SPECTROPHOTOMETRIC DETERMINATION OF PHENOL BY CHARGE-TRANSFER COMPLEXATION

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Abstract

The phenol is used in pharmaceutical domain as agent of preservation, a rapid and reliable spectrophotometric method was validated for its determination in routine control. This method is based on the formation of a charge transfer complex between phenol and 2,6-dichloroquinone-4-chloroimide (DCQ) in basic medium. This produced a blue product with maximum absorption at 610nm. Beer's law is obeyed and the calibration curve was linear (r = 0.999) over the range 7.5 10^{-6}M – 7.5 10^{-5}M.

Keywords: phenol, complex, spectrophotometry, validation, control

1. Introduction

Phenol is an anti microbial agent of conservation, it is used in the pharmaceutical industry towards bacteria (Gram + and Gram-), yeasts and fungi. It is very responded particularly in liquid dosage forms and paste forms. However, the phenol has a toxic potential [1-5], and the U.S. EPA and Health Canada established an ADI respectively 0.3 mg / kg / day and 0.12 mg / kg / day for an exhibition chronic oral [6].

Several methods for the determination of phenol are described in the literature [7-15], but the reference method is gas chromatography [16,17]. However, routine monitoring in pharmaceutical laboratories requires simple techniques to implement and quick to gain maximum time especially for controls during manufacture. Indeed during a manufacturing process, the product remains in semi worked a manufacturing step pending laboratory results to confirm the homogeneity of the batch before tackling the steps of the process or distribution.

The phenomenon of charge transfer complexation was introduced by Mulliken [18,19], since it is widely used in the field of analysis [20-24]. It is based on the power of certain molecules, called "acceptors" electrons to form complexes with molecules bearing sites "donors" of electrons, including oxygen, nitrogen and sulfur [25].

In this paper we describe a simple and fast method for the determination of phenol, by forming a colored complex with 2,6-Dichloroquinone-4-chloroimide (DCQ).

2. Materials and methods

2.1 Apparatus

The absorbance measurements were done on a spectrophotometer V-530 Jasko; using 1cm quartz cell. The pH was checked by a potentiometer 234 AMEL Model - TITRATOR and a glass electrode-type Thermo Orion.

2.2 Reagents

The reagents are analytical grade pure, phenol (Riedel-de Haen®), boric acid (Solvachim®), phosphoric acid (Solvachim®), sodium hydroxide (NORMAPUR®), ethanol (Merck®) and DCQ (Fluka Chimica®). Distilled water was used for all preparations.

A 10^{-2} M stock solution in phenol was prepared by dissolving 0.0941 g of phenol in 100ml of distilled water, 10^{-2} M DCQ was prepared by dissolving 0.2104 g in a water / ethanol mixture (50%/50%). Phosphate buffer solutions of pH (2-7) and borate buffer pH (8-14) were prepared and adjusted with a saturated solution of NaOH.

2.3 Preparation of standard solutions

Samples of 75µl, 100µl, 250ml, 500µl and 750µl of 10-3 M phenol solution are placed in test tubes of 15ml capacity, added 100µl of stock solution of 10-2M DCQ and make up to 10ml with the appropriate buffer and agitate using vortex. After 15min, performing the measurement of absorbance at 615nm against a blank prepared in the same conditions without phenol.

2.4 Validation of the method

The method validation was performed according to the criteria of the ICH and SFSTP [26,27].

3. Results and Discussion

The DCQ is an electron acceptor [28] in the presence of an electron donor such as phenol, a charge transfer complex is formed between the two molecules in blue colored and therefore spectrophotometric to 610nm (Fig. I). The complex formed can be explained by the attraction of the electrons donor hydroxyl group (-OH) of the phenol by the π DCQ bonds (Fig. II) [25,28]. The method was optimized by changing the pH of the medium, the reaction time and the ratio of molar fractions of phenol and DCQ.

Effect of pH

The Fig. III shows the evolution of the intensity of the absorbance as a function of pH. In basic medium (pka = 9.9) phenol gives the phenate. Thus the oxygen lone pairs are available to form the complex. The pH10 gives the maximum absorbance, it was therefore chosen for the optimization study.

Time of reaction

The Fig. IV shows the evolution of the intensity of the absorbance as a function of time, the optimal time is 15min and the color remains stable over an hour.

Determination of molar ratio phenol / DCQ

The study of the molar was performed according to the method of Job's [29,30], Fig. V shows a maximum absorbance in a ratio of 1/1. This indicates that the complex involves a phenol molecule linked to another of DCQ.

Method validation

The linearity of the method was studied with five concentrations covering the entire field of method from 7.5 10^{-5}M to 7.5 10^{-6}M phenol (Fig. VI), in which the Beer-Lambert law is respected. The equation calculated by the method of least squares regression is [Y = 12351X + 0,019] (n = 3). The Student t test applied to the correlation coefficient r = 0.999 showed its significance to the risk α = 5%.

The repeatability (intra-day variation) of the method was evaluated on a 2.5 10^{-5}M phenol concentration, while the intermediate precision (inter-day variation) was checked on a 7.5 10^{-6}M concentration. The results (Table 1) showed a RSD <2%. On the other hand research the accuracy was verified for three days to three sets of concentration (2.5 10^{-5}M, 5 10^{-5}M et 7.5 10^{-5}M). The recovery percentages are calculated in the range of [95% - 105%] (table 1).

4. Conclusion

This method of determination of phenol can be used in routine control, and is also a qualitative way to visualize the distribution of phenol in a mixture (indicator of homogeneity) during a manufacturing process of pasty and liquid forms. It can also have an extension in the environment, as an indicator of pollution.

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Table 1 : Data of repeatability, intermediate precision and accuracy

1.1 Repeatability: n=6

Concentration introduced [$*10^{-5}$ M]	Concentration found [$*10^{-5}$ M]	RSD %
2.50	2.53	0.45

1.2 Intermediate precision: n=6

Concentration introduced [$*10^{-6}$ M]	Concentration found [$*10^{-6}$ M]	RSD %
7.50	6.88	5.47

1.3 Accuracy : n=3

Concentration introduced [$*10^{-5}$ M]	Concentration found [$*10^{-5}$ M]	% Recovery
2,50	2.53	101.28
5.00	5.24	104.97
7.50	7.78	103.79

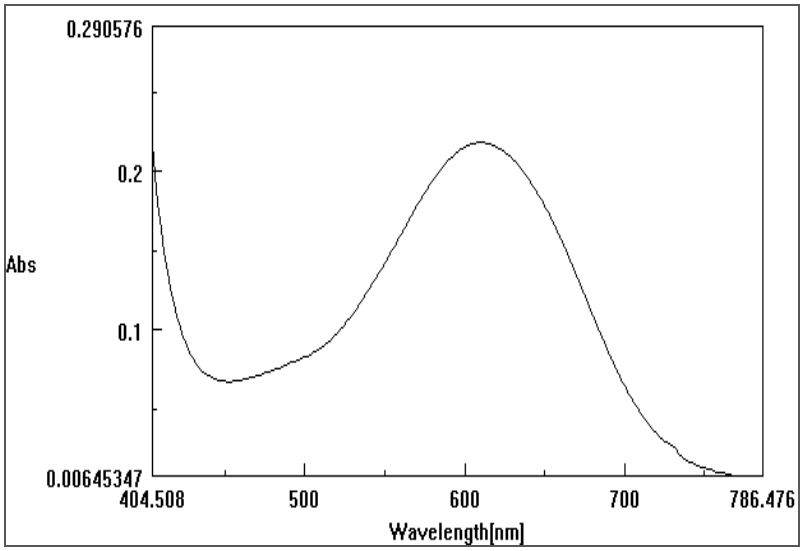

Fig. I : Absorption spectrum of the complex, phenol 10^{-5}M and 10^{-4}M DCQ

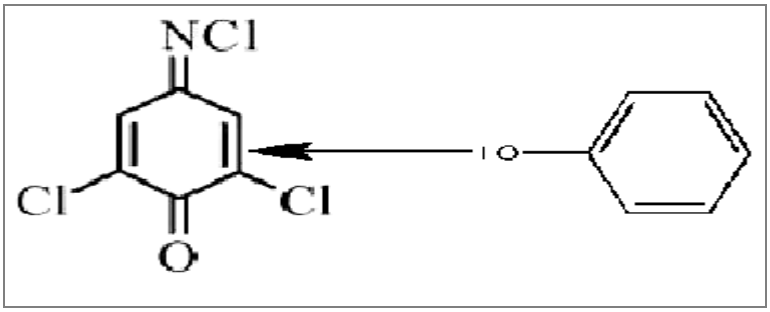

Fig. II : Scheme of the complex of phenol and DCQ

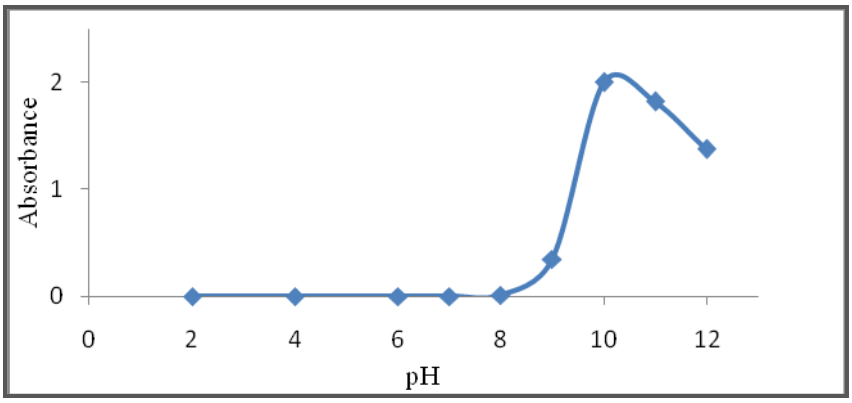

Fig. III : Absorbance versus pH: phenol 10^{-5}M, DCQ 10^{-4}M; reaction time 10min.

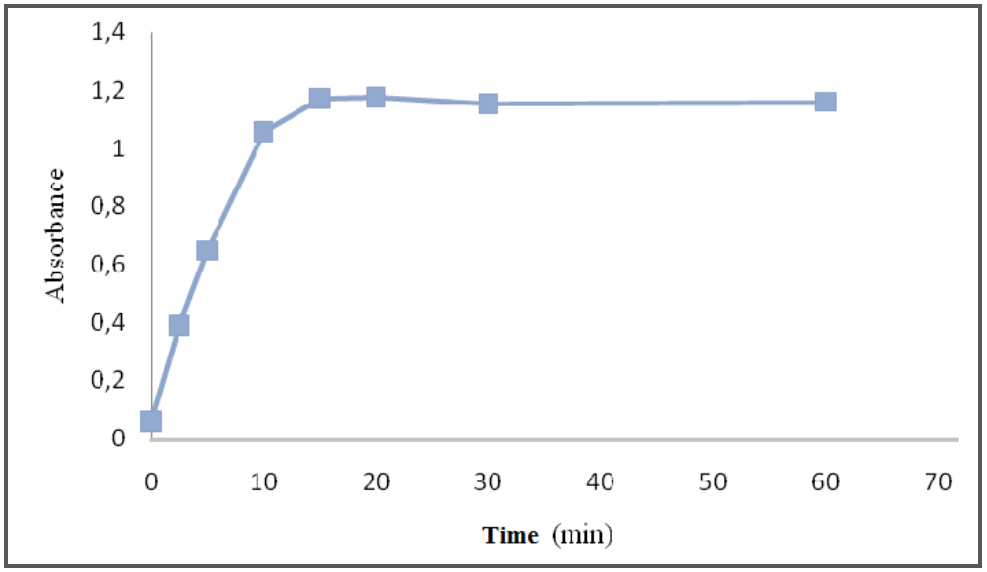

Fig. IV : Absorbance versus time : Phenol 10^{-5}M, DCQ 10^{-4}M ; Borate buffer pH 10.

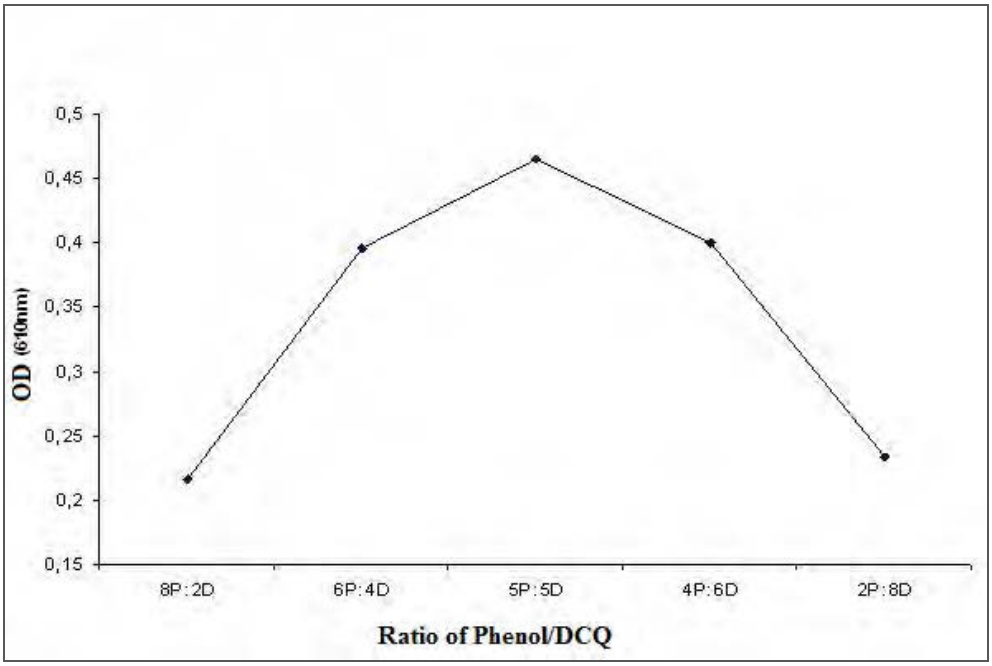

Fig. V : Optical density of different proportion of Phenol (P) 10^{-5}M and DCQ 10^{-5}M ; Borate buffer pH10.

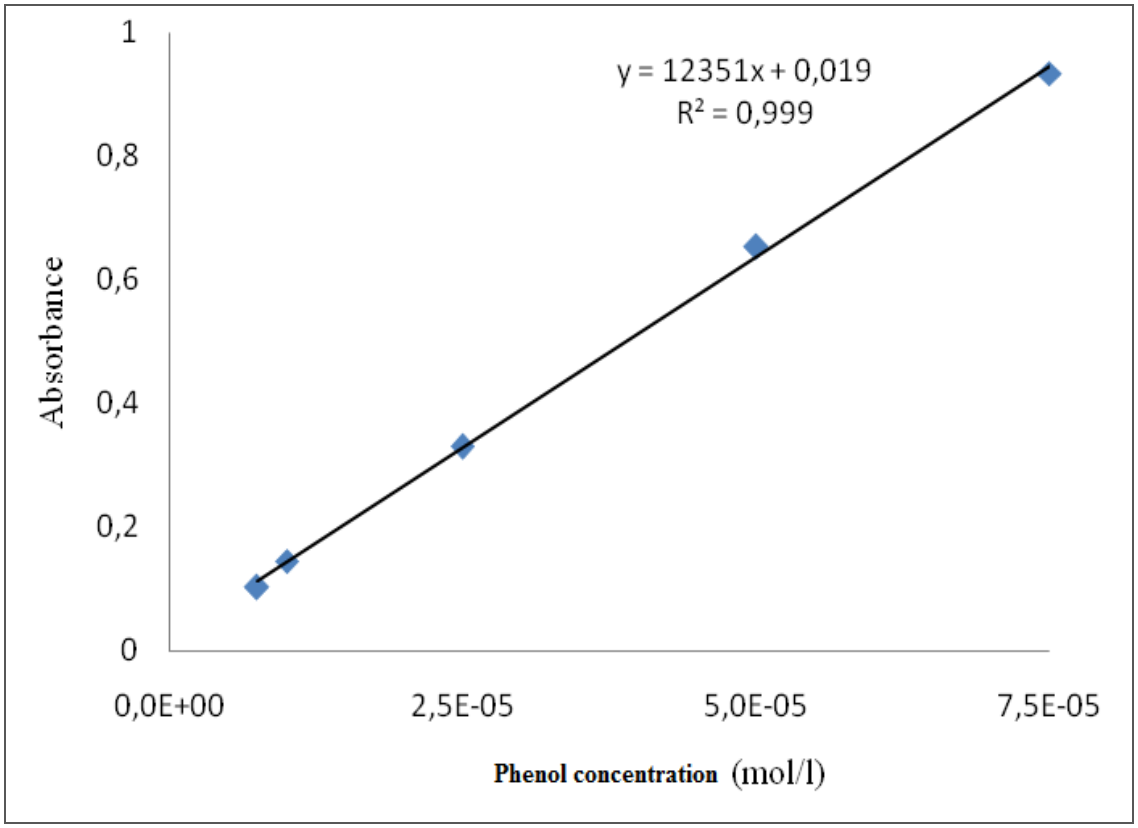

Fig. VI : Linearity curve of Phenol-DCQ (mol/l) complex