Sudan University of Science

And Technology

college of sciences

department of scientific chemical laboratories

Determination of p- amino benzoic acid in procaine drug

تقدير البارا امينو حمض البنزويك في البروكائين

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September /2015

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بسم الله الرحمن الرحيم

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المجادلة: ١١

DeDication

To the fountain of patience and optimism and hope to all in existence after Allah and His Messenger ..... Lamy expensive

To Cindy and my strength and my refuge after God. …….Abe

To the brotherhood of pleasant and distinguished themselves fulfill my brothers and tender....

To each of the finest moments they shared their seats and study my colleagues..

Acknowledgment

Firstly, all thank to Allah.

And I will give all my unbridgeable thanks to the most graceful that has provided me with lot of blessings that can never be counted.

Second, Iam grateful to Dr. Ali Altaib Jeab alla for his precious and unreserved guidance

Iam also grateful for the encouragement, help and support of many people who are behind making this study come real.

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ملخص البحث

يتضمن البحث طريقة طيفية لتقدير كميات متناهية الصغر من البارا امينو حامض البنزويك (PABA) تعتمد الطريقة علي اقتران ملح الديازونيوم لبارا امينو حمض البنزويك مع عامل الاقتران بيتا نافثول في وسط قاعدي يعطي صبغة صفراء ذائبة في الماء .واعطت هذه الصيغة اعلي امتصاص عند طول موجي (299) نانوميتر وتم تطبيق قانون بير لامبيرت في مدي تركيز من (0.5-4) مولاري في حجم نهائي (50)مل . تم تطبيق الطريقة المقترحه بنجاح لتقدير المركب الدوائي قيد الدراسة الناتج من تحلل البروكائين وكان متوسط الكفاءة يساوي 97% .

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Abstract

A Spectrophotometric method for the trace determination of p-amino benzoic acid (PABA) has been proposed .The method is based on the coupling diazotized (PABA) with p-2-naphthol in basic medium to from a yellow ,stable and water soluble .azo-dye which shows and a maximum absorption at 299 nm and obeys Beer Lambert low in consent ration range (0.5-4)ml .cm^{-3} of PABA in final volume of 50 ml. The present method has been Applied successfully to determination of PABA which result from hydrolysis of procaine drug. The accuracy which was obtained equal to 97%.

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Chapter one

Introduction

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1-1 Introduction

Procaine is a local anesthetic drug of amino ester group It is used primarily to reduce the pain of intramuscular injection of penicillin and it is also used in dentistry.

1-2 Description:- [1.2]

1-3 Nomenclature

1-3-1 Chemical Name[2]

4-amino benzoic acid ,2(diethyl amino)ethyl ester

p-amino benzoyl diethyl amino ethanol

2-diethyl amino ethyl –p-amino benzoate

Benzoic acid ,4-amino-2-(diethyl amino)ethyl ester

2-diethyl amino ethyl -4-amino benzoate

1-3-2 Nonproprietary Names

Procaine borate :Borocaine

Procaine hydrochloride :Novocain ,Ethocaine

1-3-3 Proprietary Names

Allocaine, Aminocaine ,Rocain Novocain ,Cetain, Chlorocaine ,Heisler ,Neocaine ,Paracain, Planocaine.

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1-4The Formulae:- [3]

procaine used as of the one following chemical structure showing in the table 1-1.

Empirical and Molecular Weight :CAS Number Table1-1

Procaine	$C_{13}H_{20}N_2O_2$	236.31
Procaine borate	$C_{13}H_{25}B_5N_2O_{12}$	455.40
Procaine butyrate	$C_{17}H_{28}N_2O_4$	324.42
Procaine hydrochloride	$C_{13}H_{21}N_2O_2CL$	272.77
Procaine nitrate	$C_{13}H_{21}N_3O_5$	299.33

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1-4-2 Structure(procaine base)[8]

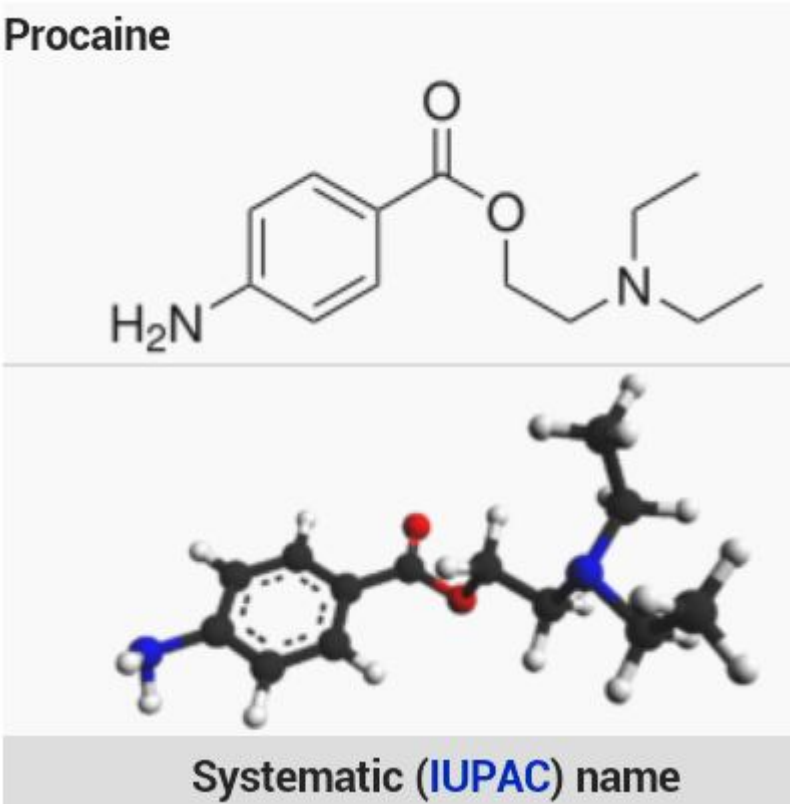

Fig 1

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1-5 Uses and Application:-[7]

Procaine is a derivative ofp-aminobenzoic acid, and is a one of the oldest used ester-type local anaesthetic agents .The compound was originally developed by Einhom and later with and Uhlfelder . This antiarrhythmic drug itself has a short half-life, but is able to form salts with other drugs which causes an increase in the duration of action Procaine is used for a wide variety of clinical nerve blocks, and is devoid of the severe local and systemic toxicity of cocaine. Adrenaline constricts blood vessels in the vicinity of the procaine injection, thus preventing procaine from being washed away into the blood supply and prolonging its duration of action . The drug remains the prototype molecule with which subsequent analogues (having the suffix ***-caines)*** are compared. Procaine exhibits considerably lower degrees of toxicity and irritation, is well-tolerated, and is characterized by superior stability in the solution phase Procaine is ineffective when administered through surface application, and is used only by injection. The onset of action for the drug is 2 to **5** minutes, and its duration of action is short. Vasoconstrictors are usually co-administered with this vasodilator drug to delay its absorption and to increase the duration of action. The drug is used for infiltration anesthesia, peripheral nerve block, and spinal anesthesia.

1-5-1 Mechanism of Action:-[7]

Procaine and the other local anaesthetic drugs prevent the generation andthe conduction of the nerve impulses. Their main site of action is the cell membrane, since conduction block can be demonstrated in giant axons from which the axoplasm has been removed Local anesthetics block conduction by decreasing or preventing the largetransient increase in the permeability of excitable membrane to that isproduced by a slight depolarization of the membrane . This local anaesthetic action is due to their direct interaction with

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voltage- sensitive Na- channels. **As** the anaesthetic action progressively develops in a nerve, the threshold for electrical excitability gradually increases. The rate of rise of the action potential declines, the impulse conduction slows, and the safety factor for conduction decreases. These factors decrease the probability of propagation of the action potential, and nerve conduction fails Raising the concentration of Ca” in the medium pathing, a nerve may relieve conduction block produced by local anesthetics. Relief occurs because Ca” alters the surface potential on the membrane, and hence the transmembrane electrical field. This, in turn, reduces the degree of inactivation of the Na’ channels and the affinity of the latter for the local anesthetic molecule.

Chapter Two

Methods of Preparation

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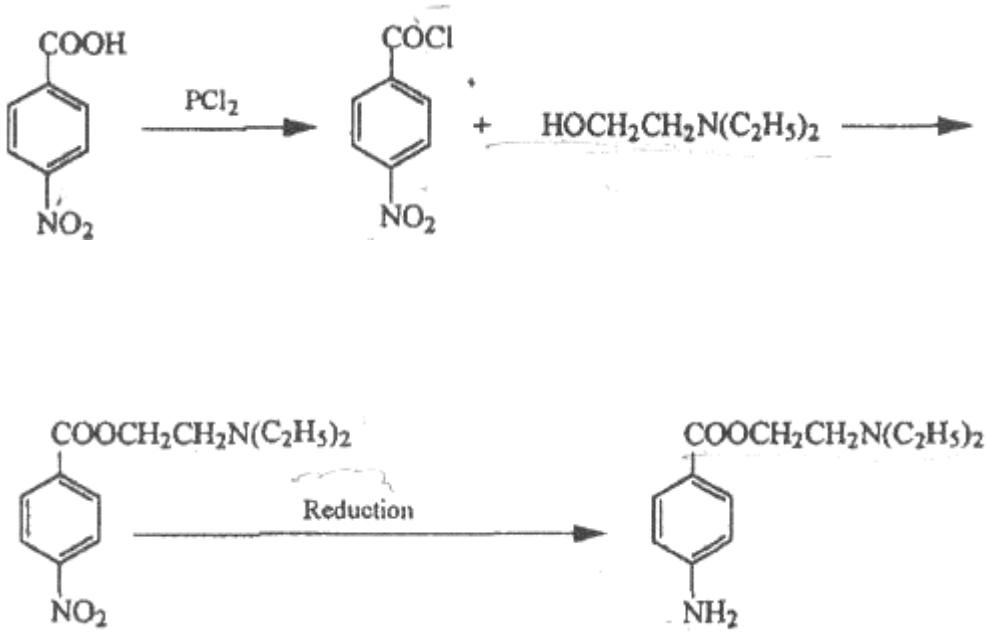
2 - Methods of Preparation:-[5]

Procaine can be prepared by one of three main routes, the basic pathways of which are illustrated in the three Schemes which follow.

Scheme I:

In one method, p-nitrobenzoic acid is converted to the corresponding pnitrobenzoyl chloride, which is allowed to interact with 2-dimethyl aminoethanol. The product of this reaction is 2-diethylaminoethyl- p-nitrobenzoate which is reduced to yield procaine



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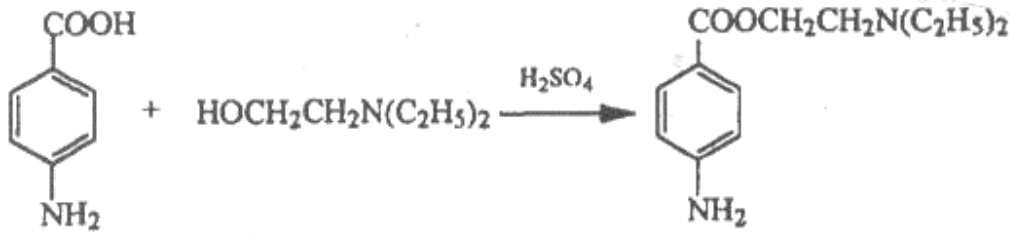
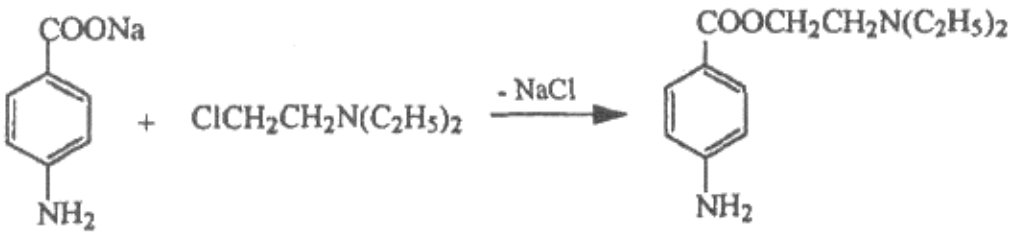
Scheme 2:

Another method entails the esterification ofp-aminobenzoic acid with 2-diethy laminoethanol using concentrated sulfuric acid as a catalyst.



***Scheme* 3:**

A third method of synthesis employs alkylation of the sodium salt **of** p-aminobenzoic acid by 2- chlorotriethylamin



Chapter Three

Methods of Analysis

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3.1 Method of Analysi:-[6.7]

3-1-1 Coulormetry :

Nikolic ***et al.*** reported the preparation and coulometric determination of quaternary ammonium iodides of procaine and of other local anesthetics **.** After extraction from 0.33 **M** NaOH, the quaternary iodide salts were prepared by precipitation with methyl iodide in ethyl ether. The quaternary iodides were then coulometrically determined with the use of aRadiometer titrator. The method used a silver cathode and anode (inelectrolytes of 2 M and **0.4 M H2S0,,** respectively), and a reference mercurous sulfate electrode. For drug determinations in the range of 0.12 to 0. **96** mg, the standard deviations were typically found to be 4 to **8 .**

3-1-2 Ultraviolet Spectrometry :-

An ultraviolet spectroscopic method was presented, and used for the assay of procaine and nitrofural in a multicomponent collagen sponge without prior separation of the drugs . Crushed Collagen Sponge (0.1 g) was dissolved in 70 mL of 1 mM HCl, and heated for ten minutes. The solution was cooled, diluted to volume, mixed, filtered, whereupon. the first 20 mL was discarded. The absorbance of the analyte solution was then measured at 290 and 373 nm (against 1 mM HCl) for procaine and nitrofural, respectively.

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3-1-3 Spectrophotornetric Methods of Analysis :-

Assay methods for Procaine have been reported which make use either of its direct ultraviolet absorption, or which are based on colorimetric reactions of the drug entity.

3-1-4 Gravimetry:-

a gravimetric method for the determination of procaine and other organic compounds .The accuracy of the gravimetric results for carbon and hydrogen were reported to depend on variation in the balance reading.

Chapter four

Practical

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4.1 The Aim :-

Determination of p-amino benzoic acid (PABA) by Aspectrophotometric method

4.2 Chemical:-

Procaine-

Ethanol-

1N hydrochloric acid-

1% sodium nitrite-

-1N sodium hydroxide

p-2-naphthol-

4-3 Apparatus:-

Beaker- pipette-volumetric- spectrophotometer .

4-4 Theory:-

Beer's Lambert's low

A=a b c

A=Absorbance

a=constant

c=concentration

step 1

PABA react with excess of nitrite from PABA diazonium solat the presence of acid .

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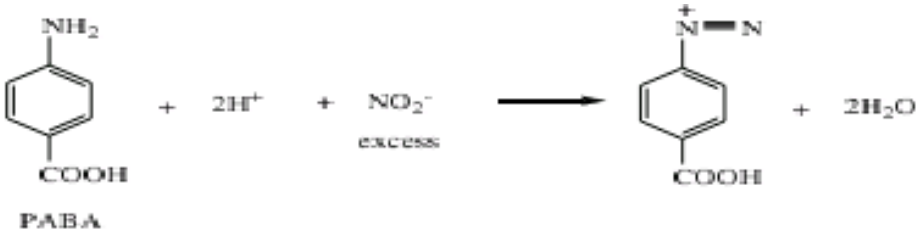
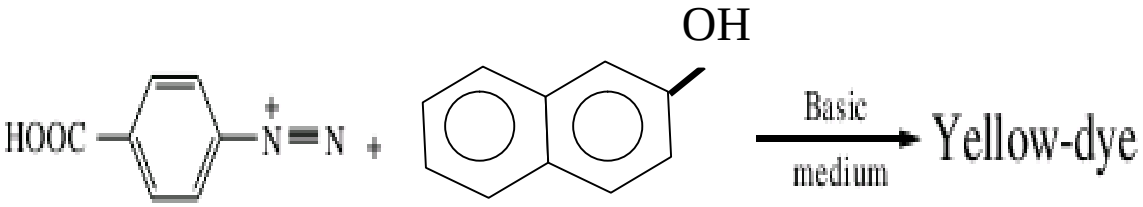


Step2

The colored solution formed by coupling diazotized PABA with p-2naphthol in basic medium.



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4-5 Procedure-:

The sample solution containing 20%(PABA) was transferred into a series of 50 ml volumetric flask. To these solutions 0.3ml of 1%sodium nitrate added ,and acidified by 0.8ml of hydrochloric acid .After shaking to one minute , 2ml of p-2naphtol and 4ml of sodium hydroxide were added and the contents diluted the mark with ethanol .After 5minute the absorbances of colored azo-dye were measured at 299 nm.

Chapter five

Results

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5-1 Result's:-

Procaine

Table 5-1

Concentration	Absorption
0.5	0.11
1	0.27
1.5	0.44
2	0.60
2.5	0.79
3	0.95
3.5	0.96
4	1.34
4.5	1.71

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Stander Amino Acid:-

Table 5-2

Concentration	Absorption
0.5	0.151
1	**0.32**
1.5	**0.470**
2	**0.65**
2.5	**0.77**
3	**0.902**
3.5	**1.05**
4	**1.31**

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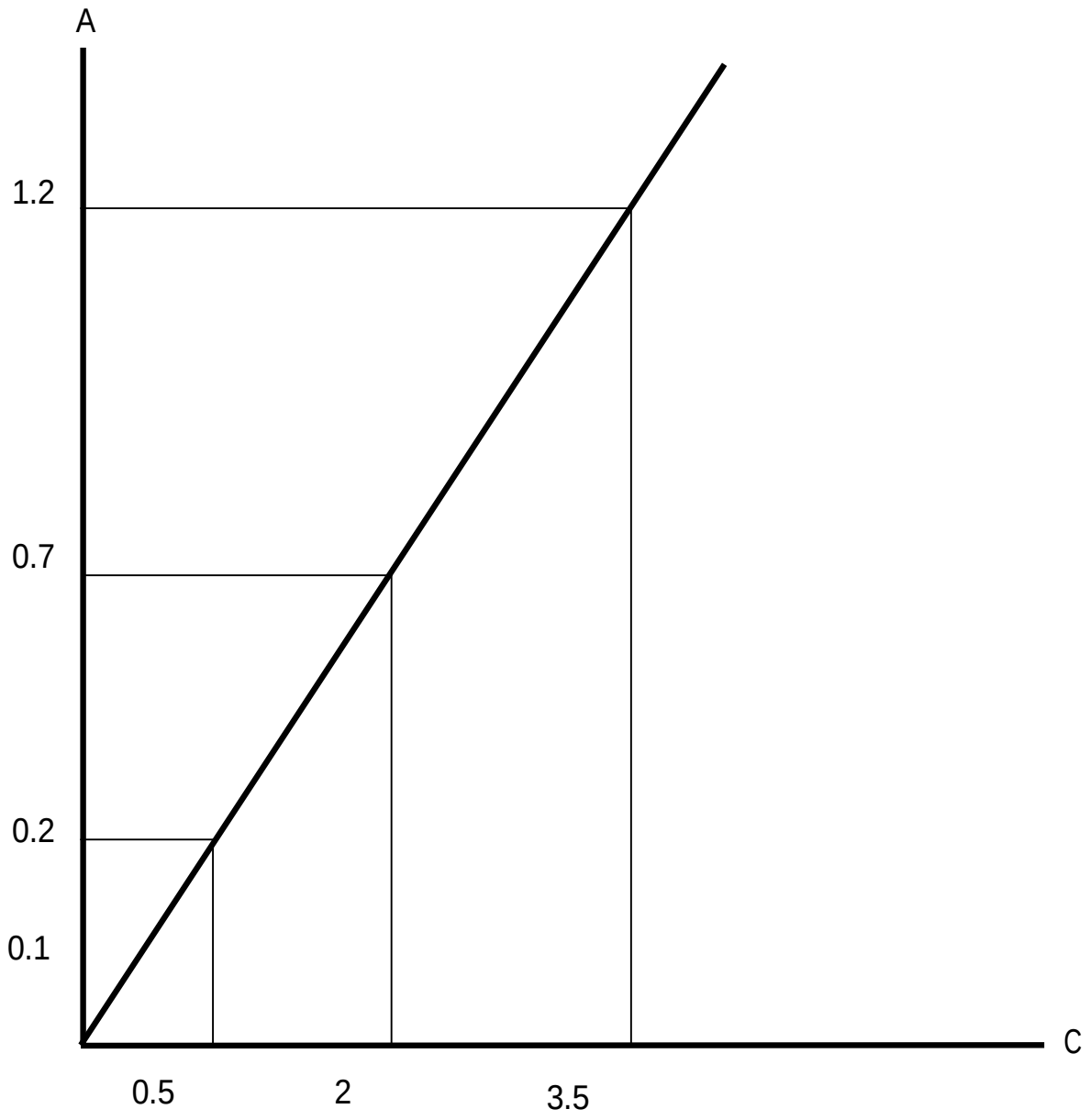
FIG (5-1)



Absorption of stander amino acid 299nm

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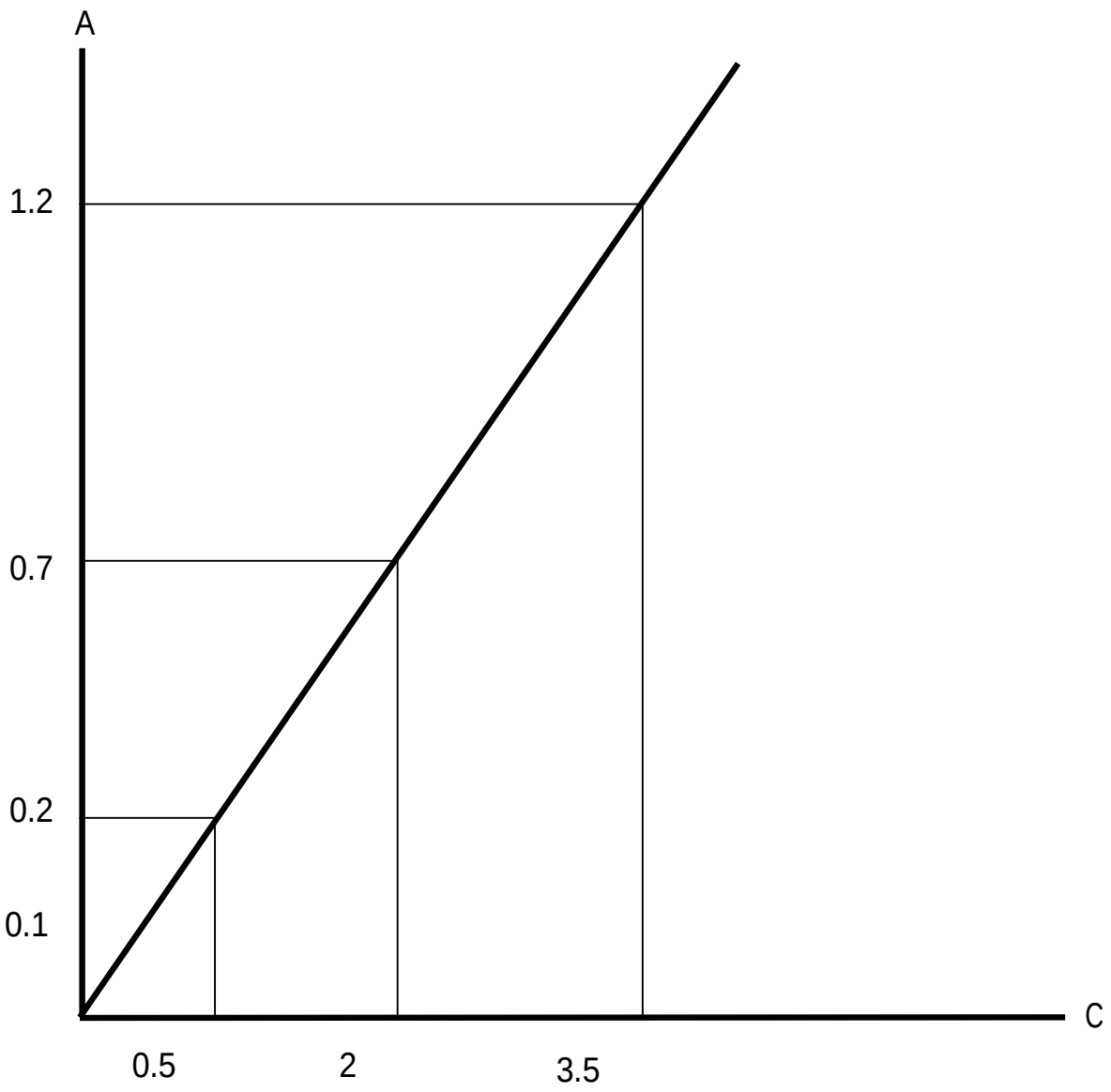
FIG (5-2)



Absorption of Procaine in 299nm

Absorption spectrum of the colored dye formed for the coupling of diazotized PABA with p-2-naphthol reagent in basic medium shows maximum absorption at 299nm .

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5-2 calculations:

At A=0.2

*C= 0.53/0.55*100 = 96%*

1.2At A =

C= 3.55/3.55*100 =100%

At A= 0.9

C= 2.2/2.3*100 =95%

Accuracy = 95+96+100/3 =97%

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5-3 conclusion:-

The experiment was done and determination the p-amino benzoic acid by spectrophotometric method this method is very fast ,cheap and simply .

The accuracy of this method equal 97%.

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