Gravimetric and Spectrophotometric Determinations of Curcuminoid Solubilities in Ethanol

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Abstract

Curcumin, a natural extract of turmeric, has many purported health benefits, but a part of its limited broader applicability is frequently attributed to its poor solubility in water. This lack of solubility is one of the primary drives for the exploration and synthesis of new analogues, seeking more greater aqueous solubility. Bioactivity assays frequently make use of ethanol solutions of these curcuminoids, followed by subsequent dilution in water. We have explored the solubility of an array of curcuminoids in ethanol to ascertain substituent effects on this property. Additionally, a few curcuminoids containing a saturated ring in their backbone have tested to determine its impact on solubility. Both gravimetric and spectrophotometric means have been utilized to measure solubility. Beer's Law plots of all local maxima in the UV-vis spectra of each curcuminoid have been produced to track linearity of the Absorbance-concentration relationship at each wavelength and correlation of each with gravimetrically determined solubilities.

Introduction

Curcumin and its related curcuminoids have been limited in the past for things such as biological uses partially due to a lack of solubility in things other than DMSO or other organohalides. By performing solubility determinations in ethanol, we have been able to find saturation points, and absorbance through the use of UV-vis. After collecting spectra, calculations were used to determine the relationship between concentration and absorbance for each substance. The calculated concentration was then compared to the concentration using the UV-vis method.

Sample Preparation Methods

Gravimetric

Three sample solutions were prepared by combining 5-10 mg of curcuminoid with 5 mL ethanol in a small vial. Sample vials were placed in a water bath maintained at 25ºC for at least 24 hours, then 5-10 mg equivalents were added as needed until the solutions reached their maximum solubility and solids were visible at the bottom. All solutions were then filtered out on glass filter frits by way of vacuum filtration. The weights of the solids were then determined by weighing by differences to determine the exact amounts of solids not dissolved in the solutions.

Spectrophotometric

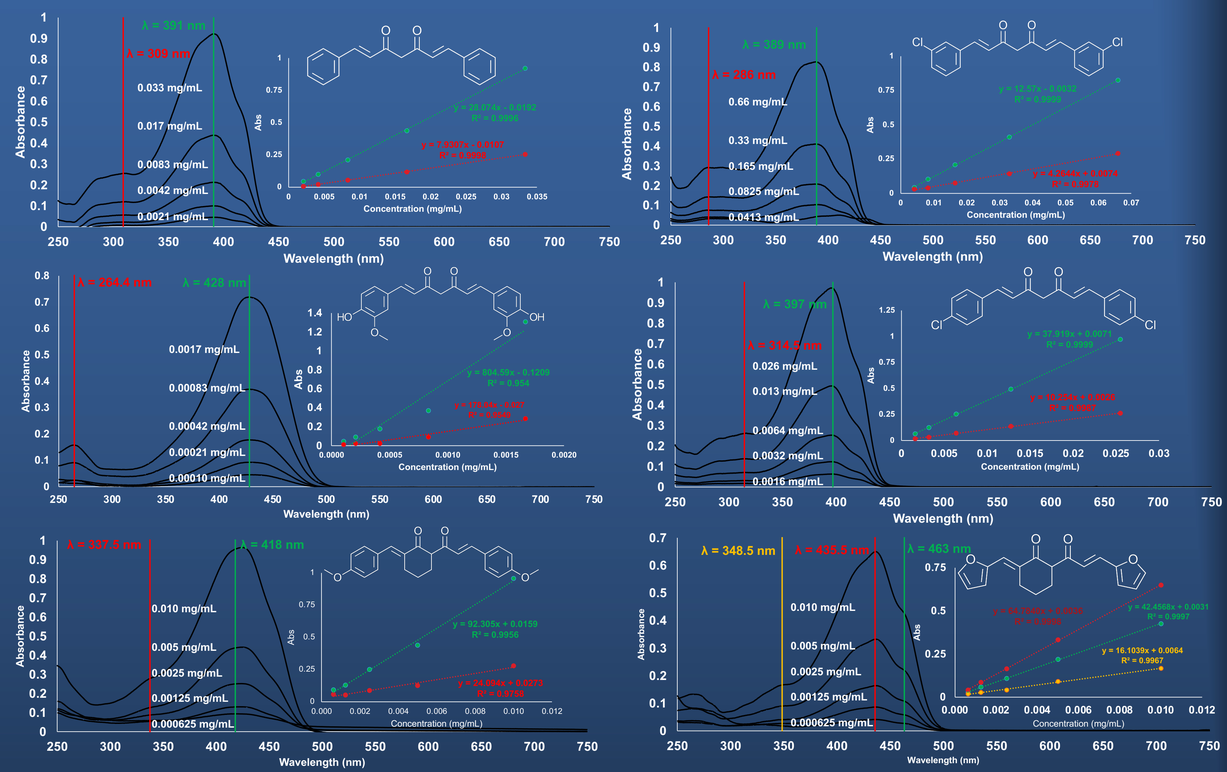
A stock solution of each analyte was prepared by combining approximately 3-5 mg of curcuminoid with 50 mL ethanol in a volumetric flask. UV-Vis spectroscopy was used to determine the absorbances of these solutions. All solutions were subjected to separate dilutions in order to reach an absorbance value under 1.

After reaching an absorbance value under 1, all solutions then underwent four more 1:1 dilutions and UV-Vis runs, for a total of 5 separate concentrations. The information obtained from these were later used to construct a calibration curve.

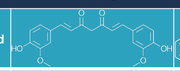
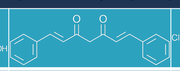
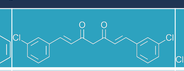
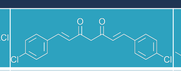
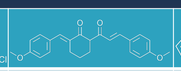
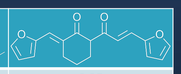
The UV-Vis spectra were all run under the same conditions, between 250-750 nm, at 0.1 nm increments, with the temperature held at a consistent 25.0ºC ± 0. 5ºC. Quartz cuvettes with 0.5 cm pathlengths were used for all sample runs.

All saturated solutions prepared under the gravimetric method were also subjected to UV-Vis analysis under the same conditions. The saturated solutions were all diluted until they were in the same absorbance range as the calibration curve.

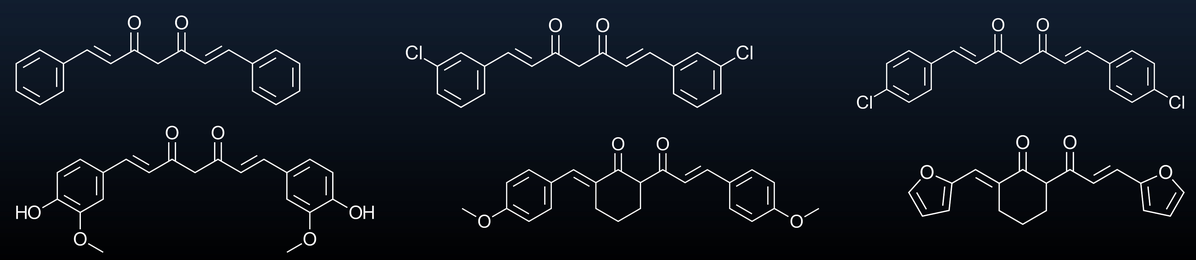
Results



Both spectroscopic and gravimetric approaches present distinct sources of error. While both approaches appear to provide reproducible results, their alignment is not perfect. Nonetheless, it is clear that with specific changes in peripheral substituents as well as changes in the central linker group, curcumin's touted low solubility is not unique and will require very specific structural modifications to improve upon this property.

Curcuminoid						
UV-vis	3.03	0.57	2.41	1.65	0.80	0.95
Gravimetric	2.98	0.61	1.77	1.00	0.74	1.03
% Difference	2.0	5.8	30.6	65.0	8.0	8.0

Analyte Structures



Conclusions

Compared to calculated concentrations, the UV-vis method shows promise in determining the solubility of curcuminoids in ethanol. This route is far more expedient compared to the gravimetric approach. Full analysis of various spectral peaks indicates that neither peaks nor shoulders should be ruled out as potential standardization wavelengths. Expansion of these analyses to other curcuminoids, and in other solvents, will be sought after by our research group.

Acknowledgements

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