

Utilization of green ATR-FTIR spectroscopic method for quantitative analysis of Ibuprofen tablets

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Abstract

Aim: The aim of this study is to propose a green and nondestructive method using the ATR-FTIR method for the quantitative analysis of Ibuprofen tablet dosage forms. Herein, the technique has been validated as an alternative green tool that evades necessary sample preparation procedures required in traditional quantitative methods.

Methods: The method depends on selecting CO of the Ibuprofen stretching band in the range 1620–1750 cm⁻¹ to quantitatively determine Ibuprofen in original samples. The peak area (AUC) from ATR-FTIR spectral scanning of samples has been determined through the first derivative measurements.

Results: The assay results indicated that no interferences between the excipients or additives and the active ingredients of the commercial tablets interferences. The linearity is excellent within the concentration range of 0.2 to 1.5 w/w % ($r = 0.9994$). A percentage of recoveries ranged between 99.7–10.5 which are in good agreement with the pharmacopeial percent recovery standards. The high degree of sensitivity of the technique was demonstrated by obtaining a 0.028 w/w % detection limit and a 0.1599 w/w % limit of quantification values.

Keywords

Ibuprofen tablet, FTIR spectroscopy, method validation, green chemistry, quantitative analysis

Introduction

Ibuprofen (IBU) is marketed under several commercial names and brands. It is available in several dosage formulations. The drug is widely popular as an antipyretic and non-steroidal anti-inflammatory (NSAID) over the counter medicine (Rainsford 2009; Bushra and Aslam 2010). IBU is a commercial name of the (±)-2-(p- isobutyl phenyl) propionic acid according to IUPAC standard nomenclature.

Traditionally, several quantitative assay techniques have been used for the analysis of commercial IBU tablets

of varied dosage forms. Many commonly validated techniques have been used in Ibuprofen determination, either alone or combined with other dosage forms, including high performance liquid chromatography (HPLC). (Sylvester et al 2015; Han et al. 2017; Alsaad et al. 2019; Borahan et al. 2019), gas chromatography (GC) (Qureshi et al. 2014), UV-visible spectrometry (El-Maraghy and Lamie 2019), spectrofluorometric (Salem et al. 2019; Magdi et al. 2021). Thin Layer Chromatography TLC-densitometry (Starek and Krzek 2010) and potentiometry (Aktaş and Ertokuş 2008; Ebeshi et al. 2009). However, United States

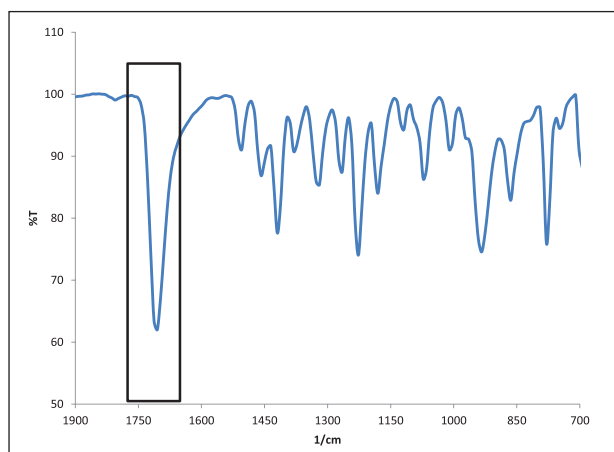


Figure 1. Spectrum of pure IBU mixed with potassium bromide (KBr; 0.6% w/w).

Pharmacopeia (USP 2013), and British Pharmacopeia (BP 2013), have adopted HPLC techniques as a standard method of IBU analysis.

Applicability of FTIR techniques in the field of pharmaceutical analysis as a qualitative method is well established. However; recent advances in manufacturing robust spectrometers equipped with powerful computer software have opened new opportunities to rediscover the qualitative feasibilities of the old technique (Bunaciu et al. 2010). More importantly, the new generation of artificial intelligence-enabled instruments has revolutionized new approaches such as chemometrics. Exploring the ability to engage infrared spectroscopy in a quantitative fashion was always appealing to scientists. The technique offers a non-destructive simple green alternative to classical methods. The dodging of tedious, environmentally harmful, and costly somehow lengthy complicated sample preparation procedures represents some of the advantages associated with IR spectroscopy in pharmaceutical analysis applications. Current work aims to shed light on the applicability of FTIR quantitative concentration measurements of active pharmaceutical ingredients (API) in several commercial IBU dosage forms. The technique offers many advantages over traditional tests. The IBU was chosen to study the quantitative applicability of the FTIR technique since it is a worldwide analgesic. Undoubtedly, the result of this study will provide an example of crucial pharmaceutical analysis using simple techniques with comparable results.

Trusting the quantitative features of IR spectroscopy applied in the analysis of many pharmaceutical products has gained tremendous acceptability in the scientific community (Bunaciu et al. 2010). It is an attractive method of analysis, particularly in examining API compared to traditional approaches, due to many factors. New FTIR spectrometers equipped with an attenuated total reflection (ATR) module have extremely simplified sampling of many drugs in different dosage forms. Accurate and reproducible FTIR spectra can be recorded for solid or liquid samples by the ATR-enabled spectrometers without any further specific sample preparations. A specific IR band selected from the recorded spectra of several standard concentrations of a partic-

ular drug can be monitored. The peak area of the selected band can then be related to the concentration. The linear relationship of AUC and the concentration of the sample allows the construction of a calibration curve. Recording an FTIR spectrum of a sample of the analyte is sufficient to determine the API in that sample. The attractiveness is that modern spectrometers can execute and manage such statistical algorithms automatically. Once a calibration curve is saved in the system, by reading the AUC of a sample from any source, the concentration of API can be obtained immediately. However; in many cases, it is essential to prepare a KBr disc of an accurately measured amount of the drug (tablet form) to record reliable spectra.

The current work, it is aimed to simplify sample preparation for the FTIR analysis even further, specifically; skipping the KBr disc requirement (Bunaciu et al. 2010). Hence, original samples taken from commercial IBU tablets were diluted with spectroscopic grade KBr within certain concentrations. Calibration curves were created by diluting standard API (pure (\pm)-2-(p-isobutyl phenyl) propionic acid) and recording the corresponding FTIR spectra. Assay tests were then performed by recording FTIR spectra of KBr-diluted commercial tablets. By reflecting the AUC of the selected band with data stored in the constructed and saved calibration curve, the API content can be accurately determined. Accordingly; the requirement of press machines is no longer essential.

Exploration of quantitative boundaries of FTIR techniques flourished recently thanks to the vast advancements made in both instrumentation or powerful computing and artificial intelligence capabilities. Additionally, FTIR spectrometers have been equipped with modern revolutionized sampling accessories including flow analysis (FA) and ATR. Such sampling fittings enabled the direct analysis of almost all types of samples (solid, liquid, solution, gas, and vapor) directly.

The implementation of quantitative FTIR analysis has opened a new era in industrial pharmacy. Not only for the purposes of accurate determinations of API contents in a variety of sources and dosages but also as a valuable and dependable quality control technique (Nugrahani et al. 2019).

The following advantages and perceptions might emphasize the opportunities of applying FTIR analysis. As the technique saves time on the run, requires little training to be operated by a technician, accepts raw samples without lengthy preparations, is sensitive, nondestructive, and is environmentally friendly as no solvent is needed, is an appealing alternative to traditional analytical chemistry techniques (Bunaciu et al. 2010). In our previous work, we used the first derivative ATR-FTIR for the quantitative analysis of diclofenac sodium tablets in which very promising results were obtained (Fahelbom et al. 2020), these results encouraged us to expand the method application with other similar dosage forms as Ibuprofen tablets.

First derivative spectra have been used in this work to analyze recorded FTIR spectra. The resolution of the obtained FTIR spectra can be greatly enhanced by this function (experimental section). The first derivative spectra

were applied to the spectrum recorded for the pure IBU standards (shown in the experimental section). The band that exhibited no overlapping with the remaining bands was selected for the construction of the calibration curve. The band also was tested to have a statistically accepted correlation with the API concentration in subsequent commercial samples analyzed. The first derivative concept was adapted for all spectral analysis throughout this work.

Materials and methods

Chemicals

The chemicals and reagents used were: Potassium bromide IR spectroscopic-grade. Reference chemical standard of Ibuprofen was provided by Adcan Pharma, Abu Dhabi, UAE.

Four different commercial tablets of Ibuprofen were purchased from local pharmacies.

Apparatus

This study was conducted using FTIR Spectrometer IRAfinity-1 CE (Shimadzu, Kyoto, Japan), with attenuated total reflectance (ATR) attachment, Pike Technologies. For the screening of data analysis, the instrument is equipped with Irresolution software. An oven (Wise Ven, Won-032, S. Korea) was used for drying tests of Potassium bromide and (AUW220D, Shimadzu) analytical balance was used in the weighing process.

Preparation of calibration curve

Ibuprofen standard calibration curve was performed by preparing different concentrations covering the range from 0.2 to 1.0% w/w; a suitable quantity of Ibuprofen was diluted with dried potassium bromide and grounded in a mortar for 10 min to obtain a homogeneous sample. The obtained FTIR spectra for each reading were converted to the first derivative spectra using Iresolution Software. A distinctive peak appeared in the range 1750–1620 cm^{-1} , which indicates the high absorbance of the C=O stretching group.

Active ingredient quantitative analysis of Ibuprofen tablets

The active pharmaceutical ingredients (API) analysis for four Ibuprofen tablet dosage forms used in this study was prepared as follows; Ten tablets from each product were weighed accurately and individually, and the weighed samples were powdered for each brand and then were thoroughly mixed with potassium bromide in order to get a concentration of 0.5% w/w of Ibuprofen. 100 mg of Ibuprofen-Potassium bromide mixture was transferred to the ATR top plate of the spectrometer over the diamond crystal. The FTIR measurements were run in triplicates and the average reading was recorded.

Results and discussion

Validation of the method

To validate ART-FTIR of this method, the ICH guidelines (International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH 2005) were used.

The following parameters were used in the validation of the method: selectivity, linearity, limit of detection, Limit of quantification, precision, accuracy, and robustness.

Linearity

To evaluate the peak Area (AUC) and its relation to the concentration of Ibuprofen, a calibration curve was constructed to assess the linear relationship of the following concentrations (0.2, 0.4, 0.6, 0.8, and 1%) with the peak area. An excellent linear relationship was obtained indicating a high correlation coefficient $R^2 = 0.99874$. The data of the Ibuprofen calibration curve was given in Table 1, While Figs 3, 4 represent the spectra of pure Ibuprofen concentrations and the linear relationship between the peak and the Ibuprofen concentration.

Table 1. Calibration curve analysis of Ibuprofen.

Wavelength (cm^{-1})	Concentration (% w/w)	Regression equation	R^2	LOD (%)	LOQ (%)
1620–1750	0.2–1.5	$Y = 1.182X - .1136$	0.9987	0.01382	0.04841

LOD: Limit of detection; LOQ: Limit of quantification; R^2 : Correlation coefficient.

Selectivity

Selectivity is an important parameter to examine the ATR- FTIR method to quantify Ibuprofen's existence in the presence of other pharmaceutical excipients. The method selectivity was evaluated by conducting a comparison between Ibuprofen tablets to pure Ibuprofen. The Ibuprofen bands were unique as shown in Figs 1, 2, in the direct and first derivative spectra. A distinctive and clear CO high absorption band at 1750–1620 cm^{-1} . Figs 5, 6 show the direct and the first derivative spectra of the Brufen tablet (as an example of Ibuprofen tablet dosage forms), and the Ibuprofen pure sample, which indicated that there is no interference due to the presence of the excipients or additives in the tablet dosage forms.

Limit of detection and limit of quantification

The LOD is defined as the lowest concentration at which the method is able to detect, while the LOQ is the lowest concentration at which the method is able to quantify (Shrivastava and Gupta 2011).

$$\text{LOD} = 3.3 \sigma / S. \quad (\text{Equation 1})$$

$$\text{LOQ} = 10 \sigma / S \quad (\text{Equation 2})$$

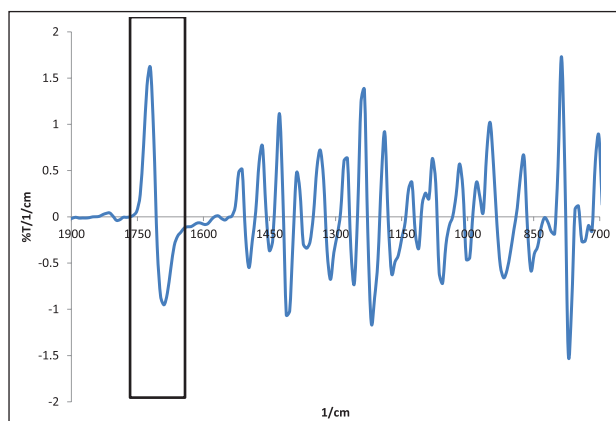


Figure 2. Spectra of the 1st derivative Ibuprofen.

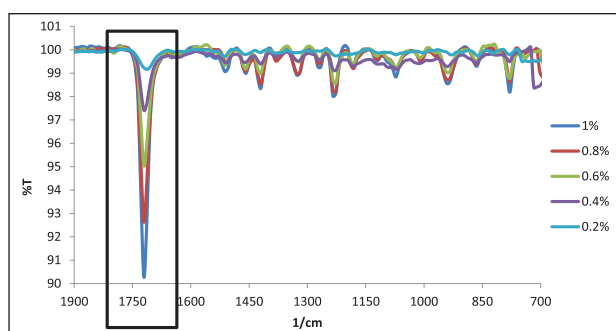


Figure 3. Overlay spectra of different concentrations of Ibuprofen.

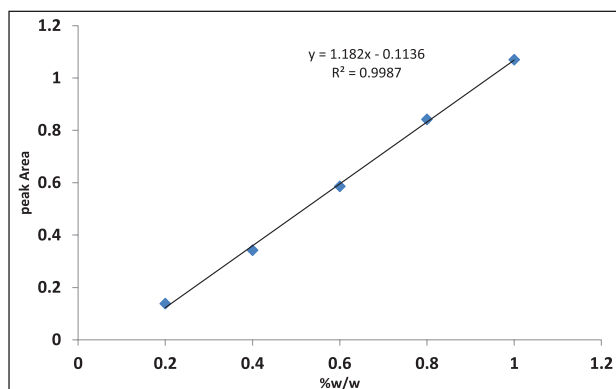


Figure 4. Ibuprofen calibration curve.

Where σ is the standard deviation and S is the slope. The results shown in (Table 1) demonstrate that the data recorded for LOD, and LOQ were 0.01382% and 0.04841%, respectively, the obtained small values for LOD, and LOQ shows the high sensitivity of this method.

Accuracy

The accuracy of this ATR-FTIR method was examined and validated by using four different brands (A, B, C, and D) of Ibuprofen tablets, which have been analyzed. Tablets of each brand were ground to a fine powder (total 10 tablets) and mixed with KBr in order to give 0.5% w/w Ibuprofen-KBr mixture. The mean recovery of each brand of these Tablets A, B, C, and D were recorded as follows; 100.4%, 100.6%, 99.9%, and 100.2%, respectively, as shown in Table 2. The results obtained in this method

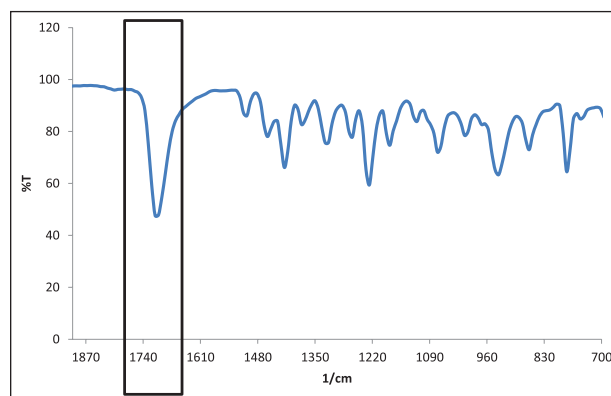


Figure 5. Spectra of Brufen Abbott tablet.

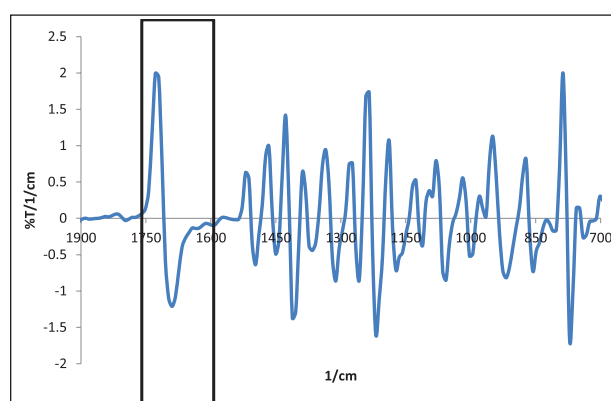


Figure 6. 1st derivative spectra of Brufen Abbott tablet.

Table 2. Quantitative analysis of Ibuprofen tablet dosage forms using ATR-FTIR.

Type of Analysis	Sample A	Sample B	Sample C	Sample D
Intra-day	101.2%	100.6%	99.0%	99.8%
	100.6%	100.4%	99.2%	101.2%
	99.4%	100.8%	99.2%	99.8%
Inter-day	100.4%	101.2%	100.4%	101.2%
	99.2%	100.0%	98.8%	99.2%
	99.6%	99.8%	101.4%	99.4%
Average	100.1%	100.5%	99.7%	100.1%
SD.	0.007865537	0.005163978	0.010171857	0.008831761
RSD	0.786029644	0.513999117	1.020587619	0.882293793

SD: Standard deviation, RSD: Relative standard deviation.

were in good agreement with the published USP and BP recovery range for Ibuprofen tablet analysis.

Precision

The precision of a method is defined as the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings. Repeatability intermediate precision studies were performed to examine and validate the proposed method's precision. The analysis was performed by determining the 0.5% w/w (mixed with KBr) peak areas (AUC) of each Ibuprofen tablet brand. Three obtained readings for each sample were recorded and analyzed in one day (for the intra-day precision) and the other three readings were recorded on two consecutive days (for the inter-day precision). The results obtained are shown in Table 2. Indicating high precision,

as represented by the standard deviations (SD), which ranged between 0.005163 and 0.01017, while the relative standard deviation (RSD) was between 0.5140 and 1.0206.

Robustness

The robustness of the analytical method can be defined as the capacity of the method to remain unaffected and give similar results by applying small deliberate variations in the method procedures. In this proposed study two parameters were used to check the method's robustness; the temperature and the time of analysis, the results indicate that changing the temperature from room temperature (20 °C) to (40 °C) does not change the obtained recovery of different Ibuprofen tablet dosage forms, as well repeating the analysis in different days show similar results with high accuracy (Table 2).

Forced degradation analysis

To demonstrate that this analysis method is stability indicating, a set of forced degradation conditions was applied according to the ICH method validation guidelines (ICH 2005). Specifically, the FTIR spectra of the reference compound (ibuprofen) were recorded under conditions of photolytic degradation, thermal degradation, and degradation in sunlight (Blessy et al. 2014). In each of the

recorded spectrums, the CO of the Ibuprofen stretching band in the range 1620–1750 cm^{-1} was monitored closely. It was found that the band correlation with the API concentration remained statistically accepted without any effects due to applied stress conditions. The percent of degradation results obtained from the recorded FTIR spectra were between 0.7–0.8 percent confirming the validity of this method as a stability indication.

Conclusion

The results obtained for the development and validation of the proposed ATR-FTIR spectroscopic method indicated that the method is nondestructive to the drug samples, has low cost, and is considered a sensitive, accurate, precise, and stability-indicating technique for the quantitative analysis of Ibuprofen in its pure and tablet dosage form. The method can be easily applied for quantitative determination and quality control.

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