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Interference of Sodium Chloride in the Determination of Lithium by Atomic Spectrometry

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Atomic spectrometry has been shown to be very attractive in the determination of lithium in biological samples because of its accuracy and convenience. However, chlorine and sodium have been reported to have interference in either flame or graphite furnace atomic spectrometry. We have investigated the interferences of sodium chloride in atomic spectrometric determination of lithium for biological samples, by nature, contain rather large amount of sodium chloride. The suppressive effect of chlorine has been found in all three kinds of detection modes (graphite furnace atomic absorption, flame atomic emission and flame atomic absorption). The possible mechanism was due to the formation of thermostable lithium chloride, which reduced the number of free lithium atoms in atomization stage. In flame atomic emission spectrometry, sodium caused a spectral interference and produced an emission signal at wavelength 670.8 nm.

Keywords: Lithium, Interference of sodium chloride, Atomic spectrometry.

INTRODUCTION

Trace elements play essential roles in the maintenance of physiological processes and appear to be consistently related to malfunctioning of the cardiovascular system. For years scientists have investigated the relationship between cardiovascular diseases and different kinds of elements, such as lithium, sodium, copper, zinc, manganese, calcium and magnesium[1-3], *etc*. Lithium levels in biological samples are to be especially attractive because it is often used for the calculation of lithium clearance[4], which is considered the best way to determine the delivery of water and sodium from the proximal tubules[5]. Besides Li is proved as an essential micronutrient and has a lot of biological action[6]. Therefore, it is very important to determine Li accurately in biological samples for clinical and medical research investigations. Several analytical methods have been developed for the determination of Li in biological samples, such as flame atomic emission spectrometry (FAES)[7-9], flame atomic absorption spectrometry (FAAS)[8,10], graphite furnace atomic absorption spectrometry (GFAAS)[1,11-18], inductively coupled plasma atomic emission spectrometry (ICP-AES)[19-21], inductively coupled plasma mass spectrometry (ICP-MS)[13,22], isotope dilution mass spectrometry (IDMS)[23], ion-selective electrode (ISE)[8] *etc*.

Among these techniques, methods of atomic spectrometry (including FAES, FAAS, GFAAS) have been shown to be very attractive for their accuracy and convenience. Flame atomic emission spectrometry and flame atomic absorption spectrometry are routinely used for monitoring therapeutic concentration of Li in serum of patients being treated with Li-containing drugs in some clinical laboratories. They were often employed as reference methods in comparison with other analytical methods because of their reliability and excellent precision[8]. Besides, FAES was also reported to determine Li at ultratrace levels in biological fluids[9]. Graphite furnace atomic absorption spectrometry is the preferred technique to determine physiological level of trace Li in biological samples since it requires low sample volume and provides adequate sensitivity, low detection limit and the possibility of measurement after just a simple dilution step (no need for sample mineralization). However, chlorine and sodium have been reported to have interference in either flame or graphite furnace atomic spectrometric determination of Li. Chlorine was reported to have distinctively suppressive effect on Li signal and influence the accuracy of analysis in GFAAS[11,12]. The experiment of ICP-AES showed that even at a low concentration of Na, the remarkable enhancement of Li intensity was observed[24].

In this paper, we investigated the interferences of sodium chloride in the determination of Li by GFAAS, FAES and FAAS, for biological samples, by nature, contain rather large amount of NaCl. The purpose of this study is to elucidate the mechanism of the interferences. Thus it is possible to select right analytical performances for the accurate measurement of Li by atomic spectrometry.

EXPERIMENTAL

All measurements were carried out using a Thermo S2 atomic absorption spectrometer (England). The analytical wavelength was set at 670.8 nm resonance line for the determination of Li by absorption or emission detection. For the measurement of the background of lithium chloride, the wavelength was set at 283.3 nm. The bandwidth of the spectrometer used was 0.2 nm. A GFS 97 graphite furnace with autosampler (England), Extended Lifetime Cuvettes (Thermo Elemental, part No. 9423 393 95041 Germany) were used for GFAAS determination. Argon was used as purge gas. The light source was a Li hollow cathode lamp (Thermo, United Kingdom) operating at 7 mA for Li determination. LiCl background signal was measured by a deuterium lamp. A stoichiometric air-acetylene flame was used for FAES and FAAS determinations. Thermo SOLAAR software was employed for the operation of the instrument.

A 100 mmol L^{-1} Li stock standard solution was employed for making standard working solutions by dilution before use. Grade of reagents and chemicals were: lithium carbonate (Li_2CO_3), extra pure (for making Li stock standard solution); nitric acid (HNO_3), guaranteed reagent; NaCl, spectrum pure. Chemicals employed without specific indications were of analytical reagent. All of them were purchased from Sinopharm Chemical Reagent Co., Ltd., Shanghai, China. High purity double distilled water was used for the preparation of all solutions.

Analytical procedure

GFAAS: The time-temperature program was based on our previous work[12] with a little modification of the ash time for the observation of the stability of LiCl during that stage. Volumes of 5 µL were injected into the atomizer for analysis.

FAES and FAAS: Samples were aspirated to the flame directly for the determination of emission and absorption signals. Results are expressed as mean ± standard deviation (SD) of triplicate determinations.

Statistical analysis: Data were analyzed as mean ± SD and evaluated statistically by one-way ANOVA with post Tukey's multiple comparison test. GraghPad Prism software was used to test whether slopes of linear regression curves were significantly different. Significance was determined as $P < 0.05$.

RESULTS AND DISCUSSION

Graphite furnace atomic absorption spectrometry

LiCl did not lose during the ash step: Severe interferences caused by the chloride matrices were considered one of the major problems encountered in the GFAAS determination of Li. It was believed that the suppression of the atomic absorption signal for Li in the presence of chloride was probably due to the formation of volatile LiCl and much of Li was lost from the graphite furnace in the form of gaseous molecular compound without contributing to the atomic absorption signal[18]. Katz and Taitel[25] pointed out that the observed signal decrease was caused by the reaction between gaseous Li and Cl and consequent formation of LiCl, which was swept out in the gaseous state from the graphite tube by the purge gas.

As the b.p. of LiCl (1360 °C) was much higher than the ash temperature for the determination of Li, it was unlikely that LiCl was lost prematurely during the ash stage. It was more likely that this kind of interference resulted from the binding of Li as a thermostable vapor phase LiCl during the atomization stage, thereby preventing some portion of Li from absorbing atomic radiation[26]. In order to obtain a deeper insight into the interference mechanism of chlorine in GFAAS, we measured 1 µmol L^{-1} Li in 0.5 % HNO_3 and in 0.03 mol L^{-1} NaCl, respectively. Then we measured 1 µmol L^{-1} Li in 0.03 mol L^{-1} NaCl by stopping time-temperature program before atomization step and run a complete cycle of the time-temperature program after addition of 0.5 % HNO_3, which was proved a very effective chemical modifier for removing the interference of chlorine in our previous work[11,12]. As shown in Fig. 1, 0.03 mol L^{-1} NaCl greatly suppressed Li signal. This kind of suppression could be eliminated by the addition of extra 0.5 % HNO_3. This result implicated that LiCl did not lose but retained from the ash step by adsorption on the graphite tube[26]. The addition of HNO_3 released Li from LiCl by formation of volatile hydrochloric acid, which was evaporated during the dry and ash steps.

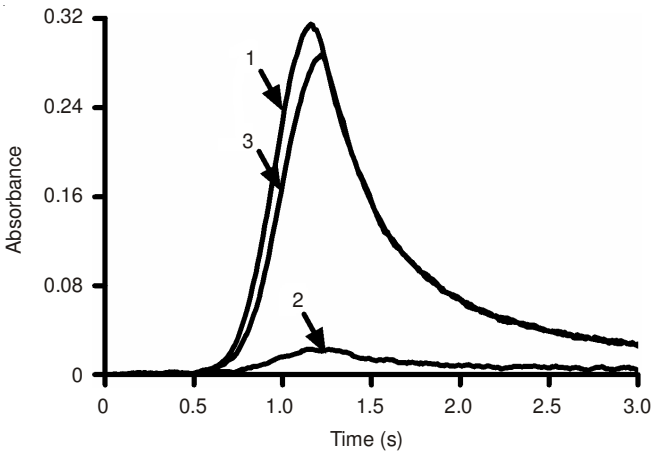

Fig. 1. Profiles of Li signals. Li concentration was 1 µmol L^{-1}. The media were: 1 = 0.5 % HNO_3; 2 = 0.03 mol L^{-1} NaCl; 3 = 0.03 mol L^{-1} NaCl, by a measurement manner of stopping time-temperature program before atomization step then performing a complete program after addition of 0.5 % HNO_3

Background absorption was LiCl concentration-dependent: To confirm that LiCl was not vaporized during the ash step, we measured LiCl background signal using a deuterium lamp at the wavelength 283.3 nm. Concentrations of LiCl were 0.01, 0.1 and 1 mol L^{-1}. The time-temperature program was exact the same as for Li determination. No apparent signal of LiCl was monitored during the dry and ash steps, but the peak was occurred during the atomization step. This background absorption was LiCl concentration-dependent (Fig. 2).

Prolonging ash time did not reduce LiCl background: To further demonstrate that LiCl did not lose during the ash step, we measured LiCl background by varying the ash time. The ash times for Figs. 3A, B and C were 10, 30 and 50 seconds respectively. There seemed no apparent differences among them.

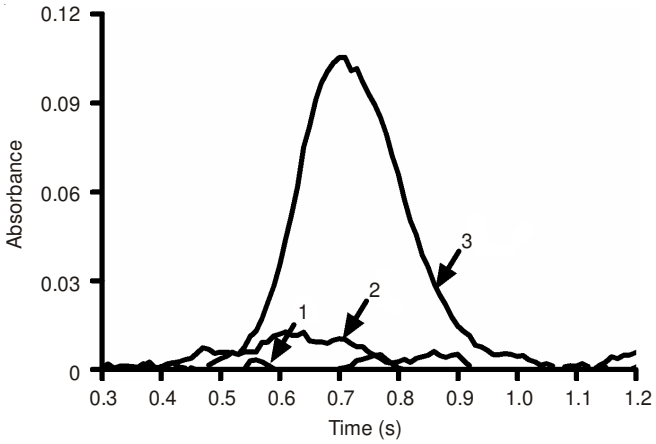

Fig. 2. Background absorption of LiCl. Background signals were measured at the wavelength 283.3 nm using a deuterium lamp. 1, 2, 3 = 0.01, 0.1, 1 mol L^{-1} LiCl, respectively

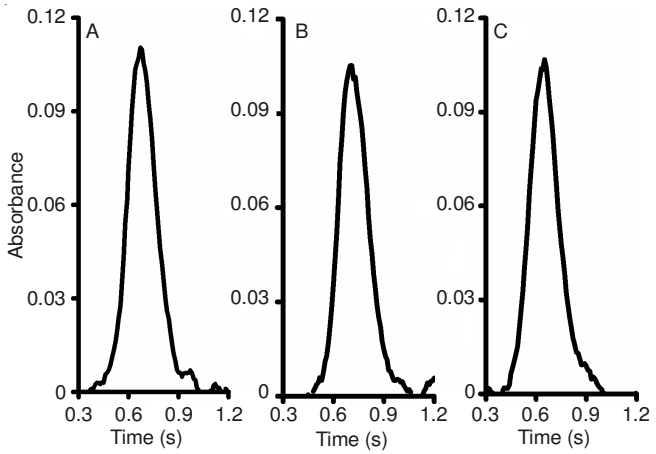

Fig. 3. LiCl background signals with different ash time. Background signals of 1 mol L^{-1} LiCl were measured at the wavelength 283.3 nm using a deuterium lamp. Ash times of the GFAAS were 10, 30 and 50 seconds for Panels A, B and C, respectively

Flame atomic emission spectrometry

Interference of NaCl: We tested NaCl interference in FAES by comparing Li standard curves in the presence of 0-0.3 mol L^{-1} NaCl. Fig. 4 shows that NaCl free standard curve bended a little bit away from the concentration axis because of the ionization interference. The addition of 0.1-0.3 mol L^{-1} NaCl overcame the issue, but caused the change of the slope of the standard curves. The more NaCl contained in Li standard solutions, the lower of its slope would be. GraghPad Prism software was employed to test whether slopes of Li standard curves in 0.1-0.3 mol L^{-1} NaCl solutions were significantly different. The result showed that the differences were extremely significant with P value < 0.001. It meant that Cl might suppress Li signal in FAES like its similar effect in GFAAS. Another finding was that there were apparent intercepts on Y axis of Li standard curves in different concentrations of NaCl solutions.

Chlorine suppressed Li signal: To confirm the suppressive effect of Cl in the determination of Li by FAES, we measured the emission signals of 10 µmol L^{-1} Li in different concentration of HCl solutions. Fig. 5 shows a dose-effect of HCl on suppressing Li signal in FAES. This result demonstrated that the suppressive effect on Li signal was truly come from Cl.

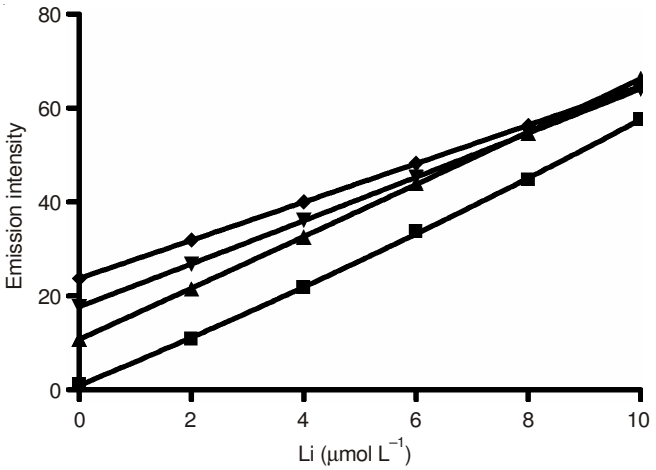

Fig. 4. Standard curves of lithium in different concentrations of NaCl (FAES). NaCl (mol L^{-1}): ■ = 0; ▲ = 0.1; ▼ = 0.2; ◆ = 0.3

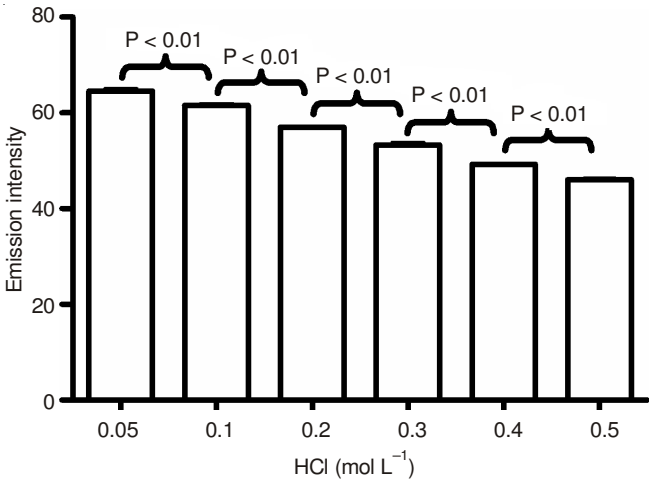

Fig. 5. Suppressive effect of chlorine. The emission intensities of 10 µmol L^{-1} Li in different concentration of HCl solutions were measured by FAES at 670.8 nm

Spectral interference of Na: Next we tried to find the cause of the intercept on the Y axis of the Li standard curves. Fig. 6A indicates that the emission intensity at the wavelength 670.8 nm was NaCl concentration-dependent. Sodium nitrate produced similar results.

To reveal whether this kind of emission signal was from Li contained in the reagents or from the interference of Na, we determined emission intensities of saturated solutions of NaCl, which were prepared with 1, 2, 3, 4 and 5-fold amount of NaCl solubility respectively, after 5-fold dilution. If the emission signal was appear in Li containing reagent, the emission signal would be increased accompanied with the adding amount of NaCl. If the emission signal was caused by Na, which was constant in the saturated solutions no matter how much NaCl over added at a certainty temperature, the emission signals should be same. As shown in Fig. 6B, the over addition of NaCl to the saturated solution caused a little increase of emission intensity. Tukey's multiple comparison test was used to compare the differences between the two contiguous groups and all of the P values were < 0.01. This meant that Li was truly contained in the test reagent but ultra-trace. As the emission signals increased slightly and was not

proportional to the adding amounts of NaCl, we believe that the intercept on the Y axis was mainly come from the spectral interference of Na. Spectral interference could not be compensated by the method of standard-addition. The interferent and the analyte need be separated prior to the measurement.

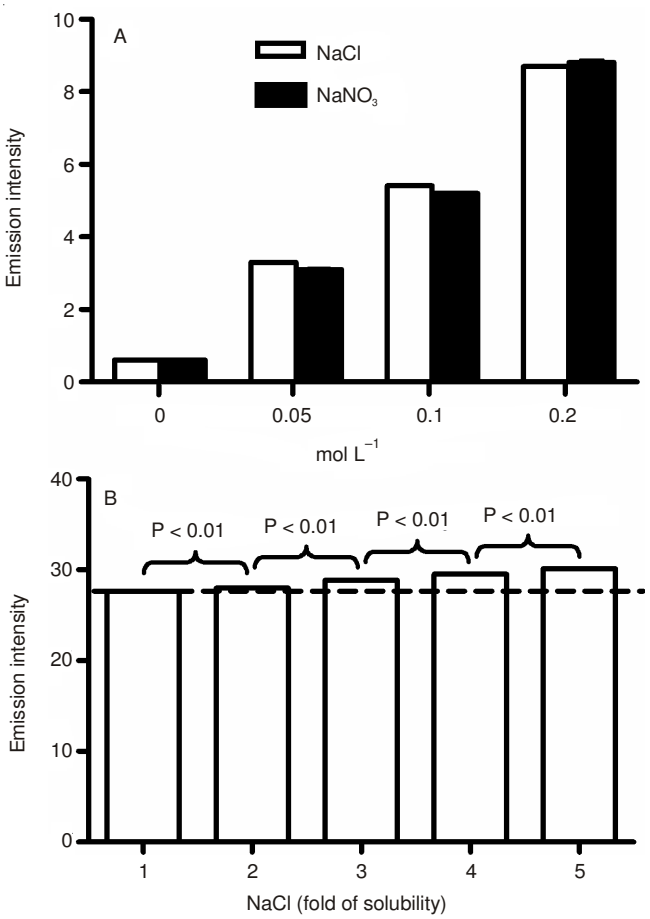

Fig. 6. Spectral interference of Na in FAES. Panel A shows the emission intensities of different concentrations of NaCl and $NaNO_3$. Panel B is the emission intensities of NaCl saturated solutions (5-fold dilution) prepared by 1, 2, 3, 4 and 5-fold amounts of NaCl solubility, respectively. The emission wavelength was 670.8 nm

Flame atomic absorption spectrometry

The solutions used for FAAS were the exact same as those for FAES and the results were shown in Fig. 7. The suppressive effect of Cl could also be seen in this detection mode, but no apparent spectral interference of Na appeared. Tiny ionization interference was still existed in NaCl free solution. The linearity of the standard curves seemed quite good though the absorbance was a little bit too low at this concentration range.

Determination of Li in serum and urine by GFAAS: As the interference of NaCl, we strongly suggest to use GFAAS with efficient chemical modifier for the physiological level of Li determination in biological samples. Table-1 shows the Li concentrations in hypertensive patients measured by GFAAS using HNO_3 as chemical modifier according to the methods reported previously[11,12]. *t*-Test was applied to examine whether the results between males and females differed significantly at the 95 % confidence level limit. There were no statistically significant differences (serum Li, P = 0.145; urinary Li, P = 0.756).

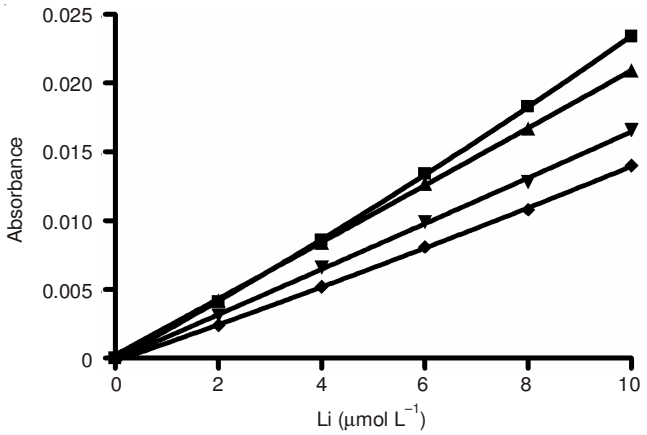

Fig. 7. Standard curves of lithium in different concentrations of NaCl (FAAS). NaCl (mol L^{-1}): ■ = 0; ▲ = 0.1; ▼ = 0.2; ◆ = 0.3

Conclusion

Taken all evidences together, we concluded that the suppressive effect of Cl in the determination of Li by atomic spectrometry could be seen in all three kinds of detection modes owing to the formation of thermostable LiCl, which reduced the number of free Li atoms during atomization stage. This kind of interference could be eliminated by chemical modifiers in GFAAS and compensated by standard addition in FAES and FAAS. In FAES, there existed a spectral interference of Na, which had to be preliminarily separated from sample matrix for the accurate determination of Li.

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TABLE-1
LI CONCENTRATION IN HYPERTENSION PATIENTS [MEDIAN (25–75 PERCENTILE)]

Sample	Total (n = 116)	Male (n = 73)	Female (n = 43)	P
Serum	0.26 (0.18,0.53)[a]	0.27 (0.17,0.66)[a]	0.24 (0.18,0.34)[a]	0.145
Urine	5.34 (3.76,7.48)[b]	5.32 (3.68,7.86)[b]	5.26 (4.07,7.28)[b]	0.756

[a]μmol L^{-1}, [b]μmol 24 h^{-1}

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