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](image1)

![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](image2)

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>DETECHIP Code</th>
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<tbody>
<tr>
<td>Caffeine</td>
<td>11111111111111000011110011001100011</td>
</tr>
<tr>
<td>Cocaine</td>
<td>11111111111111000111011001100011</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>0000000000000000000000110011001111</td>
</tr>
</tbody>
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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 7.7 ppm 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 caffeine as 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 ~7.7 ppm.

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 flat molecule consisting of a conjugated system of π-bonds.

**Figure 8:** Fluorescence spectra showing caffeine concentration dependent fluorescence of 8mM DC-2 at λ<sub>ex</sub>=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.

REFERENCES