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Polarographic Analysis of Structurally Modified Paracetamol

RAKESH CHOURE* and K.S. PITRE

Department of Chemistry,
Dr. Hari Singh Gour University, Sagar M.P.470003, India
choure_chem@rediffmail.com

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Abstract: Paracetamol is an analgesic drug. Its potency may be increased by modifying the drug by way of molecular modification. In the present study the drug has been modified by its complex formation with methanol and other organic compounds. The drug organic compound interaction has been studied using differential pulse polarography and direct current polarography. In Britton Robinson buffer as supporting electrolyte of pH 7.2±0.1, paracetamol produced a well defined peak at -1.18v and it's modified forms at relatively higher negative value. The change in peak potential and lowering in peak height indicating drug organic compound complex formation.

Keywords: Paracetamol, DCP, DPP, Polarography.

Introduction

The word acetaminophen and paracetamol both come from chemical names for the compound *para*-acetylaminophenol[1,2]. In some contexts, it is simply abbreviated as APAP, for *N*-acetyl- *para*- aminophenol.

Paracetamol is widely used over-the counter analgesic (pain reducer) and antipyretic (fever reducer)[3-5]. It is commonly used for the relief from fever, headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies in combination with non-steroidal anti-inflammatory drugs and opioid analgesics[6]. Paracetamol is used also in the management of more severe pain (such as cancer of postoperative pain)[7].

Acetanilide was the first aniline derivative serendipitously found to possess analgesic as well as antipyretic properties[8,9] was quickly introduced in to medical practice under the name of antifebrin by A. Cahn and P.Hepp in 1886. Paracetamol consists of a benzene ring core, substituted by one hydroxyl group and the nitrogen atom of an amide group in the *para* (1,4) pattern[10,11]. The amide group is acetamide (ethanamide), it is an extensively

conjugated system, as the lone pair on the hydroxyl oxygen the benzene pi cloud, the nitrogen lone pair, the *p*-orbital on the carboxyl carbon, and the lone pair on the carbonyl oxygen are all conjugated[12,13].

Experimental

Polarographic, DCP and DPP measurements were made on an (ELICO-India) pulse polarograph model CL-362. The electrode assembly in the experiment consisted of a dropping mercury electrode (DME) as a working electrode, a saturated calomel electrode (SCE) as a reference electrode and a coiled platinum electrode as an auxiliary electrode. The electrochemical cell had a provision for inserting a bubbler for deaerating the solution by passing nitrogen gas. The pH measurements were made on a systronics (India) digital pH-meter model-335.

FTIR studies were made on FTIR-8400S Shimadzu spectrophotometer. Pharmacological study were made on Analgesiometer radiant heat type mark-II Amms Allwin Mfg and Marketing Services.

Chemicals and reagents

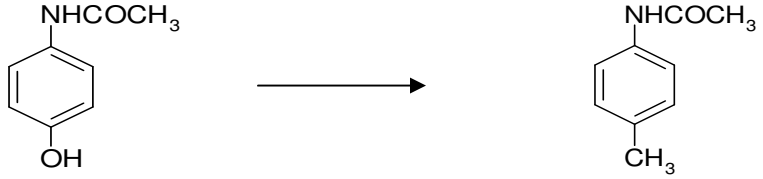
All the chemicals used to prepare in the experimental sets were of Himedia/CDH grade. Britton Robinson buffer was used as a supporting electrolyte. 1 M stock solution was prepared by dissolving a requisite amount of the respective matter in double distilled water. The drug, understudies were procured from their manufactures, *i.e*. Paracetamol [Himedia India Ltd]. The stock solution of this authentic drug was prepared using the following method.

Paracetamol

0.01 M stock solution ($C_8H_9NO_2$, M.W.151.169 g/mol. White powdered compound) of paracetamol was prepared by dissolving the required amount of the drug in water.

Synthesis and analysis of n-methyl paracetamol

Paracetamol molecule was modified by following the procedure discussed to here. Paracetamol was added to 10 mL absolute methanol and 1 mL conc.sulphuric acid, a few small chips of porous porcelain was added through the reflux condenser and the mixture was heated gently for 4 h. The excess of alcohol was distilled off and allowed to cool. The residue was poured into a 250 mL separating funnel contains water. Carbon tetra chloride was added carefully. The upper aqueous layer was rejected, lower one was washed with water and shaken for about 5 min and allowed to stand for at least half an hour with occasional shaking. The methyl paracetamol solution was filtered through a small fluting filter paper directly into a round bottom flask fitted with a still-head carrying a 360 ºC thermodeter and air condenser. A few boiling chips was added and distilled from an air bath, the temperature slowly raised at first until all carbon tetrachloride has passed over and then heated more strongly then recrystallized with chloroform. Methyl paracetamol's crystal was obtained. The process was repeated three times to take different concentration of organic substance and that the drug has been modified.



Paracetamol *N*-Methylparacetamol

Preparation of analyte and recording of the polarogram

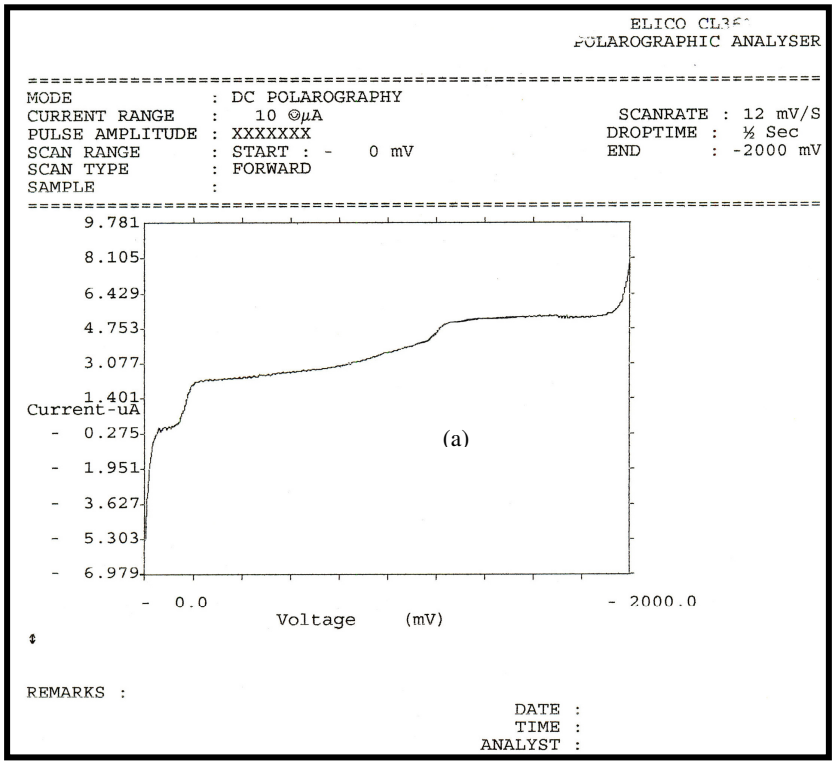
The authentic sample solution of paracetamol was obtained from CDH laboratories. The sample solution of paracetamol was prepared in water. Experimental set was prepared by taking 1 mL of sample solution and 10 mL of Britton Robinson buffer as supporting electrolyte in a polarographic cell and the total volume was made to 50 mL with distilled water. The pH of the test solution was adjusted to 7.2±0.1 with dil. NaOH/HCl solution.

Results and Discussion

The direct current polarogram (DCP) and differential pulse polarogram (DPP) of the authentic sample solution of paracetamol in Britton Robinson buffer (1 M) at pH 7.2±0.1 produced one well-defined polarographic wave/peak with E_p= -1.18V *vs* SCE.

To ascertain as to whether the wave/peak is due to paracetamol present in the solution, a known quantity of standard solution of paracetamol was added to the analyte and polarogram was recorded under above experimental conditions, An increase in wave height of the polarogram due to paracetamol was observed without any change in half wave/peak potential, thus confirming the presence of paracetamol in the solution (Figure 1).

To standardize the developed polarographic procedure for the qualitative and quantitative analysis of the said paracetamol, some experimental sets with varying concentration of paracetamol were prepared and their polarograms were recorded, under experimental conditions discussed above. The current concentration curve showed a linear relationship.



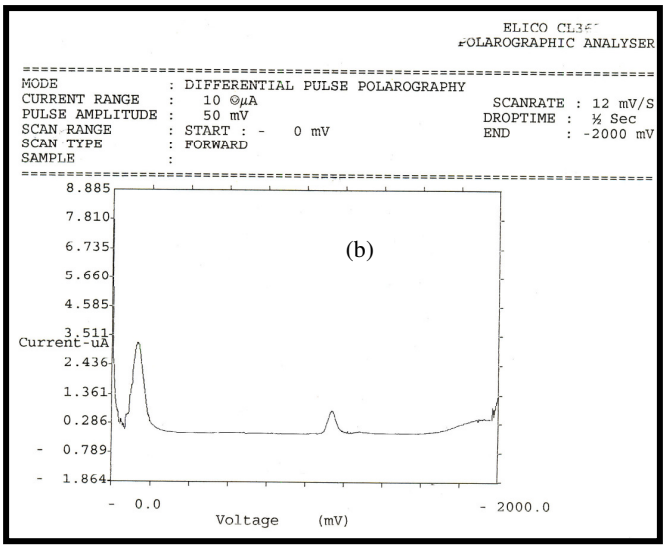
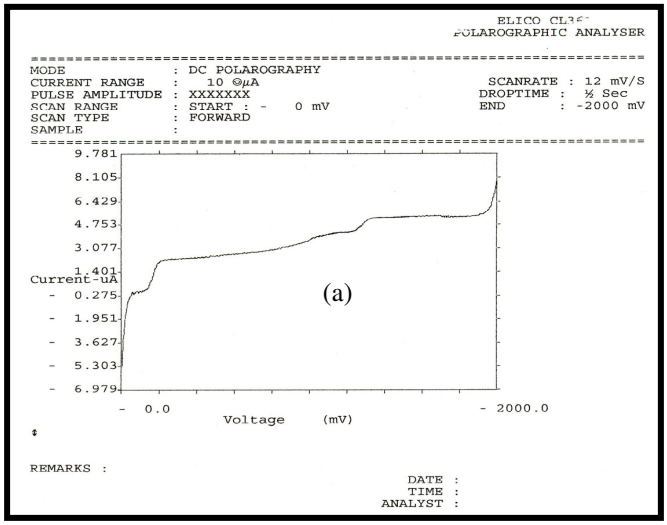


Figure 1. (a) Direct current authentic polarogram of paracetamol in Britton Robinson buffer (1 M) at pH 7.2±0.1; (b) Different pulse polarogram of authentic paracetamol in Britton Robinson buffer (1 M) at pH 7.2±0.1.

To establish the combination of paracetamol, methanol and conc. sulphuric acid the modified drug solution polarographic study was carried out in Britton Robinson buffer (1 M) at pH 7.2±0.1. The result of direct current polarogram produced well-defined polarographic peak with E_p= -1.22V *vs.* SCE on recording the polarograms of modified drug (*n*-methyl paracetamol) solution having varying concentrations of conc. sulphuric acid, methanol and paracetamol under the said experimental conditions (Figure 2). The resulting differential pulse polarography produced polarographic signals with E_P values shifting to more electropositive *i.e.* from –1.18V to –1.22V with increasing concentration of methanol and conc. sulphuric acid. Thus indicating drug methanol, conc. sulphuric acid complex formation.



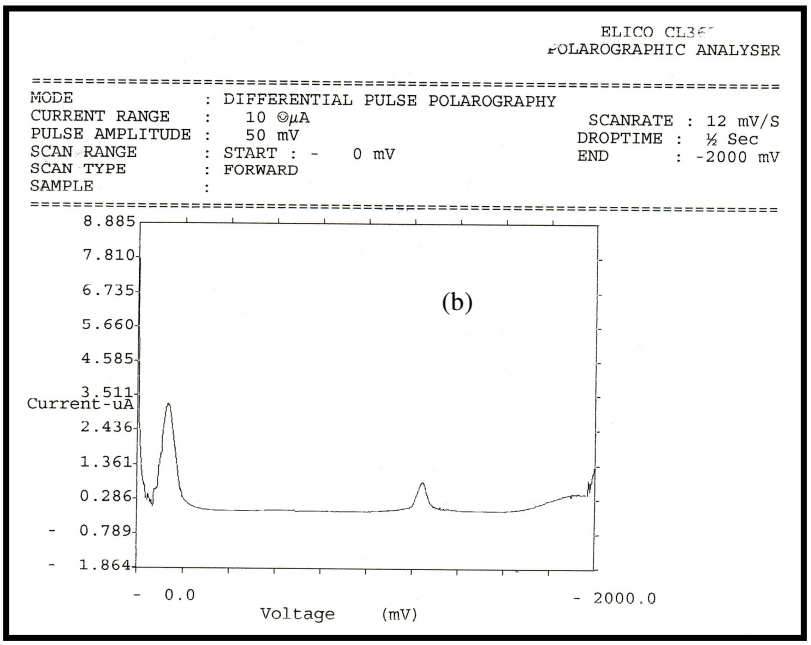


Figure 2. (a) Direct current polarogram of modified paracetamol (*n*-methyl paracetamol) in Britton Robinson buffer (1 M) at pH 7.2±0.1;(b) Different pulse polarogram of modified paracetamol (*n*-methyl paracetamol) in Britton Robinson (1 M) at pH 7.2±0.1.

IR characterization of the test samples

The observed results were also supplemented by the FTIR study on the drug and it's modified form. FTIR spectra of authentic sample clearly shows 5 characteristics signals at 3296 cm^{-1} (N-H), 3080 cm^{-1} (aromatic ring), 2584 cm^{-1} (OH), 1610 cm^{-1} (C=O) and 2881 cm^{-1} (methyl group). And the other hand modified drug (*N*-methylparacetamol) has given 5 characteristics signals at 3296 cm^{-1} (N-H), 3082 cm^{-1} (aromatic ring), 2962 cm^{-1} (methyl group) 1645 cm^{-1} (C=O) and 3014 cm^{-1} (CH_3), thus confirming the presence of methyl group in modified form.

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