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Indirect Spectrophotometric Method for Estimation of Pregabalin in Pharmaceutical Preparations

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ABSTRACT
To develop in direct colorimetric assay of pregabalin in commercial forms (capsules). This work is depend on the oxidation of pregabalin using an increasing of potassium iodate (KIO_3) in presence of sulphuric acid medium is produced by the reaction of iodide ion which in turn reacts excess iodine. To release iodine and to make sure that we interact with starch we get an active complex gives maximum absorption 600nm. The calibration plot is linear in the conc. Range of 20-240 µg.ml^{-1} with amolar absorptivity is 0.239x10^3 l/mol.cm. The (LOD) and (LOQ) are 0.0014 and 0.0048 µg.mL^{-1} respectively. The proposed method can be applied for the determination of pregabalin in pure and its capsules form.

Keywords: Pregabalin, Indirect Spectrophotometry, Pharmaceutical Capsules.
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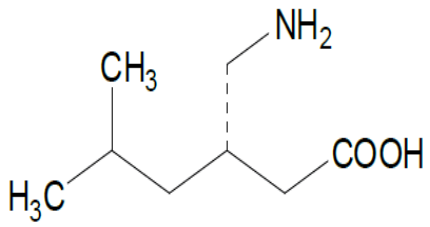
INTRODUCTION
Pregabalin is chemically (*S*)-3-(Amino methyl)-5-methylhexanoic acid, as shown in (Figure 1). It was as of late affirmed for adjunctive treatment of fractional seizures in grown-ups and for the treatment of neuropathic torment from post remedial neuralgia and diabetic neuropathy, Furthermore, it has been prescribed for gastrointestinal harm, liquor addiction, a sleeping disorder and careful dental torment insomnia [1][2][3][4][5].



$C_8H_{17}NO_2$ = 159.2
Fig. 1: Chemical Structure of pregabalin

There are many spectral methods in the sources[6][7][8], to estimate pregabalin, UV spectrofluorometric method[9][10], fluorimetric methods[11][12],RP-HPLC methods[13][14]. HPTLC method[15], LC-MS-MS method [16] and electrospray ionization tandem mass spectroscopy [17].The present method in clouded, rapid analytical indirect, colorimetric method for the estimation of pregabalin in pharmaceutical products.

MATERIALS AND METHODS
Apparatus
A Genway6405UV- visible spectrophotometer with 1.0cm quartz cells was utilized for estimations.

Reagents
The chemicals utilized in all experiments are very pure. From The (PIONER), company for pharmaceutical industries was provided the Pregabalin.

Pregabalin Standard Solution (1000ppm) (6.2x10^{-3}M)
The solution is prepared by dissolving0.1 gram of Pregabalin in 100mldistilledwaterin a calibrated flask.

Potassium Iodate Solution1 %(4.6×$^{-2}$M)
1.0 gram of Potassium iodate (BDH) was dissolved and the volume was adjusted to 100 ml with distilled water in volumetric-flask.

Sulfuric acid (2M)
Diluting 11.1ml of (18M H_2SO_4) to 100mL by D.W. in calibrated flask.

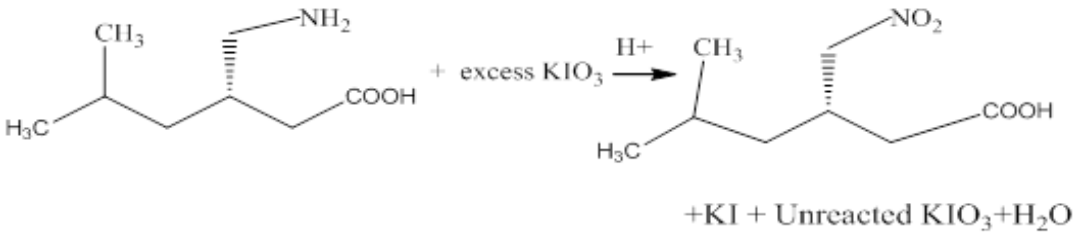
Starch solution (1%)
Mixed 1gram of starch dissolving in 5ml of water and added the Suspension got gradually With stirringto50 ml of boiling Water. Then added 50 ml of Glycerol and Gently boil the solution for 5 mints. The solution is stable for several Weeks[18].

Recommended Procedure
An aliquots of Standard Solution of Pregabalin (0.5-6 µg)we removed into 25 ml volumetric flasks followed by 2ml of (1M)H_2SO_4,4ml of (1%) starch solution and 2ml of (1%)KIO_3 solution ,finally we complete with distilled water with final volume 25ml . The absorbance was measured at 600 nm.

Procedure for Capsules
The[capsules 150 mg/cap] were provided from pioneer company(Samarra pharmaceutical –Iraq).Twenty capsules were weighed and amount of capsule Powder equivalent to 100 mg of pregabalin was weighed accurately and dissolved inabout80 ml D.W. The filtrate completedthe final volume 100mL with distilled water. The final concentration is 1.0 mg /ml. This was subsequently analyzed using a double beam UV-VIS spectrophotometer against reagent blank. The drug content of the sample was calculated by using regression analysis

RESULTS AND DISCUSSION

Spectrophotometric methods development for the determination of drugs is a very valuable technique and has been increased considerably in recent years because of their features like simplicity, economical, suitable for wide range of importance in pharmaceutical analysis[19][20].The present method involves the reaction of pregabalin with potassium iodate in acidic medium to produce nitro compound and potassium iodide[21][22]. Potassium iodide immediately reacts with the excess KIO_3 to liberate iodine which reacts with starch (I_2-Starch) complex. The formula of the product may be suggested as:



$$+KI + \text{Unreacted } KIO_3 + H_2O$$

$$KIO_3 + 5KI + 6H^+ \longrightarrow 3I_2 + 3H_2O$$

$$I_2 + \text{Starch} \longrightarrow I_2 - \text{Starch} \quad \text{(Blue color)}$$

The colored product showed maximum absorption at 600nm as shown below Fig.(2) and this wavelength was recommended for determination

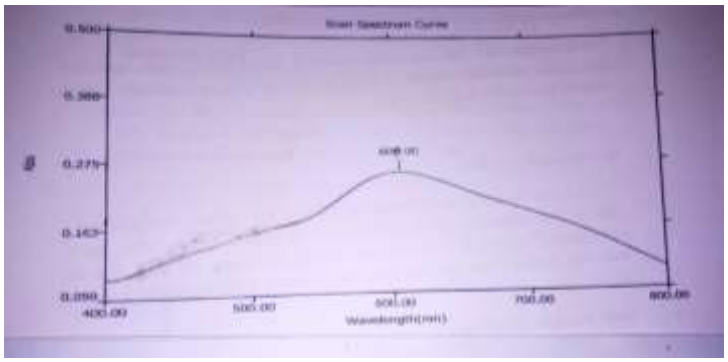


Fig. 2: Absorption spectra of 160µg/ml pregabalin-KIO_3-Starch against blank.

Study of the ideal conditions

The impact of different parameters on the absorption of the product was studied and the reaction conditions are improved.

"Effect of acid"

The absorbance of the colored product shows that when using 2 ml of 1 M sulfuric acid solution obtained maximum intensity. This value was adopted to complete the rest of the experiments.

"Effect of starch amount"

The effect of starch on the color intensity of volume (1-10) ml was studied to develop color intensity,4 ml has been incorporated for the subsequent steps.

"Effect of potassium periodate amount"

This parameters included effect of the addition of various amount of KIO_3on the absorbance, it was noticed addition of 2 ml of 1% KIO_3solution give maximum absorbance.

"Effect temperature and time"

Our result indicate that we obtain the desired color at room temperature directly and stay stable for 6 hours in any event..

Calibration graph

Under the exploratory conditions depicted, Beer's law is complied with over the focus run (20-240) µg.ml^{-1} Fig.(3). Linear regression equation: Y=0.0016x, (R^2 = 0.9988, n =7).Where "Yis the absorbance and X" is the concentration in µg/ml the apparent molar absorptivity was 0.239x10^3 L/mol.cm and Sandell's sensitivity was0.66 µg/cm^2.

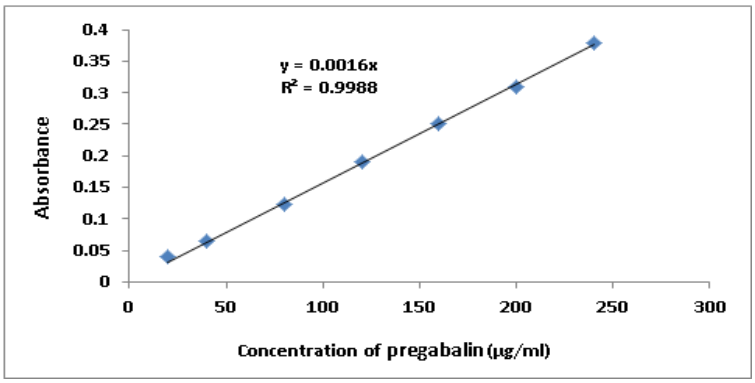


Fig. 3: Calibration graph of pregabalin

Accuracy and precision

Calculated for three concentration of the pure drug. The low value of standard deviation showed that the method was precise. The results shown in Table (1) indicate that the method has good accuracy and precision., mean recoveries being 100±89% .

Table 1: Optical characteristics and statistical dataforregressionequationof the proposed method

Parameters	Value
λ max (nm)	600
"Beer´s law limits" (µg .ml^{-1})	20-240
Molarabsorpitivity (l.mol^{-1}.cm^{-1})	0.239x10^{3}
Sandells Sensitivity(µg/cm^{2})	0.66
Correiationcoefficient (r^2)	0.9988
Recovery %	100 ± 0.89
Relativestandarddeviation (%)	< 1.5

Interferences Study

The interfering effect of foreign species often accompanied with pregabalin in pharmaceutical preparations were studied by using foreign species to 120µg/ml of pregabalin. Excipients at the concentration revealed do not interfere with the assay Table (2).

Table 2: Determination of 120 µg/ml of pregabalin in the presence of excipients and other substances

Interfering substances	Amount added(mg)	Amount of pregabalin found(µg)*	RSD %
Benzyl alcohol	1	120.09	0.88
Chlorobutanol	10	20.11	0.91
Lactose	40	120.08	0.71
Microcrystalline Cellulose	20	120.06	0.64
Magnesium Stearate	40	120.1	0.91
Hydroxyl Propyl Methyl Cellulose	40	120.1	0.93

*Average of 6 determinations

APPLICATIONS

Our results indicate that proposed method can be successfully applied to the pharmaceutical products of pregabalin. The results show in Table (3).

Table 3: Determination of pregabalin in pharmaceutical formulations

Pharmaceutical formulations	Label amount (mg)	Found by proposed method *mg	Recovery%
Capsules	150mg/caps	49.6 1	99.73

*10 determinations

CONCLUSION

The developed study describes sensitive method for the determination of pregabalin without interferences from common excipients , this method is simple, rapid and inexpensive .

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