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*Original article*

# Spectrophotometric Determination of pKa of some Paracetamol Brands Collected from Pharmacies in Abidya City

**Abdulrraziq Radad*, Suad Omar, Marwa Abas**

*Department of Chemistry, Faculty of Science, Omar Al-Mukhtar University, Abidya, Libya*

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***Corresponding Email.*** abdelraziq.soliman@omu.edu.ly

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**ABSTRACT**

*The experimental dissociation constant (pKa) value of paracetamol is presented in this work. Drugs' dissociation constant (pKa), is one of their most significant physicochemical characteristics. When considering dosage form design and pharmacological analysis, it is extremely important. A UV-visible spectrophotometric technique was mainly employed to determine the pKa of paracetamol. Considering that spectrophotometric pKa determination yields the most accurate values, the spectrophotometric methods was used for the pKa determination. It was found that the pKa of paracetamol was 4.9, 9.9, and 10.5, then understanding a substance's dissociation constant is crucial for a variety of applications and research fields.*

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## INTRODUCTION

Acetaminophen, or paracetamol, is a common medicinal ingredient used as an antipyretic and analgesic [1,2]. its systematic (IUPAC) name is N-(4-hydroxyphenyl) acetamide, a common pharmaceutical ingredient used as an analgesic and antipyretic, additionally it is a member of the pharmacological class known as aniline analgesics, farther paracetamol is a popular constituent in many combination medications intended to treat the common cold and flu as well as the treatment of mild aches, pains, and inflammations, including headaches.

The primary cause of acute gastrointestinal issues is paracetamol poisoning, even though it is normally safe to take at the recommended dosage [3], also it can be categorized as an NSAID (non-steroidal anti-inflammatory drug), paracetamol is sold as a single pharmacologically dynamic chemical substance or in details in combination with other pain relieving drugs that incorporate headache medicine, caffeine or a few opioid pain relieving drugs [4,5]. The dissociation constants can be found in a variety of ways, it is found by measuring an analyte's physical property as a function of a solution's pH in the majority of these techniques. The study was conducted to assess the use of the spectrophotometric approach for measuring the paracetamol pka.

## MATERIALS AND METHODS

### *Sample collection*

Samples collected from different pharmacies in albida city (Libya).

### *Materials*

Paracetamol pure samples, Potassium dihydrogen orthophosphate, Methanol, Hydrochloric acid, and Sodium hydroxide.

***Instrumentation***

Spectrophotometric study was conducted on UV/VIS Spectrophotometer operated at a wavelength range of 200–800 nm. The pH of the buffer solution was measured using digital pH meter.

***Table 1. The pharmaceutical samples***

| Number of samples | Drug name |
|---|---|
| **1** | Adol caplets |
| **2** | Panadol advance |
| **3** | Paracerol vial iv aroma |
| **4** | Paracetamol pl holder |
| **5** | Paracetamol 1000 mg/100 |
| **6** | Windol |

***Methods***

for buffer solutions preparations, about 27.18 g of $KH_2PO_4$ was transferred to a 100 ml volumetric flask, dissolved and the volume made up to 100 ml, resulting in 0.2 M in 100 ml of $KH_2PO_4$. A similar formula was followed to prepare exactly 100 ml of 0.2 M NaOH. Next, 50 ml of 0.02 M and then $KH_2PO_4$ were placed in a 200 ml volumetric flask and a sufficient amount of 0.2 M NaOH was added, then the volume is brought up to 200 ml.

An acid phosphate buffer was prepared, where 0.02 M $KH_2PO_4$ was added to a 250 ml volumetric flask, an observed volume of 0.2 M HCl was prepared and then added, the volume was brought to 250 ml with water, finally buffer solution measured by digital PH meter, and the absorbance of the paracetamol preparation solution in each buffer was measured with a UV-visible spectrophotometer at a wavelength of 277 nm [6].

## RESULTS AND DISCUSSION

Since a drug's hydrophilicity is assessed by the partition coefficient and its ionization state with respect to a solution's pH is determined by its dissociation constant pKa. pKa plays a crucial role in establishing the drug's pharmacokinetic profile. In its ionized state, a drug molecule is less membrane permeable than its counter form, but it is more soluble in water. When a medicine is poorly soluble in water, pKa becomes even more important from a pharmacokinetic perspective. Also, pka is broadly utilized by therapeutic chemists in early medicate advancement stages to check the productivity of medicate to reach its target, proficiency of authoritative at target and likely time for which it'll stay in body. Consequently, pKa is the cardinal variables which have to be considered within the pharmaceutical investigation and measurement shape plan of the medicate [7].

In figure 1, the first curve showed the absorption spectrum of standard paracetamol. It was found that the highest wavelength of paracetamol was at 277 after preparing a series of standard solutions of paracetamol and measuring them with a spectrophotometer, the other curves from 2 to 7 show the equation for calculating the pka, where the value of the pka is equal to the pH value at A1/2 (Figure 2).

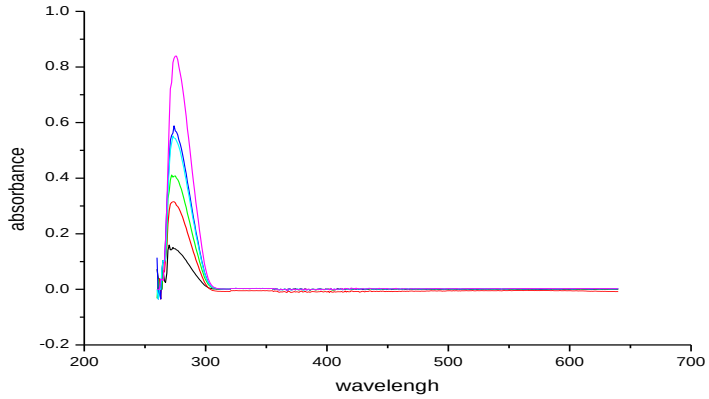


***Figure 1. Absorption spectrum of paracetamol***

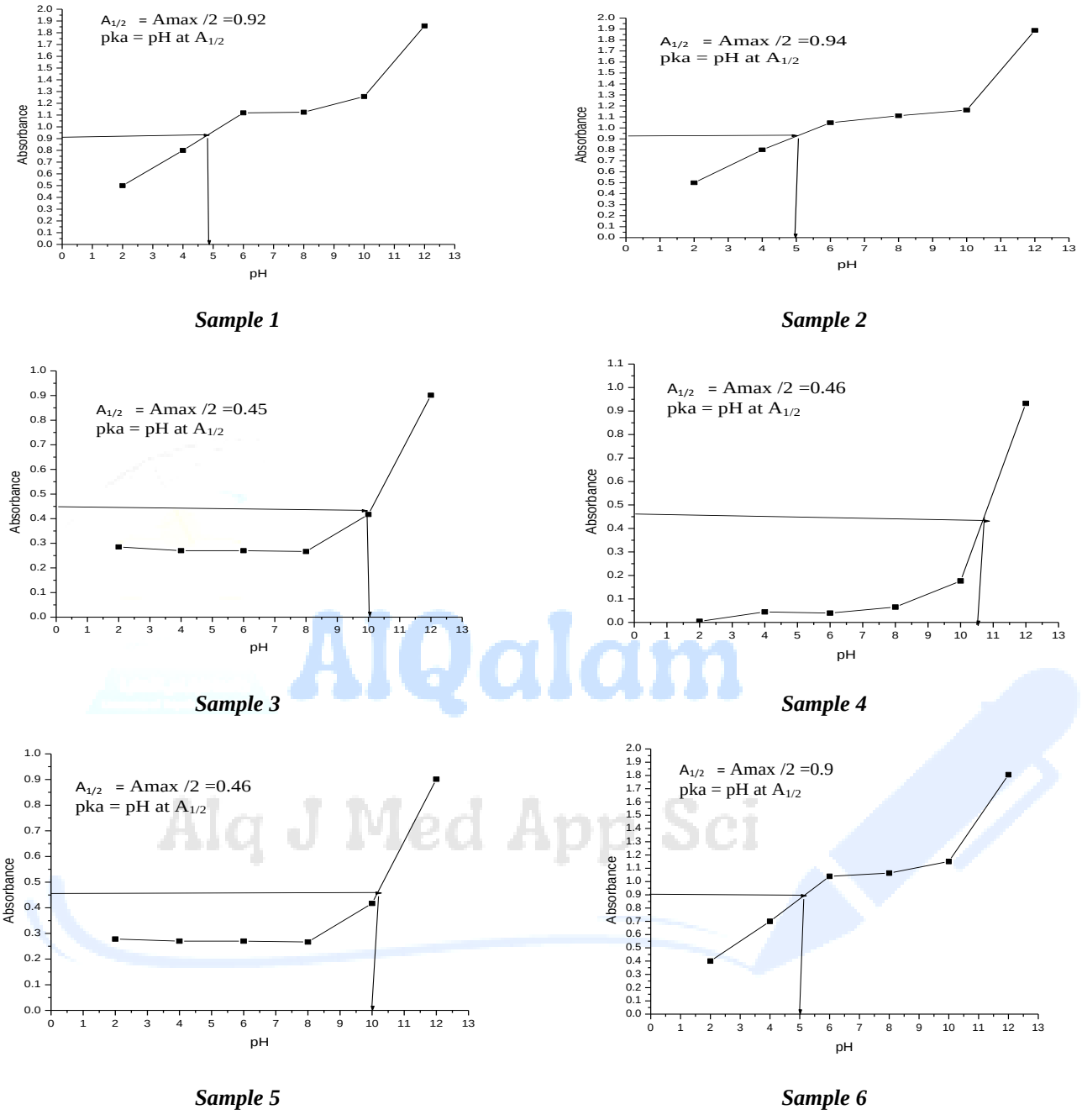


***Figure 2. curve for calculating the value of the pka of each paracetamol sample***

The values of the ionization constant for the different samples are not equivalent, as shown in table 2, they ranged from 4.9 to 10.5 and does not agree closely with the values of the pka calculated previously in the references, this may be due to incorrect transport or storage conditions for the drugs, or perhaps in the product during preparation, as in table 2, also shows the values of Ka, which is equal to the antilogarithmic pka.

***Table 2. The pka and ka values***

| Number of samples | pka | ka |
|---|---|---|
| **1** | 4.9 | $1.2 * 10^{-5}$ |
| **2** | 4.9 | $1.2 * 10^{-5}$ |
| **3** | 9.9 | $1.2 * 10^{-10}$ |
| **4** | 10.5 | $3.16 * 10^{-11}$ |
| **5** | 9.9 | $1.2 * 10^{-10}$ |
| **6** | 4.9 | $1.2 * 10^{-5}$ |

## CONCLUSION

This study was carried out to learn more about the molecular behavior of paracetamol. The pKa of paracetamol was determined experimentally. We noticed variation in the values of the pka for paracetamol, where the results ranged from 4.9 to 10.5 and these values differed from the values calculated for paracetamol in the references. There is necessity of using a group of other techniques for the purpose of increasing and ensuring accuracy of these results. There is also a need to increase control over medicines and periodically monitor their quality and safety.

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# تقدير الطيفي لـ pKa لبعض ماركات الباراسيتامول المجمعة من الصيدليات بمدينة البيضاء

**عبد الرازق ردادا*، سعاد عمر، مروة عباس**

قسم الكيمياء، كلية العلوم، جامعة عمر المختار، البيضاء ، ليبيا

**المستخلص**

يتم تقدير قيمة ثابت التفكك للباراسيتامول في هذا العمل . يعد ثابت تفكك الأدوية أحد أهم خصائصها الفيزيائية والكيميائية. ومن وجهة نظر التحليل الصيدلاني وتصميم أشكال الجرعات، فهو مهم للغاية. تم استخدام تقنية مطياف الضوء المرئي و فوق البنفسجي بشكل رئيسي لتحديد ثابت تفكك الأدوية للباراسيتامول. طرق التحليل الطيفي اعطت قيم عالية الدقه لثابت تفكك الأدوية، وقد وجد أن ثابت تفكك الأدوية للباراسيتامول تراوحت من 4.9، 9.9 و10.5. وهنا يعد فهم ثابت تفكك المادة أمرًا بالغ الأهمية لمجموعة متنوعة من التطبيقات ومجالات البحث.

**الكلمات الدالة.** ثابت التفكك، الباراسيتامول، مقياس الطيف الضوئي ، الأدوية والأشعة فوق البنفسجية المرئية.