DETECHIP®: Developing a Molecular Sensing Device

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ABSTRACT

Detechip® is a detection system made of various sensors that has been shown to detect and discriminate between small molecules of interest, including various illicit drugs for and over-the-counter medications, explosives, pesticides and food spoilage metabolites. Detechip® employs an array of sensors from which an analyte is tested and based on changes in color; a code specific to the analyte is developed. Detechip® offers possibilities for a simple, sensitive, selective, and affordable alternative to costly immunoassays. Results from NMR, UV-VIS and fluorimetry studies suggest that the color and fluorescence changes are a result of intermolecular interaction between the analytes and sensors ranging from non-covalent covalent bonding of supramolecular structure to proton exchange between the analyte and sensor molecules. Current efforts are focused on miniaturization of Detechip® to the micro and nanoscale.

Keywords: Detechip®, Sensor, drug detection, colorimetric array, RGB Code

1. INTRODUCTION

Detechip®, short for detection chip, is a developing technology consisting of molecular sensors that can be used to identify analytes by colorimetric changes due to differential interactions with analytes [1]. A quick, sensitive, and selective detection system is required for many applications, such as alerting security officers to the presence of explosives or their precursors, pre-incident monitoring/screening for homeland security purposes such as weapons of mass destruction, and detection and quantification of doping compounds in competitive sports [2]. The most common methods currently used require skilled operators and cannot be miniaturized, e.g. gas chromatography-mass spectrometry (GC-MS) [3], ion trap mobility spectrometry, wet colorimetric assays, spot tests such as Marquis, Scott Drug Testing Company drug tests (www.scottcompany.com), or the b-Glucuronidase Drug Analysis Bundle (Sigma-Aldrich) and Magnotech technology testing [4].

Detechip® employs an array of sensors, a sample of four is shown in **Figure 1**, which rely on color and fluorescence changes due to analyte-sensor interactions. Unlike other color tests which provide a single "yes" or "no" response, Detechip® gives multiple simultaneous responses in the form of color and fluorescent changes using two different buffers at pH =7, allowing users to quickly identify suspect materials, **Figure 2**.

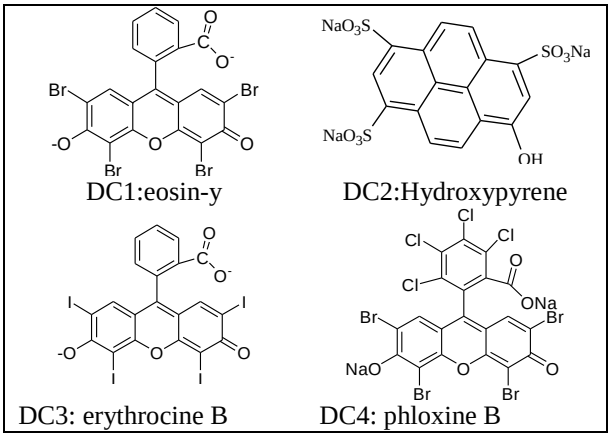

Figure 1: Structures and names for some Detechip® sensors

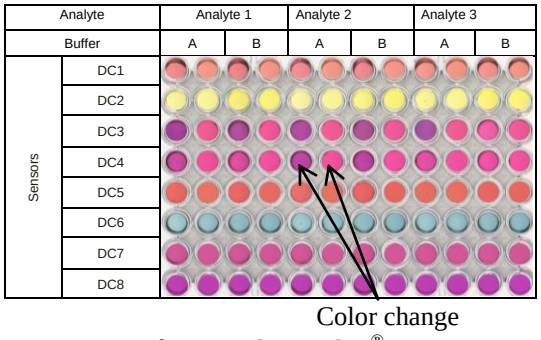

Figure 2: Set-up of a typical Detechip® assay in a 96-well plate showing presence or absence of color changes of the sensors in presence of analytes.

A library of Detechip® codes has been established for over 100 illicit, over-the-counter (OTC) and prescription drugs. **Table 1** shows a sample of the codes.

Table 1: Detechip® codes for selected drugs

Drug	DETECHIP Code
Caffeine	11111111110000111100110011000011
Cocaine	11111111110000111100110011000011
Ibuprofen	00000000000000000000110011001111

Our studies using NMR methods, UV-Visual and fluorescence spectroscopies [5,6], show that the color changes result from a range of intermolecular interaction between Detechip® sensors and analytes from non-covalent.

2. RESULTS AND DISCUSSION

^{1}H-NMR spectra with peaks assigned for sensor, DC-1 **Figure 3** and analyte, caffeine in **Figure 4**. A spectrum for the mixture of caffeine and DC-1 is shown overlaid along those of the pure components is shown in **Figure 5**. A pentet-like peak is observed at 7.7ppm for the mixture that resembles one observed for DC-1 at pH=4. This along with the slight down-field shift for the DC-1 peaks in the aromatic region, are characteristic of protonated DC-1. Caffeine peaks in the mixture spectrum show an up-field shift, suggesting de-protonated caffeineas seen in **Figure 6**. This was confirmed by COSY and DOSY-NMR spectra (not shown) which showed the presence of a two-component solution. A proposed mechanism for the proton abstraction from caffeine to DC-1 is given in **figure 7**.

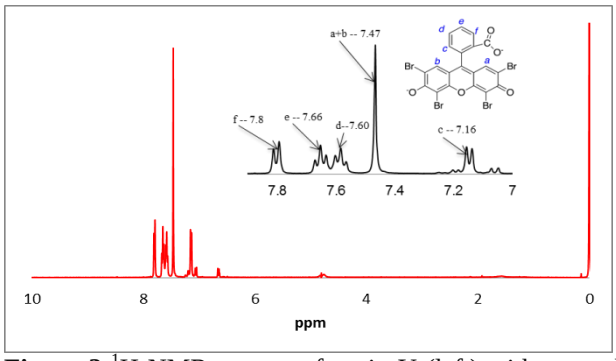

Figure 3: ^{1}H-NMR spectra of eosin-Y (left) with expanded aromatic region (inset) showing peak assignments

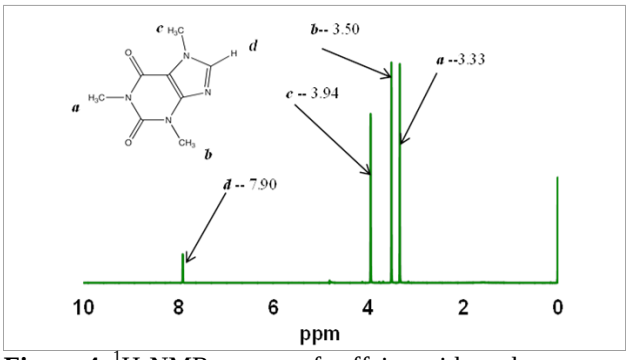

Figure 4: ^{1}H-NMR spectra of caffeine with peak assignment.

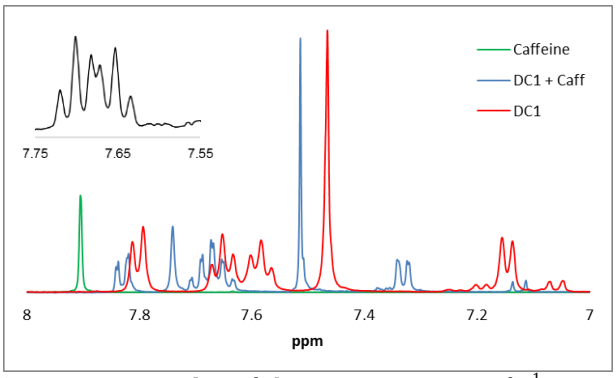

Figure 5: An overlay of the aromatic region of ^{1}H-NMR spectra of caffeine, DC-1, and a mixture of caffeine and DC-1. Inset is an NMR spectrum of DC-1 at pH=4 showing a pentet-like peak at 7.7 ppm that is similar to one observed in the caffeine-DC-1 mixture at ~7.7ppm**.**

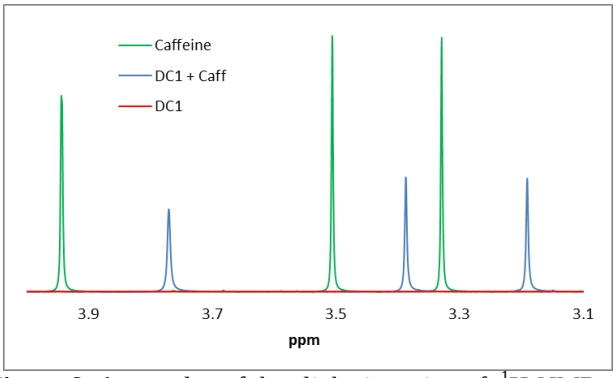

Figure 6: An overlay of the aliphatic region of ^{1}H-NMR spectra of caffeine, DC-1, and a mixture of caffeine and DC-1.

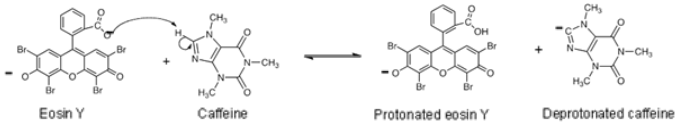

Figure 7: Proposed Mechanism for proton transfer from caffeine to eosin Y

Fluorescence and NMR studies on DC-2 and caffeine suggest the formation of π-stacks. **Figure 8** shows a sequential quenching of fluorescence as caffeine concentration increases at a constant DC-2 concentration. This compares well with the quenching of fluorescence observed in increasing concentrations of DC-2 at higher molarities (2M and above) attributed to π-stacking due to a flate molecule consisting of a conjugated system of π-bonds.

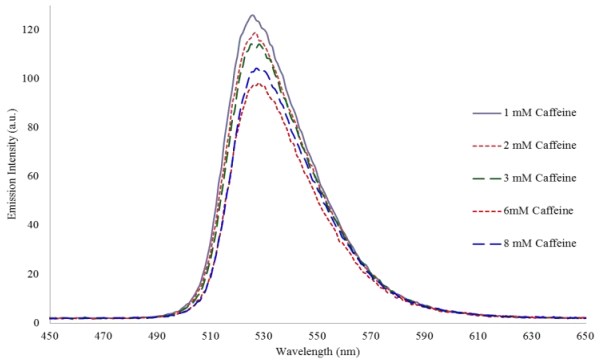

Figure 8: Fluorescence spectra showing caffeine concentration dependent fluorescence of 8mM DC-2at λ_{ex}=330 nm.

Figure 9: Micro-Detechip® Device

Figure 10: A cartridge for the Micro-Detechip device. The little white square on the cartridges contains the nano-size membrane on which the sensor arrays are printed

3. CONCLUSION

Detechip® is based on fluorescence and color changes from which a unique identification has been developed for many drugs. The results in this study have shown that some of the color and fluorescence changes observed in Detechip® assays may be a consequence of a proton transfer reaction between the sensors and the analyte molecules. Further detailed studies are in progress for the interaction between other Detechip® sensors and other analyte. Detechip® has been developed into a miniature toaster-size reader (**Figure 9**) that uses microchips with the sensor-arrays printed on a nano-size membrane as shown in **Figure 10**[7-9]. Studies are in progress to expand the Detechip® library of codes to include steroids and hormones. The ultimate goal is to develop a hand-held device the size of a cellphone that can be used by anybody to test for drugs.

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