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College of pharmacy

Evaluation Spectrophotometric studies of Some pharmaceutical preparation

A project

Submitted by Department of pharmaceutical chemistry in the college of pharmacy / University of Basrah in partial fulfillment of the requirements for the BSc degree in pharmacy

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Abstract

The objective of this work to develop a spectrophotometric method for the determination of gabapentin in commercial dosage form . the method is based on the chelation of the drug with fe(III) to form pink coloured metal chelate at room temperature which absorbed maximally at 330nm

INTRODUCTION

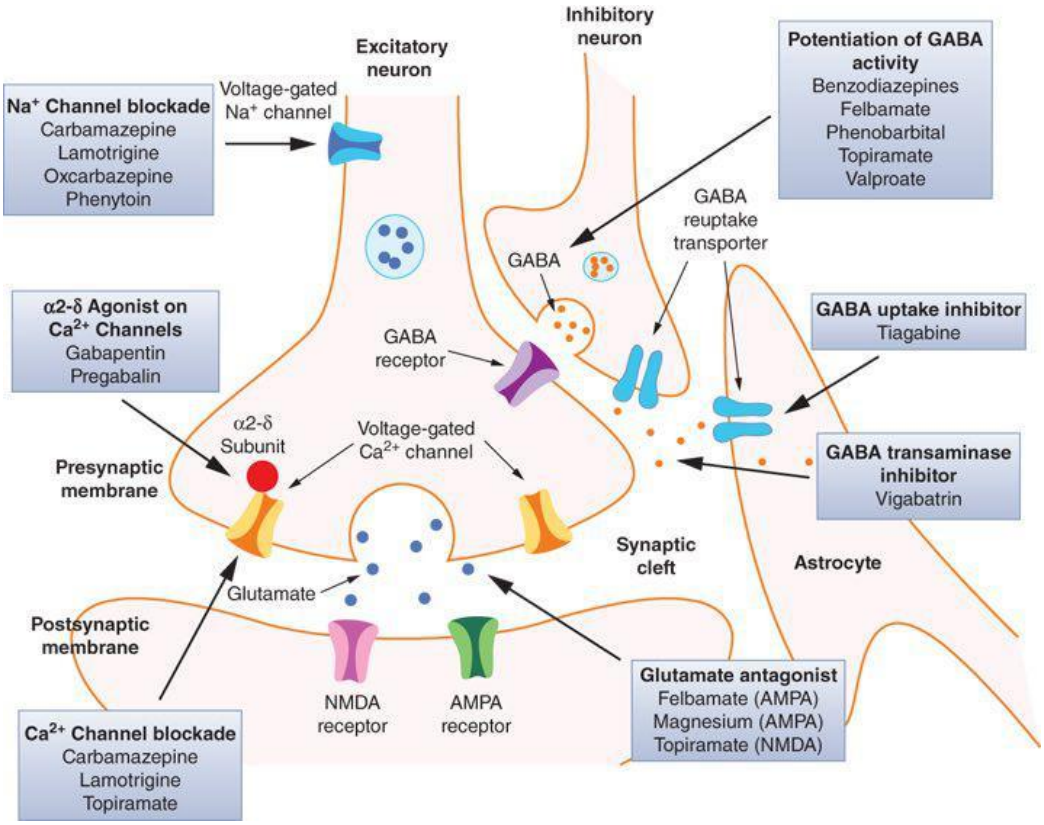
Antiepileptic drugs Are the main form of treatment for people with epilepsy, and up to 70% people with epilepsy have their seizure controlled with AEDs .there are 26 AEDs used in treatment of seizures ,different AEDs used for different type of seizures.(1)

How they work?

It is important to understand the mechanism of action and the pharmacokinetics of AEDs so that these agents can be used effectively.(2)

- Sodium channel blockers
- Calcium channel blockers
- GABA enhancers
- Glutamate blockers
- Carbonic anhydrase inhibitors
- Sex hormones
- SU2A binding agents.

Mechanism of action of AEDs



History:

The first AED was bromide, suggested in 1857 by british gynecologist Charles Hancock, who used it in treatment of women with hysterical epilepsy.(5)

Phenobarbital was first discovered in 1912 as sedative and antiepileptic,in 1930 phenytoin was discovered by Tracy Putnam and Houston meritt, the advantage of discover is to lower the sedative action with treatment of epilepsy.(3)

-In 1940,Trixidone discovered,in1958 ethosuximide discovered,

In 1960 carbamazepine was discovered by schindler,In 1963 ,valporic acid discovered by Beverly S.Burtn in 1882. (4)

The value of benzodiazepines for treatment of epilepsy was rapidly recognized after their discovered and development by Leo steruback during working in swiss pharmaceutical company Roche in 1960(6)

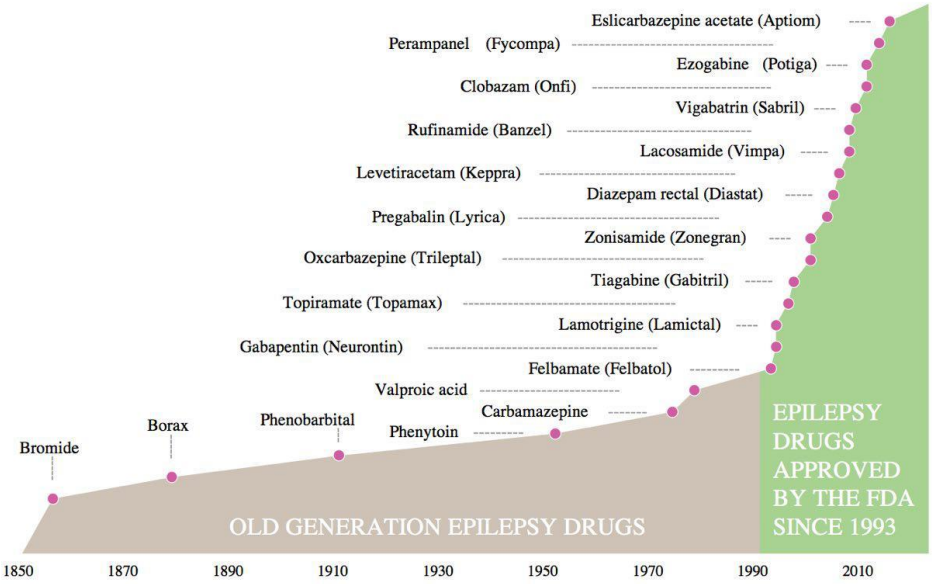
The modern era development began in 1975 by national institute of neurological disorders and stroke in USA ,when established anticonvulsant drug development programme , they found more than 28,000 new chemical entity , these AEDs appear to have unique mechanism of action despite demonstrating efficacy against a similar range of seizure models ,they all have in common the ability to decrease neuronal excitation or increase neuronal inhibition by more pharmacological process ,including modulation of voltage gated cation channel, potentiation of GABA ergic activity ,inhibition of glutamatergic process and modification of neurotransmitter release.(7)

The most important new era AEDs

- Vigabatrin 2009
- Zonisamide 2000
- Lamotrigin 1994
- Gabapentine 1993
- Topiramate 1996
- Tiagabine 1997
- Oxacarbazepine 2000

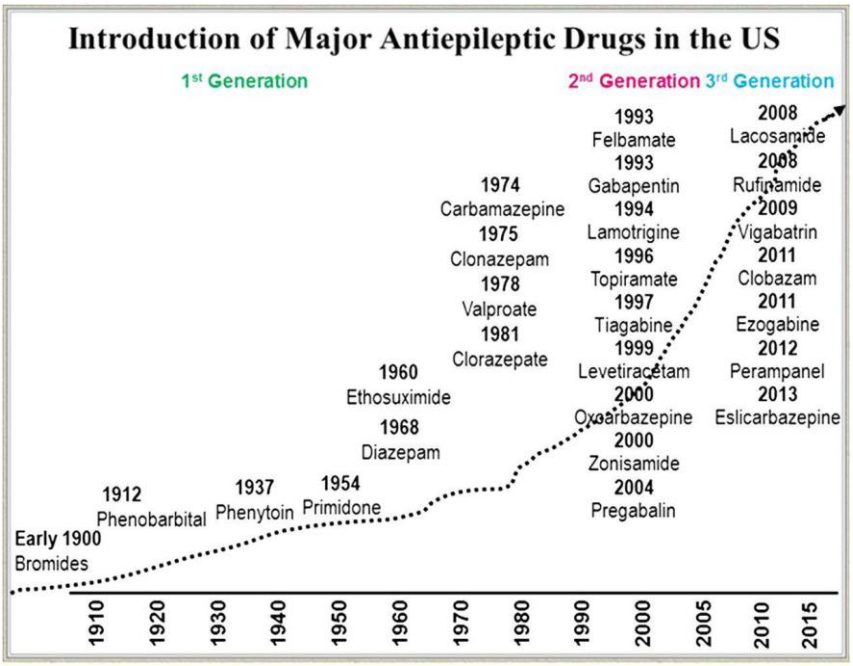
- Pregabalin 2004
- Lacosamide 1998
- Eslicarbazepine acetate

History of ADEs discovery



The classification of antiepileptic drugs

usually presented in two ways as classical ,here the AEDs classified as newer and classical according to the time of discovery and according to the mechanism of action of them .(8)



Pharmacological uses of AEDs

- -Psychratric disorder
- -Trigeminal neuralgia
- -Neuropathic pain
- -Migrane
- -Essential tremor
- -Neuropathic pain syndrome particulary diabetic neuropathy
- -Bipolar disorder
- -Antimanic action

Side effect of AEDs

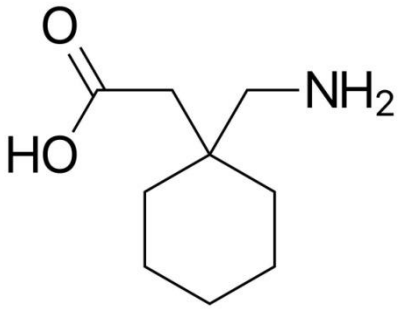
- Allergic reaction
- Idiosyncratic side effect
- Problem with liver and pancreas
- WBCs reduction in count (reduced immunity)
- Platelets reduction in count (Bleeding)
- Most dangerous side effects are aplastic anemia and liver failure.
- Others ,feeling tired ,stomach upset or discomfort , dizziness and blurred vision

Gabapentin

Gabapentin is a synthetic analogue of the neurotransmitter gamma-aminobutyric acid with anticonvulsant activity. Although its exact mechanism of action is unknown, gabapentin appears to inhibit excitatory neuron activity. This agent also exhibits analgesic properties(9).

Brand and Other Names:Neurontin, Gralise

Classes: GABA Analogs



Dosage Forms & Strengths

capsule

- 100mg
- 300mg
- 400mg

tablet

- 300mg (Gralise)
- 600mg (Gralise, Neurontin)
- 800mg (Neurontin)
- oral solution
- 250mg/5mL

Therapeutic indication

- Postherpetic Neuralgia
- Restless legs syndrome
- Cocaine withdrawal
- Insomnia
- Diabetic Neuropathy
- Tremors in multiple sclerosis
- Hot flashes-cancer related

Adverse effect

- Dizziness
- Drowsiness
- Fatigue
- Constipation
- Depression
- Dry mouth
- Dyspepsia
- Increased appetite
- Leukopenia
- Myalgia
- Nervousness
- Peripheral edema
- Pruritus
- Vasodilation
- Weight gain
- Arthralgia
- Vertigo
- ngioedema
- Blood glucose fluctuation
- Breast enlargement

Materials and method

All solvents and materials were of analytical grade and all experiments were performed with distilled water . the drug used is Gabapentin

Apparatus

All absorbance measurements and spectral made on a Shimadzu UV-visible 1100 spectrophotometer (Japan)

Materials and method

All reagent s used at analytical grade

- 0.005 M ferric sulphate (m.w 399.88)
  Solution was freashly prepared in distilled water
- Gabapentin reference standard drug was purchased from sigma chemical company (USA) and 1000 mg/ml used as stock solution

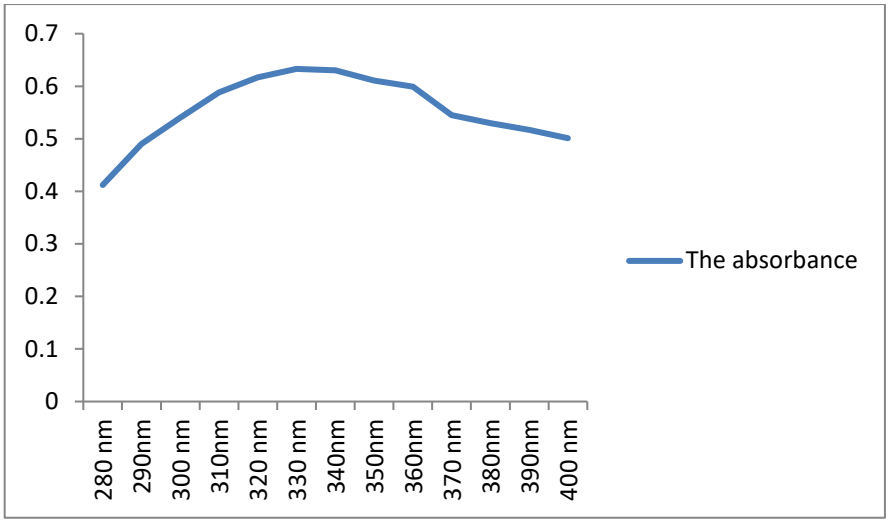
Optimum condition

Absorbance spectra of the complex

the solution of gabapentin absorbed maximally at 205nm , while the ferric sulphate solution in distilled water was peaking at 213nm when the two solutions were mixed together , there was a red shift in the wave length due to the complexation reaction between Gabapentin and ferric sulphate ,Thus gabapentin was allowed to react with ferric sulphate resulting in the formation at pink color metal chelate peaking at 330nm . the reaction was carried out at room temperature .

Table (1) show the data obtained and fig (1)

Lambda	The absorbance
280 nm	0.412
290nm	0.490
300 nm 310nm	0.540 0.588
320 nm	0.617
330 nm	0.633
340nm	0.630
350nm	0.611
360nm	0.599
370 nm	0.545
380nm	0.530
390nm	0.517
400 nm	0.501



2.The effect of the solvent

The effect of the solvent such as water and diluted hydrochloric acid 0.1M was investigated on the absorbance of the colored complex , from the result table (2) and figure (2) we see the complex stability in water is more than in Hcl (0.1m) . as we see above the complex stability in water is more than in HCL , the complex tend to have an almost stable readings in water this owing to degradation complex more readily in acidic media by oxidative degradation , and after saturation of amino group the strong acid work to destruct the whole stracture og gabapentin , so we will use the water in farther investigation .

Table (2) results effect of the solvents

Time	Absorbance at 330nm when the Hcl is the diluents	Absorbance at 330 nm when the diluents is water
0	0.636	0.448
2	0.635	0.454
4	0.635	0.459
6	0.632	0.462
8	0.629	0.466
10	0.628	0.469
12	0.625	0.470
15	0.612	0.470
20	0.616	0.471
25	0.607	0.471
30	0.603	0.472

35	0.598	0.472
40	0.598	0.471
45	0.597	0.466
50	0.596	0.464
55	0.544	0.462
60	0.544	0.455

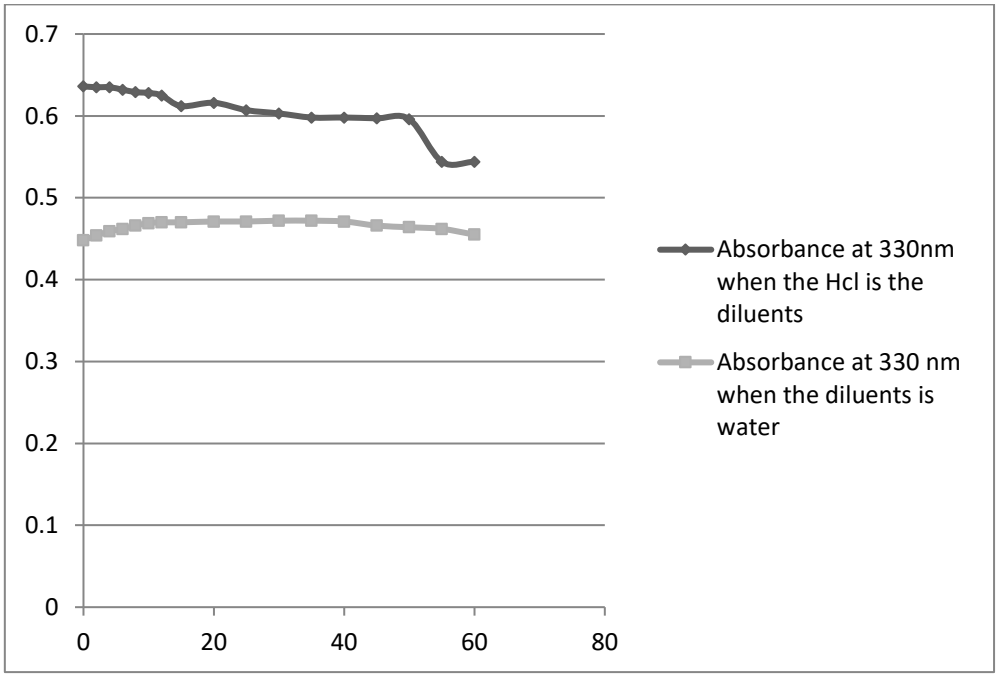


Figure (2) effect the solvent on absorbance

3.the effect of the concentration of fe(III)

The concentration of the ferric sulphate used for the development at proposed method was optimize by perfuming a series at experiment . the influence at the concentration at ferric sulphate on the absorbance at pinked colored complex was examine in different volume range (0.2-2.2ml) of the ferric sulphate , it is evident from fig(3) and table (3) that the maximum absorbance was obtained with 2ml (0.005M) ferric sulphate solution.

Table (3) effect of fe(III) volume on absorbance

Fe +3 concetration	Absorbance at 330nm
0.2ml	0.035

0.4 ml	0.054
0.6ml	0.098
0.8ml	0.1044
1ml	0.163
1.2ml	0.395
1.4ml	0.512
1.6 ml	0.589
1.8ml	0.669
2ml	0.745
2.2ml	0.667

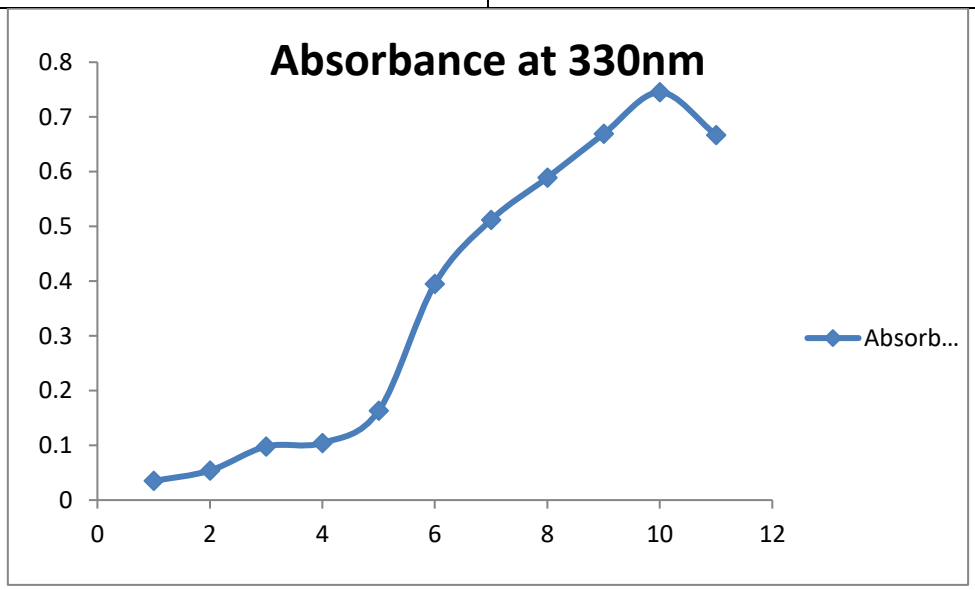


Fig (3) effect of fe(III) on the absorbance

4.Linearity (effect of gabapentin concentration)

Under the optimize experimental condition the absorbance was plotted against the concentration of the drug and found out to be linear over the concentration range (5-35mg/ml) . as showen in Table (4) and figure (4)

Table (4) effect of drug concentration on absorbance

Gabapentin concentration mg/ml	Absorbance
5	0.166
10	0.339
15	0.456
20	0.622
25	0.767
30	0.909
35	1.070

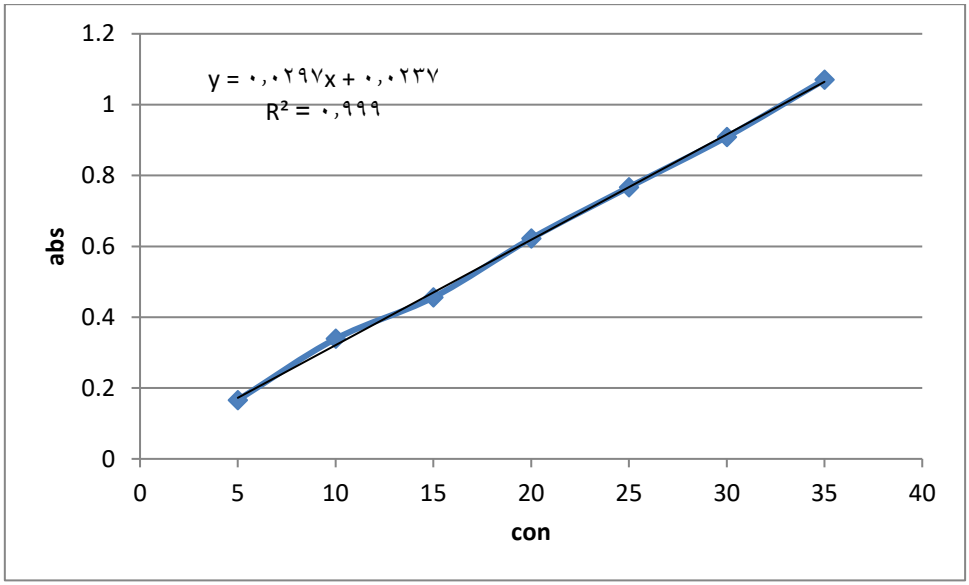


Figure (4) linearity

Table (5) summarized the analytical parameter

Table (5) analytical parameter

Parameter	Analytical data
λ max (nm)	330
Beer's law limits	5-35mg/ml
Correlation coffecient	0.999
LOD	0.75mg/ml

The conculsion :

The aim of this study is to develop a new methods of assay and quality control of ADE Gabapentin and optimize the conditions to get best results , The method has the advantage of using commonly available solvent i.e methanol and ferric sulphate which is less expensive and non-toxic reagent . The proposed method is avoiding the use of hazrduos metal ion , acid , buffer solution and heating of the reaction product .

Reffernce :

Books

-lippincott

- antiepileptic drugs pharmacology and thearpuetics

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