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The Spectrophotometric Determination of Antiepileptic Drug in Standard and Pharmaceutical Formulations by Diazotization Coupling Reaction and Some Metals Complexes

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ABSTRACT
A rapid, sensitive spectrophotometric method has been proposed for the determination of Gabapentin antiepileptic drug in pure and in pharmaceutical preparations was developed. The method is based on the coupling reaction between Gabapentin with8-hydroxy quinoline in to form an olive colored azo dye which gave maximum absorption at 365nm.The optimum reaction conditions like: pH, Temperature affected and time of reaction were evaluated. The ligand and its complexes were characterized by UV-visible spectroscopy, infrared FT-IR, (C.H.N.) analysis and Molar conductivity. The ratio of (metal: ligand) of all complexes was (1:2) by using molar ratio method and jop's method. Beer's law is obeyed for ligand and its complexes with (Cu^{2+}, Ni^{2+},Cd^{2+}, Co^{2+} and Zn^{2+}) in concentration ranges (2 - 20, 1.5 - 25, 1 - 20, 2 - 25 and 2-30µg ml^{-1}) respectively . The molar absorptivity also calculated and it's found to be (1.396×10^4, 2.0208×10^4, 2.295×10^4, 1.684×10^4 and 1.862×10^4 $L.mol^{-1}.cm^{-1}$) for Cu^{2+}, Ni^{2+},Cd^{2+}, Co^{2+} and Zn^{2+}complexes respectively. The detection of limit and quantification of limits are also calculated. The stability constant of complexes equal to(3.273×10^6, 1.695×10^2, 7.859×10^6, 1.851×10^5 and 1.588×10^2 $L^2.mol^{-2}$) for Cu^{2+}, Ni^{2+},Cd^{2+}, Co^{2+} and Zn^{2+} complexes respectively. The method is successfully used for the determination of Gabapentin in pharmaceutical formulations. Analytical parameters like accuracy and precision for the method have been established and evaluated statistically to assess the application of the proposed method. No interferes observed in the proposed method. The complexion with five ions (Cu^{2+}, Ni^{2+}, Cd^{2+}, Co^{2+} and Zn^{2+}) were studying. The aim of present work was devoted to investigate the reaction between Gabapentin and 8-hydroxy quinoline to form color Azo dye and use this product in the development of sensitive and simple spectrophotometric method for determination of Gabapentin in its pure and pharmaceutical preparations and spectrophotometric studies of a azo dye formed and it's metal complexes with Cu^{2+}, Ni^{2+}, Cd^{2+}, Co^{2+} and Zn^{2+} ions.

Key words: Azo compound, Diazotization, Gabapentin, Metals complexes.

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INTRODUCTION
Gabapentin drug is known chemically as [1-(amino-methyl) cyclohexaneacetic acid)], it is antiepileptic drug which is a structural analogue of the inhibitory neurotransmitter yaminobutyric acid (GABA) [1]. Gabapentin crosses the blood brain barrier and is used for the treatment of partial seizures. It has demonstrated analgesic effects in patients with chronic neuropathic pain states [2].Gabapentin anticonvulsant preparation drugs used in both epilepsy treatment and neuropathic pain, as an adjunct therapy for partial seizures in children and adults [3-4]. Many analytical methods have been used for the assessment of Gabapentin drug in pharmaceutical formulations such as (HPLC) high performance liquid chromatography [5-7], voltammetry [8], visible spectrophotometry [9-11], capillary electrophoresis [12], chemiluminometry [13], UV-spectrophotometry [14-16] electrophoresis [17], fluorimetry using sequential injection [18], fluorimetry using sequential injection [19]. spectrofluorimetry [20], potentiometric sensor [21] spectrofluorimetry [22] voltammetry [23], using piezoelectric pumping [24].Many analytical methods for therapeutic monitoring also have been wrote in the literature explain the quantitative determination of Gabapentin in human serum or plasma using GC [25], CE [26].

EXPERIMENTAL
All absorbance measurements and spectral were carried out by used a Jena Model 1100, UV-Visible spectrophotometer(Germany) in pharmaceutical chemistry department, college of pharmacy, university of Basrah, Iraq. The UV-Visible spectrophotometer was equipped with a quartz cell with a 10mm path length. E. Meter electrical balance is used for weighting the sample. The pH measurements are performed using Philips PW 9421 pH meter.FTIR-8400 shimadzu, single beam bath laser spectra were recorded as KBr in the range of (4000-400) cm^{-1}.The CHN analysis measurements for the synthesized compounds were performed by using Euro Vector model EA3000A (Italy), and Molar conductivity was measured at 25 ℃ for 10-3M solution of DMSO .Melting points were determined by using Stuart melting point apparatus PH7110.

Reagents
All chemicals used were of analytical grade. Gabapentin pure was purchased from Sigma-Aldrich Co. The commercial drugs used in the present work were taken from commercial markets. Pharmaceutical preparation of Gabapentinlikes Gabtin capsules-100 mg (Al-Debeiky pharmaceutical products for Delta pharma, Egypt), and Gabix capsules (Getz pharma, Karachi, Pakistan), contain 100mg GAB. per capsule. GABATREX capsules (HIKMA) contain 100 mg Gabapentin per capsule.