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A Simple Spectrophotometric Determination of Diclofenac Sodium in Commercial Dosage Forms using 2,3-Dichloro-5, 6-Dicyano-1,4-Benzoquinone (DDQ)

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Abstract

A rapid, simple and sensitive spectrophotometric method has been developed for the determination of diclofenac sodium in pure and tablet formulations. The method depends on the charge–transfer complexation between diclofenac sodium as n-electron donor with 2,3-Dichloro-5, 6-Dicyano-1,4-Benzoquinone (DDQ) in acetonitrile medium as π-acceptor to give a colored complex which absorbs maximally at 545 nm. Beer's law has been obeyed in the concentration range of 13-275 μg ml^{-1} with molar absorptivity of 2.5×10^3 L $mole^{-1}$ cm^{-1}. The proposed method is precise, accurate and specific for routine quantitative analysis of the drug in bulk and dosage forms.

Key words: Spectrophotometric determination, Diclofenac sodium, 2,3-Dichloro-5, 6-Dicyano-1, 4-Benzoquinone

Introduction

Diclofenac, derived from benzeneacetic acid, is a NSAID (non-steroidal anti inflammatory drug) of cyclooxygenase (COX) inhibitor. Chemically, it is described as 2-[(2,6-dichlorophenyl)amino] benzene acetic acid. The sodium or potassium salts of diclofenac are soluble in water and administered orally. They are widely used for the treatment of inflammatory disorders and painful conditions such as rheumatoid arthritis, gout, bursitis, painful menstruation and headache. They are effective in the relief of pain and fever [1].

Several analytical techniques are reported for the determination of diclofenac sodium in pharmaceutical formulations such as colorimetry [2-3], ultraviolet [4-7] and visible [8-14] spectrophotometry, fluorometry [15] gas [16-18] and liquid [19-21] chromatography and flow injection analysis with spectrophotometric detection [22]. Spectrophotometric methods provide practical and economical advantages over other methods. Most of these methods involve the determination of diclofenac sodium indirectly by means of either the formation of colored species with reagents (such as Methylene Blue, Methylene Violet, Copper (II) acetate, Iodine, 2,3-dichloro-5,6-dicyanol, 2,4-dichloro-6-nitro-phenol and ferric chloride / 2,2-bipyridine) followed by extraction [8,11,13,22] or *via* oxidation with $KBrO_3$, ceric ammonium sulfate or potassium ferricyanide [12,14]. Accuracy and precision of these methods are similar to those obtained by chromatographic methods. Nevertheless, they are time consuming and usually involve a solvent extraction step.

In this study, a sensitive, accurate and rapid spectrophotometric method has been optimized for the determination of diclofenac sodium in pharmaceutical preparations.

Experimental

Equipment

All spectrophotometric measurements were carried out using a UV-VISIBLE spectrophotometer (Model U 1100 Hitachi, Japan) with quartz cells of 1 cm thickness.

Chemicals and reagents

All reagents and chemicals used were of Analytical Reagent Grade. Diclofenac sodium was supplied by BioFine pharmaceuticals (Pvt.) Ltd. Multan, Pakistan. Diclofenac Sodium tablets were purchased from the local market of Multan, Pakistan. Stock solution of diclofenac sodium was prepared by dissolving 100 mg powder in sufficient amount of methanol then diluted with acetonitrile (99.9%). Standard diclofenac sodium solutions were prepared from the stock solution by appropriate dilution with acetonitrile. 0.2 % solution of 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone (DDQ) (*Fluka, Hong Kong)* was prepared in acetonitrile.

Proposed Procedure

To different aliquots of diclofenac sodium (13-275 µg ml^{-1}, final concentration) in 10 ml flask, add 1 ml 0.2% of 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone (DDQ) solution. Keep the mixture for 5 minutes at room temperature (25±5 °C). Make the volume upto the mark with acetonitrile. Measure the absorbance of the solution at 545 nm against the reagent blank.

Procedure for the assay of diclofenac sodium in pharmaceutical formulations

Twenty tablets were accurately weighed and powdered. A portion equivalent to 100 mg of diclofenac sodium was stirred with 30 ml methanol. The residue was filtered with Whatman filter paper # 1 and washed with methanol. The filtrate and washings were diluted to 100 ml using acetonitrile. To 2 ml of this solution, 1 ml of 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone (DDQ) solution was added. The reaction mixture was kept at room temperature (25±5 °C) for 5 minutes. Final volume was made up to 100 ml with acetonitrile. Absorbance measurements were made at 545 nm against reagent blank.

Results and Discussion

Charge Transfer (CT) reaction has been widely studied recently. Many drugs are easy to determine by spectrophotometry based on colored Charge Transfer (CT) complexes formed with electron acceptors [23,24]. DDQ is π-electron acceptors as a result of the strong electron withdrawing halo- and cyano- groups conjugated with the π- system [25,26]. This complex is formed by the lone pair of electron donated by the diclofenac sodium as *n*-donor and the charge transfer reagent as an electron acceptor, which a partial ionic bond ($D^+ A^-$) is assumed to be formed.

$$\underset{\text{Donor}}{D} + \underset{\text{Acceptor}}{A} \longrightarrow \underset{\text{Donor-acceptor complex}}{[D \longrightarrow A]} \longrightarrow \underset{\text{Radical anion}}{D^+ + A^-}$$

Optimization of Analytical Parameters Choice of solvent and absorption spectrum

Different solvents have been tried in order to achieve maximum sensitivity and product stability. Dichloromethane, chloroform and 1,4-dioxane were suitable solvents for CT complexes. However, acetonitrile was the best solvent for DDQ complexes with respect to molar absorptivity and color stability. The complex formed between diclofenac sodium and DDQ reagent shows maximum absorption at 545 nm (Fig.1).

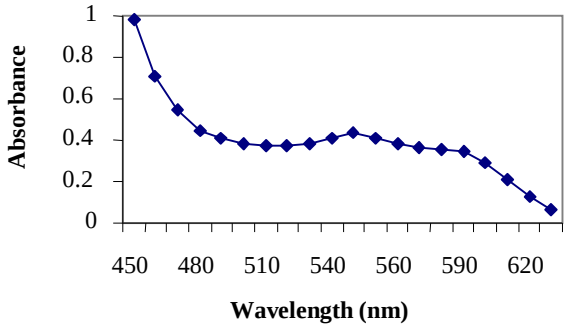

Fig. 1. Wavelength of maximum absorption of Diclofenac sodium-DDQ system

Stoichiometric Relationship

The molar ratio of the complexes formed between the studied drug and DDQ reagent used was investigated by applying the molar ratio [27] and continuous variation Job's methods [28] using equimolar solutions of the drug and reagent. The result indicated that the complex was formed in the ratio of 1 : 1 (Fig.2) . This finding supports that the interaction of the studied drug and the reagent takes place at only one site, which was the more sterically free terminal basic amino group.

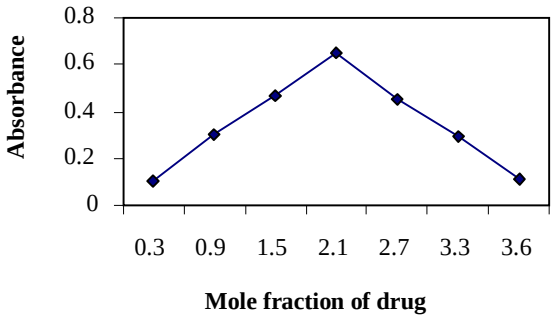

Fig. 2. Stoichiometric ratio of the complex

Effect of temperature, reaction time, reagent concentration and color stability

To optimize the reaction conditions different parameters such as temperature, reaction time, reagent concentration and color stability have been investigated. It was observed that the reaction occurred at room temperature (25±5 °C). The optimum reaction time to develop maximum color was found to be after five minutes at room temperature (Fig.3).

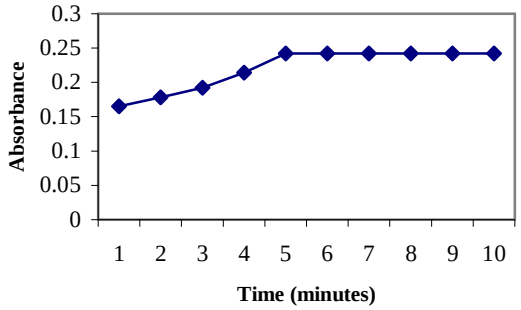

Fig. 2. Effect of time on color development

Effect of DDQ concentration on the color development was investigated. It was observed that absorbance increased with the addition of 0.2 % DDQ reagent. Absorbance remained constant after 1 ml of 0.2% DDQ reagent was added (Fig. 4) Therefore, 1 ml of 0.2% of DDQ reagent was chosen as the optimum in the procedure.

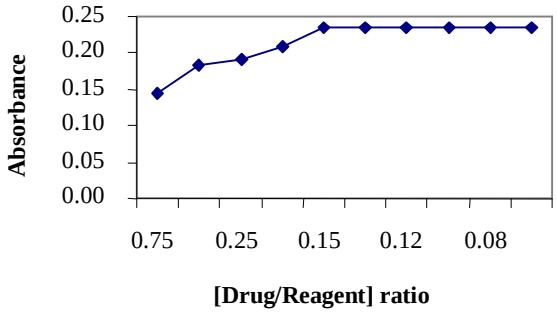

Fig. 4. Plot of Drug/Reagent Concentration ratio *vs* Absorbance

Developed color was stable up to three hours which was considered sufficient time to carry out a spectrophotometric determination. Beer's law was verified in the concentration range of 13-275 µg mL^{-1}.

Interference studies

More than 99 % recovery of diclofenac sodium was obtained in the presence of possible excipients and other additives such as talc, lactose, starch, sodium starch glycolate, microcrystalline cellulose and magnesium stearate. Under the experimental conditions employed, to a known amount of drug (diclofenac sodium 30 µg ml^{-1}), excipients in different concentrations were added and analyzed. Results of the recovery analysis are presented in Table 1. Excipients up to the concentrations shown in the Table do not interfere with the assay. In addition, recoveries in most cases were 100% and the smaller values of standard deviation indicate the good precision of the method.

Table - 1. Determination of diclofenac sodium in the presence of excipients

Excipients	Amount taken ($\mu g\ ml^{-1}$)	% Recovery ± s (n = 5)
Talc	50	99.64 ± 0.82
Microcrystalline cellulose	300	101.32 ± 0.75
Sodium starch glycolate	100	100.84 ± 0.66
Glucose	100	99.21 ± 0.56
Lactose	300	100.2 ± 0.52
Magnesium Stearate	50	98.2 ± 0.57
Starch	200	100.02 ± 0.75

Optical characteristics and validation of the method

Optical characteristics and statistical data for the regression equation of the proposed method are given in Table 3. Commercial formulations were successfully analyzed for diclofenac sodium by proposed method and compared with reference method [29] (Table 2). The calculated student's t-test values and F-test values did not exceed the theoretical values, which indicate the absence of any difference between the methods compared. The proposed method gives good results for diclofenac sodium in pure and pharmaceutical formulations.

Table -2. Optical characteristics and statistical data for the regression equation of the proposed method

Parameters	Values
λ_{max}	545 nm
Beer's law limit ($\mu g\ ml^{-1}$)	13-275
Molar absorptivity (L $mole^{-1}$ cm^{-1})	2.5×10^{3}
Sandell's sensitivity ($\mu g\ cm^{-2}$)	1.2×10^{-1}
Regression equation (Y*)	
Slope (b)	8.1×10^{-3}
Intercept (a)	1.4×10^{-3}
Correlation coefficient (r)	0.999
Relative Standard Deviation** (%)	0.652
Limit of Detection ($\mu g\ ml^{-1}$)	11.08
Limit of Quantification ($\mu g\ ml^{-1}$)	36.56

Y* = a + bC
Where C is the concentration of analyte ($\mu g\ ml^{-1}$) and Y is absorbance unit.
** = Calculated from five determinations

Applicability of the method

The proposed method is successfully applied for the determination of diclofenac sodium in pure and in pharmaceutical dosage forms and results are compared statistically with reference method [29] as shown in Table 3. Percent recovery of diclofenac sodium in the presence of excipients is more than 98 % with standard deviation values in the range of 0.52 – 0.82, which indicates that the method is precise and accurate. The precision and accuracy of the method was further compared statistically using Student's t-test and variance ratio F-test. At a 95% confidence level, the calculated t-values and F-values do not exceed the tabulated values.

Table - 3. Determination of diclofenac sodium formulations by the proposed and reference method [29].

Formulation	Proposed method		Reference method		t-test	F-test
	*Recovery (%)	RSD (%)	Recovery *(%)	RSD (5)		
(Tablets)						
Dyclo	91	0.71	100.25	0.49	0.668	2.125
Volmax	100.05	0.66	101.14	0.37	0.412	3.021
Dicloran	99.86	0.68	100.09	0.47	0.872	2.194
Diclokalium	99.23	0.52	99.97	0.45	0.623	3.121
Diclorep	101.25	0.61	100.63	0.58	0.525	2.192
(Injection)						
Dyclo	100.65	0.48	101.24	0.67	0.628	4.18
Diclodyn	98.67	0.51	100.89	0.73	0.596	3.98
Diacron	99.48	0.49	98.78	0.66	0.642	4.55

*Average of 3 independent analyses

Conclusion

The proposed spectrophotometric method is simple, rapid, accurate, precise and economical for the routine analysis of diclofenac sodium in pharmaceutical quality control laboratories. The method is statistically valid. The color reaction does not require stringent conditions like temperature and pH. The color is stable up to three hours, which is sufficient time for an analytical chemist to perform analysis. Proposed method is also applicable for determination of diclofenac potassium salts.

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