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Ensuring Therapeutic Consistency And Safety: A Comprehensive Physicochemical Quality Assessment Of A Commercially Available Potassium Gluconate Oral Suspension

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Abstract
The present study was conducted to perform a comprehensive quality control analysis of KALIGON 15% syrup, a pharmaceutical product, to verify its compliance with the specifications of the European Pharmacopoeia.
A series of analyses were performed on the finished product. The organoleptic properties (color, odor, and consistency) were evaluated. Physicochemical parameters, including pH, density, and average fill volume, were measured. The concentration of the active ingredient, potassium gluconate, and of potassium ions was determined using a calibration curve method. Finally, High-Performance Liquid Chromatography (HPLC) was employed for the identification and quantitative assay of the preservatives, methylparaben (Nipagine) and propylparaben (Nipazol).
The results obtained show that the organoleupeptic evaluation yielded a syrup with a slightly yellowish color, a raspberry odor, and a homogeneous consistency. The physicochemical analysis produced a pH of 5.67, a density of 1.3097 g/cm³, and an average fill volume of 124.22 ml. The assay for the active ingredient determined the potassium gluconate concentration to be 14.47 g/100ml and the potassium ion concentration to be 2.41 g/100ml. Finally, the analysis of preservatives found the Nipagine (methylparaben) concentration to be 0.09664 g/100ml and the Nipazol (propylparaben) concentration to be 0.02085 g/100ml.
All of these measured values fall within their respective acceptance ranges as specified by the European Pharmacopoeia.
Keywords: *Quality control, Physicochemical analysis, Kaligon 15%, syrup.*

INTRODUCTION

The pharmaceutical industry, a pillar of global healthcare systems, contributes significantly to improving the health and well-being of billions of people through the development and distribution of medicines. This sector, one of the most regulated in the world, is subject to strict controls by agencies such as the Food and Drug Administration (FDA) in the United States **[1]** and the European Medicines Agency (EMA) **[2]**. The quality of a medicine is directly linked to patient safety, and any failure can have serious consequences, ranging from ineffective treatment to major health risks for consumers. According to the World Health Organisation **[3]**, in low- and middle-income countries, one in ten medicines is of poor quality or counterfeit, highlighting the crucial importance of quality control.

To guarantee the quality, safety and efficacy of products, rigorous controls, governed by Good Manufacturing Practices (GMP) **[4,5,6]**, are implemented at every stage of the production process. These controls apply to raw materials as well as semi-finished and finished products, and aim to prevent any non-compliance or contamination. In addition, stability studies are conducted to ensure that the medicine retains its physical, chemical and microbiological properties throughout its shelf life **[7].**

In Algeria, industrial group is a major player in local pharmaceutical production **[8],** playing a strategic role in the country's health sovereignty policy. Among the many medicines manufactured by this group is Kaligon, a 15% potassium gluconate oral suspension. This medicine is indicated for the treatment of hypokalemia, a potassium deficiency in the blood that can lead to muscle weakness, cramps and heart rhythm disorders. Liquid pharmaceutical forms such as suspensions present particular challenges in terms of formulation and stability, making their control all the more important.

The objective of our study was to conduct a thorough physico-chemical characterization of the finished product Kaligon 15% oral suspension, in order to verify its compliance with pharmacopoeial specifications and to ensure its quality, stability, and suitability for therapeutic use.

MATERIAL AND METHODS

Organoleptic characteristics Observe the syrup with the naked eye (whether it is syrupy liquid, clear, amber, viscous...), and check the smell

pH It indicates the concentration of hydrogen in a liquid and allows to measure the degree of acidity or alkalinity of an aqueous solution. It is determined using a 780 pH meter 780 Metrohm TM.

Density measurements were carried out using a BioSan densitometer. All measurements were performed under standardized conditions to ensure accuracy and reproducibility.

Quantitative analysis of UV-visible spectrophotometry relies on the Beer-Lambert law which establishes a relation between the absorption of light by a substance and its concentration in a solution. The Beer-Lambert law is valid in the case of monochromatic light, diluted solutions, and in the absence of interferences from reflection, scattering, or fluorescence. In the present study, analyses were performed using Perkin Elmer, UV-Vis spectrophotometer. A quartz cell was used for all analyses.

Quantitative analysis by High-Performance Liquid Chromatography (HPLC) is based on the separation of components in a mixture according to their interactions with the stationary and mobile phases. The choice of detector depends on the chemical properties of the analyte and may include refractive index, fluorescence, or mass spectrometry. In this study, analyses were performed using a Waters 2695 HPLC system equipped. A C18 reverse-phase column, 250 mm × 4.6 mm, 5 µm column was used, with temperature and flow rate carefully controlled to ensure reproducibility and accuracy of the results.

RESULTATS AND DISCUSSION

I. Primary analyses

The preliminary stage of the analysis of the finished product KALIGON 15%, during which the organoleptic characteristics, pH, density, and volum were checked.

Organoleptic control

Organoleptic testing of KALIGON 15% syrup yielded satisfactory results. The syrup has a slightly yellowish color and a characteristic raspberry odor, which attests to its compliance with the specifications established according to the principles of the European Pharmacopoeia **[9]**. The observed coloration is an acceptable visual indicator and is potentially due to formulation components. The raspberry flavor plays a crucial role in masking the taste of the active ingredient, thus promoting better patient compliance. All these stable, expected sensory characteristics confirm the integrity and quality of the finished product, guaranteeing its release to patients.

PH measurement

The pH measurement of KALIGON syrup, taken directly using a calibrated pH meter, revealed a value of 5.67. This result is clearly within the acceptable range of [5.0–6.0] as prescribed by the European Pharmacopoeia **[9]**, thus confirming the product's compliance with this critical specification. Strict control of pH is of paramount importance for a liquid pharmaceutical formulation, as it directly affects several essential quality attributes. Indeed, maintaining the pH within this slightly acidic range is fundamental to ensuring the chemical stability of the active ingredient and excipients, preventing any premature degradation that could compromise the efficacy and safety of the medicine. In addition, this pH level is optimised to ensure good patient tolerance, avoiding the risk of mucosal irritation, and also contributes to the microbiological preservation of the syrup by creating an environment that is unfavourable to bacterial growth. Therefore, the value obtained of 5.67 not only represents regulatory compliance, but also demonstrates control over the manufacturing process, ensuring that a fundamental parameter for the quality, safety and efficacy of KALIGON syrup is perfectly controlled.

Determination of density

The density of the KALIGON 15% suspension, measured using a densimeter, was 1.3097 g/cm^3, which is within the acceptance limits [1.28-1.32]. As can be clearly seen, the density of the suspension remains within the compliance range.

Average volume:

9 bottles are randomly selected from the batch and the average volume of the 9 bottles is determined using a 250mL graduated cylinder. Using a test tube, the volume of 9 vials is measured individually and the average volume calculated.

According to the European phrmacopoeia **[9]**, the average volume of the vials should be between [114-126] mL. The volumes measured are summarised in Table

Table 1: volumes of KALIGON syrup finished product suspensions.

N° Flask	01	02	03	04	05	06	07	08	09
Volume (mL)	122	124	122	123	126	125	124	127	125

The average volume calculated is 124,22mL. There were no volumes outside the limits [114-126] mL. Consequently, the volume contained in the vials is declared to be uniform. This result means that the average volume calculated meets the specifications.

Determination of active ingredient and potassium ion:

The solutions used for physico-chemical quality control are also used to determine the concentrations of potassium ion and potassium gluconate in the KALIGON suspension. The relationship used to determine the concentrations of potassium ion and potassium gluconate is as follows:

Dg= Dp×6

Dp = n×5

Dg: Potassium gluconate concentration (g/100ml)

Dp: Potassium concentration in 100ml of syrup, expressed as (g/100ml).

n : Concentration of potassium ion in the syrup (determined from the calibration curve), expressed in (mg/ml).

According to the calibration curve shown in **Figure 1** we have :

y =784x -202.2

y=176, n=x

$x=\frac{y+202.2}{784}$ = 0.48 mg/ml=n

Dp = n×5 = 0.48×5=2.41g/100ml.

So : Dg=2.41×6= 14.47g/100ml

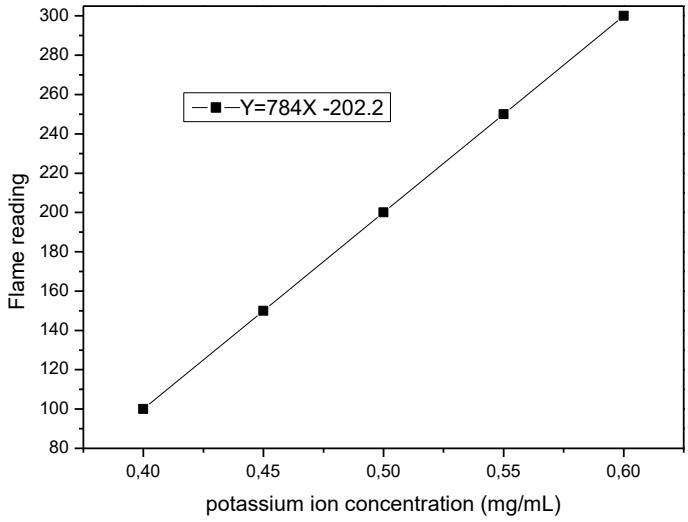

Figure1: Calibration curve for potassium ion in syrup.

The values determined lie within the following acceptance ranges:

Determination of potassium gluconate: [14.25-15.75] g/100 ml.

Potassium ion assay: [2.375-2.625] g/100ml.

Consequently, the concentrations of potassium gluconate and potassium ion in the KALIGON analysed are declared to comply with the requirements.

II. Preservative identity control and assay:

Identification of preservatives

Once the test and standard solutions are ready, identification is carried out by HPLC, by comparing the retention times obtained with the test solution (t_{essai}) with those obtained with the standard solution,($tr_{étalon}$) for each of the two preservatives. HPLC analysis was carried out under the same chromatographic conditions.

The chromatograms obtained are presented in Figures 2.A and 2.B below:

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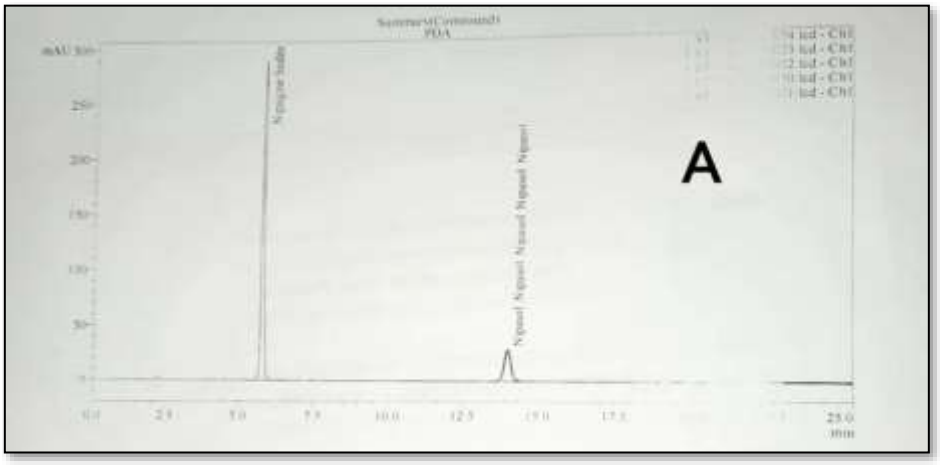

Figure 2.A : chromatograms of preservatives

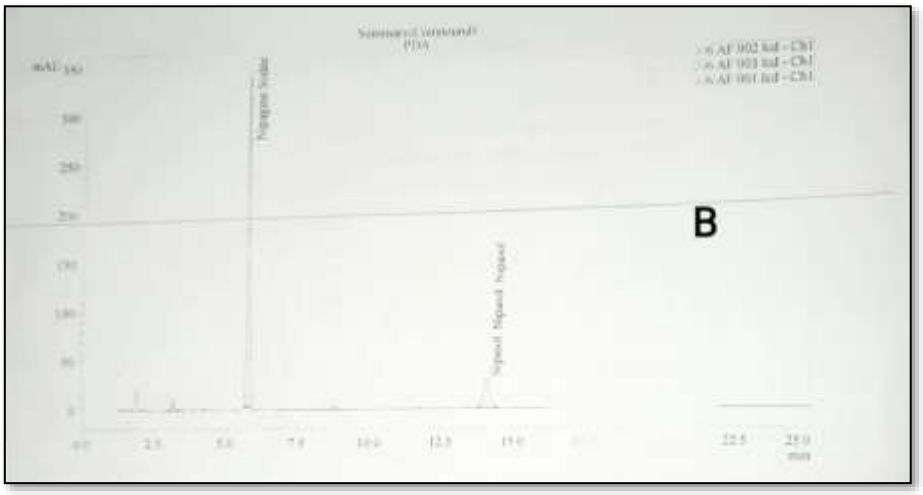

Figure 2.B: Chromatograms of the standard solution.

The retention times observed are summarised in Table below:

Table: Identity check of preservatives in KALIGON (syrup)

Retention time (min	Standard solution	Test solutioN
Nipagine	**Peak 1 : 5.754**	5.782
Nipazol	**Peak 2 :14.002**	14.101

As the retention times of peaks 1 and 2 in the test are very close to those of the Nipagine and Nipasol standards respectively, it can be verified that the preservatives contained in the KALIGON medicinal suspension are indeed methyl paraben and propyl paraben. The identities of the preservatives were confirmed.

Determination of the preservatives

The results obtained (peak area and retention time) for the determination of the preservatives 'Nipagine and Nipazol' by HPLC are summarised in the following tables 1 and 2:

Table 1: Determination of retention time and average surface area for sodium nipagine

N° Injection	Retention time (min)	Height	Concentration	Area	area average
Std: inj01	5.762	287064	0.09660	1874768	
Std : inj 02	5.757	289124	0.09660	1878468	
Std : inj 03	5.755	288638	0.09660	1880499	1879430
Std : inj 04	5.747	290175	0.09660	1880211	
Std : inj 05	5.751	289118	0.09660	1883205	
KALIGON : inj01	5.781	337528	0.10964	2127767	

KALIGON: inj 02	5.789	337008	0.11016	2137915	2139314
KALIGON : inj 03	5.776	339579	0.11090	2152258	

Table 2: Determination of retention time and average surface area for nipasol

Repeatability	Retention time (min)	Height	Concentration	Area	area average
Std : inj01	14.026	28907	0.02080	447989	
Std : inj 02	14.011	29004	0.02080	448628	
Std : inj 03	14.004	29055	0.02080	449277	449624
Std : inj 04	13.978	29273	0.02080	450260	
KALIGON: inj01	14.101	28411	0.02060	443662	
KALIGON : inj02	14.131	28270	0.02059	443190	443461
KALIGON : inj03	14.071	28598	0.02059	443531	

The relationship used to determine the concentrations of each of the two preservatives is as follows:

$$\boldsymbol{T = \frac{Sex}{Sst} \times \frac{Pst}{DILst} \times \frac{DILex}{Vex}\, t}$$

T: preservative content, in g/100mL.
Sex: peak area of the preservative in the solution to be examined.
Sex: area of the preservative peak in the standard solution.
Pst: preservative test sample in g.
DILst: dilution of the standard solution in mL.
DILex: dilution of the solution to be examined in mL.
Vex: volume of syrup taken from the solution to be examined in mL.
t: titre of preservative, expressed as a percentage.

Table 3: Concentrations of each of the two preservatives

Preservatives	Nipagine	Nipasol
Concentration (T)	0.09664 g/100ml	0.02085 g/100ml

The values thus determined fall within the following acceptance ranges:
Nipagine assay: [0.090-0.110] g/100 ml.
Nipazol dosage: [0.018-0.022] g/100ml.
According to the specifications described in the European Pharmacopoeia **[9]**, the preservative levels comply with the standards.
The levels of preservatives in the KALIGON analysed are declared to be in compliance with the requirements.

CONCLUSION

The comprehensive quality control analysis of KALIGON 15% syrup demonstrates that the product fully complies with the stringent standards set forth by the European Pharmacopoeia. Each parameter evaluated, from organoleptic characteristics to physicochemical properties and quantitative assays, yielded results within the specified acceptance limits.
The satisfactory organoleptic profile, with its characteristic color, odor, and consistency, confirms the integrity of the formulation and the reproducibility of the manufacturing process. The pH value of 5.67 is optimally positioned to ensure the chemical stability of the active ingredient, patient tolerance, and microbiological preservation. Furthermore, the conformity of the density and average fill volume attests to the precision of the production and batch uniformity.
Crucially, the assays for the active ingredient confirmed that the concentrations of potassium gluconate (14.47g/100ml) and potassium ion (2.41g/100ml) meet the required therapeutic levels. The analysis of preservatives, Nipagine and Nipazol, also verified that their concentrations are appropriate for ensuring the stability and safety of the product throughout its shelf life.

In summary, the collective evidence from this study confirms that KALIGON 15% syrup meets all critical quality attributes. The product is declared to be of high quality, safe, and effective, justifying its release for distribution to patients. This rigorous adherence to quality standards is consistent with Good Manufacturing Practices and ensures that KALIGON 15% is a reliable pharmaceutical product.

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