-based studies, but the probable inadequacy of Li in field-based studies with wild populations.

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