



## STUDY OF VARIOUS SOLVENTS FOR PHOLCODINE DETERMINATION USING UV SPECTROPHOTOMETER

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### ABSTRACT

Pholcodine is an opioid cough suppressant (anti-tussive). The objective of this work was study of various solvents for Pholcodine determination using UV Spectrophotometer and to develop a new method for determination of the Pholcodine by using UV-Visible Spectrophotometer that would be more accurate and cheapest. A number of solvents were used during the study those were methanol, chloroform, water, 0.1N KOH and 0.1N HCL that were soluble in Pholcodine and by using absorbance method at (285±1) nm wave length we finds that methanol ( $r^2=0.999$ ) and 0.1N HCL ( $r^2=0.999$ ) are the best solvents for the determination of Pholcodine by using UV Spectrophotometer.

**Key Words:** Pholcodine, absorbance method, UV, method development.

### INTRODUCTION

Pholcodine (7, 8-didehydro-4, 5 $\alpha$ -epoxy-17-methyl-3-[2-(morpholine-4-yl) ethoxy] morphian-6 $\alpha$ -ol.) is a semi-synthetic opium alkaloid, which is widely used as an anti-tussive agent. It is synthesized<sup>1</sup> by treating an aqueous solution of morphine with an equivalent amount of sodium hydroxide, before the addition of a solution of Chloroethylmorpholine hydrochloride, previously neutralized with sodium hydroxide.

Pholcodine is readily absorbed from the gastrointestinal tract and freely crosses the blood brain barrier. It acts primarily on the C.N.S, causing depression of the cough reflex, partly by a direct effect on the cough centre in the medulla. It is metabolized in the liver and its action may be prolonged in individuals with hepatic insufficiency (i.e. liver problems). its use in therefore contraindicated in patients with liver disease while care is advised in patients with hepatic impairment. It slowly biotransforms in the body via oxidation and conjugation to a series of metabolites that are eliminated primarily in the urine. With an average half life of 2-3 days, steady state in someone taking the drug chronically would not be reached for nearly 2 weeks<sup>2,3</sup>.

Pholcodine is a white or almost white, crystalline powder having a molecular formula C<sub>23</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub> with molecular mass 398.55g/mol. It is soluble in Benzene, Chloroform, Acetone and slightly dissolved in ethyl ether. Melting point of Pholcodine is 98°C and maximum plasma concentration attained 4-8 hr. after oral dose<sup>4,5</sup>.

Overdosing may cause the dizziness and gastrointestinal disturbances such as nausea or vomiting. Adverse effects such as respiratory depression, excitation, constipation, ataxia, drowsiness also have been reported occasionally or after large doses. Pholcodine is found in cough lozenges. In UK, the preparation is almost exclusively an oral solution, typically 5 mg/5ml. Adult dosage is 5-10ml up to 3-4 times daily.

### METHODS AND MATERIALS

UV-Visible spectrometer UV wavelength range from (200-400) nm (Systronics) was used, all the glassware were soaked overnight with chromic acid solution and washed thoroughly with water and detergent, then rinsed with distilled water before use. Volumetric flask (10ml-100ml), Pipette (0.1ml-10ml), Beaker, Magnetic stirrer, glass rod, ultra-sonicator, UV-Visible spectra-photometer. The solvent use in this study includes (methanol, chloroform, water, 0.1N HCL solution, 0.1N KOH solution) with were of high quality at least analytical grade.

#### Sample Preparation Procedure

1000 ppm solution has been prepared by adding 10  $\mu$ g of Pholcodine in to 10 ml of solvent (methanol, chloroform, water, 0.1N HCL, 0.1N KOH). After that further dilutions have been done from 1000 ppm to make (5-30) ppm solutions. Poured the solution into (1 cm) quartz UV cell and place into the sample holder of the spectrometer and measure the sample. The sample is measured by precision and Accuracy.

### RESULTS AND DISCUSSION

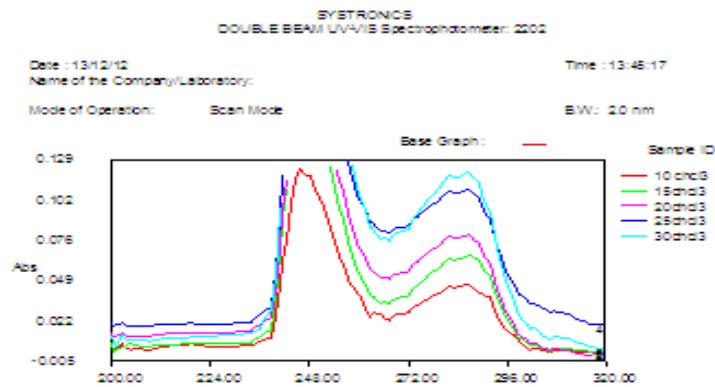
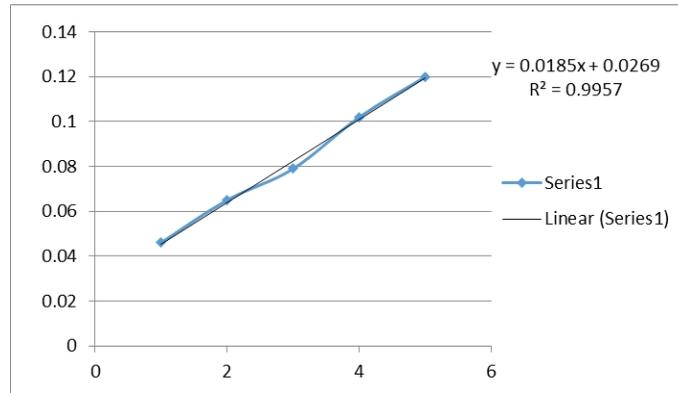
Many solvents were studied to find best one for dissolving Pholcodine. Standard calibration curve were obtained for each solvent as shown in figures, It is clear from figure that methanol and 0.1N HCL solution are the two best solvents because of calibration curves of these two have the highest value of correlation coefficient i.e. 0.999 so we considered both methanol and 0.1N HCL solution best solvents.

#### Linearity

The calibration graph was generated Six different concentrations of Pholcodine from 5 ppm to 50 ppm were analyzed according to experimental conditions. Then the calibration curve was established according to the response (peak area) and the concentration of Pholcodine in standard solutions. The results show a good relationship.

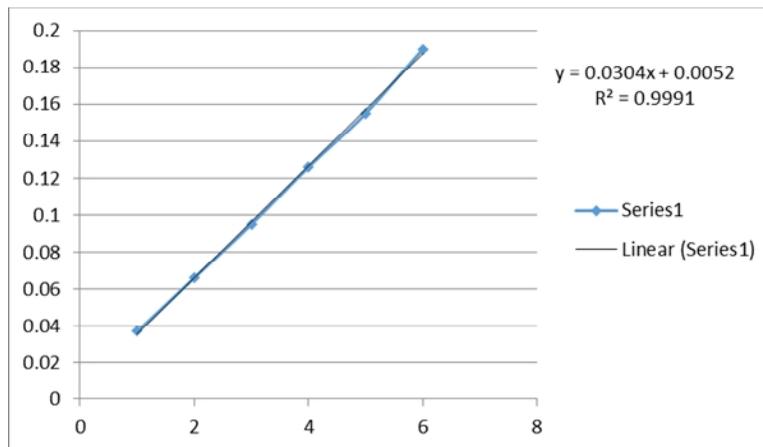
**Chloroform:-**

Concentration	Abs. (285nm)
5 ppm	No Abs
10 ppm	0.046
15 ppm	0.065
20 ppm	0.079
25 ppm	0.102
30 ppm	0.120



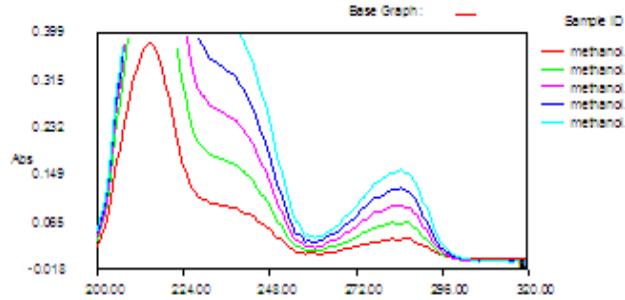
**Methanol:-**

Concentration	Abs. (285nm)
5 ppm	0.037
10 ppm	0.066
15 ppm	0.095
20 ppm	0.126
25 ppm	0.155
30 ppm	0.190



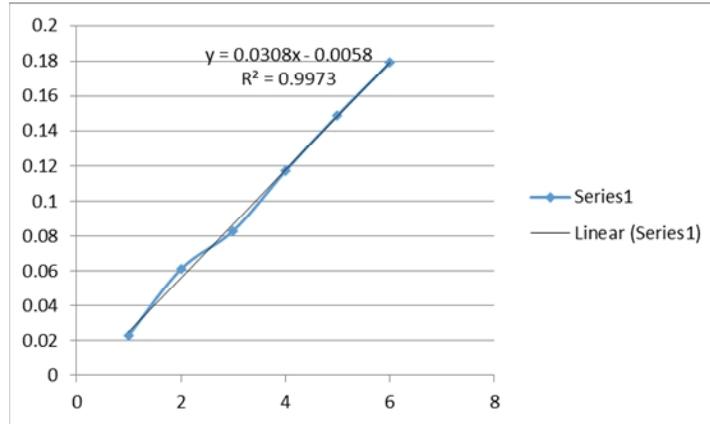
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Mode of Operation: Scan Mode BW: 20 nm



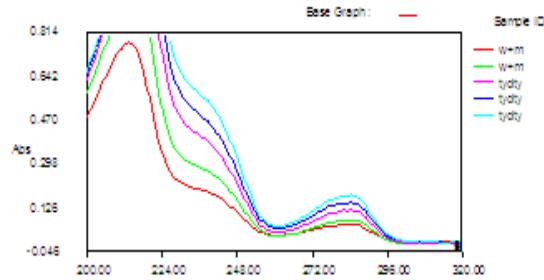
Water:-

Concentration	Abs. (284nm)
5 ppm	0.023
10 ppm	0.061
15 ppm	0.083
20 ppm	0.117
25 ppm	0.151
30 ppm	0.179



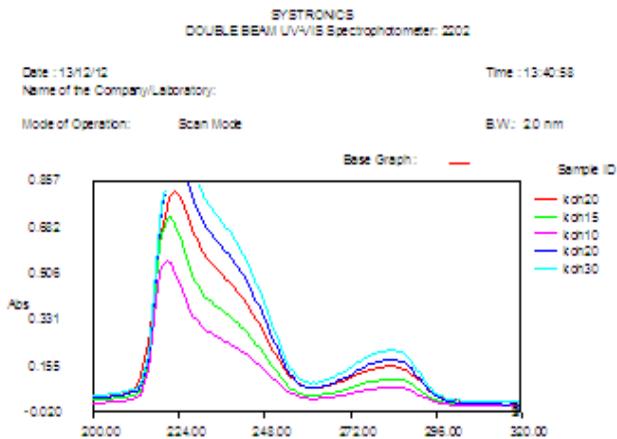
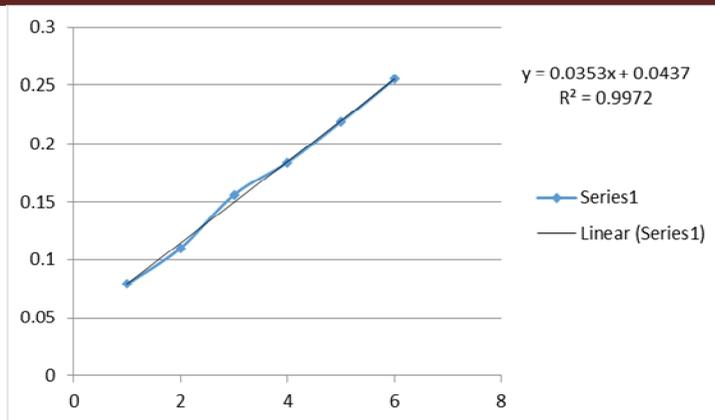
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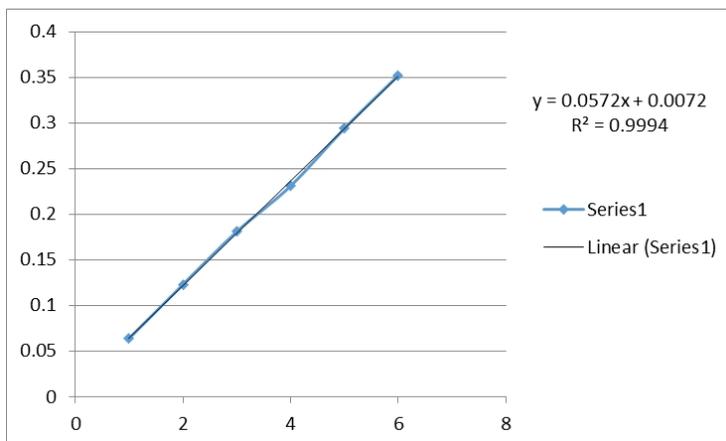
0.1N KOH solution:-

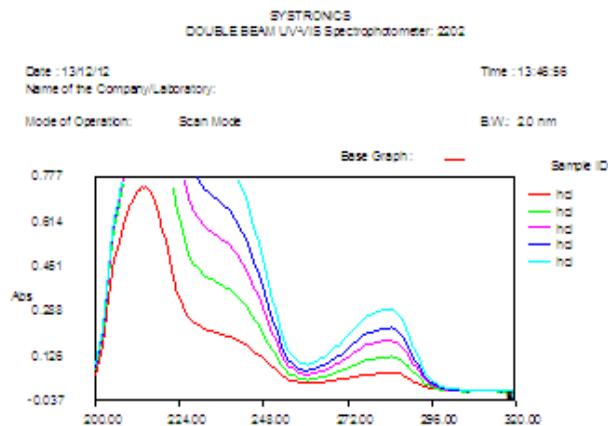
Concentration	Abs. (284nm)
10 ppm	0.076
15 ppm	0.110
20 ppm	0.156
25 ppm	0.184
30 ppm	0.219
35 ppm	0.255



**0.1N HCL solution:-**

Concentration	Abs. (284nm)
5 ppm	0.064
10 ppm	0.123
15 ppm	0.181
20 ppm	0.231
25 ppm	0.294
30 ppm	0.352





Parameter	Chloroform	Methanol	Water	0.1N KOH	0.1N HCl
Range	10-30 µg /mL	0-30 µg /mL	0-30 µg /mL	10-35 µg /mL	0-30 µg /mL
Slop	0.018	0.030	0.030	0.035	0.057
Intercept	0.026	0.005	0.006	0.043	0.007
Correlation Coefficient	0.9957	0.999	0.997	0.997	0.999
S.D	0.029314	0.056846	0.057837	0.066107	0.107098

### CONCLUSION

Simple and accurate method for the determination of Pholcodine using UV visible spectrometer was developed; the best solvents were methanol and 0.1N HCL solution. Standard linear calibration curve was run to obtain the linear range of sample analysis, correlation factor was with accepted value 0.999 for both (methanol and 0.1N HCL) and standard calibration curve was linear over range (0-30) ppm with equation (for methanol  $y=0.030x+0.005$ ) (for 0.1N HCL  $y=0.057x+0.007$ ).

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9. ICH TOPIC Q 2 A Validation of analytical methods: Definition and Terminology Step 5(CPMP/ICH/381/95).

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