Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 4, 2013

Research Article

SFSTP GUIDELINE 1992 – BASED VALIDATION OF DIRECT POTENTIOMETRIC METHOD FOR QUANTIFICATION OF SODIUM BICARBONATE IN BABY'S BLISS GRIPE WATER AVAILABLE IN YEMEN

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Received: 23 July 2013, Revised and Accepted: 21 Aug 2013

ABSTRACT

Objective: The study aims to validate a direct potentiometric method based on classical approach namely SFSTP guideline 1992 for quantification of sodium bicarbonate (SB) in grip water syrup marketed in Yemen.

Methods: A potentiometric automatic titration method was used to SB in pharmaceutical products. The method was validated and applied to assay of SB in original and generic products.

Results: The validated method was very precise to each analyte with percent relative standard deviation (RSD %) of intraday (0.96 %) and RSD % of interday (1.11%). The accuracy test of the validated method exhibited well mean recovery value of 99.46 % with confidant interval (98.68 % – 100.24 %). Furthermore, the coefficient correlation (R^2) value was 0.9996. In addition, the results showed low dosage of active component which did not meet the acceptance criteria for SB in some generic products in the USP: 93%–107% of the stated amount per unit.

Conclusion: The described analytical method is a simple, sensitive, specific, more accurate and useful for the assay of SB in grip water syrup and the findings showed poor quality of some generic grip water syrups available in Yemen and this problem may affect the efforts to control gastrointestinal discomfort. Efficient regulatory systems of drugs quality control should be implemented.

Keywords: Validation, Potentiometric, Quality Control, Sodium Bicarbonate, Grip Water Syrup, Yemen.

INTRODUCTION

Gripe water is a home remedy for infants with colic, gastrointestinal discomfort, teething pain, reflux and other stomach ailments, gripe water is recommended by some pediatricians and alternative practitioners as a naturopathic treatment option[1]. On other hand, this product contains sodium bicarbonate (SB) that is a very quick-acting antacid. It should be used only for temporary relief [2,3]. Several studies have been done on assay of SB in different matrix. The European Pharmacopoeia (EP) described assay of SB as a raw material based on titration potentiometric method [4] while the United State Pharmacopoeia (USP) described its assay in tablet, powder and syrup pharmaceutical forms according to atomic absorption method [5]. In addition, the British Pharmacopoeia (BP) used titration method for determination of SB in eye drops, tablet, lotion, intravenous infusion and oral solution [6]. The first objective of our study was to develop and validate the direct potentiometric method for quantification of SB as the major active pharmaceutical ingredient available in grip water syrup based on guideline of Society French of Sciences and Pharmaceutical Techniques (SFSTP – 1992) [7] with the aid of International Conference Harmonization (ICH) guideline [8]. The second objective was to evaluate the quality of original and generic grip water products marketed in Yemen.

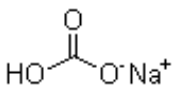

Fig. 1: Chemical Structure of SB

MATERIALS AND METHODS

Standard, samples, chemicals and apparatus

The potentiometric system consists of electrode (Metrohm – USA). Data acquisition was performed by the x lab software data registration, Balance of Precisa (Switzerland), 98.2 % SB standard was obtained from Sigma-Aldrich (Germany).Hydrochloric acid was supplied by Merck KGaA (Germany). Five samples namely one original and four generic grip water syrups were collected from licensed pharmacies in Yemen, Hodeidah city.

Potentiometric conditions

Instrument: potentiometric equipped with Metrohom 702 Titrino with keyboard, and 649 titre stand or Metrohom 798 with keyboard and 728 stirrers. Electrode: Combined pH electrode KCl (3.0 M) as electrode (Metrohom 6.0222.100 or 6.0258.000 were suitable). The titration parameters were volume step: 0.1 ml, titre rate: maximum ml/min, signal drift: 50 mV/min, equilibrium time : 25 seconds and temperature : 25 °C.

Validation of potentiometric method

Analytical method was validated on based on SFSTP guideline – 1992 associated with the ICH guidelines Q_2R_1 – 2005 which required two solutions of calibration standards (CSs) and validation standards (VSs). For estimation of linearity and accuracy of parameters, CSs were prepared separately by accurately weighting 12.5 mg, 25 mg, 50 mg, 75 mg and 100 mg of SB RS and diluting them, respectively in 50 ml of water. These solutions were mixed and sonicated for 10 min. Each level was repeated three times in three series of analysis. Altogether 3 (series) × 5 (levels) × (replicates) = 15 standards solutions were prepared and independently measured. The original product (SB in matrix) was used as VS to reach five concentrations levels like the CS [7,8]. For estimation of precision, six VSs with target concentration (50 mg/50 ml water) were prepared in three days (6 × 3). The Samples prepared: into a measuring beaker and titrate with hydrochloricacid (0.1N) for determination the end point potentiometrically.

RESULTS AND DISCUSSION

Validation of analytical method

Specificity

The specificity of the developed potentiometric method for quantification of SB in grip water was investigated in order to obtain an indication of the possible interferences from the drug substance with other components at routine analysis. The results in figure 2 – A and B showed that there were no difference between CS and VS.

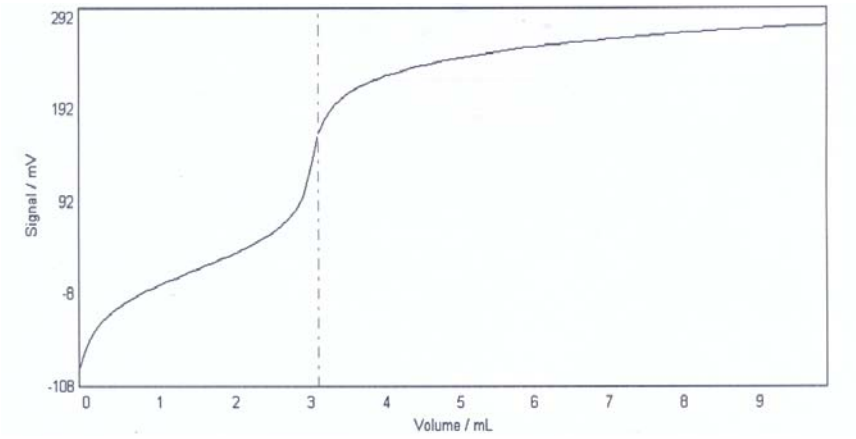

Fig. 2A: Potentiometric titration method of CS of SB (API only) with HCl 0.1 N

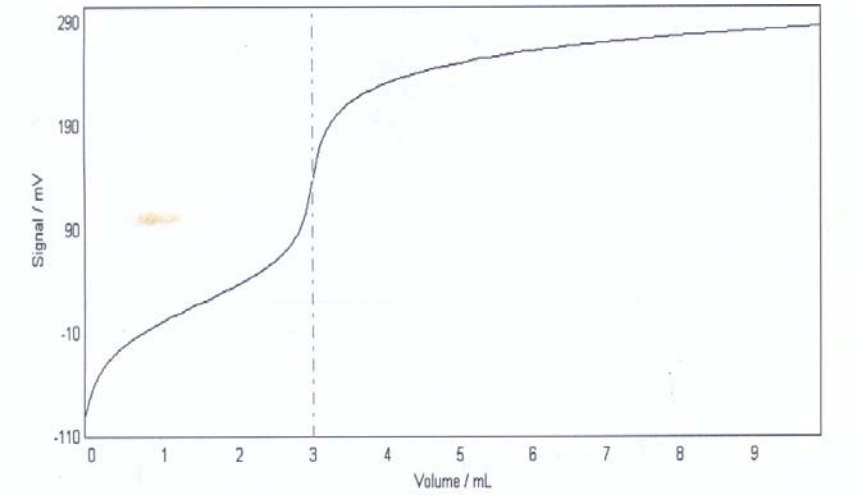

Fig. 2B: Potentiometric titration method of VS of SB (API in matrix) o SB with HCl 0.1 N

Linearity

Five calibration standards of SB were prepared in order to evaluate the relationship between the volume and the concentration (Figure 3). The homogeneity of the variances through all the concentration levels of the CS and VS was estimated by Cochran Test and the results showed no different significant between different concentrations levels ($p > 0.05$). On the other hand, the linearity of the relationship was evaluated in a concentration range of 0.25 mg /ml to 2.00 mg /ml, covering the normal range of concentrations obtained when analyzing the SB with slope 0.118, intercept - 0.025 and correlation coefficient (R^2) equal to 0.9997. In addition, for comparison between slop and intercept of CS and VS, the data obtained were compared by Test student, the p-value more than 5 % ($p > 0.05$) draw the conclusion that exists a no statistically significant difference (Table 1- A).

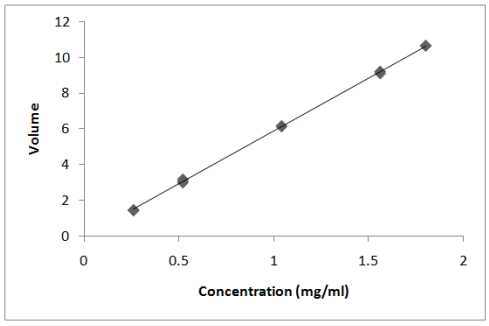

Fig. 3: Linearity of validated method

Table 1A: Results of analytical method validation

Linearity of validated method	SB	SB in matrix
Cochran Test	p > 0.05	p > 0.05
Slope	0.119	0.118
Intercept	- 0.067	- 0.025
R^2	0.9996	0.9997
Comparative between two slops	p > 0.05	
Comparative between two intercepts	p > 0.05	

Accuracy

Accuracy parameter was determined by using of CS at three levels with concentrations ranging from approximately 0.5, 1 to 1.5 mg/ml. Recoveries of validated method ranged from 98.68 % – 100.24 % with a mean of 99.46 %. The homogeneity of the recoveries through all the three concentrations levels of the VS was estimated by Cochran Test and the results obtained showed no significant different between them ($p > 0.05$). On the other hand, the data obtained of the recovery in different levels were compared by using F test and the results proved the existence of no significant difference between them ($p > 0.05$) (Table 1 - B).

Precision

The repeatability (Intraday) of the method was tested by analyzing six replicate samples of 1.5 mg /ml of SB; the percent relative standard deviation (RSD %) was 0.96 %. The intermediate precision (Interday) of the same concentration of SB was evaluated over 3 days by performing six measurements every day and the RSD % was found to be 1.11 % (Table 1 - C).

Table 1B: Results of analytical method validation

Accuracy of validated method – Recovery (%)	
Level	
1	99.09 %
2	99.47 %
3	99.81 %
Homogeneity of recoveries	p > 0.05
Analyze of variance	p > 0.05
Mean (%)	99.46
Confidence Interval (%)	98.68 – 100.24

Routine analysis

Five samples (original and four generic products) were collected from licensed pharmacies of Hodeidah city, Yemen. Assay of active pharmaceutical ingredient namely SB was measured and the results were shown in Table 4. From the table, 40 % of the sampled SB in grip water syrup showed low dosage of active component which did not meet the acceptance criteria for SB in pharmaceutical products in the USP: 93%–107% of the stated amount per unit. These were two products (generic 1 and 2) sampled from Egypt and Yemen showed the lowest percentage of active pharmaceutical ingredient (%): 93.66 % and 80.00 %, respectively.

Table 1C: Results of analytical method validation

Precision of validated method (RSD %)	
Day	
Day 1	1.60 %
Day 2	0.38 %
Day 3	0.21 %
Homogeneity of recoveries	p > 0.05
Repeatability (Intraday)	0.96 %
Intermediate precision (Interday)	1.11 %

Table 4: Routine analysis of SB in grip water syrup

Products	Assay (%)	RSD (%)	Manufactures Countries
Reference	98.99	0.90	England
Generic 1	93.66	1.33	Egypt
Generic 2	80.00	0.88	Yemen
Generic 3	99.00	1.11	Egypt
Generic 4	98.80	1.27	Egypt
Acceptance criteria for assay of SB in pharmaceutical products according to USP : 95 % – 105 % [5].			
Acceptance criteria for precision of analytical method at routine analysis according to ICH : (< 2%) [8].			

CONCLUSION

Direct potentiometric method was developed and validated using a classical approach namely the SFSTP guidelines 1992 for the assay of SB in liquid pharmaceutical forms. This approach gives enough guarantees for the results that will be generated by this method during routine analysis. The present study showed that the potentiometric method could be used more accurately to assay the SB in grip water syrup marketed in Yemen. This study showed poor quality of some products sampled from Yemen and this could be attributed to the absences of efficient regulatory systems. Poor quality of these products may affect the efforts to control gastrointestinal discomfort and providing high quality of drug products will significantly reduce diseases. Although, grip water syrups treatment failure against gastrointestinal discomfort in children are usually due to low compliance or the use of grip water preparations of poor quality could also contribute to this failure.

ACKNOWLEDGEMENT

The authors would like to thank the director and staff of the Drugs Quality Control Laboratory of Rabat, Morocco and Mr Khaldoon Saeed B.Sc. Pharmacy, for their fruitful assistance.

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