

## Direct spectroscopic determination of carbamazepine using a carbonyl reagent

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### Abstract:

A new sensitive method was developed for the determination of carbamazepine using an organic reagent, and this method showed good and rapid results. Carbamazepine and the organic reagent (hydroxy-3-methoxybenzaldehyde) react in an acidic medium at laboratory temperature, resulting in a yellow compound. Maximum absorbance was observed at a wavelength of 450 nm using vanillin as a reagent. It obeyed Beer's law (linear concentration) in the range of (5-60) µg/mL, while the molar absorptivity was (4229.22) L/mol.cm, the detection limit was (1.54) µg/mL, and the quantitation limit was (4.67) µg/mL. Thus, the method was effective for the spectrophotometric estimation of carbamazepine in its pure form and in its pharmaceutical preparation.

Key words: carbamazepine, vanillin, Spectrophotometric, methylolamide.

### التقدير الطيفي المباشر للكاربامازيبين باستخدام كاشف كاربونيلى

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### مستخلص:

تم تطوير طريقة جديدة وحساسة لتحديد الكاربامازيبين باستخدام كاشف عضوي، وقد أظهرت هذه الطريقة نتائج جيدة وسريعة. يتفاعل الكاربامازيبين والكاشف العضوي (هيدروكسي-3-ميثوكسي بنزالدهيد) في وسط حامضي عند درجة حرارة المختبر، مما ينتج عنه مركب أصفر اللون. لوحظ أعلى امتصاص عند 450 نانومتر باستخدام الفانيلين ككاشف. وكان متوافقاً مع قانون بيرلامبرت (التركيز الخطي) في نطاق (5-60) ميكروغرام/مل، بينما كان معامل الامتصاص المولاري يساوي (4229.22) لتر/مول.سم، وكان حد الكشف (1.54) ميكروغرام/مل، بينما كان حد الكمية (4.67) ميكروغرام/مل. بذلك كانت الطريقة فعالة لتقدير الكاربامازيبين طيفياً في شكله النقي وفي مستحضره الصيدلاني. الكلمات المفتاحية: كاربامازيبين، فانيلين، التحليل الطيفي، مثيلول اميد.

## 1- INTRODUCTION:

Carbamazepine (Fig.1)<sup>(1)</sup>, It is a tri-cyclic compound from the dibenzazepine family<sup>(2)</sup>. Carbamazepine is as effective as phenytoin in treating grand mal epilepsy and psychomotor epilepsy. It is the drug of choice for treating trigeminal neuralgia.<sup>(3)</sup> It is used (either alone or in combination with other treatments) to control specific types of seizures, and it is also used in treating facial nerve pain. It helps reduce the formation of pain-transmitting nerve signals, which is why it is used as a remedy for neuropathic pain, and it is also used in treating certain cases of bipolar disorder. Carbamazepine does not cure epilepsy, but it helps control seizures by reducing their frequency<sup>(4)</sup>. Therefore, it is not recommended to stop treatment simply because the patient's condition has improved, as seizures may recur after discontinuing the medication <sup>(5)</sup>Carbamazepine has previously been estimated by several methods, including UV-visible spectrophotometry<sup>(6)</sup>, HPLC <sup>(7)</sup>, RP-HPLC<sup>(8)</sup> GC-MS <sup>(9)</sup>, and LC <sup>(10)</sup> . .

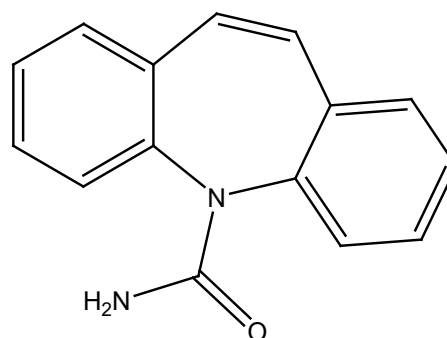


Fig.1,Carbamazepine

## EXPERIMENTAL:

### Apparatus: I

- UV-Vis. Spectrophotometer.
- cell's 1cm glass.
- UV-Vis. Spectrophotometer single beam
- Sensitive balance
- Oven

### Materials:

- C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O (SDI; Samarra. Iraq).
- C<sub>8</sub>H<sub>8</sub>O<sub>3</sub> 98% from (Fluka),
- CH<sub>3</sub>CH<sub>2</sub>OH 99,9 % from (Merck) ,
- HCl 37% from (Scharlan),

### Solutions:

- (Carbamazepine 1000 µg/ml): Weight 0.1 gm of CBZ.; was dissolved in 100 ml of distilled water.
- (Hydrochloric acid1.0 M): Prepared at an approximate concentration of dilute 12.9 ml of concentrated acid to a volume of 150 ml of distilled water.

- (Vanillin 0.01 M): Dissolve 0.152 g of vanillin in 100 ml of absolute ethanol.

### Procedures:

#### Determination of Carbamazepine & Vanilin:

Preliminary tests were conducted on the product formed from the reaction of carbamazepine with the organic reagent to determine the optimal reaction conditions. This was achieved by adding 1.0 ml of a carbamazepine solution

at a concentration of  $250 \mu\text{g/ml}$  to a 10 ml volumetric flask, then after waiting for 5 minutes, 1.5 ml of 1M hydrochloric acid was added. After 5 minutes, 2 ml of the organic reagent used was added, followed by adjusting the volume to 10 ml with distilled water. The resulting product was yellow in color with a maximum absorbance of 0.753 at a wavelength of 450 nm at room temperature, Figures (2) and (3).

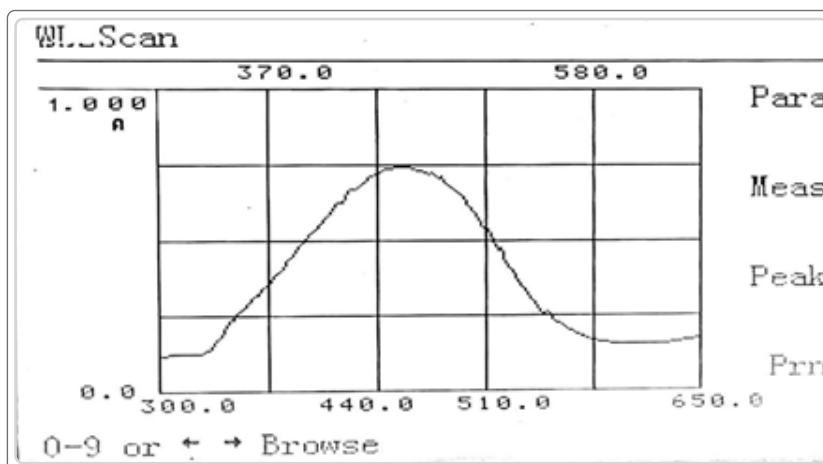


Fig. 2: Absorption spectrum of CBZ- Van against blank

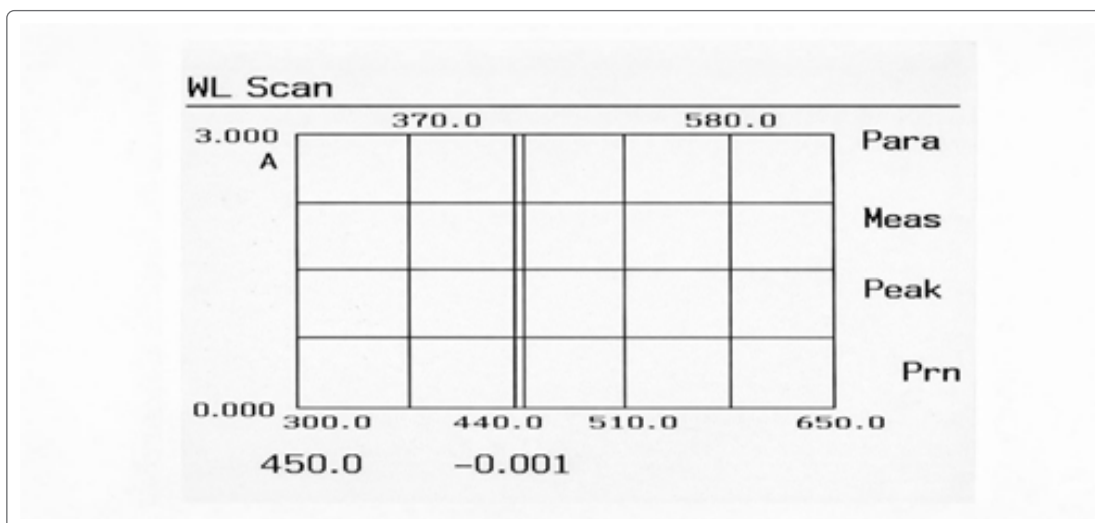


Figure. 3: Absorption spectrum of blank against distilled water

### Optimal Conditions

#### Effect of the different acids:

A set of strong and weak acids (HCl, H<sub>2</sub>SO<sub>4</sub>, HNO<sub>3</sub>, CH<sub>3</sub>COOH) was used, each at a concentration of 1 M, and a volume of 1.5 ml of each acid was added to determine which one gives the best absorption for the sample measurement. The best results were obtained using hydrochloric acid, as shown in table (1).

#### Effect of acid volume:

After adding varying amounts of hydrochloric acid to determine the volume at which the best absorption occurs, the results obtained showed that the optimal added volume is 1.5 ml., As shown in Fig, (4).

Table (1): Effect of different acids

Acid	Abs.
HCl	0.753
HNO <sub>3</sub>	0.238
H <sub>2</sub> SO <sub>4</sub>	- 0.146
CH <sub>3</sub> COOH	- 0.104

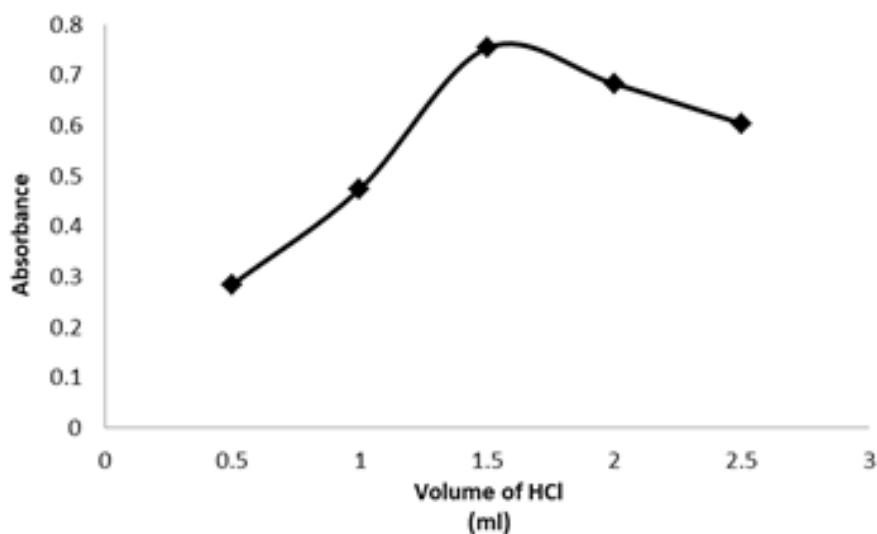


Fig 4. Effect the Volume of (HCl)

#### Effect of Vanillin volume:

To determine the effect of the amount of reagent used in the reaction on the absorption values of the resulting product, and by adding different volumes of organic reagent, with the same concen-

tration 0.01 M, it was found that the best absorption occurred when 2 ml of it was added while keeping the other reaction volumes constant. as shown in Fig5 .

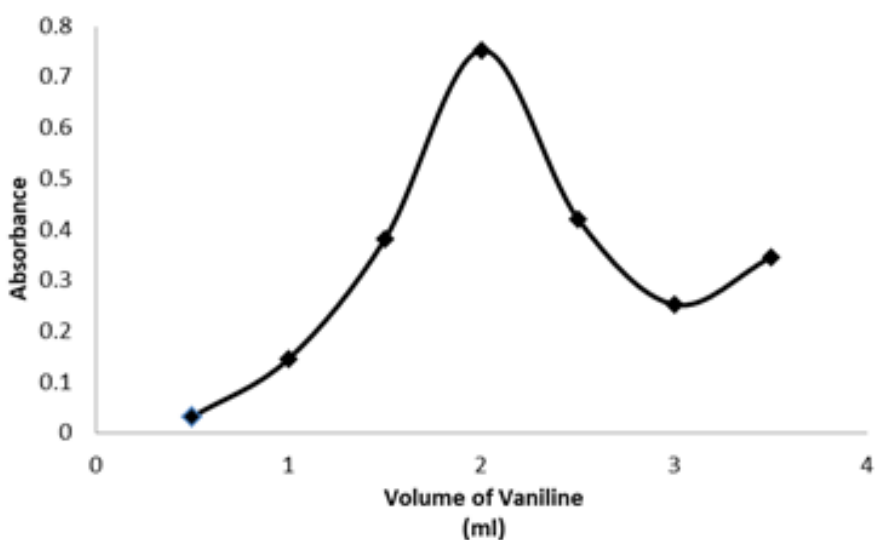


Figure. (5): Effect the volume of vanillin

**Effect of Time:**

Experiments conducted on the resulting complex showed that the stability of the product's absorption is high during the first eight hours, then

it begins to gradually decrease., exceeding approximately 24 hours, and at the same wavelength , as shown in table (2).

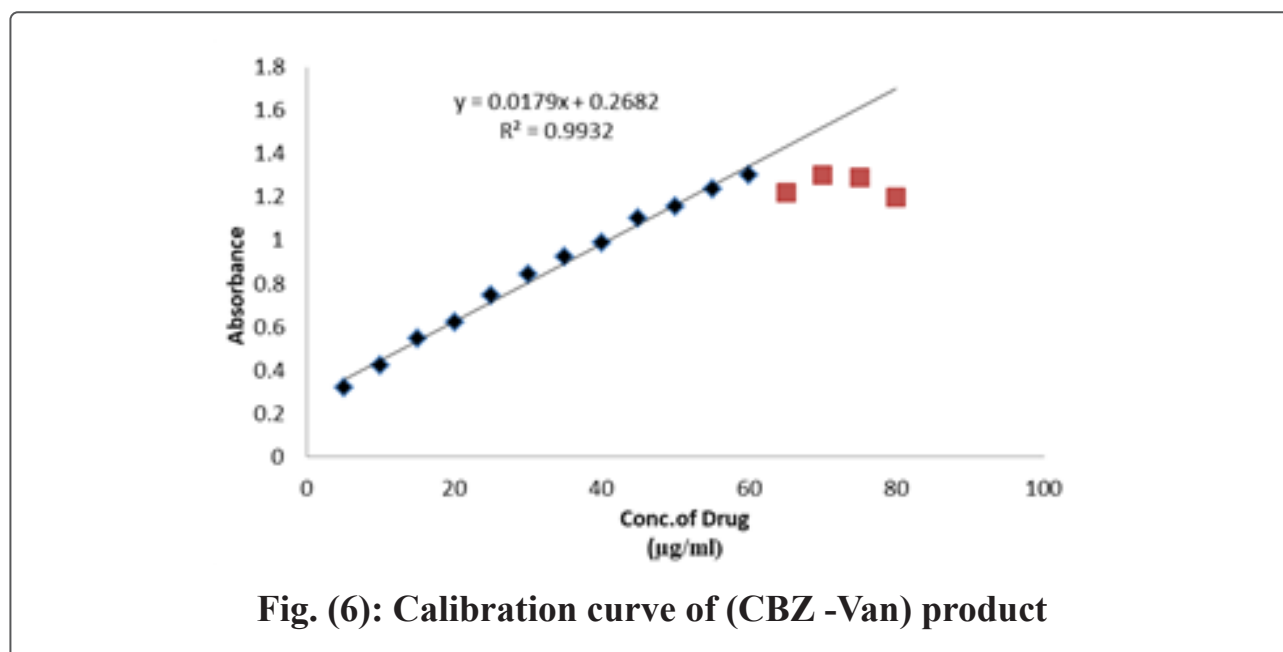
**Table (2): Effect of Time**

Time	0	8	16	24	48	72
Abs	0.753	0.758	0.730	0.714	0.704	0.628

**Calibration Curve:**

In the pure form of the drug with the organic Vanillin reagent, the titration

curve appeared linear in the concentration range of 5-60 µg/mL, as shown in Figure (6).



**Fig. (6): Calibration curve of (CBZ -Van) product**

**Application of the Proposed Method:**

The accuracy and precision of the method were evaluated by measuring three different concentrations of carbamazepine, namely 15, 35, and 50 µg/

mL, under the same optimal conditions established in the procedure. It was found that the method has good accuracy and precision, as evidenced by the results shown in Table (3).

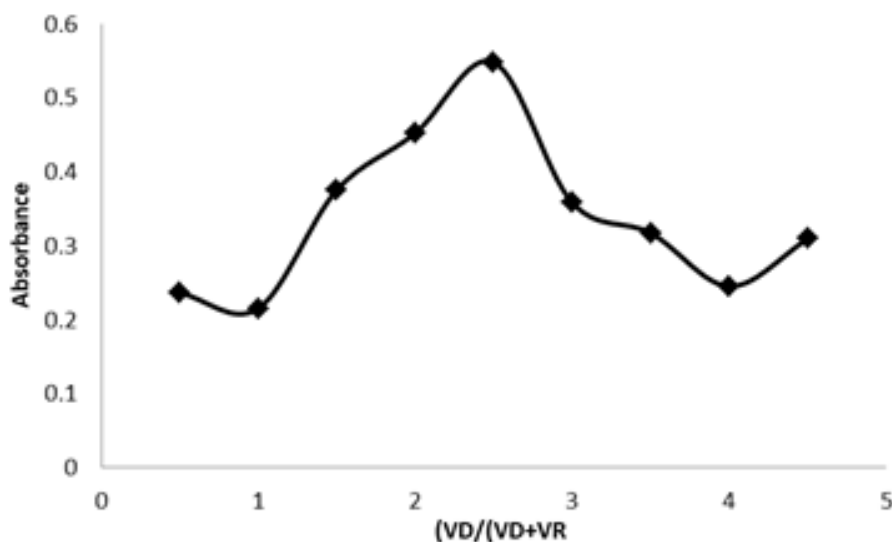
**Table (3): Determination of CBZ (as tablet)**

Pharmaceutical preparation	Content ( $\mu\text{g}$ ) declared	Found ( $\mu\text{g}$ ) by proposed method	%Recovery
Taver	15	15.09	100.60
	35	35.15	100.43
	50	50.15	100.30

**The Stoichiometry of the product:**

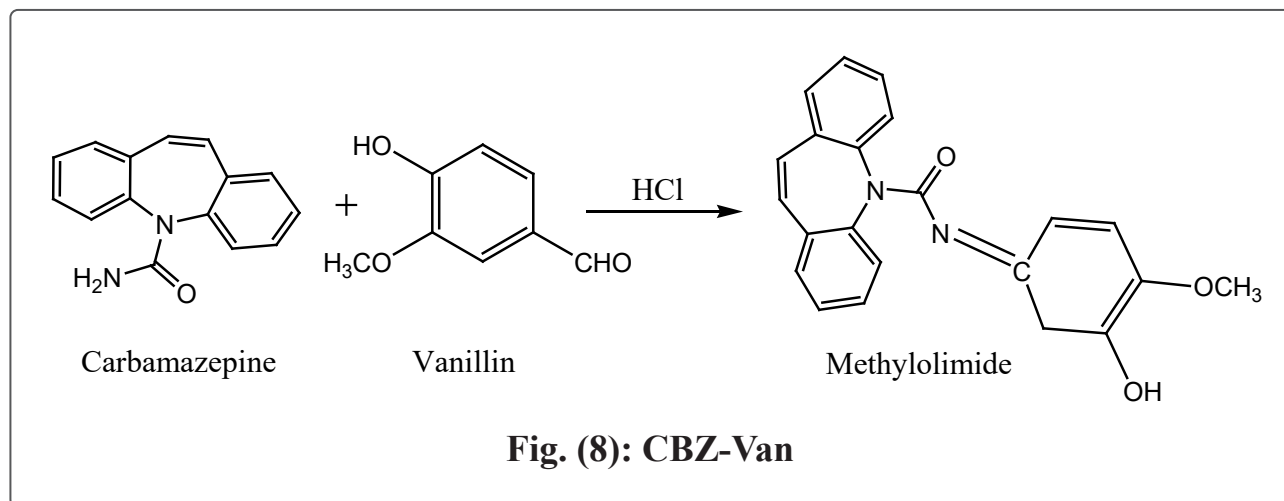
To determine the ratio of the association between carbamazepine and the organovanillin reagent in the spectral product, the method of continuous change was applied. The method was applied in an initial concentration of  $2 \times 10^{-4}$  molar to a fixed volume of 1.0

ml of carbamazepine, following the same initial steps and conditions used in the standard curve drawing. The “equivalence of output” was studied in the Job method and the valence ratio between carbamazepine and the reagent was 1:1. as shown in Figures(7).

**Figure. (7): Continuous variation method of CBZ****:The proposed reaction equation**

The proposed reaction to form a chelating complex between the organic

reagent (vanillin) and the drug carbamazepine is methylolamide. <sup>(11)</sup>.



**Table (4): Optical characteristics of the calibration curve of the formed product**

Parameters	Value (vanilin)	Value (C.V) <sup>(12)</sup>
$\lambda_{\text{max.}}$ (nm)	450	592
Molar absorptivity (L/mol.cm)	4229.22	3992.95
Correlation coefficient (r)	0.9932	0.9991
Limit of Detection ( $\mu\text{g/ml}$ )	1.54	0.16
Limit of quantification ( $\mu\text{g/ml}$ )	4.67	0.48
Slope	0.0179	0.0169
%RSD	0.18	0.29

\*The detection limit and quantity limit were calculated using the following laws.

$$\text{L.O.D} = 3.3 \text{ S} / \text{b}$$

$$\text{L.O.Q} = 10 \text{ S} / \text{b}$$

### CONCLUSION:

The proposed reaction method for estimating carbamazepine is rapid, sensitive, simple, and inexpensive, as it was conducted under uncomplicated working conditions and is easy to obtain. It showed good results compared to other estimation methods and can

be applied to determine the drug in its pure form as well as in pharmaceutical preparations.

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