

Quantitative Determination of Paracetamol in Pharmaceutical Formulations by FTIR Spectroscopy

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Abstract

The aim of this work was to use a spectrophotometric method for the determination of paracetamol in pharmaceutical formulations. The quantification of paracetamol through infrared spectroscopy was developed and validated for pharmaceuticals in tablet forms. The method involves the extraction of the active ingredient with chloroform and the measurement of the area of the infrared band corresponding to the carbonyl group centered at 1650cm^{-1} . The specificity, linearity, detection limits, precision and accuracy of the calibration curve, paracetamol extraction, infrared analysis and data manipulation were determined in order to validate the method. The statistical results were compared with the quantification of paracetamol through UV detection. The recovery values obtained in the analysis of pharmaceuticals are within the range 98-105%.

Keywords: FTIR analysis, Paracetamol quantification, pharmaceuticals ,UV analysis.

التقدير الكمي للباراسيتامول في المستحضرات الصيدلانية بواسطة مطيافية الأشعة تحت الحمراء FTIR

الخلاصة

تم في البحث الحالي استخدام طريقة طيفية (مطيافية الأشعة تحت الحمراء المعززة بتحويلات فوريير FTIR) لتقدير الباراسيتامول المتواجد بشكل حبوب تقديراً كمياً. تتضمن الطريقة استخلاص المادة الفعالة للباراسيتامول بواسطة المذيب العضوي الكلوروفورم، ومن ثم تحضير محاليل قياسية للباراسيتامول وقياسها بواسطة جهاز مطيافية الأشعة تحت الحمراء FTIR ثم حساب مساحة الحزمة العائدة إلى مجموعة الكربونيل والواقعة في المدى 1650سم^{-1} ، تم تحويل قيمة النفاذية (T%) التي يسجلها جهاز الأشعة تحت الحمراء FTIR إلى قيمة الامتصاصية (A) وذلك لغرض رسم منحنى المعايرة القياسي للمحاليل القياسية المقاسة بواسطة جهاز الأشعة تحت الحمراء. تم معالجة القيم المستحصلة من القياسات احصائياً وتقييم كل من الخطية، حدود الكشف، الدقة لمنحنى المعايرة القياسي، كذلك تقييم استخلاص المادة الفعالة للباراسيتامول بواسطة المذيب، ومن ثم مقارنة هذه النتائج الاحصائية مع النتائج المستحصلة من التقدير الكمي للباراسيتامول بواسطة مطيافية الأشعة فوق البنفسجية. كانت قيمة الاسترداد للباراسيتامول تتراوح بين 98 - 105 %.

1. Introduction

Paracetamol [N-(4-hydroxyphenyl) acetamide] is widely used as an analgesic and antipyretic drug [1]. This pharmaceutical is the active ingredient of a variety of oral medicines in tablets and syrup forms that are used worldwide due to the higher efficiency and tolerance, lower adverse effects and toxicity than other substances [2]. Many assays have been described for paracetamol including potentiometric titration [3], direct titration with Ceric ammonium sulphate [4], high performance liquid chromatography [5], flow injection [6], and UV spectroscopy [7]. Potentiometric titrations avoid the interference of the excipients since the completion of the reaction is detected through the slope change of the electromotive force emf (or pH) versus volume of titrant. This method is suitable to analyze raw paracetamol and tablets using tetrabutylammonium in acetonitrile [8]. The direct titration with Ceric ammonium sulphate is economical, easily applicable and is described in the European Pharmacopeia for the quantification of raw paracetamol (European Pharmacopeia 2005) [9]. But, non-soluble excipients contained in tablets may interfere in the observation of the completion of the reaction through a chemical acid-base indicator [10]. The analysis of paracetamol through high performance liquid chromatography is used worldwide for quality control of pharmaceuticals. This method allows to analyze both paracetamol

and products of degradation [11]. However, the pretreatment of the sample may be difficult if the excipients or the active ingredient are non-soluble in the mobile phase.

Infrared spectroscopy is the method described by the pharmacopoeias to identify paracetamol, the present investigation shows the development and validation, according to the US Pharmacopoeia recommendation of the quantitative analysis of paracetamol in tablets through infrared spectroscopy. The results allowed to improve that a standard FTIR spectrometer is suitable to be used both to identify and quantify active ingredients of pharmaceuticals. The technique was compared with the results obtained from UV spectroscopy.

II. Methods

Chemicals and Pharmaceuticals

Paracetamol (99.8%) that used as standard for physico-chemical assays was provided by the SDI (Samara drug industry) of Iraq.

Infrared Spectroscopy

The IR analyses were performed in a Shimadzu FTIR 8400S equipment. Quantitative analyses of solutions of paracetamol in chloroform were performed in a cell with CaF_2 windows. Qualitative analyses of solid samples were performed through thin discs with KBr.

UV-VIS Spectroscopy

Quantitative analyses of solutions of paracetamol in chloroform were measured by using a Shimadzu UV-VIS equipment and 1 cm pathlength

cell. The absorbance was measured at 243 nm.

III. Results and Discussion

A. Extraction of paracetamol from pharmaceutical formulations in tablet form

The extraction of paracetamol from pharmaceuticals in tablet forms was achieved through the selective dissolution of the active ingredient with chloroform according to the indications of the USP for the identification of paracetamol (US Pharmacopoeia, 2005) [12]. Ten tablets of a pharmaceutical (SDI 500 mg) were weighed, powdered and homogenized. An accurately weighed quantity of the powder was dissolved in 10.00 ml of chloroform, stirring for 10 minutes and centrifuged in order to separate the excipients. The supernatant solution was diluted to 25 ml with chloroform in a volumetric flask.

Figure 1 shows the IR spectra of paracetamol as active ingredient (standard) and the active ingredient (solution of paracetamol tablets in chloroform) recovered after the extraction.

B. Linearity

The relationship between the concentration of a substance and its absorbance of radiation is given by the Beer-Lambert law :

$$A = \log (I_0 / I) = \epsilon b c$$

Where A is absorbance, (I_0 / I) is the ratio between the intensities of incident and transmitted radiation that goes through a substance with C concentration contained in a cell of width b. The parameter ϵ , known molar absorptivity, is a property of the substance [13].

The range of linearity of absorbance versus concentration of paracetamol and the molar absorptivity at constant

b was determined through a series of solutions of different concentrations of paracetamol in chloroform. Each of them was analyzed through infrared spectroscopy and the area of the signal corresponding to the carbonyl species (typically in the 1650 cm^{-1} range) was determined.

The limits of detection and the parameters of the linear regression are presented in table 1.

C. Precision and Accuracy

The precision and accuracy were determined from the following steps of the analytical method: the preparation of standard solutions of paracetamol, the determination of the IR spectra of the solutions and the extraction of paracetamol from the tablets.

The precision and accuracy of the preparation of standard solutions was investigated through the preparation of six solutions containing 0.3 % w/v of standard paracetamol in chloroform that were further analyzed through IR spectroscopy.

The IR analysis and data processing involve transferring a solution to the cell, digitalize the infrared spectra and the mathematical manipulation of the data for area calculation. The statistical study of those steps was performed through the preparation of three solutions containing concentrations of paracetamol that correspond to the limits (0.056 % w/v and 0.500 % w/v) and center of the calibration curve (0.300 % w/v) obtained in section B. Each of those solutions was analyzed three times through IR spectroscopy and the area of the infrared signal of the carbonyl species was determined.

Finally, the precision and accuracy of paracetamol extraction was determined treating ten tablets of the

same commercial pharmaceutical with chloroform as described in section A.

Table 2 shows the theoretical concentration of paracetamol, the relative standard deviation (RSD%) of peak areas, the relative error and the recovery values, obtained on the experiments described above. The RSD values are an indication of the repeatability (precision) and reproducibility of an experiment and the error and recovery values shows the accuracy of the analytical determination. The RSD values presented in table 2 indicate that the extraction of paracetamol from the pharmaceuticals possesses the lowest repeatability (3.8 %). However, the recovery values demonstrate that the quantification of the active ingredient is highly accurate at concentrations of ~0.300 % w/v (center of the calibration curve) and above.

These results were compared with the quantification of paracetamol through UV spectroscopy.

A calibration curve was determined by measuring the UV absorbance at 243 nm of solutions containing different concentrations of paracetamol in chloroform. The limits of detection and the parameters of the linear regression are presented in table 1.

The accuracy and precision of the determination of absorbance of a series of solutions of standard paracetamol in chloroform along with the data processing, and the quantification of paracetamol in pharmaceuticals are presented in table 3.

The extraction of paracetamol from the pharmaceutical possesses the lowest repeatability (~5%) as observed previously (see table 2

for comparison). The UV detection allows a more accurate quantification of lower concentrations of paracetamol compared with the IR analysis. The relative error and the recovery values indicate that the UV quantification is highly accurate at concentrations below 0.160 % w/v while the FTIR analysis possesses a high accuracy even at concentrations of 0.5 % w/v. This is an important observation considering that most of the paracetamol based pharmaceutical possess 500mg or more of the active ingredient therefore, the IR analysis avoids further dilutions that diminish the accuracy of the quantification.

D. Comparison with other methods and quantification of paracetamol in pharmaceuticals

Table 4 compares the precision, accuracy and recovery of the present method with other techniques reported in the literature such as high performance liquid chromatography and titrimetric.

The quantification of paracetamol through infrared spectroscopy either with a conventional cell for liquid analysis or a flow injection device possesses similar accuracy and recovery values. Although the FTIR method presents lower precision than the non-official assays, is similar to HPLC which is the most frequently used for quality control of pharmaceutical formulations.

IV. Conclusions

The quantification of paracetamol through infrared spectroscopy accomplishes with the requirements of precision and accuracy in order to be used as a method for the quality control of pharmaceuticals. Moreover, the method may be suitable for the quantification of

major components of bulk drug substances or active ingredient in finished pharmaceutical products, according to the US Pharmacopoeia (US Pharmacopoeia, 2005).

This technique extends the use of a standard IR spectrophotometer, typically used for identification purposes, to the reliable quantification of paracetamol. The present method opens the possibility of applying IR spectroscopy to quantify other active ingredients than paracetamol.

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Table (1) Linear regression equations ($y = A + Bx$) for paracetamol quantified through IR and UV spectroscopy.

Method	detection limits (% w/v)	A	B	Correlation coefficient r
IR spectroscopy	0.000-0.609	0.00	168.38	0.998
UV spectroscopy	0.000-0.200	0.00	10.61	0.993

Table (2) Precision and accuracy of the different steps of the quantitative analysis of paracetamol in tablets through IR spectroscopy.

Step	Theoretical concentration of paracetamol (%w/v)	RSD (%)	Accuracy (%)	Recovery (%)
preparation of solutions of standard	0.300	2.0	0.7	99.0
Spectroscopic analysis and data manipulation	0.056	1.9	34.0	68.0
	0.300	1.0	0.3	100.0
	0.500	0.2	2.4	98.0
quantification of paracetamol in pharmaceutical	0.400	3.8	10.2	110.2

Table (3) Precision and accuracy of the different steps of the quantitative analysis of paracetamol in tablets through UV spectroscopy.

Step	Theoretical concentration of paracetamol (%w/v)	RSD (%)	Accuracy (%)	Recovery (%)
spectroscopic analysis and data manipulation	0.020	0.9	1	100.0
	0.100	1.1	1	100.0
	0.200	0.4	6.5	93.5
quantification of paracetamol in pharmaceutical	0.160	5.4	5.0	95.0

Table (4) Comparison of precision, accuracy and recovery of the quantification of paracetamol through IR and other reported methods, [14], [15], [16].

Method	Reference	Precision (%)	Accuracy (%)	Recovery (%)
HPLC	Carina de A.Bastos et al.,2009	1.72	1.6	99-101
HPLC	ALTUN M. 2002	2.02	0.6	100.24
Titrimetric	Kumar K.G. et al.1997	1	0.4	99.5
FTIR spectroscopy	This work	3.8	0.3-2.4	98-100
UV spectroscopy	This work	5.4	5	95

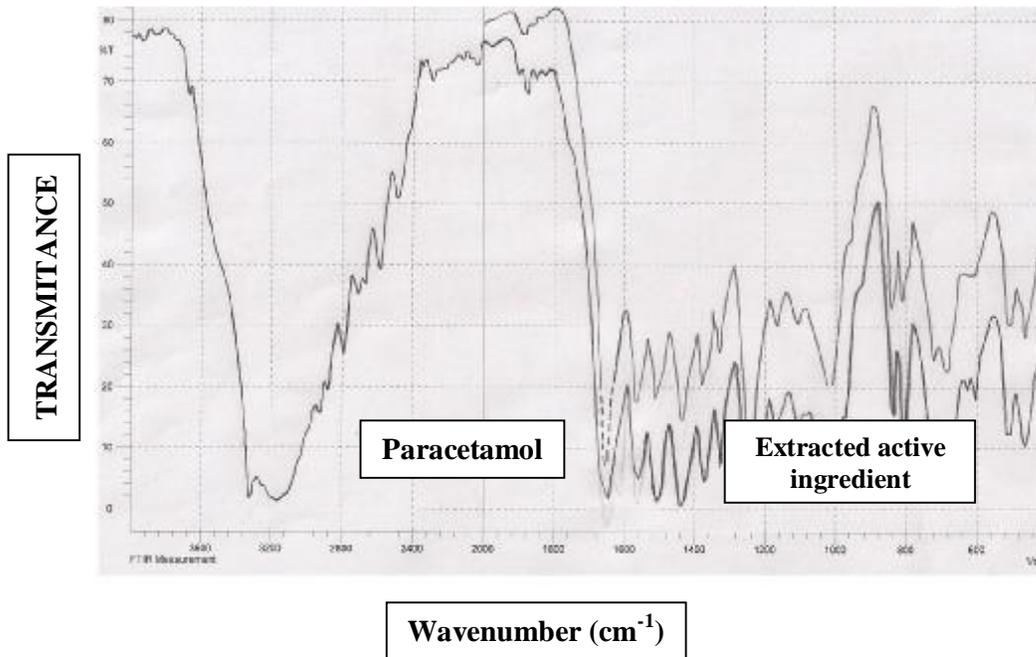


Figure (1) Infrared spectra of paracetamol (standard) and active ingredient after extraction with chloroform.