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Simultaneous UV-spectrophotometric estimation of ibuprofen and moxifloxacin in pH 6.8 phosphate buffer

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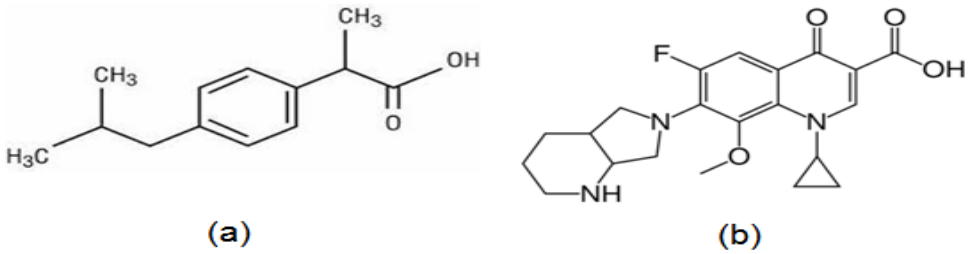
ABSTRACT

Rapid development of research in the field of periodontal drug delivery poses challenges in developing new analytical methods to estimate combination of drugs used to treat infections. Preferably, the anti-inflammatory agent is a non-steroidal anti-inflammatory drug (NSAID), such as ibuprofen should be employed in subgingival infections along other anti-microbial agents such as moxifloxacin. The aim of the present investigation is to develop a precise and rapid simultaneous estimation of ibuprofen and moxifloxacin using a UV spectroscopic method in pH 6.8 phosphate buffer. Ibuprofen and moxifloxacin showed absorbance maxima at 224.5 nm and 287 nm in 6.8 pH phosphate buffer respectively. The validation parameters proved that the developed method could be employed successfully for simultaneous routine determination of these drugs in formulations such as *in situ* gels intended for periodontal infections.

Keywords: Ibuprofen, moxifloxacin, Simultaneous estimation, UV-spectrophotometric method, periodontal infections, *in situ* gels.

INTRODUCTION

Gram-negative enteric rods were associated with periodontal diseases in several populations including chronic periodontitis. Moxifloxacin appeared capable of eradicating these organisms from periodontal pockets. Its good activity against Gram-negative enteric rods and periodonto pathogens suggests the potential use of moxifloxacin as an adjunctive antibiotic in the treatment of mixed periodontal infections[1]. Post-surgical discomfort is usually treated with over-the-counter medications such as ibuprofen or the application of ice packs[2]. Preferably, the anti-inflammatory agent is a non-steroidal anti-inflammatory drug (NSAID), such as ibuprofen should be employed in subgingival infections. The formulation could include one anti-inflammatory agent and at least one other anti-microbial agent[3]. Rapid development of research in the field of periodontal drug delivery poses challenges in developing new analytical methods to estimate combination of drugs used to treat infections.



(a) (b)

Figure 1: Structures of (a) ibuprofen and (b) moxifloxacin

The 2-arylproprionic acid derivative, ibuprofen [RS-2-(4-isobutyl-phenyl) propionic acid] (Figure 1a), is one of the most potent orally active antipyretic, analgesic and nonsteroidal anti-inflammatory drug (NSAID) used extensively in the treatment of acute and chronic pain, osteoarthritis, rheumatoid arthritis and related conditions. This compound is characterized by a better tolerability compared with other NSAIDs[4].

Moxifloxacin is chemically1-cyclopropyl-7-[(S,S)-2,8-diazabicyclo [4.3.0]non-8-yl]-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3 quinoline carboxylic acid (Figure 1b)[5]. It is a slightly yellow crystalline powder with formula $C_{21}H_{24}FN_3O_4$ and molecular weight 401.43 g/mol. It has been found to be effective in acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, community acquired pneumonia, skin, and skin structure infections. In literature survey many analytical methods includes and UV-Spectroscopic[6], RP-HPLC[7] and HPTLC[8] methods. A few methods have also been described for the simultaneous determination of Dexamethasone and fluoroquinolones with other drugs such as Chloramphenicol and Prednisolone[9-12]. Some analytical methods are also available for the estimation of moxifloxacin alone or in combination[13-15]. Similarly few spectroscopic methods are available for the estimation of ibuprofen alone and in combination with various drugs[16,17]. To the best of our knowledge no analytical methods are reported for the simultaneous estimation of ibuprofen and moxifloxacin. Therefore the aim of the present investigation is to develop a precise and rapid simultaneous estimation of ibuprofen and moxifloxacin using a UV spectroscopic method in pH 6.8 phosphate buffer. The present study encompasses to estimate these drugs in bulk and in any dosage form expected to come out in the coming future based on above literature projection. We expect that the combination of these two drugs is used to treat periodontal infections. A combination formulation is also expected to come out in the market in the coming days.

MATERIALS AND METHODS

Chemicals

Working standard of ibuprofen and moxifloxacin were pursued as a gift sample from Alkem Laboratories, Mumbai, India. All chemicals and solvents of AR grade were purchased from Merck India Ltd, Mumbai, India.

Instrumentation

UV- spectrophotometer (Elico-India, SL-164) with spectral b and width of 2 nm and 10 mm matched quartz shells was used for development analytical method over the range of 200–400 nm.

Preparation of standard stock solutions

An accurately weighed quantity of both ibuprofen and moxifloxacin equivalent to 10 mg was taken in two different 100 mL volumetric flasks and it was dissolved by using 5 mL of ethanol and volume was made to mark with 6.8 pH phosphate buffer to give a 100 µg/mL each of both drugs. The aliquot portion of standard stock solution of ibuprofen and moxifloxacin were diluted with 6.8 pH phosphate buffer to obtain concentration 10 µg/mL.

Selection of analytical wavelengths

Appropriate dilutions were done for the drugs from the standard stock solutions and scanned in the spectrum mode from 200–400 nm. Ibuprofen and moxifloxacin showed absorbance maxima at 224.5 nm and 287 nm in 6.8 pH phosphate buffer respectively.

Construction of calibration curves

From the above stock solution 2, 4, 6 and 8 mL were taken and diluted up to 10 mL with phosphate buffer pH 6.8 to get 2, 4, 6 and 8 µg/mL concentrated solutions of both ibuprofen and moxifloxacin respectively.

Absorbance of solution was measured at 224.5 and 287 nm in 6.8 pH phosphate buffers using the buffer as blank for ibuprofen and moxifloxacin respectively. The graphs were plotted for concentration vs. absorbance to get calibration curves of the drugs.

Determination of drug content in *in situ* gels prepared

Drug content uniformity in the drug delivery system is an important aspect that determines the performance of the system in *in vivo* conditions. If the drug is not distributed uniformly throughout the formulation, it could either lead to availability of sub therapeutic dose or toxic dose. Drug content uniformity was also performed to ensure minimum batch to batch variations. The drugs content of formulated gels which was analyzed spectro photometrically at λ_{max} 224.5 nm (ibuprofen) and 287 nm (moxifloxacin) in pH 6.8 phosphate buffer. The prepared formulations were analyzed for the drug content by taking 1 mL of the smart gel in 50 mL volumetric flasks, 3 mL of 6.8 pH buffer was added and shaken to dissolve the drugs. The volume was made up to the mark by 6.8 pH phosphate buffer and the solution was left overnight. The drug content was determined by measuring the absorbance at 224.5 nm for ibuprofen and 287 nm for moxifloxacin using an UV-Visible spectrophotometer.

Method validation

Precision

The precision of the proposed method was ascertained by actual determination of six replicates of fixed concentration of the drug within the Beer's range and finding out the absorbance by the proposed method. From this absorbance mean, standard deviation and % RSD were calculated.

Accuracy

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (50 %, 100 % and 150%) of bulk samples of ibuprofen and moxifloxacin within the linearity range were taken and added to the pre-analyzed formulation of concentration 8 µg/mL for both the drugs. From that the percentage recovery values were calculated.

Repeatability

Repeatability is given by inter-day and intra-day precision. Intra-day precision was determined by analyzing the three different concentration of drug for three times in the same day. Inter-day precision was determined by analyzing the three different concentration of drug for three days in a week. From the data the % RSD was determined.

Recovery

Recovery studies were carried out by addition of standard drug solutions to pre-analysed sample solutions of ibuprofen and moxifloxacin at three different concentration levels taking into consideration percentage purity of added bulk drug sample.

Ruggedness

Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot in different laboratories using similar operational and environmental condition.

RESULTS AND DISCUSSION

A UV-spectrophotometric method was developed for the simultaneous estimation of ibuprofen and moxifloxacin in pH 6.8 phosphate buffer. The λ_{max} obtained for ibuprofen and moxifloxacin were 224.5 and 287 nm for ibuprofen and moxifloxacin respectively. The summary of the optical characteristics are shown in Table 1 and Figure 2.

Table 1: Optical characteristics of ibuprofen and moxifloxacin (n=6).

Parameter	Ibuprofen	Moxifloxacin
Working λ_{max} (nm)	224.5	287
Beer's Law limit (µg/mL)	2-10	2-8
Regression equation	y=0.0365x+0.0268	y=0.0555x+0.0274
Correlation coefficient (R^2)	0.9927	0.09978
Slope	0.0365	0.0555
Intercept	0.0268	0.0274
LOD (µg/mL)	0.85	0.74
LOQ (µg/mL)	2.6	2.36

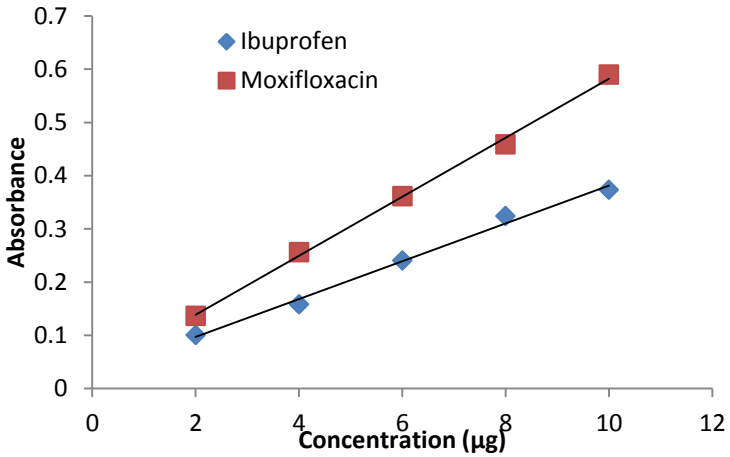


Figure 2: Linearity plots of ibuprofen and moxifloxacin.

Precision of the method was verified by using stock solutions in concentration containing 2 µg/mL of ibuprofen and moxifloxacin. System repeatability was done by repeating the assay three times of six replicate dilutions of the same concentration after every 2 h on the same day for intra-day precision. Inter-day precision was carried out by performing the assay of six sample sets after 24 and 48 h. The result of precision study is given in Table 2.

Table 2: Results of precision (n=6).

Drug	Parameter	Intra-day	Inter-day
Iburpofen	Mean	99.75	99.42
	%RSD	0.1588	0.1685
Moxifloxacin	Mean	99.57	99.83
	%RSD	0.1799	0.1252

To check the accuracy of the developed method and to study the interference of formulation additives, analytical recovery experiments were carried out by the standard addition method. The recovery studies were carried out at three different levels, i.e. 50%, 100% and 150% level. The percentage recovery values were shown in Table 3.

Table 3: Accuracy studies (n=6)

Drug	% Recovery			% RSD		
	50%	100%	150%	50%	100%	150%
Ibuprofen	99.75	100.03	100.15	0.365	0.398	0.429
Moxifloxacin	99.84	99.89	100.07	0.274	0.417	0.386

To check the degree of repeatability of method, suitable statistical evaluation was carried out. Repeatability was performed for six times with prepared formulation. The standard deviation, coefficient of variance and standard error was calculated. The results of statistical evaluation are shown in Table 1.

The LOD and LOQ of ibuprofen and moxifloxacin by proposed method were determined using calibration standards. LOD and LOQ were calculated as 3.3σ/S and 10σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of response. The results of the same are shown in Table 1.

Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot in different laboratories using similar operational and environmental conditions and the coefficent of variation was found to be less than 2%.

The selectivity of the method was checked by monitoring a standard solution of ibuprofen and moxifloxacin in presence of excipients (prepared *in situ* gels) at the same concentration level as used in the gels using the method described in the procedure for calibration curve. The excipients did not show any effect on the estimation of both the drugs. Hence, the determination of ibuprofen and moxifloxacinin the *in situ* gels were considered to be free from interference due to the excipients. This reveals that the potential utility of this method for the routine analysis of ibuprofen and moxifloxacinin pharmaceutical preparations.

The drugs content was estimated in the formulated in situ gels of ibuprofen and moxifloxacin intended to use as subgingival drug delivery systems. The results are summarized in Table 4.

Table 4: Analysis of *in situ* gel formulations (n=6).

Drug	Label claim (mg)	Amount estimated (mg)	% Label claim	% RSD
Ibuprofen	50	50.24	100.04	0.536
Moxifloxacin	50	49.86	99.16	0.427

CONCLUSIONS

The developed UV spectrophotometric method was simple, precise, accurate, linear, reproducible, and repeatable for the estimation of ibuprofen and moxifloxacin in pH 6.8 phosphate buffer. This developed method could be applied to estimate these drugs in pharmaceutical dosage forms such as *in situ* gels without any interference from the excipients. This method has been developed based on future thrust in the area of periodontal treatment using combination therapy of these drugs.

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