Optimization of a lithium assay method in oil fields brines by using experimental design methodology and its validation by the accuracy profile approach

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ABSTRACT

To cover the excessive demand of lithium compounds, especially for the manufacture of vehicle batteries, several extraction technologies from natural resources and mainly geothermal brines are applied. These brines are distinguished by the complexity of its chemical composition. So, the quantification of lithium amount by spectroscopic methods will be disturbed by some interferences due to the cohabitation of major cations and anions. The originality of this investigated work is to optimize, by using the response surface methodology, and to validate, by the application of the accuracy profile approach, the analytical method for lithium assay by flame emission spectroscopy. After identification of the major ions in the oilfield brine sample (Ca, Mg, Na, K and Cl), a specificity test is applied, which reveals the presence of chemical interferences. For this reason, a spiked synthetic solution by a lithium standard (20 mg/L) is prepared for each run of the Doehlert design. Four studied factors, which are the major cations ($[Ca^{2+}]$ (X_1), $[Mg^{2+}]$ (X_2), $[Na^+]$ (X_3) and $[K^+]$ (X_4)), are used to build this design and to determine their effects on the lithium recovery yield response ($Y(\%)$). As resulted outcomes, a polynomial valid and predictive model is statistically qualified and used to plot the iso-responses curves of the chosen response. Consequently, the optimal conditions are determined by: $[Ca^{2+}]$ (X_1) = 1.7 mol/L, $[Mg^{2+}]$ (X_2) = 0.02 mol/L, $[Na^+]$ (X_3) = 0.36 mol/L and $[K^+]$ (X_4) = 0.01 mol/L, which correspond to 64.128, 2.43, 60 and 2 g/L, respectively and the theoretical lithium recovery yield is nearby 98% in five-fold diluted composition. Moreover, the validation by the accuracy profile approach is performed after the robustness test. The resulted β-expectation tolerance interval is within the acceptability limits, which means that the analytical method, used for lithium assay by flame emission spectroscopy, is valid and the response variances are almost constant (homoscedasticity) over the predefined range concentration (8–50 mg/L) and it can be used for routine analysis.

Keywords: Lithium; Oil field brine; Optimization; Validation; Accuracy profile; Uncertainty

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1. Introduction

Lithium, the lightest alkaline metal, is considered a valuable strategic element and the focus of modern and innovative industries [1–4]. The greenhouse gas emissions from cars that consume fuels and the need to find an alternative energy source are potential factors to cause the demand increase of lithium compounds [1,4–6]. Its applications are widespread; [4,7], for example, lubricants, polymers, pharmaceuticals, ceramics, glass, and especially in the manufacture of vehicle batteries because it has a high redox potential and the best heat capacity [8]. To satisfy this demand is a challenge. For this reason, the manufactures are obliged to multiply the lithium resources. There are many extraction resources of this element, such as pegmatites, brines, thermal waters and others [9]. Some studies have shown that brines are the abundant and economically lithium resources [10]. These salty brines are subdivided into three types: geothermal, evaporative and oil fields ones which are generally contain major cations such as sodium, magnesium, calcium and potassium and major anions such as chloride and sulphate [9,11–13]. Moreover, the oil fields brines are about 3% of the total resources [9], and they are the least investigated and exploited. These complex matrices inhibit the determination of the real lithium concentration, which is due to interferences. Xianming et al. [14] studied the elimination of chemical interferences by adding spectroscopic buffers in the brine samples in order to increase the sensitivity for the lithium assay by flame atomic absorption spectroscopy. Mannapperuma et al. [15] compare the validation method of lilthium assay by the flame photometer and ion-selective electrode in serum samples. In fact, the obtained results reveal a fair agreement between the two analysis methods. Sampson et al. [16] evaluate precision, recovery and interferences by drugs and inorganic elements (Na, K, Ca, Mg and Br) for the lithium assay in sera patients by eight analytical methods: five kinds of ion-selective electrodes, colorimetric method, flame atomic absorption and atomic emission spectroscopy. Hence, the outcomes show that the values obtained by the use of the ion-selective electrodes Baxter, Beckman, and Corning are in fair agreement with the results given by flame atomic emission, but the AVL and Nova ones provide inferior values and the Ektachem analyser furnishes superior ones given by the same spectroscopic equipment. Payehghadr et al. [17] conclude that the direct determination of lithium concentration in the brine is difficult. For this reason, a solid phase extraction by some metallic ions complexes, such as: 2,2-pyridine 2,6-diyil bis(nitrilo (E) methyliden Schiff base ligand in ethanol at 25°C, is applied, as a better way, in order to eliminate the interferences and to quantify accurately the lithium content by flame photometer. In this respect, the development and the validation of the lithium assay method are crucial in order to determine accurately the real lithium concentration in the brine. The aim of this original paper is firstly to optimize the lithium assay method in an oilfield brine by using the response surface methodology (RSM) [18–20] and secondly to validate it by using the accuracy profile approach in order to provide a well performed routine analysis [21–24]. The RSM is useful to all persons undertaking scientific or industrial research. They are applicable to all disciplines and industries in order to model or to optimize many properties (responses) by modifying the parameters (factors). Moreover, it is a statistical methodology, which is significantly helpful and it has many advantages like economic (a smaller number of tests and less time consuming), efficient (focusing accurately the optimal conditions) and well didactic (providing the best way to show the obtained outcomes). Concerning the validation by the accuracy profile is a suitable mean to visualize graphically the lower and upper quantification limits for lithium assay method. Indeed, this harmonization approach is characterized by two important interdependent parameters, which are the acceptability limits (±λ) (it represents the "*true biais*" which means the maximum tolerable deviation for each level of concentration), and the β-expectation tolerance interval (It signifies the "*true precision*" which defines an interval where the expected proportion of future results will fall) [21]. This approach acquires many assets comparatively to the other procedures, which are only based on some complicated statistical tests used as tools for diagnostic aim and not decision. Among these advantages, the accuracy profile approach is in fair agreement with the validation definition in the international vocabulary of metrology [25]. This definition is built on three important pillars; setting the method objectives (acceptability limits), providing of tangible evidence in the form of validation criteria and checking that this evidence is in fair agreement with these predefined objectives. Moreover, this approach enables the determination of the precision in each level of concentration, which is in accordance with the empirical Horwitz theory. Finally, contrary to the other validation approaches, which is characterized by the greater the error, the worse the precision, the more valid the adopted method. In addition, they generally treat trueness and precision separately. While our investigated procedure shows simultaneously these two statistical criteria in the same graph, which is in fair agreement with the accuracy and uncertainty definition [25].

To achieve these goals (optimization and validation of the assay lithium method), the physico-chemical properties of the oilfield brine are firstly characterized. Secondly, a synthetic salt solution is prepared and it is spiked by a known lithium concentration. After that, an optimization, by using the RSM, of the lithium assay method by using the flame photometer equipment is applied. Finally, the validation by the accuracy profile approach is applied on this analytical method in order to obtain a well-performed routine analysis.

2. Material and methods

2.1. Oilfield brine samples

The investigated oilfield brine is sampled from the governorate Nabeul located in the northeast of Tunisia. This brine is treated to remove the organic phase and many kinds of transition metals. The resulted electrolytic solution is used as investigated samples in this currently work.

2.2. Analytical equipment's

The pH, conductivity and density of the studied samples are determined by pH-meter 827 pH-Lab (Metrohm),

conductimeter consort multiparameter analyzer (3010) and laboratory electronic balance AXIS (Max = 220g; d = 0.0001 g), respectively. Two anionic and cationic chromatography systems fitted with an ionic exchange column, ((Metrosep A, 150 mm × 4 mm, eluent: dipicolinic acid in ultrapure water, suppressor module: H_2SO_4 (50 mmol/L)) and (Metrosep C, 150 mm × 4 mm, eluent: 0.18 mol/L Na_2CO_3/0.17 mol/L $NaHCO_3$ (100 times concentrated) in H_2O, suppressor module: H_2SO_4 (50 mmol/L), respectively, and coupled with a conductivity detector monitored by ICNET software (Metrohm, France) are used to determine the major anionic and cationic composition in the oilfield brine. The mineral elements (sodium, potassium and lithium) assays are determined by flame photometer (BWB XP) after calibrating it by diluted known standards.

2.3. Steps of the analytical assay method

Firstly, the ionic chromatography is applied to determine the major cation and anionic compositions of the oilfield brine. Then, magnesium and calcium content are analyzed by ethylenediaminetetraacetic acid complexometry method by using a graduated burette (borosilicate, 25 mL, increment = 0.05 mL, Pyrex V ± 0.030 mL). Next, sodium, potassium and lithium amounts are assayed by the calibrated flame photometer. At the end, the potentiometric method is applied in order to quantify the chloride-weighted concentration [26].

2.4. Chemical reagents

The mineral compounds used to prepare the synthetic solution are: anhydrous $CaCl_2$ powder (purity ≥ 97% and 110.98 g/mol molecular weight; Sigma-Aldrich), $MgCl_2 \cdot 6H_2O$ (98% purity and 203.30 g/mol molecular weight; OXFORD LAB FINE CHEM LLP), KCl powder (ACS Reagent, purity > 99% and 74.55 g/mol molecular weight; Sigma-Aldrich), extra-pure NaCl powder (99.9% purity and 58.44 g/mol molecular weight; Sisco Research Laboratories (SRL)) and Li_2CO_3 powder (ACS Reagent, purity ≥ 99.0% and 73.89 g/mol molecular weight; Sigma-Aldrich). Reference buffers (4.01, 7.00 and 10.00 at 25°C; Labo and Co.) are used to calibrate the pH-meter. The electrical conductivity meter is calibrated by HANNA reference buffers (1,413; 12,880 and 111,800 µS/cm at 25°C).

3. Results and discussion

In order to optimize and validate the lithium assay method by flame emission spectroscopy, a harmonized approach is applied. Firstly, the chemical composition of the oilfield brine is identified by analytical quantification methods. Secondly, the specificity test is adopted with the aim to know the interferences caused by the natural and synthetic brines, which are considered as chemical complex matrixes. Thirdly, an experimental design methodology is applied allowing to model and optimize the lithium recovery yield and to determine the robustness of the adopted method. At the end, the optimized lithium assay method is validated by the accuracy profile approach in order to determine its real value in the strong electrolytic solution and assess accurately the efficiency of the lithium extraction method in further study.

3.1. Identification of the major chemical elements

Fig. 1A and B show the chromatograms of the ionic composition of the oilfield brine obtained by the above-mentioned ion chromatography. These outcomes are obtained by injection a 500-fold diluted brine. Firstly, Fig. 1A reveals that the major cations are: sodium (Na), calcium (Ca), magnesium (Mg) and potassium (K) and Table 1 summarizes their concentrations, which are 78.576, 41.082, 2.500 and 2.107 g/L, respectively in the natural oilfield sample. Secondly, as shown in Fig. 1B, the most abundant anion is the chloride ion with concentration around 203.3 g/L, whereas the others (sulfate, nitrite, nitrate and phosphate) are on a trace scale. The current oilfield brine differs from the majority-studied brines in our laboratory [11,26,27]. In fact, these latter are characterized by the high magnesium content, which is more important than that of calcium, and generally the cohabitation of sulphate ions. While the former has a calcium content more important than that of magnesium and sulfate-free. Furthermore, the initial density, pH and the conductivity of the investigated sample are equal to 1.2092 g/cm³, 5.94 and 174.100 mS/cm, respectively.

3.2. Specificity test

After identification of the chemical composition of the major elements, a spiked sample method is adopted for specificity test. Indeed, doped natural and synthetic brines are prepared by adding a known lithium quantity (0, 10, 20, 30, 40 and 50 ppm) as well as the calibration standards in ultrapure water. As shown in Fig. 2, the linear curves of the spiked natural and synthetic brines are almost parallel, which means that their slopes are statistically equal (175.18 ± 8.09 and 175.42 ± 8.88, respectively). Moreover, the intercept of the natural brine line is positive (1,339.7 ± 245), which reveals that the lithium has an initial concentration before standard addition (obtained by intersection between extrapolated linear curve and the x-axis). The two above-mentioned curves intersect with the linear calibration curve indicating the existence of chemical interferences due to the matrix effect.

To tackle this challenge, an optimization of the lithium assay method by the experimental design methodology is applied in the following step.

3.3. Modelling and optimization of the lithium recovery yield by the experimental design methodology

3.3.1. Modelling

3.3.1.1. The Doehlert matrix

Table 2 summarizes the four investigated factors and their levels, which are the major cations: $[Ca^{2+}]$ (X_1), $[Mg^{2+}]$ (X_2), $[Na^+]$ (X_3) and $[K^+]$ (X_4). Their intervals are in mol/L: 0–0.4, 0–0.04, 0.36–1.25 and 0–0.02, respectively. The domains are chosen on the one hand by framing the initial chemical composition of our oilfield brine sample and on the other hand by approaching to the chemical composition of the
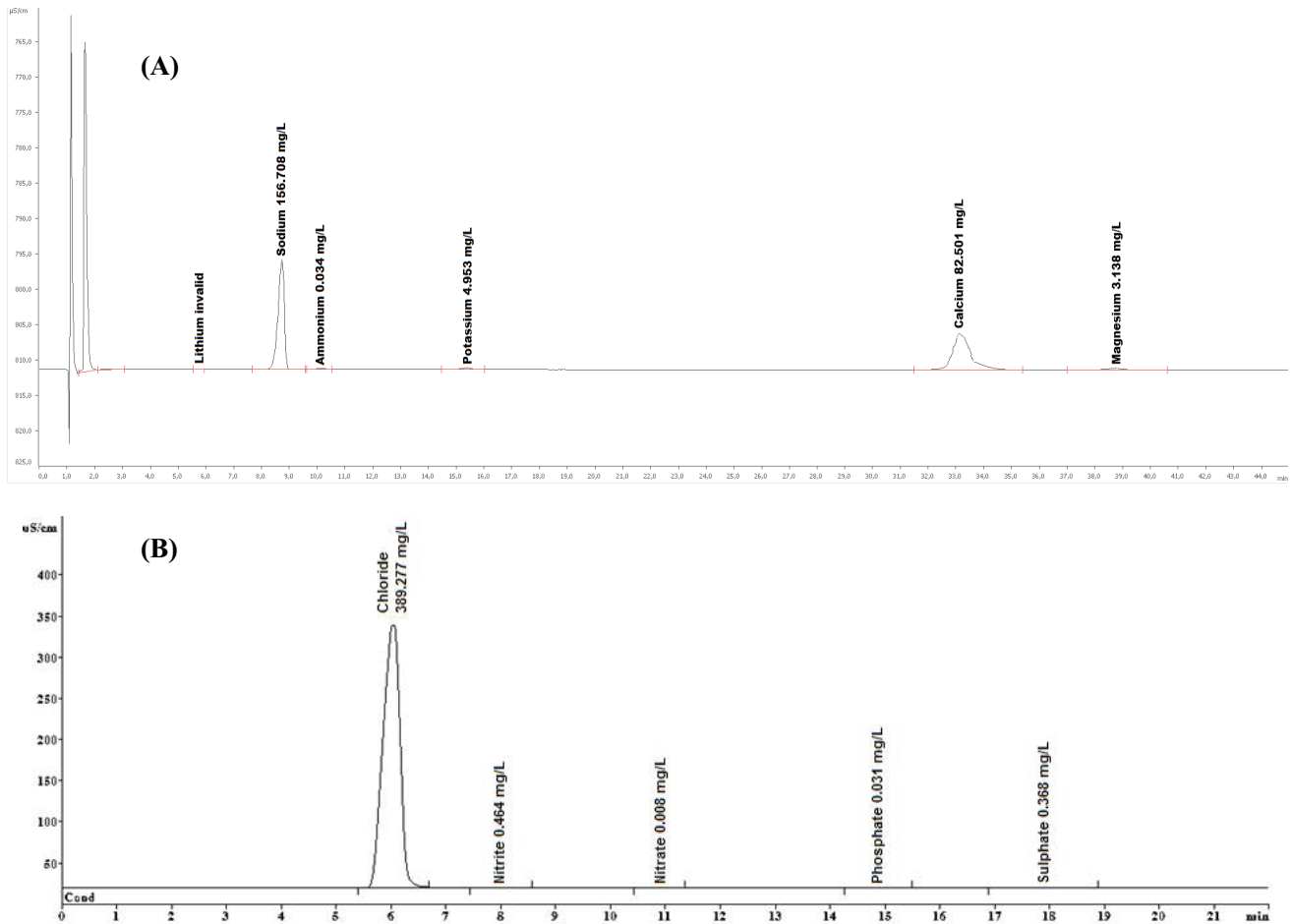
Fig. 1. Chromatograms of the major cations and anions into the investigated oilfield brine: (A) major cations and (B) major anions.

Table 1
Major chemical composition of the treated oilfield brine

Symbol	Major cations				Major anions
	Ca^{2+}	Mg^{2+}	Na^+	K^+	Cl^-
Concentration (g/L)	41.082	2.500	78.576	2.107	203.270

Table 2
Levels of the investigated factors

Factor name	Unity	Coded name	Levels		
			−1	0	+1
$[Ca^{2+}]$	(mol/L)	X_1	0	0.2	0.4
$[Mg^{2+}]$	(mol/L)	X_2	0	0.02	0.04
$[Na^+]$	(mol/L)	X_3	0.360	0.805	1.250
$[K^+]$	(mol/L)	X_4	0	0.01	0.02

geothermal and conventional mine brines given by Table 1 [28]. Table 3 resumes the experimental Doehlert matrix and the chosen response (lithium recovery (Y(%))). Twenty runs in different levels constitute this matrix and five repetitive centered runs in order to calculate the estimation of the experimental variance. The used products to prepare the synthetic brine are based on chloride compounds: such as $CaCl_2$, $MgCl_2 \cdot 6H_2O$, NaCl and KCl. A 5-fold diluted concentration of each considered cation and a fixed lithium content (20 ppm) in ultrapure water constitute the resulting mixture of each trial.

$y = 221{,}09x - 596{,}78$
$R° = 0{,}9886$

$y = 175{,}42x - 429{,}87$
$R° = 0{,}991$

$y = 175{,}18x + 1339{,}7$
$R° = 0{,}9925$

Fig. 2. Specificity test of the lithium assay method by the flame photometer equipment.

Table 3
Doehlert experimental matrix of the investigated lithium recovery yield (fixed concentration [Li] = 20 ppm)

N°Exp	[Ca^{2+}]	[Mg^{2+}]	[Na$^+$]	[K$^+$]	Recovery yield
	X_1	X_2	X_3	X_4	Y_{obs} (%)
1	1	0	0	0	99.588
2	–1	0	0	0	88.104
3	0.5	0.866	0	0	93.179
4	–0.5	–0.866	0	0	90.872
5	0.5	–0.866	0	0	95.332
6	–0.5	0.866	0	0	92.000
7	0.5	0.2887	0.8165	0	90.001
8	–0.5	–0.2887	–0.8165	0	93.282
9	0.5	–0.2887	–0.8165	0	93.743
10	0	0.5774	–0.8165	0	95.127
11	–0.5	0.2887	0.8165	0	87.130
12	0	–0.5774	0.8165	0	86.053
13	0.5	0.2887	0.2041	0.7906	91.949
14	–0.5	–0.2887	–0.2041	–0.7906	91.539
15	0.5	–0.2887	–0.2041	–0.7906	94.358
16	0	0.5774	–0.2041	–0.7906	94.666
17	0	0	0.6124	–0.7906	92.718
18	–0.5	0.2887	0.2041	0.7906	90.565
19	0	–0.5774	0.2041	0.7906	91.180
20	0	0	–0.6124	0.7906	97.383
21	0	0	0	0	90.872
22	0	0	0	0	91.539
23	0	0	0	0	91.744
24	0	0	0	0	91.231
25	0	0	0	0	89.847

Table 4
Signification of the studied factors on the chosen response

Coefficient	Value	SD	t.exp.	Signification (%)
b_0	91.0466	0.3341	272.52	<0.01***
b_1	3.6142	0.3341	10.82	0.102**
b_2	0.5063	0.3341	1.52	20.4
b_3	–3.9492	0.3341	–11.82	0.0829***
b_4	–0.3486	0.3341	–1.04	35.7
b_{11}	2.7994	0.6250	4.48	1.23*
b_{22}	1.4658	0.6251	2.35	7.9
b_{33}	–1.3023	0.5866	–2.22	9.0
b_{44}	2.6040	0.5540	4.70	1.06*
b_{12}	–1.8943	0.8626	–2.20	9.3
b_{13}	2.1456	0.9644	2.22	9.0
b_{23}	0.1636	0.9644	0.17	86.7
b_{14}	–0.7697	1.0022	–0.77	48.9
b_{24}	–1.7269	1.0022	–1.72	15.9
b_{34}	–5.9167	1.0022	–5.90	0.530**

(*), (**) and (***): levels of signification at $p < 5\%$, $p < 1\%$ and $p < 0.1\%$, respectively.
SD: standard deviation.
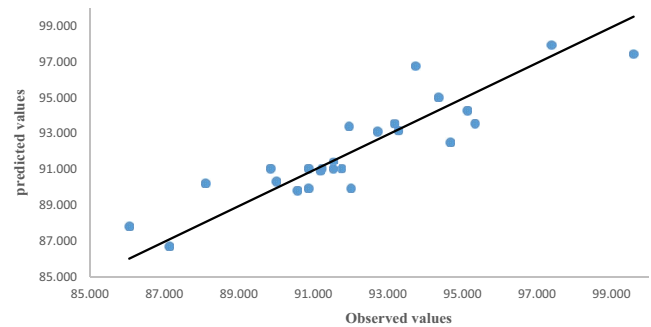t.exp.: calculated t-value of the student test.

Fig. 3. The trueness plot of the predicted vs. observed values.

3.3.1.2. Statistical signification of the regression coefficients

As presented in Table 4, the signification of the regression coefficients are statistically determined by using the NemrodW software (LPRAI, France 2000). Indeed, the most significant regression coefficients on the chosen response (p-value < 1%) are b_0, b_1, b_3 and b_{34} which are assigned to the intercept, [Ca^{2+}] (X_1), [Na$^+$] (X_3) and the interaction between the factors [Na$^+$] (X_3) and [K$^+$] (X_4). The quadratic regression coefficients b_{11} and b_{44} are less significant (p-value < 5%). The remaining coefficients are not significant (p-value > 5%), it means that the independent variables [Mg^{2+}] (X_2) and [K$^+$] (X_4) have no effect on the lithium recovery yield due to their low concentration in the studied sample. Therefore, it is better to continue this work by fixing these two factors at the initial concentrations (0.01 and 0.05 mol/L, respectively) in the synthetic brine. The function that relates the independent variables (X_i) to the interest response (Y) is given by the Taylor polynomial Eq. (1):

$$Y_{cal} = b_0 + \sum_i b_i X_i + \sum_{ij} b_{ij} X_i X_j + \sum_{ii} b_{ii} X_{ii}^2 \qquad (1)$$

where Y_{cal}, b_i and X_i are the calculated response, the regression coefficients and the independent variables, respectively.

The resulted quadratic model, composed with only by the significant regression coefficients, is given by Eq. (2):

$$Y_{cal} = 91.0466 + 3.6142 X_1 - 3.9492 X_3$$
$$- 5.9167 X_3 X_4 + 2.7994 X_{11}^2 + 2.6040 X_{44}^2 \qquad (2)$$

The aim of the obtained model is to predict the lithium recovery response with a minimum of total error, that is, a little difference between the calculated and observed values. For this a reason, the residuals analysis is applied.

3.3.1.3. Residual analysis

As shown in Fig. 3, the graph reveals a points cloud with coordinates the observed values in *x*-axis and the predicted values in *y*-axis. These points are distributed on a straight line, which means the fair agreement between the observed and calculated responses and the total error is quite small. Therefore, the postulated model is relatively

valid. To confirm the validity of the obtained model between the chosen response and the significant independent variables, an analysis of variance occurred.

3.3.1.4. Analysis of variance

Table 5 resumes the analysis of variance of the previous model. In fact, the value of the ratio between the means squares of the lack-of-fit and the pure error (3.651) is inferior to the critical F-value ($F_{15,4,0.05}$ = 5.86), it means that the systematic error is neglected and the only resource of error is due to the random error. Accordingly, the postulated model is valid. Moreover, the value of the ratio between the means square of the regression and the residuals (21.150)

Table 5
Analysis of variance of the recovery yield response

Source of variance	SS	DF	MS	Ratio	Signification
Regression	182.516	5	36.503	21.150	<0.01***
Residuals	32.792	19	1.726		
Lack-of-fit	30.560	15	2.037	3.651	11.000
Pure error	2.232	4	0.558		
Total	215.308	24			

SS: Sum square.
DF: Degree of freedom.
MS: Mean square.
(***): Level of signification ($p < 0.01\%$).

is superior to the critical F-value ($F_{5,19,0.05}$ = 2.74), which reports that the regression coefficients used to elaborate the model have a significant effect on the lithium recovery yield.

3.3.2. Optimization of the lithium recovery yield

The aim of this part is to determine the optimal conditions that minimize the effect of the interferences due to the chemical complex matrix and provide the true value of the lithium concentration. This value enables to know, in the subsequent study, the efficiency of the direct lithium extraction methods, firstly in the synthetic brine and secondly in the natural oilfield brine. Figs. 4 and 5 show the 2D and 3D iso-responses curves, which are theoretical plotted from the relationship between the chosen response and each combination of two factors within their intervals delimited by the red circle. On the basis that the regression coefficient of the factors [Ca^{2+}] (X_1) and [Na$^+$] (X_3) are positive and negative, the increase of the recovery yield (more than 90%) is obtained at the levels (+1) and (–1), respectively. Whereas Fig. 5E shows that the variation of the chosen response values is practically constant, which confirm the neglected effects of the factors [Mg^{2+}] (X_2) and [K$^+$] (X_4) on the lithium recovery yield ($Y(\%)$). Thus, the resulted optimal composition is determined by the major cations concentrations: [Ca^{2+}] (X_1) = 2 mol/L, [Mg^{2+}] (X_2) = 0.02 mol/L, [Na$^+$] (X_3) = 0.36 mol/L and [K$^+$] (X_4) = 0.01 mol/L to obtain more than 90% of lithium recovery yield.

In order to focus more and to determine accurately the coordinates of the optimal conditions, the desirability
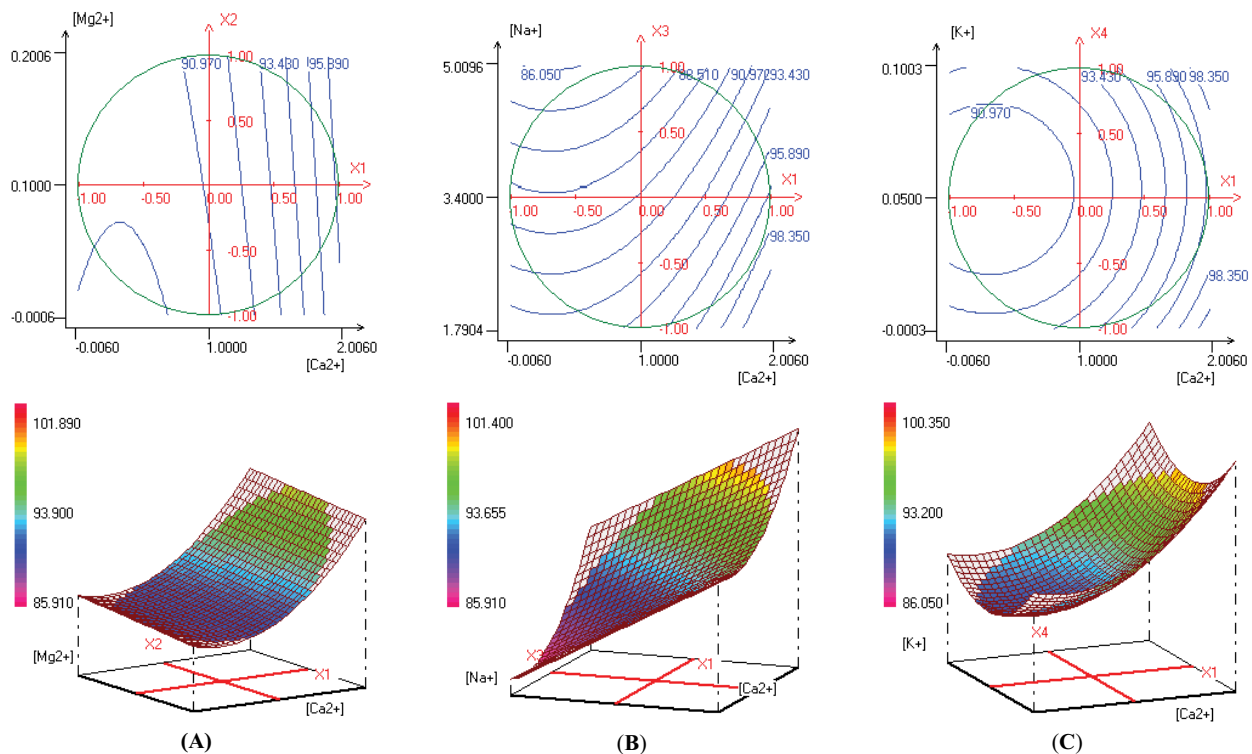

Fig. 4. The 2D and 3D iso-responses curves of the recovery lithium response vs. the two factors combinations: (A) [Ca^{2+}]-[Mg^{2+}], (B) [Ca^{2+}]-[Na$^+$] and (C) [Ca^{2+}]-[K$^+$].
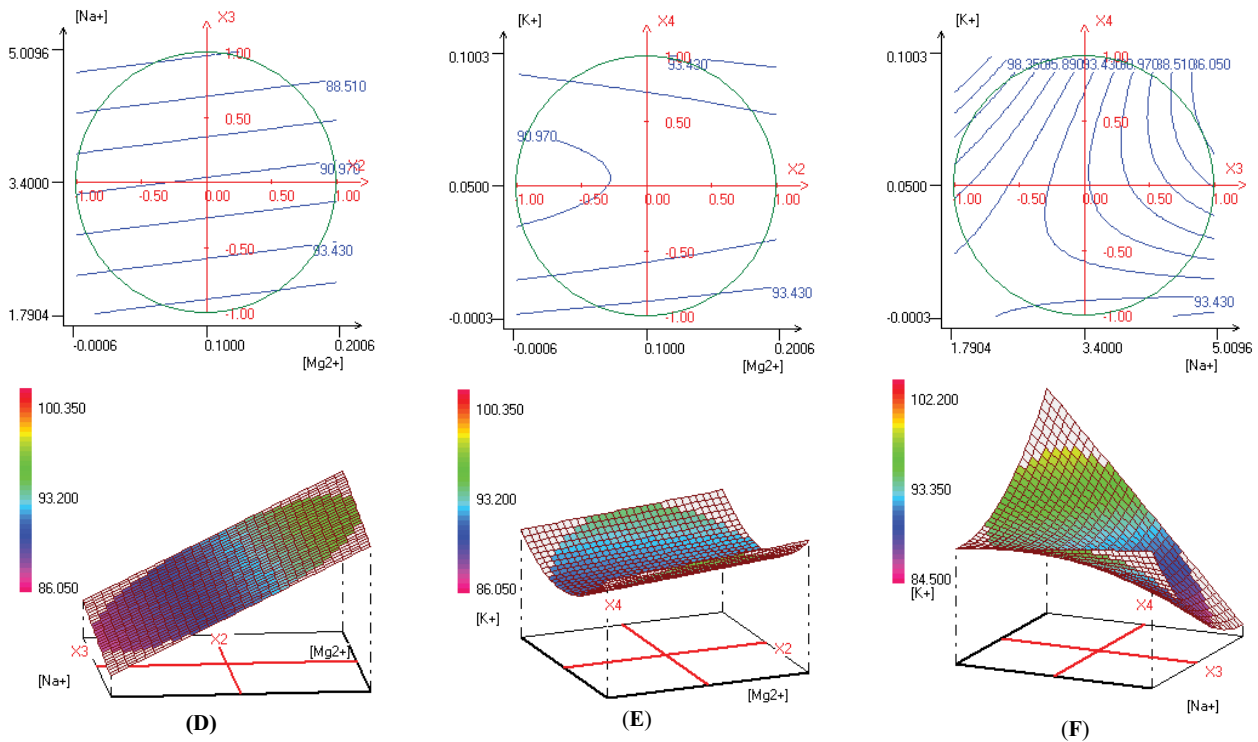
Fig. 5. The 2D and 3D iso-responses curves of the recovery lithium response vs. the two factors combinations: (D) $[Mg^{2+}]$-$[Na^+]$, (E) $[Mg^{2+}]$-$[K^+]$ and (C) $[Na^+]$-$[K^+]$.

approach is applied in this part and in the validation by accuracy profile method developed later. This objective function is determined by a relationship between the global desirability (D), bounded by 0% and 100% (totally satisfied), and the individual desirability (d_i) of each chosen response [20,29]. This approach is an efficient theoretical method offered by the statistical software (NemrodW). In our case, the only chosen response is the lithium recovery yield ($Y(\%)$). Fig. 6 shows the desirability profile of this response by assigning to 95% and 99% of lithium recovery and the global desirability D = 0% and 100%, respectively. Hence, the resulted optimal conditions are focused by: $[Ca^{2+}]$ (X_1) = 1.7 mol/L, $[Mg^{2+}]$ (X_2) = 0.02 mol/L, $[Na^+]$ (X_3) = 0.36 mol/L and $[K^+]$ (X_4) = 0.01 mol/L, which correspond to 64.128, 2.43, 60 and 2 g/L, respectively and the theoretical lithium recovery yield is nearby 98% in 5-fold diluted composition. These operating conditions are checked by the robustness test in the following paragraph.

Given that $[Na^+]$ (X_3) and $[K^+]$ (X_4) factors are not significant, they are fixed at their medium levels (0.02 and 0.01 mol/L, respectively) and the robustness test is only investigated by the significant factors ($[Ca^{2+}]$ (X_1) and $[Na^+]$ (X_3)). Table 6 summarizes these factors and their levels, which are incremented by ±0.1 mol/L around the optimal conditions. In fact, the studied ruggedness intervals become (1.6 mol/L; 1.8 mol/L) and (2.6 mol/L; 2.8 mol/L) for the significant factors ($[Ca^{2+}]$ (X_1) and $[Na^+]$ (X_3)), respectively. As summarized in Table 7, the robustness test is applied by using a full factorial matrix 2^k. Four runs in the –1 and +1 levels and four centered points (0) compose this matrix. Each run is performed by preparing a lithium spiked synthetic
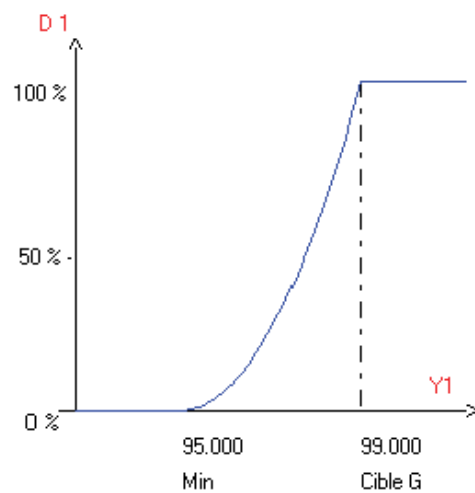

Fig. 6. Desirability function of the response: lithium recovery yield (Y).

Table 6
Levels of the significant factors for the robustness test ($[Mg^{2+}]$ = 0.020 mol/L and $[K^+]$ = 0.01 mol/L)

Factor name	Unity	Coded name	Levels		
			–1	0	+1
$[Ca^{2+}]$	(mol/L)	X_1	1.60	1.70	1.80
$[Na^+]$	(mol/L)	X_3	2.60	2.70	2.80

Table 7
Full factorial matrix 2^2 of the robustness test ($[Mg^{2+}]$ = 0.020 mol/L and $[K^+]$ = 0.01 mol/L and [Li] = 20 ppm)

N°.Exp	$[Ca^{2+}]$	$[Na^+]$	Recovery yield (%)
	X_1	X_3	Y_{obs}
1	−1	−1	99.177
2	1	−1	99.690
3	−1	1	97.639
4	1	1	98.152
5	0	0	98.306
6	0	0	99.536
7	0	0	99.946
8	0	0	98.511

Table 8
Signification of the investigated factors in the robustness test

Coefficient	Value	SD	t.exp.	Signification (%)
d_0	98.870	0.280	353.085	<0.01***
d_1	0.256	0.396	0.647	56.356
d_3	−0.769	0.396	−1.942	14.744
d_{13}	0.000	0.396	0.000	100.000

(***): Level of signification at $p < 0.1\%$, respectively.
SD: Standard deviation.
t.exp.: Calculated t-value of the student test.

brine ([Li] = 20 ppm). Table 8 resumes the signification of the above-mentioned factors and their interaction by using the statistical student test. This later reveals that all regression coefficients: d_1, d_3 and d_{13} are not statistically significant ($p > 5\%$), which means that the optimal conditions for determining the lithium recovery yield are statistically robust within the investigated ruggedness range. Consequently, the following step, which is a validation by the accuracy profile approach by setting the chemical composition of the synthetic brine at the above optimal conditions.

3.4. Validation of the lithium assay method by using flame emission spectroscopy: the accuracy profile approach

As already detailed above, this efficient approach is applied in this part by, firstly, starting with the use of the normality test (Shapiro–Wilk test). Then, the within-laboratory validation of the lithium assay method is applied based on two important interdependent parameters, which are the acceptability limit (λ) and the β-expectation tolerance interval. At the end, the resulted accuracy profile assessment is performed by using the desirability function method.

3.4.1. Shapiro–Wilk test

After checking the robustness of the lithium assay method by the flame emission spectroscopy, a Shapiro–Wilk test is carried out [30]. Sixteen-repeated runs are identically made as the centered points at the above-mentioned optimal

conditions (Table 7). The calculation of the experimental Shapiro–Wilk value, W_{exp} (n = 16; α = 5%) = 0.9286, is superior to the critical value, W_c (n = 16; α = 5%) = 0.8370, which means that the null hypothesis is accepted ($p > 5\%$) and the resulted measurements came from a normally distributed population. In light of the previous result, a validation of the lithium assay method by accuracy profile approach is performed and detailed in the following paragraph.

3.4.2. Validation by the accuracy profile approach

The aim of the validation is to prove that the analytical procedure for lithium assay has a guarantee to quantify the future concentration measurements (x) as close enough to the unknown "true value" (μ_T) with high proportion in routine analysis, that is, a good trueness (little bias) and a high intermediate precision (minimum of total error (systematic error + random error)). For this reason, two predefined interdependent parameters are required to reach this intended use: the acceptability limits (λ) and the β-expectation tolerance interval. The former is given by Eq. (3):

$$-\lambda < x - \mu_T < \lambda \Leftrightarrow |x - \mu_T| < \lambda \qquad (3)$$

where x, μ_T and λ are the expected measurement, the unknown "true value" and the acceptability limit, respectively. In fact, a procedure, giving the measurements inside these limits, is considered valid. However, it is practically impossible to obtain all expected measurements into the acceptability limits. Therefore, the second required parameter (β-expectation tolerance interval) must be determined based on the objective of the analytical method (biological, chemical or physical analysis). The most used theoretical β-values are 66%, 80% and 95% as proportions of the future concentration measurements that must fall inside the acceptability limits to decide that the analytical procedure is valid [21]. Eq. (4) resumes the relationship between the expected measurements (x), the unknown "true value" (μ_T), the acceptability limit (λ) and the proportion β. In our case, the chosen values of the two last parameters are 10% and 80%, respectively.

$$P\left(|x - \mu_T| < \lambda\right) \geq \beta \qquad (4)$$

The majority of the normative or regulatory documents (ISO, ICH, AFNOR and FDA) describe the validation criteria, but they do not provide the experimental strategies and are limited to general definitions (e.g., trueness, precision, accuracy, linearity, LOD, and LOQ). While the accuracy profile procedure provides a more reliable and appropriate experimental design by the good selection of the series (such as day, equipment and operator), the number of repetition and the levels of lithium concentrations according to many criteria (such as: feasibility, manipulation time, LOQ, etc.) in order to estimate the statistical parameters as close enough as the "true bias" and the "true variance" [22].

In our case, 3/3/5 and 3/2/3 experimental designs are the optimal and pragmatic procedures; the validation and the calibration designs, respectively, which are performed simultaneously [24]. Indeed, the two previous plans are similar in number of series (3 d), but they are different in

number of repetition (3; 2) and levels of concentrations (5; 3), respectively. Furthermore, the only chemical composition difference between the two kinds of designs is that the validation standards are prepared in synthetic brine, but the calibration standards are diluted in ultrapure water. Table 9 resumes the obtained intensity values of the validation design by varying, three times (3 repetitions), five predefined concentrations levels (8, 10, 25, 40 and 50 ppm) split in 2 at low, 1 in medium and 2 in high levels of the validation domain for each day [22]. The previous intensity values are used to back-calculate the lithium concentration by the daily-elaborated relationship. There are many kinds of used regressions such as linear through zero, linear through intercept, quadratic, weighted linear, linear after square-root transformed data and linear after log-transformed data. In the current study, the most appropriate regression is the linear through intercept. As can be shown in Fig. 7, the three linear curves are almost overlapped and the slope varies only about 1% between the highest (233.87 ± 8.60) and lowest values (231.87 ± 8.60), which confirms the robustness

Table 9
Intensity values of the validation matrix

Series (d)	Concentration levels (ppm)	Intensity values		
		Repetition		
		1	2	3
	8	693.717	756.794	724.088
	10	1,165.629	1,114.233	1,200.672
Day 1	25	4,688.619	4,595.171	4,716.653
	40	8,178.902	8,449.901	8,309.729
	50	10,482.395	10,645.929	10,622.567
	8	726.548	714.776	750.092
	10	1,338.692	1,126.796	1,150.340
Day 2	25	4,634.852	4,776.116	4,823.204
	40	8,472.524	8,244.147	8,166.452
	50	10,386.651	10,497.308	10,473.764
	8	710.087	735.885	737.058
	10	1,251.851	1,120.515	1,175.629
Day 3	25	4,661.918	4,685.371	4,769.801
	40	8,325.276	8,347.556	8,238.500
	50	10,434.873	10,572.074	10,548.621

Fig. 7. Daily elaborated calibration curves.

Day 1 → y = 231,87x − 1148,1 R² = 0,9993
Day 2 → y = 233,87x − 1122,7 R² = 0,9993
Day 3 → y = 232,87x − 1135,4 R² = 0,9993

of the current analytical method of lithium assay. In addition, the lowest value of the correlation coefficient is equal to 99.93%, which reveals that the relationship between the intensity response (dependent variable) and the lithium concentration (independent variable) is statistically significant. Therefore, the unknown lithium amount will be back-calculated not only in the validation step but also in routine analysis by using the daily-elaborated equation.

Table 10 summarizes all necessary statistical parameters for the built of the accuracy profile, which is a reliable and graphical tool to analyst to visualize and decide about the validity and the capability of the analytical method. For each predefined reference value (8, 10, 25, 40 and 50 ppm), average recovered concentration x, intermediate precision standard deviation (s_{IP}), tolerance standard deviation (s_{TT}) and coverage factor (k_{TT}) are computed by using the back-calculated values of the lithium concentration in the validation design. In addition, RSD values range of the intermediate precision (1.220%–1.390%) reveals a slight variation, which means that the response variances are almost constant over the validation range of lithium concentration (homoscedasticity).

Based on the predefined values of the acceptability limit and the proportion β (10% and 80%, respectively), two sided limits are computed for each parameter. As shown in Table 10, the upper and lower limits of the absolute and relative bias are calculated by using ppm and percentage units, respectively. Fig. 8 shows the resulted accuracy profile built by using the recovery yield and the relative upper and lower β-tolerance and acceptability limits. The x and y-axes show the predefined lithium concentration and the relative values of the sides of each interval (acceptability limits and tolerance interval), respectively. As can be seen the graph, the relative upper and lower β-tolerance limits did not exceed the acceptability limits (λ = ±10%), which is in fair agreement with Eq. (4). Consequently, the analytical method for lithium assay is valid over the concentration range (8–50 ppm) and it can be used lately for the routine analysis in order to estimate its amount in the oilfield brine samples. In addition, the low limit of quantification (LOQ) is inferior to 8 ppm in the resulted optimal composition.

For the level assessment of the validation satisfaction, a global desirability function approach is applied. This latter, named accuracy index I_A, depends on three individual desirability indexes, which are the dosing range index I_{DR}, the trueness index I_T and the precision index I_P. The relationships used to calculate on one hand these indexes and on the other hand the accuracy index I_A [23]. Firstly, a significant I_{DR}-value (100%) is reached, which confirms that the method is valid in the whole investigated range (8–50 ppm). Secondly, the resulted I_T-value (99.60%) is close to 100%, which proves that the measurements are almost not biased. Thirdly, a slightly significant I_P-value is achieved (73.70%) showing that this procedure is fairly precise. Finally, 90.20% of I_A-value is obtained, which resumes a high level of accuracy reached by this analytical lithium assay method.

3.4.3. Determination of the expanded relative uncertainty

As resumed in last line of Table 10, the expanded relative uncertainty (u_R) is calculated for each concentration level. This statistical parameter is almost proportional to

Table 10
Computed statistical parameters to build the accuracy profile

| Level	A	B	C	D	E
Reference value μ_T (ppm)	8	10	25	40	50
Average recovered concentration x (ppm)	8.001	9.955	25.083	40.534	50.045
Intermediate precision standard deviation (s_{IP})	0.111	0.121	0.322	0.537	0.610
RSD of intermediate precision (%)	1.390	1.220	1.284	1.325	1.220
Degree of freedom (ν)	6.230	7.714	7.714	7.714	2.951
Coverage factor (k_{IT})	1.434	1.402	1.402	1.402	1.650
Tolerance standard deviation (s_{IT})	0.119	0.366	0.339	0.566	0.688
Lower β-tolerance limit (L) (ppm)	7.829	9.441	24.608	39.741	48.911
Upper β-tolerance limit (U) (ppm)	8.172	10.468	25.559	41.328	51.180
Lower acceptability limit (L) (ppm)	7.20	9.00	22.50	36.00	45.00
Upper acceptability limit (U) (ppm)	8.800	11.000	27.500	44.000	55.000
Recovery yield (%)	100.009	99.545	100.333	101.336	100.090
Relative lower β-tolerance limit (L) (%)	97.868	94.412	98.432	99.351	97.821
Relative upper β-tolerance limit (U) (%)	102.149	104.678	102.234	103.321	102.359
Relative lower acceptability limit (L) (%)	90	90	90	90	90
Relative upper acceptability limit (U) (%)	110	110	110	110	110
Expanded relative uncertainty u_R (%)	2.985	7.356	2.703	2.794	2.748
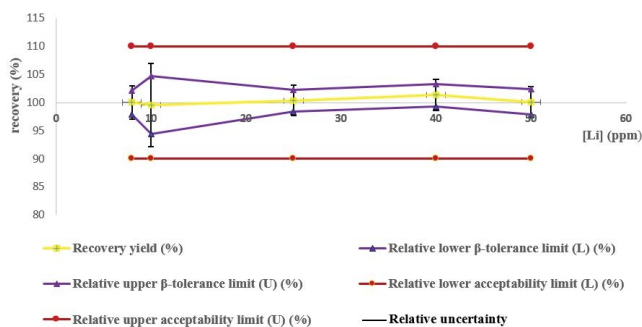
Fig. 8. Accuracy profile of the validated lithium assay method by flame photometer equipment and illustration of relative uncertainty.

the relative tolerance standard deviation, which is the ratio between s_{IT} and x-values. In fact, the maximum achieved value of the expanded relative uncertainty (u_R) is equal to 7.40% at [Li] = 10 ppm, which is considered fairly accurate because it is within the acceptability limits (±10%). Fig. 8 shows the expanded relative uncertainty bar for each lithium concentration level, which is relatively larger than the tolerance interval and it is explained that the former characterizes the dispersion of the quantity values being attributed to a measurand, but the later represents the future expected values quantified by the analytical method.

4. Conclusion

In this investigated work, a harmonized approach, divided into four steps, is chronologically applied in order to implement an accurate analytical method used for the routine analysis of the lithium assay. The first step is assigned to the specificity test indicating the presence of the chemical interferences due to the cohabitated major

cations in the synthetic and natural brines, which are considered complex matrixes. For this reason, an experimental design methodology is applied, as a second step, by studying the effect of four factors (major cations: [Ca^{2+}] (X_1), [Mg^{2+}] (X_2), [Na$^+$] (X_3) and [K$^+$] (X_4)) on the lithium recovery yield response (Y%). Indeed, a Doehlert design is used in this study in order to model and to optimize the chosen response. A fixed lithium concentration (20 ppm) is prepared in 5-fold diluted synthetic solution for each run. Therefore, the resulted outcomes from the statistical analysis of the previous design by the software NemrodW are a valid and predictive model and lithium recovery yield at nearby 98% obtained under the optimal chemical composition: [Ca^{2+}] (X_1) = 1.7 mol/L, [Mg^{2+}] (X_2) = 0.02 mol/L, [Na$^+$] (X_3) = 0.36 mol/L and [K$^+$] (X_4) = 0.01 mol/L. After that a robustness test is performed, as a third step, and the statistical analysis proves the capability of the used analytical method for lithium assay. Finally, a validation of the previous method is occurred by using the accuracy profile method as a graphical and reliable tool to the analyst in choose the right decision. Indeed, the resulted β-expectation tolerance interval is within the acceptability limits and doesn't exceed it, which proves that this analytical procedure is valid and the response variances are almost constant (homoscedasticity) over the predefined range of lithium concentration (8–50 ppm). In addition, the assessment of the within-laboratory validation is performed by using the global desirability function, which reveals that dosing range I_{DR}, trueness I_T, precision I_P, and accuracy I_A indexes, equal to 100%, 99.6%, 74% and 90.2%, respectively, are statistically significant and very convincing about the efficiency of the analytical method and it can be adopted for the routine analysis. Moreover, the expanded relative uncertainty (u_R) bars are within the acceptability limits (inferior to 10%) and they are relatively wider than the tolerance range, which

indicates the authenticity and the accuracy of the lithium assay method used to estimate its amount in the oilfield brine and assess the efficiency extraction process in a further study.

Disclosure statement

Acknowledgments

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