Rapid Calibration Free, Semi-Quantitative Analysis of Defined Drug Formulations Using FTIR Pre-computed Mixture Spectra

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Purpose: Rapid screening of commercial and illicit drug mixtures.

Introduction

The **FDM ATR Drug Kit** is a spectral library designed to rapidly screen bulk drug mixtures. ATR/FTIR spectra of neat active pharmaceutical ingredients and common binders, coatings, etc. were selected and digitally combined to render mixture spectra. ATR has become the primary sampling technique for FTIR because of the ease of sample preparation. Using the library avoids (a) the time and expense of planning, preparing and running multicomponent standards and (b) time consuming and computationally intensive multi-component searches. Searching the library provides rapid and effective screening of commonly encountered bulk drug mixtures, and gives relative concentrations, prior to further analysis. No quantitative calibrations are required. The reported percentages are estimates of relative concentration.

Experimental

Most spectra were run on a PIKE GladiATR with a monolithic diamond ATR crystal. The Cocaine spectrum was run on a GoldenGate ATR. No baseline correction was performed. Optical resolution was 4 cm^{-1}. Caplets were powdered in an inexpensive plastic pill crusher and placed on the ATR with no additional preparation.

Search Method

The full range of the sample spectra were searched against the library. The search algorithms were correlation coefficient or first derivative correlation coefficient.

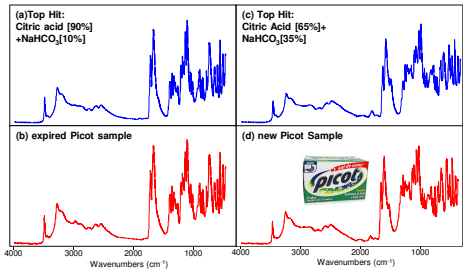
Picot Experiment

A Picot antacid packet contained 5.01 grams of powder. The label indicated 1.948g Citric acid and 2.485g of NaHCO3 or 49.6% and 38.9% relative concentration, respectively. ATR/FTIR spectra were obtained from samples from two packets in February, 2016. The expiration dates were August, 2014 and July, 2017.

Picot Discussion: Expired Product Decomposition

Searching the ATR/FTIR spectrum of the expired Picot sample showed estimated relative concentrations of 90% Citric acid and 10% $NaHCO_3$, meaning very little $NaHCO_3$ was detected. Searching the spectrum from the new sample showed estimated relative concentrations of 65% Citric acid and 35% $NaHCO_3$, which was less than the label indicated but presumably still met product specifications. Searching the library with the two samples clearly shows one sample has far less $NaHCO_3$. See Figure 1. This has applications for validating the expiration dates of pharmaceutical formulations.

FIGURE 1: Picot Antacid powder. (a) and (c) (blue) are library spectra. (b) is the expired sample and (d) is the new sample.



expired Picot Results	
Score	Name
0.9967	Citric acid [90%] + $NaHCO_3$ [10%]
0.9949	Citric acid [85%] + $NaHCO_3$ [15%]
0.9894	Citric acid [80%] + $NaHCO_3$ [20%]
0.9799	Citric acid [75%] + $NaHCO_3$ [25%]
0.9666	Citric acid [70%] + $NaHCO_3$ [30%]
0.9494	Citric acid [65%] + $NaHCO_3$ [35%]

new Picot Results	
Score	Name
0.9559	Citric acid [65%] + $NaHCO_3$ [35%]
0.9555	Citric acid [70%] + $NaHCO_3$ [30%]
0.9514	Citric acid [75%] + $NaHCO_3$ [25%]
0.9512	Citric acid [60%] + $NaHCO_3$ [40%]
0.9448	Citric acid [80%] + $NaHCO_3$ [20%]
0.9397	Citric acid [55%] + $NaHCO_3$ [45%]

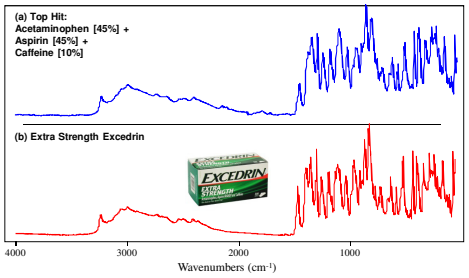
Excedrin Experiment

An Extra Strength Excedrin tablet was 0.73 grams. The label indicated 250 mg Acetaminophen, 250 mg Aspirin and 65 mg Caffeine plus various inactive ingredients. An ATR/FTIR spectrum was collected and searched against the library.

Excedrin Discussion

Searching the ATR/FTIR spectrum readily confirmed the nature of the sample is consistent with the label. Furthermore, results showed good agreement within 12% relative concentration for Acetaminophen and Aspirin and within 2% for Caffeine. Searching identified the mixture components even when one, Caffeine, was less than 10% of the sample mass. Inactive ingredients are 175 mg (24.0% of the total). When the relative concentrations of the active ingredients are calculated the search results are excellent.

FIGURE 2: Extra Strength Excedrin tablet: (a)(blue) is the library spectrum and (b)(red) is the sample spectrum.



Excedrin Results	
Score	Name
0.8785	Acetaminophen [45%] + Aspirin [45%] + Caffeine [10%]
0.8761	Acetaminophen [50%] + Aspirin [50%]
0.8741	Acetaminophen [40%] + Aspirin [50%] + Caffeine [10%]
0.8734	Acetaminophen [40%] + Aspirin [45%] + Caffeine [15%]
0.8732	Acetaminophen [50%] + Aspirin [40%] + Caffeine [10%]
0.8725	Acetaminophen [55%] + Aspirin [45%]
0.8724	Acetaminophen [45%] + Aspirin [40%] + Caffeine [15%]

Table 1: Excedrin Results

Active ingredient	% Total based on Label	% Relative Active Ing.	% Best Search Result
Aspirin	34.2	44.2	45
Acetaminophen	34.2	44.2	45
Caffeine	8.9	11.5	10

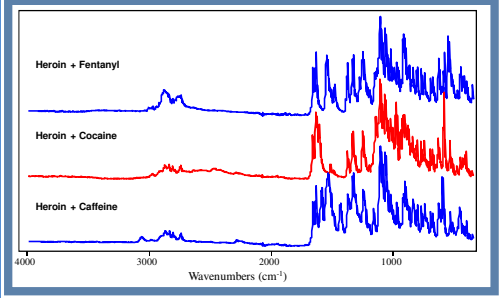
Discussion

(1) The Excedrin scores are lower than the Picot scores because the inactive ingredients are not modelled in the library spectra.

(2) The fact that good results were obtained, even with 24% of the sample unidentified (and not modelled), strongly suggests the library has broad utility screening in bulk drug mixtures. The drugs could be on DEA Schedule I, active pharmaceutical ingredients, binders, diluents, excipients and so on.

(3) In Figure 3, modelled spectra of three common street mixtures from the library are readily distinguishable from each other. Thus, we expect the library can readily screen such mixtures.

FIGURE 3: Modelled spectra in the FDM ATR Drug Kit



Conclusions

Searching the **FDM ATR Drug Kit** is shown to be effective for screening two bulk mixtures containing drugs. Such screening can help any analyst decrease total analysis time by rapidly providing estimates of relative concentration prior to using other analytical methods. The library is expected to be useful in screening bulk mixtures of many controlled and uncontrolled substances on any device that can produce an ATR/FTIR spectrum.

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