Spectrophotometric Analysis of Ibuprofen According to USP and EP Monographs

Performing pharmaceutical identification tests with an Evolution UV-Visible Spectrophotometer

Introduction

Monographs outlined by the United States Pharmacopeia (USP) and European Pharmacopoeia (EP) contain tests, procedures, and acceptance criteria that help to ensure drug ingredients and drug products conform to the published requirements for strength, quality, and purity. These monographs contain detailed instructions utilizing a variety of analytical instrumentation for performing identification tests, purity tests, and tests to limit the amount of undesirable impurities. Although the general requirements governing the performance of an analytical instrument used in a monograph will be outlined in its own general chapter, additional instrument requirements needed to perform a test may be indicated in the individual monographs.

This document will highlight the utilization of UV-Visible spectrophotometers to perform essential monograph tests. As spectrophotometric tests are featured in hundreds of monographs, UV-Visible spectrophotometers are essential analytical instrumentation for every pharmaceutical quality control laboratory. In this work, a Thermo Scientific™ Evolution™ Pro using Thermo Scientific™ Insight™ Pro Software will be used to perform the USP and EP spectrophotometric identification tests for ibuprofen highlighted in their respective monographs.

Ibuprofen is an active pharmaceutical ingredient that is used as a medication for treating pain, fever, and inflammation. The Ibuprofen monographs published by USP and EP contain a variety of identification tests utilizing infrared absorption spectroscopy, ultraviolet visible spectroscopy, melting point analysis, and chromatography to help confirm the quality of ibuprofen samples.
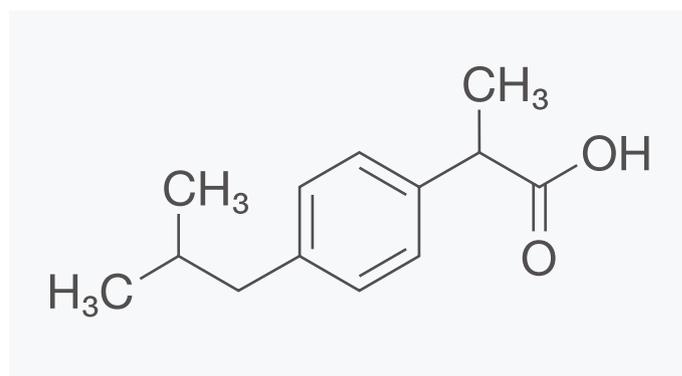

Figure 1. Chemical Structure of Ibuprofen, $C_{13}H_{18}O_2$.

Experimental

EP Identification Test

The spectrophotometric ibuprofen identification test according to the EP ibuprofen monograph requires measuring a test sample and comparing the ratios of its absorbance values to confirm they are within an acceptable range.

A 500 µg/mL ibuprofen solution was prepared by dissolving 50 mg in a solution of 0.1 M sodium hydroxide in a 100 mL volumetric flask using the sodium hydroxide solution to fill to the total volume. The sodium hydroxide solution was used as the blank. The monograph required a spectrum of the ibuprofen solution to be obtained with a wavelength range of 240 nm – 300 nm, a bandwidth of 1 nm, and a scan speed of less than or equal to 50 nm/min. The Insight Pro software experimental parameters used to obtain the spectrum are shown in Figure 2. The programed ratio equations for evaluating the results are shown in Figure 3.
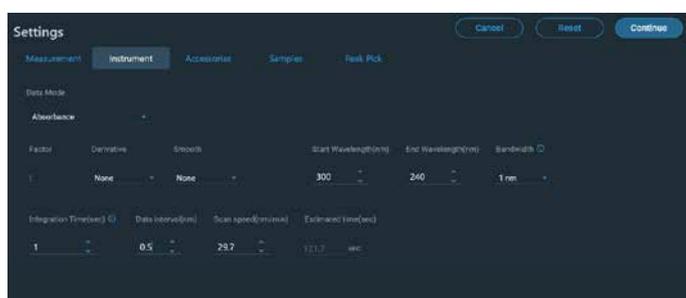
Figure 2. Experimental parameters of EP ibuprofen test.

The spectrum of the ibuprofen test sample is shown in Figure 4. Visual inspection of the spectrum shows absorption maxima at 264 nm and 272 nm and a shoulder at 258 nm which align with the monograph requirement for the identification of ibuprofen.

Along with this spectrum, Insight Pro Software automatically calculates the ratio values required to verify the identity of ibuprofen using the programed equations from Figure 3. The absorbance ratio of A_{264}/A_{258} was 1.25 which was within the 1.20 – 1.30 requirement highlighted in the ibuprofen monograph. The Absorbance ratio of A_{272}/A_{258} gave a result of 1.00 which was also within the monograph requirement of 1.00 – 1.10. These absorbance ratios along with the visual inspection of the spectrum confirm the identity of ibuprofen according to the Ultraviolet and visual absorption spectrophotometry test in the EP ibuprofen monograph.


Figure 3. Ratio calculations for EP ibuprofen test.
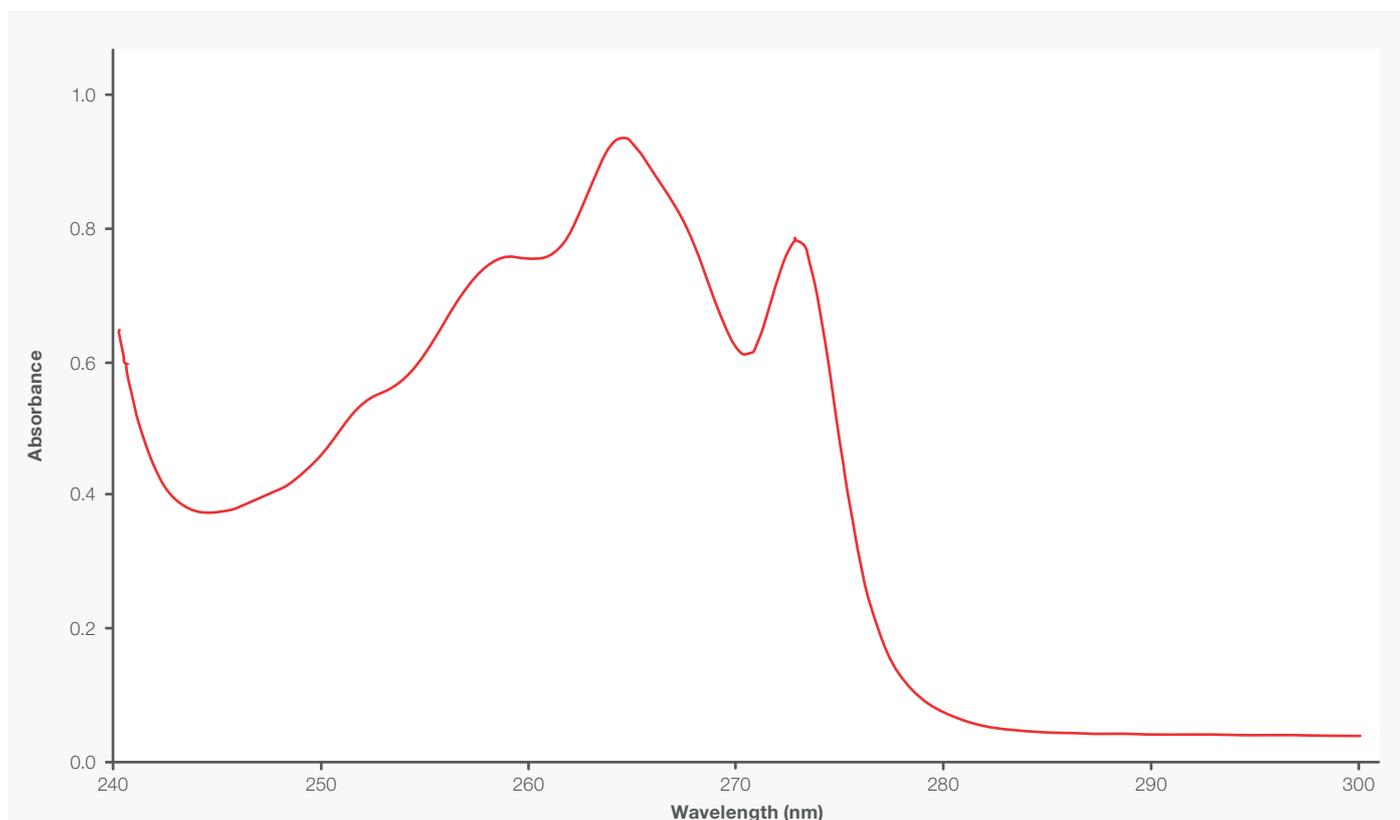
Figure 4. EP ibuprofen test sample spectrum.

USP Identification Test

In the USP spectrophotometric identification test for ibuprofen, a reference standard sample and a test sample are prepared using identical procedures and the spectra are compared to confirm the test sample exhibits absorption maxima and minima only at the same wavelengths as those of the reference sample. Additionally, the molar absorptivity at two different wavelengths are calculated and compared between reference standard and sample to ensure they do not differ within a certain percentage.

A 250 µg/mL solution of an ibuprofen standard was prepared by dissolving 25 mg in a solution of 0.1M sodium hydroxide in a 100 mL volumetric flask using the sodium hydroxide solution to fill to the total volume. A test ibuprofen solution was prepared in the same way as the standard. The sodium hydroxide solution was used as the blank in the experiment.

Spectral measurements of the reference standard and sample were obtained using a similar procedure as the EP Identification Test in Figure 2 but scanning from 200 nm – 400 nm. The spectral data should be similar to the results shown in Figure 4 with maxima and minima at the same wavelengths.

The absorbance values at 264 nm and 273 nm of both the standard and test solution were measured according to the USP guidelines using the Fixed method on the Evolution Pro Spectrophotometer with the following parameters as shown in Figure 5.
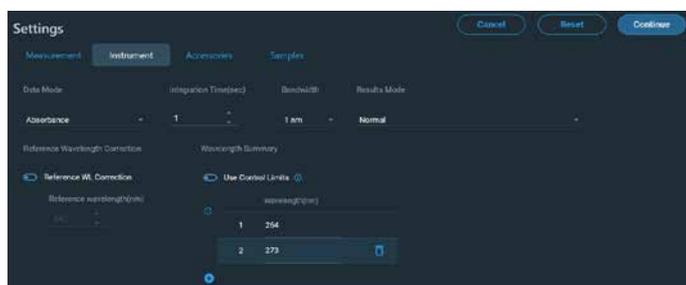
Figure 5. Experimental parameters of USP ibuprofen test.

	Weight (mg)	A_{264}	A_{273}	ε_{264}	ε_{273}
Standard	25.8	0.4732	0.3905	385.83	318.35
Sample	24.9	0.4644	0.3849	378.61	313.85

Table 1. USP Measurement Data.

The absorptivity values at each wavelength for both the standard and test sample were calculated using the Beer-Lambert Law where ε is the molar absorptivity in L/mol•cm units, A is the absorbance value, l is the pathlength in cm and c is the concentration in mol/L:

$$\varepsilon = \frac{A}{l \times c}$$

The molar absorptivity is calculated using the absorbance values and the weight of the samples. An example is shown below where the molar absorptivity of the standard sample at 264 nm was calculated as shown below:

$$\varepsilon = \frac{0.4732}{1 \text{ cm} \times 0.00122649 \text{ mol/L}}$$

$$\varepsilon = 385.83 \text{ L/mol}$$

The measured weight, absorbance at each wavelength, and calculated absorptivity at each wavelength for the reference standard and test sample are shown in Table 1.

The percent difference between the absorptivities of the sample and standard at both 264 nm and 273 nm were calculated using the following formula where the Average ε is the average of the Test ε and Standard ε at each respective wavelength:

$$\text{Percent Difference} = \frac{\text{Sample } \varepsilon - \text{Standard } \varepsilon}{\text{Average } \varepsilon} \times 100$$

Using this formula, we obtain a percent difference between the Standard and Sample of 1.9% for the 264 nm absorptivity and 1.4% for the 273 nm absorptivity. The USP test requires the difference between the respective absorptivities at 264 nm and 273 nm to be less than or equal to 3.0%. Since the test sample has a percent difference of less than 3.0% at both wavelengths, it meets the identification requirement in the ibuprofen USP monograph.

Conclusion

Spectrophotometers are utilized in hundreds of pharmaceutical monographs which make them essential instrumentation for confirming the identity of drug ingredients and drug products. The Thermo Scientific Evolution Series Spectrophotometers are ideal for performing these tests due to their versatility, ease of use, and superior performance. In this document both the USP and EP identification tests for each respective ibuprofen monograph was completed with an Evolution Pro Spectrophotometer. The identity of an ibuprofen test sample was confirmed according to the USP requirements when compared to a standard ibuprofen sample. The identity of an ibuprofen test sample was also confirmed according to the EP requirements through visual inspection and by comparing absorbance ratios.

References

1. United States Pharmacopeia and National Formulary (USP 43-NF 38), Monographs, Ibuprofen

2. European Pharmacopeia (EP 9.6), Monographs, Ibuprofen

Ordering information

Product	Part number
Evolution One UV-Vis Spectrophotometer	840-341400
Evolution One Plus UV-Vis Spectrophotometer	840-341500
Evolution Pro UV-Vis Spectrophotometer	840-340200

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