



Separation and preconcentration of aluminum in parenteral solutions and bottled mineral water using different analytical techniques

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ABSTRACT

A new method is reported for the separation of aluminum ions [Al(III)] from interfering elements in parenteral and pharmaceutical solutions (PS) and bottled mineral water (BMW) samples, through solid-phase extraction with 2-methyl-8-hydroxyquinoline (quinaldine) adsorbed onto activated silica gel. While the enrichment step of separated Al(III) was carried out by cloud point extraction (CPE) using 8-hydroxyquinoline as complexing reagent, the resulted complex was entrapped in a non-ionic surfactant octylphenoxy polyethoxyethanol (Triton X-114). The enriched Al(III) in sample solutions were determined by spectrofluorometry (SPF) at $\lambda_{\text{excitation}}$ 370 nm and $\lambda_{\text{emission}}$ 510 nm, and flame atomic absorption spectrometry (FAAS) for comparative purpose. The variables affecting the complexation and extraction steps were studied and optimized. The validity of methodology was checked with certified reference material of water and standard addition method. The enrichment factor and detection limit of Al(III) for the preconcentration of 50 ml of PS and BMW were found to be 100 and 0.25 $\mu\text{g/L}$, respectively. The proposed method has been applied for the determination of trace amount of Al(III) in PS and BMW samples with satisfactory results. In PS the levels of Al(III) are above than permissible limit (25 $\mu\text{g/L}$).

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1. Introduction

Aluminum [Al(III)] is recognized as a non-essential toxic metal to which humans are frequently exposed. During recent years, much interest has been aroused by the toxicity and biological effect of Al(III) [1]. Some studies suggested that Al(III) may be accumulated in the brain via different routes (drinking waters, food and pharmaceutical formulations) and may interfere with the normal activities of nervous system [2]. The Al(III) accumulation may increase the risks of neurological and bone diseases, e.g., Alzheimer's disease, Parkinson's disease, encephalopathy, and osteomalacia [2,3]. The brains of uremic patients receiving aluminum for long term, developed neuro-developmental impairment, especially in pre-term infants who are receiving nutrition from parenteral solution (PS) [4]. The patients can unintentionally receive significant high amounts of Al(III) from PS as a contaminant, which is above the recommended values [5,6]. The most commonly

described toxicities have been reported in the bones of patients undergoing treatment with peritoneal dialysis and hemodialysis [7,8].

Premature newborns receiving endogenous therapy are patients with a high risk of suffering from Al(III) overload due to parenteral exposure. This way of entry avoids the intestinal barrier and the renal immaturity of newborns impairs its elimination [9]. Many sources have been shown to be contaminated PS with Al(III) included raw materials, containers, medicines containing Al(III), such as aluminum-containing phosphate binding gels, processed human serum albumin and other environmental and industrial sources [10].

The Al(III) is present at low levels in natural waters, significant amounts are added to water supplies as a flocculating agent, increasing its final concentrations. The addition of Al(III) based coagulants has the potential to leave Al(III) contents in the treated drinking water. Further treatment of water to prepare bottled water, sold in market with trade name 'bottled mineral water (BMW)', contains certain high quantities of Al, depending on its initial levels. The BMW in developing countries are especially used only for children and patients, due to their high cost.

Therefore, the evaluation of Al(III) levels in PS and BMW for prevention of Al overload has attracted considerable attention in the field of nutritional and clinical chemistry. There are a variety of ana-

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lytical techniques such as flame atomic absorption spectrometry (FAAS), inductively coupled plasma-atomic emission spectrometry and spectrofluorometry (SPF) used for the determination of Al(III) [11,12]. However, all of the techniques require enrichment methods for the determination of trace amounts of Al(III) [13].

Due to the presence of interfering cations such as iron, chromium, copper and zinc in BMW and PS or the presence of Al ions below the detection limit, it is hard to accurately determine Al ions by spectroscopic techniques [13–15]. So, the separation and preconcentration steps for Al ions are necessary to applying simple and less expensive techniques such as SPF and FAAS [15]. The widely used techniques for the separation and preconcentration of Al(III) include liquid–liquid extraction [16], ion exchange [17], solid-phase extraction [18] and cloud point extraction [19]. Separation and preconcentration based on cloud point extraction (CPE) are becoming an important alternative and have a lot of practical applications in the field of surface chemistry [20].

The CPE offers a most frequently used extraction methodology that is simple, cheap, most efficient and less toxic than other extraction methods [21]. The CPE is based on the preconcentration of metal ions after the formation of sparingly water-soluble complexes in the surfactant-rich phase prior to their determination [22,23]. In addition, the cloud point strategies can enlarge the FAAS application, which depends on preconcentration/enrichment factors, to enhance its sensitivity significantly, thus making the method more advantageous when compared with those based on direct determination using ETAAS or ICP techniques [24]. The complexing reagent 8-hydroxyquinoline (oxine) has been acknowledged as one of the most sensitive organic ligand used for the determination of Al(III) [25,26]. It forms a highly fluorescent complex with some metals such as zinc and aluminum, without showing any intrinsic fluorescence itself.

The aim of present work was to develop and establish a separation/preconcentration of trace quantity of Al ions in samples of pharmaceutical formulations (parenteral solutions). In Pakistan over 60% of the population is severely affected by contaminated water. In the present study, the Al(III) level was also determined in BMW to check their suitability for drinking, especially by children and diseased patients. For separation of Al ions from other interfering cations, 2-methyl-8-hydroxyquinoline (quinaldine) was used, while for enrichment, a CPE was applied. The Al(III) reacts with 8-hydroxyquinoline and resulted complex entrapped by Triton X-114 prior to its determination by SPF and FAAS using nitrous oxide–acetylene flame. Several experimental variables affecting the method sensitivity and stability were investigated in detail. The proposed method has been applied for determination of trace amount of Al(III) in PS and BMW with satisfactory results.

2. Experimental

2.1. Instrumentation

WIROWKA Laboratoryjna type WE-1, nr-6933 centrifuge (speed range 0–6000 rpm, timer 0–60 min, 220/50 Hz, Mechanika Pheczyjna, Poland) was used for centrifugation. The pH was measured by pH meter (720-pH meter, Metrohm). Fluorescence measurement of Al–oxine complex was made on a Shimadzu RF-5301 PC spectrofluorophotometer equipped with a 150 W Xenon lamp and using 1.00 cm quartz cells. Instrument excitation and emission slits were adjusted to 10 nm. The concentration of Al(III) in extracts was also determined by a double beam PerkinElmer model A Analyst 700 atomic absorption spectrometer (Norwalk, CT, USA), equipped with burner at wave length (nm) 309.3, slit width (nm) 1.3, lamp current (10 mA), burner height (12.5 mm) Fuel (acetylene 0.45 kg/cm) and oxidant (nitrous oxide as oxidant = 1.6 kg/cm²).

2.2. Reagents

Ultrapure water obtained from ELGA labwater system (Bucks, UK), was used throughout the work. The non-ionic surfactant octylphenoxypolyethoxyethanol (Triton X-114) was obtained from Sigma (St. Louis, MO, USA) and was used without further purification. Stock standard solution of Al(III) at a concentration of 1000 µg/L was obtained from the Fluka Kamica (Bush, Switzerland). Working standard solutions were obtained by appropriate dilution of the stock standard solutions before analysis. Concentrated nitric acid and hydrochloric acid were of analytical reagent grade from Merck (Darmstadt, Germany) and were checked for possible trace Al(III) contamination by preparing blanks for each procedure. The quinaldine and oxine (Merck) were prepared by dissolving appropriate amounts of both reagents in 10% ethanolic acetic acid (0.01 M) and kept in refrigerator (4 °C) for one week. The acetate buffer was used to control the pH of the solutions. The pH of the samples was adjusted to the desired pH (3–8) by the addition of 0.1 M HCl or NaOH solution in acetate buffer (0.01 mol/L). For the accuracy of methodology, a certified reference material of water SRM 1643e (National Institute of Standards and Technology (NIST), Gaithersburg, MD, USA) was used. The glass and plastic wares were soaked in 10% nitric acid overnight and rinsed many times with deionized water to avoid experimental errors.

2.3. Sampling

Parenteral and pharmaceutical solutions of four different batches packed on different dates ($n = 13$) were purchased from different pharmaceutical stores. The 20 different bottled mineral water samples of different brands packed on four different dates (five samples of each brand) were collected from local market of Pakistan. On arrival to laboratory, the PS and BMW were stored at -20°C till further analysis.

2.4. Preparation of real samples

For separation of Al ions from different interfering elements present in matrices of PS and BMW, a glass column with an inner diameter of 20 mm and a length of 25 cm was filled up to a height of about 20 cm with activated silica gel. Prior to use, the column was preconditioned with buffer solution (pH 6), and passed 10 mL of 0.1 mol/L quinaldine solution prepared in 0.1 mol/L acetic acid–ethyl alcohol. For Al(III) separation and preconcentration, aliquots of 25 mL standard solution containing the Al(III) (in the range of 5–50 µg/L), while triplicate samples of 100 mL of each PS and BMW samples were passed through the column to separate Al ions from other interfering ions at the flow rate of 1.0 mL/min. The eluents of each PS and BMW were divided in two sub-samples (50 mL of each) and subjected to CPE for preconcentration of Al ions. The same sub-samples of PS and BMW (50 mL in volume), without removing interfering cations were taken in a graduated centrifuge tube (100 mL in capacity) and subjected to CPE.

For CPE added 0.1–0.6 mL of oxine solution (1.37×10^{-3} mol/L), 2.0 mL of Triton X-114 (0.05–0.2%, v/v) and 2 mL of different buffers to adjust a pH range of 4–8 were added. The tubes were kept in an ultrasonic bath at 40–80 °C for 10–30 min. After different time intervals the separations of the two phases were achieved by centrifugation for 5 min at 3500 rpm. After cooling in ice-bath, the surfactant-rich phase became viscous and the aqueous phase decanted carefully.

To decrease the viscosity of one of the duplicate extracts 0.5 mL of ethanol–water mixture was added and fluorescence intensity of obtained Al–oxinate in the micellar phase was measured by SPF at $\lambda_{\text{excitation}} 370 \pm 3$ nm and $\lambda_{\text{emission}}$ at 510 ± 3 nm. While simultaneously the viscosity of other sub-sample was decreased by adding

Table 1
Validation of cloud point extraction of Al in parenteral solution after (AS) and before (BS) pre-separation of interference ions.

Flame atomic absorption spectrophotometry				Spectrofluorometer		
	AS	BS	Paired <i>t</i> -test ^a , <i>t</i> _{Experimental}	AS	BS	Paired <i>t</i> -test ^a , <i>t</i> _{Experimental}
SRM 1643e (water), certified value of Al(III) (141.8 ± 8.6)						
SRM	141 ± 6.4 (98.7%)	140 ± 7.2 (97.3)	0.238	139 ± 7.5 (98.0%) ^c	130 ± 8.4 (93.5%)	1.27
Standard addition method (added Al(III) μg/L)						
PS6	29.4 ± 3.12 ^b	29.0 ± 3.6 (98.6) ^c	0.154	28.3 ± 3.38 ^b	26.7 ± 1.05 (93.2)	1.23
5	34.0 ± 1.65 (98.8)	33.7 ± 1.82 (98.0)	0.242	32.8 ± 1.47 (98.0)	31.5 ± 2.21 (94)	1.56
10	39.0 ± 1.45 (99)	38.5 ± 2.94 (97.7)	0.182	37.8 ± 2.1 (98.2)	36.3 ± 3.12 (94.3)	1.64
20	48.8 ± 2.94 (98.8)	48.3 ± 4.1 (98)	0.287	47.5 ± 2.75 (97.9)	45.4 ± 3.21 (93.6)	1.82

*t*_{Critical} at 95% confidence limit = 2.57.

^a Paired *t*-test between AS vs BS, degree of freedom (*n* - 1) = 5.

^b Average value ± confidence interval (*p* = 0.05).

^c () Values in parenthesis %recovery.

acidic ethyl alcohol (0.1 mol/L HNO₃) and introduced into flame by conventional aspiration, for comparison purposes. Calibration was performed against aqueous standards submitted to the same CPE procedure. A blank submitted to the same procedure was measured parallel to the calibration solutions of standards, and real samples.

2.5. Validity and applicability

The calibration graph using the preconcentration step for Al(III) was linear with a correlation coefficient of 0.9997 at 5–50 μg/L. The validity and accuracy of the proposed method was checked by certified reference material of water (SRM 1643e) and standard addition method at three concentration levels of Al(III) (5–20 μg/L), results are shown in Table 1. The preconcentration factor (PCF), which is defined as the concentration ratio of the analyte in the final diluted surfactant-rich extract ready for its determination and in the initial solution was 100 for Al(III) in PS and BMW. The PCF achieved in this work was higher than those obtained in other CPE methods used for extraction and preconcentration of Al(III) [6]. The limit of detection (LOD) of Al(III) for the preconcentration of 50 mL of parenteral solution was 0.25 μg/L as three times the standard deviation of the blank signals. The obtained LOD was sufficiently low as to be valuable for detecting Al(III) in different PS and BMW. The method was successfully applied for the determination of Al(III) in PS and BMW samples at different concentrations levels.

The Student's *t*-test showed that the %recoveries of Al(III) with and without pre-separation of interference elements were significantly different at 95% confidence level using SPF, it was reduced 6–7%, indicating the interferences of matrices species in fluorescence intensity of Al-oxine complex. While the differences were not significant in those results obtained by FAAS (Table 1).

The validity of the proposed method was checked by CRM and standard addition method by adding certified standards at three concentration levels in sub-sample of PS (PS 6). The accuracy of CPE method is determined as relative standard deviation for six replicates containing 20 μg/L of Al(III) was <5%, after pre-separation of interferent elements by both techniques.

3. Results and discussion

The proposed separation/preconcentration methodologies were easy, rapid and interference free, and did not require any particular technical skill: for instance, the analysis time of samples and calibration curve of standards including manually operated chelation, extraction, and fluorescence determination, required less than 15 min, apart from conventional extraction methods. We used these methods to evaluate the contamination of Al(III) in PS and BMW samples at trace levels. The influence of different analytical parameters (pH, amounts of reagents, concentration of non-ionic surfactant, time and temperature) were studied for the

optimum recovery of Al(III) in different matrices. The oxine is a strong chelating agent for Al(III) and gives rise to fluorescent complexes [26,27]. The interferences of different elements were eliminated by using quinaldine, that form chelates with most of the metal ions except Al(III), which was not complexed with quinaldine due to steric hindrance of the methyl group at the 2-position of aromatic ring [28]. The silica gel is an active adsorbent and also plays a role as solid material coated with complexing reagent (quinaldine) solution in ethanol–0.1 M acetic acid. In addition, other advantages of silica gel are local availability, high surface area and thermal resistance [29,30]. To check the accuracy of the cloud point extraction procedure, the results obtained by SPF were compared with those obtained by FAAS using nitrous oxide–acetylene flame.

3.1. pH effects

Extraction yield depends on the pH at which complex formation is carried out. The CPE of Al(III) was performed in different pH buffer solutions. The replicate six standard solutions of Al(III) (20 μg/L) were adjusted to the different pH with the buffer solutions covering the pH range of 3–8. Fig. 1 shows the effect of pH on the extraction recovery of Al(III), which was calculated based on the amounts of analyte in the surfactant-rich solution after extraction at the starting pH 3 (Fig. 1). As can be seen that quantitative extraction (>95%) was obtained for Al(III) in the pH range of 5–6 and starts to decrease after pH 7.0. Hence, pH 5.5 was chosen for CPE of Al(III).

3.2. Effect of oxine concentration

The %recovery of Al(III) as a function of concentration of the chelating agent, 8-hydroxyquinoline (oxine), is shown in Fig. 2, where standard, SRM and real sample solution containing Al(III) were treated with oxine solutions in the range of 1.37×10^{-5} to 8.22×10^{-5} (0.1–0.6 mL of stock reagent (1.37×10^{-3} mol/L)) and appropriate buffer solution was added to keep pH level at

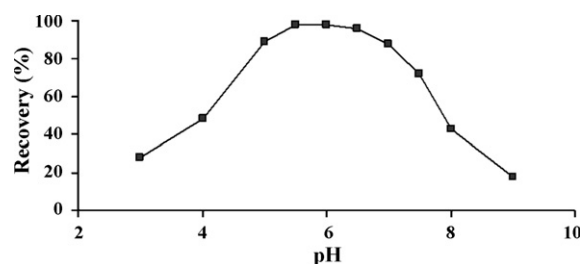


Fig. 1. Effect of pH on the spectrofluorimetric responses: 100 μg/L Al, 5.48×10^{-5} mol/L 8-HQ, 0.1% (w/v) Triton X-114, temperature 45 °C, and stirring time 20 min.

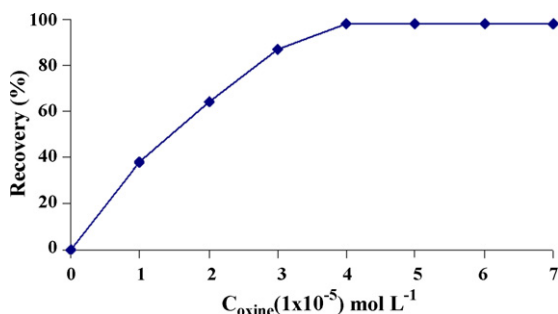


Fig. 2. Effect of oxine concentration on the %recovery: 100 $\mu\text{g/L}$ Al, 0.1% (w/v) Triton X-114, pH 5.5, temperature 45 °C, and stirring time 20 min.

6.0. The complex was entrapped in 0.1% (w/v) Triton X-114 to preconcentrated traces of Al(III) in understudy samples. The extraction efficiency of Al(III) in PS and BMW were increased up to 5.48×10^{-5} mol/L of oxine, reaching a plateau, which is considered as complete extraction. The concentrations above this value have no significant effect on the efficiency of CPE. The stoichiometry of the Al–oxine ternary complex, as reported in literature is 1:3 ratios [28].

3.3. Effect of Triton X-114 concentration

In the present work, Triton X-114 was chosen because of its higher extraction efficiency as well as its lower cloud point temperature as compared to other reported surfactants [31]. The low cloud point temperature avoids back extraction during centrifugation. Fig. 3 shows the variation in extraction efficiency of Al–oxine complex within the concentration range of 0.05–0.2% of Triton X-114. The 60–70% recovery was observed at 0.05% of Triton X-114, while the extraction efficiency reached a maximum at the concentration of 0.1%. So, a concentration of 0.1% was chosen as the optimum surfactant concentration in order to achieve the highest possible extraction recovery of Al(III) from standards, SRM and real samples, while <0.1% the extraction efficiency of complexes is low probably because of the inadequacy of the assemblies to entrap the hydrophobic complex quantitatively. While concentrations >0.1% (w/v), the signals decrease because greater amounts of diluents (ethanol–water for SPF and ethanol–0.1 M nitric acid for FAAS) were used to reduce the viscosity of the surfactant.

3.4. Effect of time and temperature

A sufficiently long reaction time was allowed for the Al–oxine complex formation to proceed, up to 300 min at room temperature [31]. While subjecting to heating in ultrasonic bath in the range of 10–60 min, the formation of complex was optimum at 20 min. We preferred to stop the reaction at 60 min, as a longer reaction time did not increase fluorescence intensity and %recovery of Al(III). The

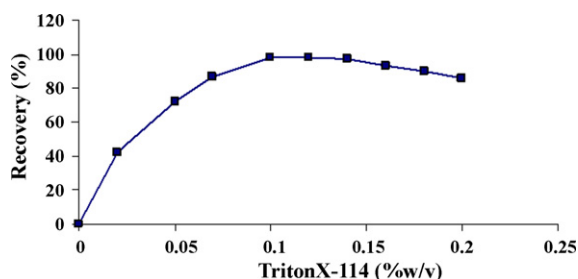


Fig. 3. Effect of Triton X-114 on the %recovery: 100 $\mu\text{g/L}$ Al, 5.48×10^{-5} mol/L 8-HQ, pH 5.5, temperature 45 °C, and stirring time 20 min.

effects of temperature on the analytical signal were studied in the range of 30–60 °C. Since, in the present study >40 °C was used for optimum extraction efficiency of Al–oxine complex. It was observed that at 45 °C, maximum extraction efficiency was obtained, while at higher temperature (80 °C) the fluorescent intensity of Al–oxine complex was lowered.

3.5. Interferences

The interferences are those relating to the preconcentration step, i.e., cations that may react with 8-HQ or species that may react with Al(III) and decrease the extraction efficiency as well as effects on the determination of fluorescence intensity of Al–oxine complex, using SPF technique. The interferences study was carried out on CPE of Al(III) in CRM and real samples, with and without pre-separation of Al(III) from other matrices' elements using 2-methyl-8-hydroxyquinoline. Duplicate of 25 mL solution containing 20 $\mu\text{g/L}$ of Al (III) and interfering ions in different (interfering ions to analyte ratios) were subjected to CPE. The determination of Al(III) in the presence of Zn produces positive error and broad band in emission spectrum was observed, while Fe(III), Cd(II), Pb(II) and Cu(II) can interfere with the determination of Al(III), to produce negative error effects. The interference from these ions can be eliminated by using quinaldine that form chelates with these metal ions except Al(III), which was not complexed with quinaldine due to steric hindrance of the methyl group at the 2-position of aromatic ring. Our results are not consistent with other study to determine simultaneously Al(III) and Zn using oxine as chelating agent [32].

3.6. Application

The optimized procedure was carried out on PS and BMW samples without any previous treatment prior to subjecting separation/preconcentration steps. It was observed that concentration of Al (III) in most of the PS and BMW samples were within permissible limit, except in few cases. The obtained results are shown in Tables 2 and 3. The tables also include the comparison of the found values of Al(III) with preconcentration using CPE and determination with SPF and FAAS. In understudy samples, the commonly encountered matrix components such as alkali and alkaline earth elements generally do not form stable complexes and are not extracted into the surfactant-rich phase. The iron is present at trace levels in PS and BMW and it was removed by complexation with quinaldine.

The concentration of Al(III) in some samples of BMW (samples 5, 7, 8, 9, 13, 16, 19, 20), was found higher than the recommended permissible limit of Al for drinking water (200 $\mu\text{g/L}$), indicating that the manufactures were using alum for water purification rather than using standard water purification methods [3]. While the concentration of Al(III) in remaining 16 BMW samples is within the permissible limit. Now a days more than 100 samples of branded as well as many non branded bottled water are available in Pakistan. This wide selection, reflects diverse consumer demand for safe and good quality of water falling within WHO recommendation. For present study, we have selected twenty different brands of mineral water.

The concentrations of Al(III) in different PS were found in the range of 22.5–668 $\mu\text{g/L}$. It was observed that the understudy PS samples used as parenteral nutrition have high Al(III) contents which exceeds the suggested threshold concentration of 25 $\mu\text{g/L}$ recommended by the American Society for Clinical Nutrition and the American Society for Parenteral and Enteral Nutrition [5,6,33].

The Al(III) content of the BMW and PS depends primarily on its content in the water with which they are prepared; there may be some contribution from the chemicals used in the concentrate which is added to the water. Some domestic tap-water supplies

Table 2
Aluminum in bottled mineral water (BMW) samples ($\mu\text{g/L}$).

Samples	SPF	FAAS
BMW-1	65.6 \pm 4.5	68.2 \pm 5.7
BMW-2	125 \pm 12.0	127 \pm 11.0
BMW-3	75.2 \pm 6.0	76.9 \pm 7.2
BMW-4	140 \pm 13.5	143 \pm 11.0
BMW-5	643 \pm 81.4	640 \pm 70.3
BMW-6	94.2 \pm 9.1	95.8 \pm 9.4
BMW-7	277 \pm 15	280 \pm 24.5
BMW-8	281 \pm 17.3	82.5 \pm 8.1
BMW-9	253 \pm 25.0	256 \pm 22.0
BMW-10	91.4 \pm 8.7	92.9 \pm 9.2
BMW-11	214 \pm 8.6	220 \pm 8.4
BMW-12	216 \pm 6.9	218 \pm 8.5
BMW-13	756 \pm 26.2	760 \pm 18.9
BMW-14	65.3 \pm 6.6	66.7 \pm 5.5
BMW-15	54.6 \pm 5.9	55.2 \pm 5.6
BMW-16	268 \pm 16.3	270 \pm 14.9
BMW-17	97.4 \pm 7.8	98.6 \pm 9.1
BMW-18	142 \pm 7.28	141 \pm 8.12
BMW-19	252 \pm 10.5	256 \pm 12.5
BMW-20	378 \pm 22.4	382 \pm 24.8

Table 3
Aluminum contents in parenteral solutions (PS) and pharmaceutical formulations (PhF) ($\mu\text{g/L}$).

PS/PhF	Package	SPF	FAAS
PS1	Plastic	27.8 \pm 2.78	28.5 \pm 2.24
PS2	Plastic	40.8 \pm 5.23	41.6 \pm 4.84
PS3	Glass	42.9 \pm 4.52	43.8 \pm 3.87
PS4	Plastic	33.4 \pm 4.87	34.2 \pm 4.56
PS5	Plastic	30.6 \pm 4.34	31.5 \pm 3.64
PS6	Plastic	28.8 \pm 3.38	29.4 \pm 2.86
PS7	Glass	45.9 \pm 4.92	46.7 \pm 3.72
Sodium bicarbonate	Glass	668 \pm 35.4	675 \pm 32.6
Sodium heparin	Glass	210 \pm 20.4	214.7 \pm 17.8
Vitamin solution	Glass	56.7 \pm 4.56	58.3 \pm 3.56
Human albumin	Glass	205 \pm 18.7	208 \pm 15.8
Amino acid 10%	Glass	23.0 \pm 3.12	23.8 \pm 2.42

contain Al(III) in high concentration, either naturally or because aluminum compound (alum) has been added as a flocculent in the purification process. This often results in increased water concentrations of Al(III), but if the treatment process is functioning optimally, the addition of Al(III) may actually result in lower Al values in the treated water than in the raw water [34]. For the preparation of PS the process of deionization and particularly reverse osmosis is much more effective in removing aluminum from the water used for preparation of these very important pharmaceutical formulations.

It was reported in literature that certain substances when stored in glass containers have a leaching action and Al(III) can be released into the solutions and it can also be present as contaminant from some pharmaceutical products [35]. It is reported that the Al(III) contamination may be a potential hazard to patients with prolonged parenteral nutrition [36]. The great variability between the solutions of different manufacturers and of different batches suggests that the contamination takes place during manufacturing. Thus, the production of these medicines in pharmaceutical laboratories calls for very strict quality control, because they are injected directly into the blood stream at high volumes.

4. Conclusion

The results demonstrated the usefulness of proposed separation/preconcentration methods to quantitative extraction of Al(III) in different PS and BMW with low cost, simple, efficient and non interfering effects of matrices' elements. The proposed CPE method

gives low LOD, good RSD and solvent-free extraction of the Al(III) from its initial matrix without previous treatment. The main advantages of this novel method are: a much higher sensitivity has been obtained by SPF and FAAS techniques and the interference of elements can be efficiently eliminated by reaction with quinaldine, because Al is not reacted with quinaldine due to steric hindrance effect of methyl group. Due to these efficiencies, it can be applied to the monitoring of Al(III) in various environmental and biological samples. Careful clinical and biochemical monitoring are warranted to determine whether it will be necessary to eliminate aluminum contamination of PS used in patients, particularly infants, with reduced kidney function who may be at risk for aluminum intoxication.

References

- [1] M. Venturini-Soriano, G. Berthon, Aluminum speciation studies in biological fluids. Part 4. A new investigation of aluminum–succinate complex formation under physiological conditions, and possible implications for aluminum metabolism and toxicity, *J. Inorg. Biochem.* 71 (1998) 135–145.
- [2] H. Sinczuk-Walczak, W. Matczak, G. Razniewska, M. Szymczak, Neurological and neurophysiological examinations of workers occupationally exposed to aluminum, *Med. Pract.* 56 (2005) 9–17.
- [3] T.P. Flaten, Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water, *Brain Res. Bull.* 55 (2001) 187–196.
- [4] N.J. Bishop, R. Morley, J.P. Day, A. Lucas, Aluminum neurotoxicity in preterm infants receiving intravenous feeding solutions, *N. Engl. J. Med.* 336 (1997) 1557–1561.
- [5] L. Sombra, M. Luconi, F. Silva, R.A. Olsina, L. Fernandez, Spectrophotometric determination of trace aluminium content in parenteral solutions by combined cloud point preconcentration–flow injection analysis, *Analyst* 126 (2001) 1172–1176.
- [6] G.L. Klein, Aluminum: new recognition of an old problem, *Curr. Opin. Pharmacol.* 5 (2005) 637–664.
- [7] E. Advenier, C. Landry, V. Colomb, C. Cognon, D. Pradeau, M. Florent, O. Goulet, C. Ricour, O. Corriol, Aluminum contamination of parenteral nutrition and aluminum loading in children on long-term parenteral nutrition, *J. Pediatr. Gastr. Nutr.* 36 (2003) 448–453.
- [8] T. Baydar, A. Aydin, S. Duru, A. Isimer, G. Sahin, Aluminum in enteral nutrition formulas and parenteral solutions, *Clin. Toxicol.* 35 (1997) 277–281.
- [9] K. Popinska, J. Kierkus, M. Lyszkowska, J. Socha, E. Pietraszek, W. Kmietek, J. Ksiazek, Aluminum contamination of parenteral nutrition additives, amino acid solutions, and lipid emulsions, *Nutrition* 9 (1999) 683–686.
- [10] C.W.K. Chow, S.D. Thomas, D.E. Davey, D.E. Mulcahy, M. Drikas, Development of an on-line electrochemical analyser for trace level aluminium, *Anal. Chim. Acta* 499 (2003) 173.
- [11] B. Bocca, A. Alimonti, F. Petrucci, N. Violante, G. Sancesario, G. Forte, O. Senofonet, Quantification of trace elements by sector field inductively coupled plasma mass spectrometry in urine, serum, blood and cerebrospinal fluid of patients with Parkinson's disease, *Spectrochim. Acta B* 59 (2004) 559–566.
- [12] M. Soy lak, U. Sahin, A. Ülgen, L. Elçi, M. Dogan, Determination of aluminium at trace level in water samples by visible absorption spectroscopy with a laser diode, *Anal. Sci.* 13 (1997) 287–289.
- [13] I. Narin, M. Tüzen, M. Soy lak, Aluminium determination in environmental samples by graphite furnace atomic absorption spectrometry after solid phase extraction on Amberlite XAD-1180/pyrocatechol violet chelating resin, *Talanta* 63 (2004) 411–418.
- [14] M. Tuzen, M. Soy lak, Biosorption of aluminum on *Pseudomonas aeruginosa* loaded on Chromosorb 106 prior to its graphite furnace atomic absorption spectrometric determination, *J. Hazard. Mater.* 154 (2008) 519–525.
- [15] J. Komarek, R. Cervenka, T. Ruzicka, V. Kuban, ET-AAS determination of aluminium in dialysis concentrates after continuous flowsolvent extraction, *J. Pharm. Biomed. Anal.* 45 (2007) 504–509.
- [16] S.B. Erdemoglu, K. Pyrzyniska, S. Gucer, Speciation of aluminum in tea infusion by ion-exchange resins and flame AAS detection, *Anal. Chim. Acta* 411 (2000) 81–89.
- [17] M.B. Luo, S.P. Bi, Solid phase extraction–spectrophotometric determination of dissolved aluminum in soil extracts and ground waters, *J. Inorg. Biochem.* 97 (2003) 173–178.
- [18] A.B. Tabrizi, Cloud point extraction and spectrofluorimetric determination of aluminium and zinc in foodstuffs and water samples, *Food Chem.* 100 (2007) 1698–1703.
- [19] S. Rubio, D. Perez-Bendito, Supramolecular assemblies for extracting organic compounds, *Trace Trends Anal. Chem.* 22 (2003) 470–485.
- [20] M. Ghaedi, A. Shokrollahi, F. Ahmadi, H.R. Rajabi, M. Soy lak, Cloud point extraction for the determination of copper, nickel and cobalt ions in environmental samples by flame atomic absorption spectrometry, *J. Hazard. Mater.* 150 (2008) 533–540.
- [21] J.L. Manzoori, A.B. Tabrizi, Cloud point preconcentration and flame atomic absorption spectrometric determination of Cd and Pb in human hair, *Anal. Chim.*

- Acta 470 (2002) 215–221.
- [22] M. Ghaedi, A. Shokrollahi, K. Niknam, M. Soyulak, Cloud point extraction of copper, zinc, iron and nickel in biological and environmental samples by flame atomic absorption spectrometry, *Sep. Sci. Technol.* 44 (2009) 773–786.
- [23] A. Shokrollahi, M. Ghaedi, M.S. Niband, H.R. Rajabi, Selective and sensitive spectrophotometric method for determination of sub-micro-molar amounts of aluminium ion, *J. Hazard. Mater.* 151 (2008) 642–648.
- [24] F. Papadimitrakopoulos, X. Zhang, K.A. Higginson, Chemical and morphological stability of aluminum tris (8-hydroxyquinoline)(Alq3): effects in light-emitting devices, *IEEE J. Sel. Top. Quant.* 4 (1998) 49–57.
- [25] R.H. Zhu, W.T. Kok, Determination of trace metal ions by capillary electrophoresis with fluorescence detection based on post-column complexation with 8-hydroxyquinoline-5-sulphonic acid, *Anal. Chim. Acta* 371 (1998) 269–277.
- [26] A. Alonso, M.J. Almendral, M.J. Porras, Y. Curto, C. Garcia de Maria, Flow-injection solvent extraction with and without phase separation, Fluorimetric determination of aluminum in water, *Anal. Chim. Acta* 447 (2001) 211–217.
- [27] M. Buratti, C. Valla, O. Pellegrino, F.M. Rubino, A. Colombi, Aluminum determination in biological fluids and dialysis concentrates via chelation with 8-hydroxyquinoline and solvent extraction/fluorimetry, *Anal. Biochem.* 353 (2006) 63–68.
- [28] A. Ohashi, A. Tsuguchi, H. Imura, K. Ohashi, Synergistic cloud point extraction behaviour of Al(1 1 1) with 2-methyl-8-quinolinol and 3,5-dichlorophenol, *Anal. Sci.* 20 (2004) 1091–1093.
- [29] P.K. Jal, S. Patel, B.K. Mishra, Chemical modification of silica surface by immobilization of functional groups for extractive concentration of metal ions, *Talanta* 62 (2004) 1005–1028.
- [30] K. Sharma, S. Mittal, M. Koel, Analysis of trace amounts of metal ions using silica-based chelating resins: a green analytical method, *Crit. Rev. Anal. Chem.* 33 (2003) 183–198.
- [31] J.L. Manzoori, A. Bavili-Tabrizi, Cloud point preconcentration and flame atomic absorption spectrometric determination of cobalt and nickel in water samples, *Microchim. Acta* 141 (2003) 201–207.
- [32] R.M. Acheson, *Chemistry of Heterocyclic Compounds: A Series of Monographs*, second ed., 2008.
- [33] M.M. Pluhator-Murton, R.N. Fedorak, R.J. Audette, B.J. Marriage, R.W. Yatscoff, L.M. Gramlich, Trace element contamination of total parenteral nutrition. I. Contribution of component solutions, *J. Parenter. Enteral. Nutr.* 23 (1999) 222–227.
- [34] R.D. Letterman, C.T. Driscoll, Survey of residual aluminum in filtered water, *J. Am. Water Works Assoc.* 80 (1988) 154–159.
- [35] D. Bohrer, P. Cicero do Nascimento, R. Binotto, S.C. Pomblum, Influence of the glass packing on the contamination of pharmaceutical products by aluminium. Part I. Salts, glucose, heparin and albumin, *J. Trace Elem. Med. Biol.* 15 (2001) 95–101.
- [36] J.L. Greger, J.E. Sutherland, Aluminium exposure and metabolism, *Crit. Rev. Clin. Lab. Sci.* 34 (1997) 439–474.