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QUANTITATIVE DETERMINATION OF FLURBIPROFEN IN BOTH BULK AND FORMULATIONS USING ACID-BASE TITRATION

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ABSTRACT

Flurbiprofen, a propionic acid derivative, is a non steroidal anti-inflammatory agent (NSAIA) with antipyretic and analgesic activity. Oral formulations of flurbiprofen may be used for the symptomatic treatment of rheumatoid arthritis, osteoarthritis and anklylosing spondylitis. Flurbiprofen may also be used topically prior to ocular surgery to prevent or reduce intra-operative miosis. In the present study, simple titrimetric method was developed. Respective quantities of Flurbiprofen were taken in aqueous methanol titrated against 0.1N sodium hydroxide acid using phenolphthalein as an indicators for acid-base titration. This method were found to be sensitive and inexpensive, do not require any sample processing steps and can be utilized for estimation of flurbiprofen in bulk and formulations.

Keywords: Flurbiprofen, Titrimetry, Sodium hydroxide, Methanol

INTRODUCTION

Flurbiprofen [(±)-2-(2-fluoro-4-biphenylyl) propionic acid] is an important non-steroidal, anti-inflammatory drug (NSAID), effectively used in the treatment of rheumatoid arthritis [3]. Flurbiprofen demonstrates comparable efficacy to other NSAIDs, e.g. aspirin [4], indomethacin [10], ibuprofen [7] and Naproxen [6] in the treatment of rheumatoid arthritis. Flurbiprofen is indicated for the management of vernal kerato conjunctivitis [15], Post-operative ocular inflammation [12], herpetic stromal keratitis, excimer laser photo refractive keratectomy [14] and ocular gingivitis [5].

Recent reports suggest potential topical and systemic use of flurbiprofen in radio-protection [13] inhibition of colon tumor [8], protection of post-irradiation myelo suppression [11], pain management after foot surgery [16] and peridontal surgery [17].

With its ever increasing use and the number of formulations entering into the market, there is always a need for simple, sensitive, accurate, rapid, reproducible analytical method for the estimation of flurbiprofen in pure form and in formulations which can be easily adapted for routine analysis in quality testing laboratories.

The present work aims to develop a simple, rapid and sensitive, accurate and economic titrimetric method for the determination of flurbiprofen in pure form and pharmaceutical preparations using 0.1N sodium hydroxide and this method do not require any sample processing and extraction steps and can be used for the quality control of these drugs in industry. The developed method was validated as per ICH guidelines and USP requirements, suitable statistical tests were performed on validation data.

MATERIALS AND METHODS

Materials: Flurbiprofen, sodium hydroxide, phenolphthalein, potassium hydrogen phthalate, triple distilled water, starch, magnesium stearate, microcrystalline cellulose, talc

Preparation of 0.1N Sodium hydroxide: It was prepared by adding accurately weighed 4gm of sodium hydroxide was dissolved in 1000 ml of distilled water using standard volumetric flask.

Standardization of 0.1N sodium hydroxide: Accurately measured quantity of 20.4gm of standard potassium hydrogen phthalate and dissolved in 1000ml of distilled water, 5ml was pipette out into a clean conical flask and phenolphthalein indicator was added. Then the contents in the conical flask were titrated against standard solution of 0.1N sodium hydroxide, solution.

Titration was carried out until color changes from colorless to pale pink. Results were obtained in triplicate for standardization using the fallowing formula $N_1V_1=N_2V_2$, (Where N_1 and V_1 are the normality and volume of standard potassium hydrogen phthalate N_2 and V_2 are the unknown normality and consumed volume of sodium hydroxide).

Equivalent factors: The exact amount of base consumed by the drug can be determined by stoichiometric equations was described in **Figures 1**. In this step, one mole of drug was undergone reaction with sodium hydroxide. Therefore, Each 1 ml of 0.1N sodium hydroxide is equivalent to 0.024426 gm of flurbiprofen.

Assay procedure using 0.1N sodium hydroxide: Aliquots of flurbiprofen were prepared by dissolving different amounts of drug (100-500mg)add 25 ml of methanol and add 25 ml of triple distilled water. Aliquots were titrated using previously standardized 0.1N sodium hydroxide using phenaphthalein as an indicator to pale pink was observed for end point identification. Results were obtained in triplicates and flurbiprofen was assayed. Assay reaction for titration is shown in **figure 1.**

Linearity: To establish the linearity of proposed methods, five separate series of solutions of drug ranging from 100mg-500mg were dissolved in 25 ml of methanol and add 25ml of distilled water. Then the resulting solution was titrated against 0.1N sodium hydroxide by using phenolphthalein as an indicator, end point pale pink color.

Specificity: Specificity is the ability of an analytical method to differentiate and quantify the analyte in the presence of other components in the sample [1]. The specificity of these methods were determined by adding inert excipients such as starch, microcrystalline cellulose, magnesium stearate and talc individually with known concentration of the drug and titrated by using standard solutions.

Estimation from excipient blends: The in-house prepared tablet formulation blends were prepared, since no marketed formulations were available. These tablet blends were prepared by adding immediate release excipients such as starch, microcrystalline cellulose, magnesium stearate and talc. The crushed blend equivalent 100 mg and 250 mg were transferred to conical flask and respective solvents were added; solutions were filtered through Whatman filter paper number (#40) and the filtrate was titrated with standard solutions using indicators. Assay results were shown in T**able 2 and 3.** Calibration curve was shown in **figure-2.**

RESULTS AND DISCUSSIONS

The mean five normality values are calculated and approximate values obtained, which were equivalent to normality of 0.1.25 ml of methanol was used to dissolve flurbiprofen. Add 25ml of distilled water, did not produce any precipitate. The proposed reactions were found to be simple acid- base titration of flurbiprofen using basic solvent like sodium hydroxide. During the process of titration, the amount of base consumed was calculated.

An accurately consumed 13.9±0.04 ml (RSD 1.27) of 0.1N sodium hydroxide is equivalent to 303.84 mg of flurbiprofen The correlation coefficient was found to be 0.9996 for 0.1N sodium hydroxide.

The assay procedure was performed and percent recovery values were determined for actual drug and blend equivalents (Table 2 and 3). The estimated drug content with extremely low value of RSD established the precision of the proposed methods. Recovery experiments using the developed assay procedures further indicated absence of interference from pharmaceutical excipients used in the selected formulation blends.

CONCLUSION

A new titrimetric method has been developed to be routinely applied to estimate in flurbiprofen bulk and formulation. This method has proved to be specific, linear, well recovered. Hence the method is recommended for routine quality control analysis.

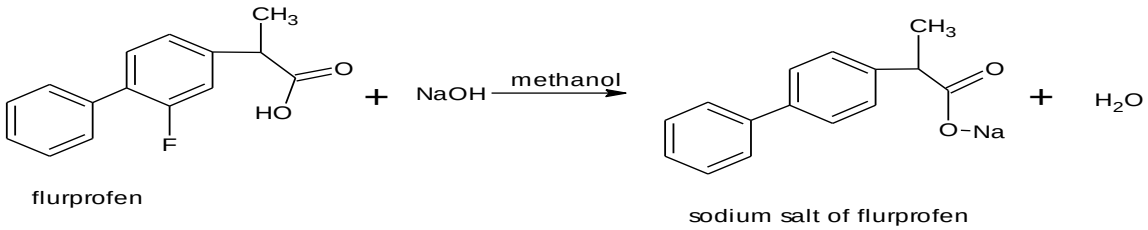

Figure 1: ACID-BASE titration with 0.1N sodium hydroxide

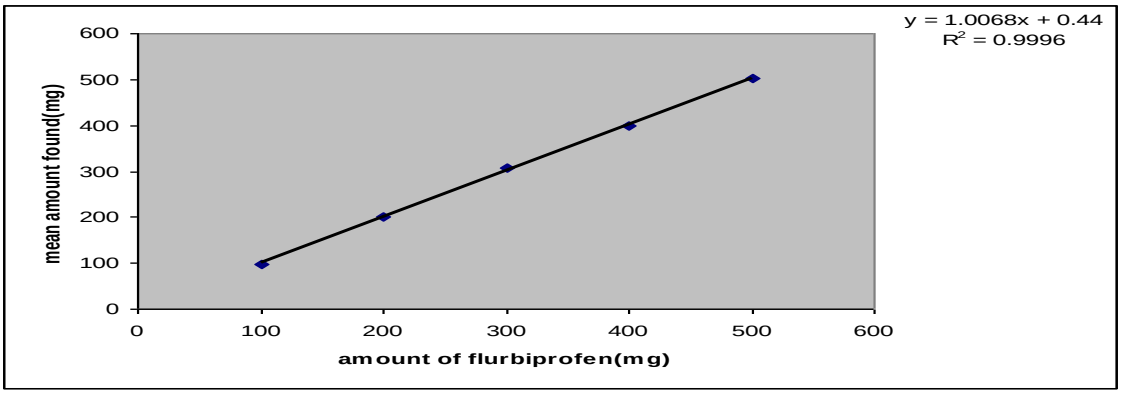

Figure-2: Calibration curve- Assay of Flurbiprofen with 0.1N sodium hydroxide

Table -1: Acid-Base titration (Standardization values of the 0.1N sodium hydroxide)

Volume of potassium hydrogen pthalate(ml)	**Volume of sodium hydroxide consumed (ml)**
05	5.3
05	5.4
05	5.3

Mean volume of sodium hydroxide consumed	5.34ml
Standard Deviation	0.889443
RSD	1.66
Normality of sodium hydroxide consumed	0.092N

*Relative standard deviation (n=5)

Table 2: Assay of Flurbiprofen with 0.1N sodium hydroxide

Amount of drug added (mg)	**Mean volume of sodium hydroxide consumed(ml)**	**RSD*(mg)**	**Mean amount found (mg) †**	**% Recovery**
100	4.5±0.02	1.85	98.95	98.95
200	9.2±0.1	1.71	202.2	101..12
300	14.02±0.2	1.77	307.76	102.58
400	18.2±0.2	0.91	400.04	100.02
500	22.9±0.1	1.31	503.42	100.68

Table 3: Assay of Flurbiprofen in Blend with 0.1N sodium hydroxide

Blend equivalent (mg)	Mean volume of sodium hydroxide consumed(ml)	RSD*(mg)	Mean amount found (mg) †	% Recovery
100 mg	4.62±0.03	1.81	102.3	102.3
250 mg	11.12±0.04	1.33	249.3	99.7

*Relative standard deviation (n=5)
† Each 1 ml of 0.1N S0dium hydroxide is equivalent to 0.024426 gm of flurbiprofen

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