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The Dynamic Shift to Green Chemistry: Investigating the Spectral Behavior of Natural Deep Eutectic Solvents (NADES) and their Performance as MALDI-TOF Matrices

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Introduction

Recently, natural deep eutectic solvents (NADES), the combination of two or more solid compounds to produce a stable liquid through hydrogen bonding, have emerged as a green alternative to toxic and dangerous solvents such as methanol and ethanol. Notably, one of the most frequently used analytical instruments in chemistry is Matrix Assisted Laser Desorption Ionization - Time of Flight (MALDI-TOF), which requires the use of a solvent matrix, often one that is volatile and expensive, to analyze a sample of interest. However, the crystallization and heterogeneity of 4-Chloro-α-cyanocinnamic acid (CHCA) spots, the gold standard of MALDI matrices, on the MALDI plate inhibits its long-term use as an effective matrix. A desirable matrix produces a homogeneous spot and exhibits high sensitivity, low vapor pressure, optimal spectral absorbance, making the development of new liquid matrices a complex task. Because NADES exhibits the qualities listed above, we attempted to utilize NADES as an alternative MALDI matrix by investigating its spectral behavior and performance with small analytes.

NADES Fabrication & Experimental

We created several different NADES formulations by heating and stirring solid compounds in a vial to create a stable liquid. We then diluted the NADES with 50:50 acetonitrile and water solution to improve viscosity for use in the spectrophotometer and MALDI. Next, we investigated the absorbance shift of the NADES using a spectrophotometer to confirm their absorption at 337 nm, matching the absorption of the laser in the MALDI. Once confirmed, we spotted our NADES on the matrix plate with a selection of different analytes using various spotting techniques and evaluated the performance of the NADES using the mass to charge output provided by the MALDI.

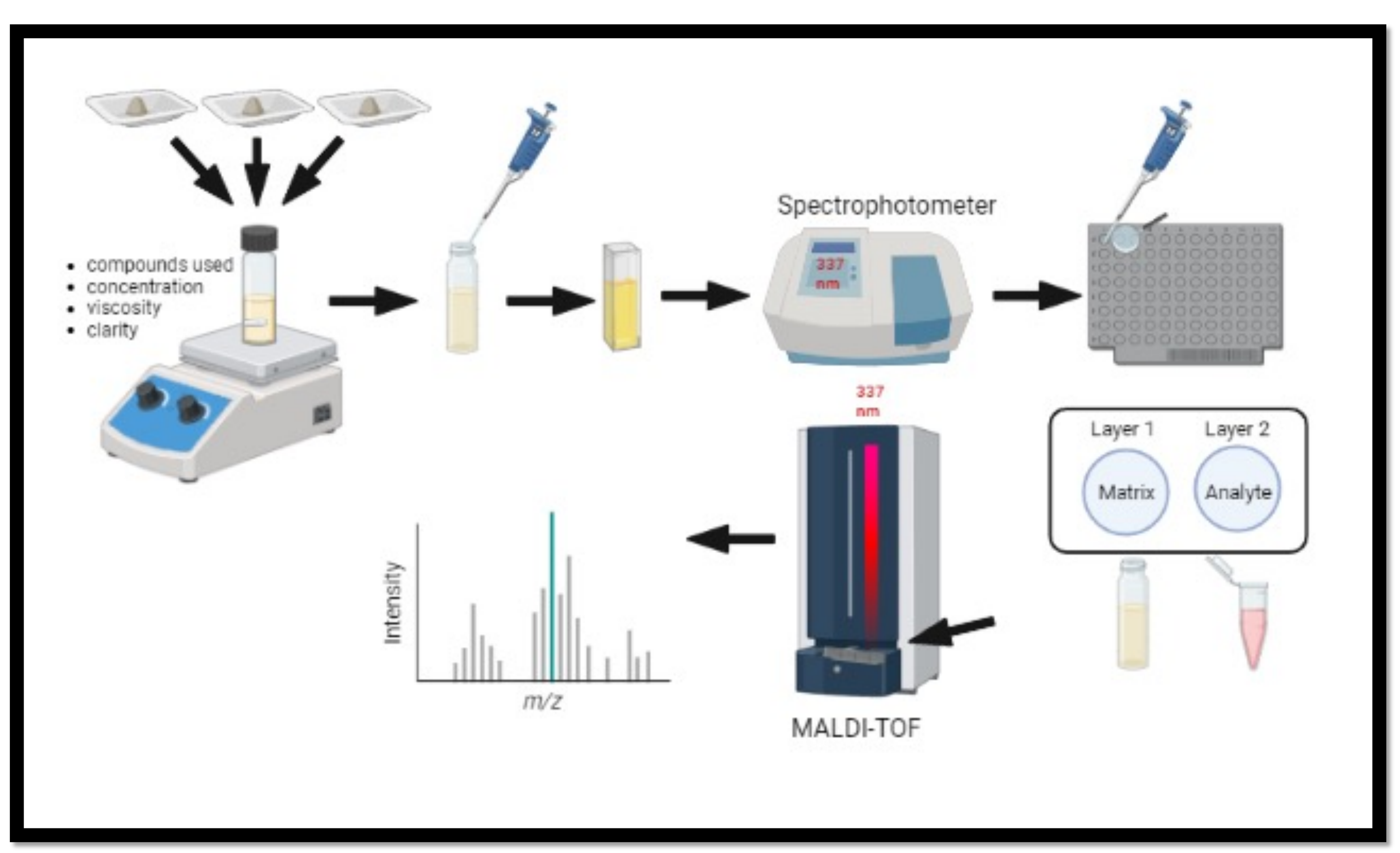

Figure 1: Schematic representation of NADES experimentation

Results

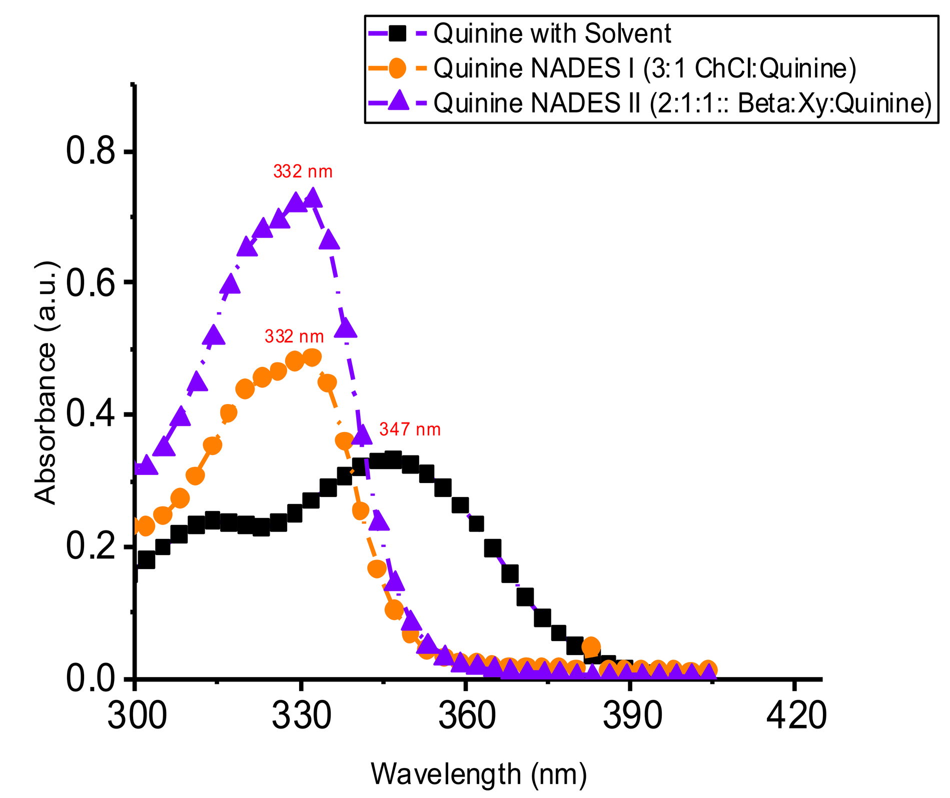

Figure 2. Comparing UV-VIS absorbance spectrum of quinine and solvent with 2 NADES formulations containing quinine NADES I --- 3:1:: Choline Chloride: Quinine NADES II--- 2:1:1:::Betaine:Xylitol:Quinine

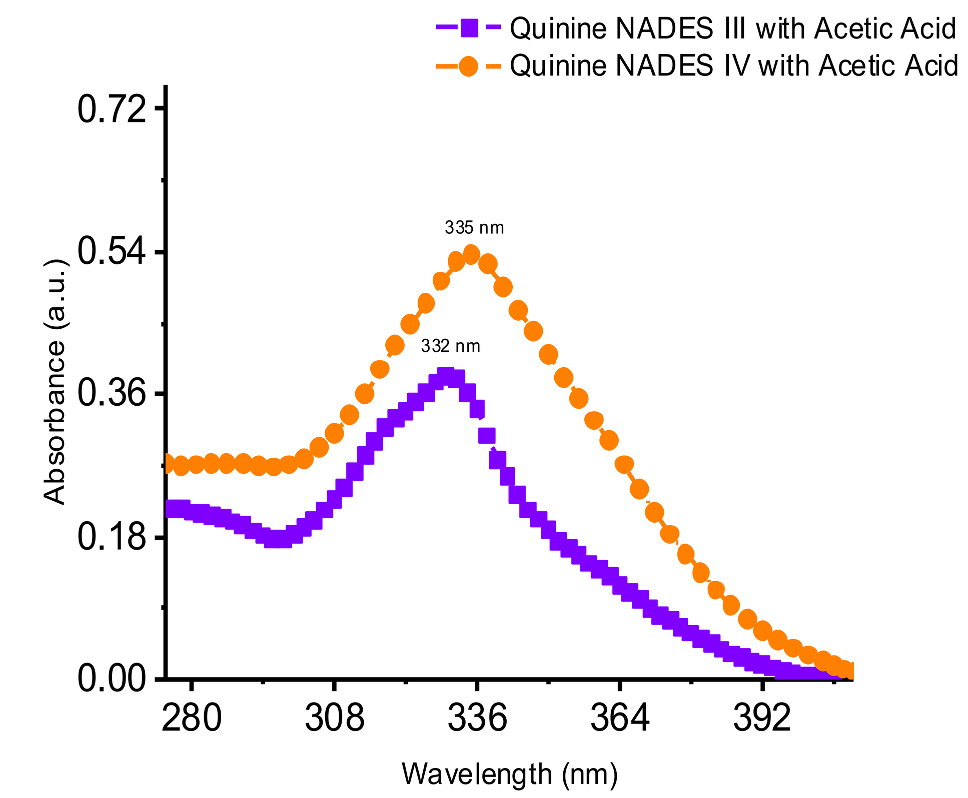

Figure 3. UV-VIS absorbance spectrum of 2 NADES formulations containing quinine NADES II --- 2:3:1:::Betaine:Xylitol:Quinine with Acetic Acid NADES IV --- 4:4:1::: Choline L-bitartrate:Xylitol:Quinine with Acetic Acid

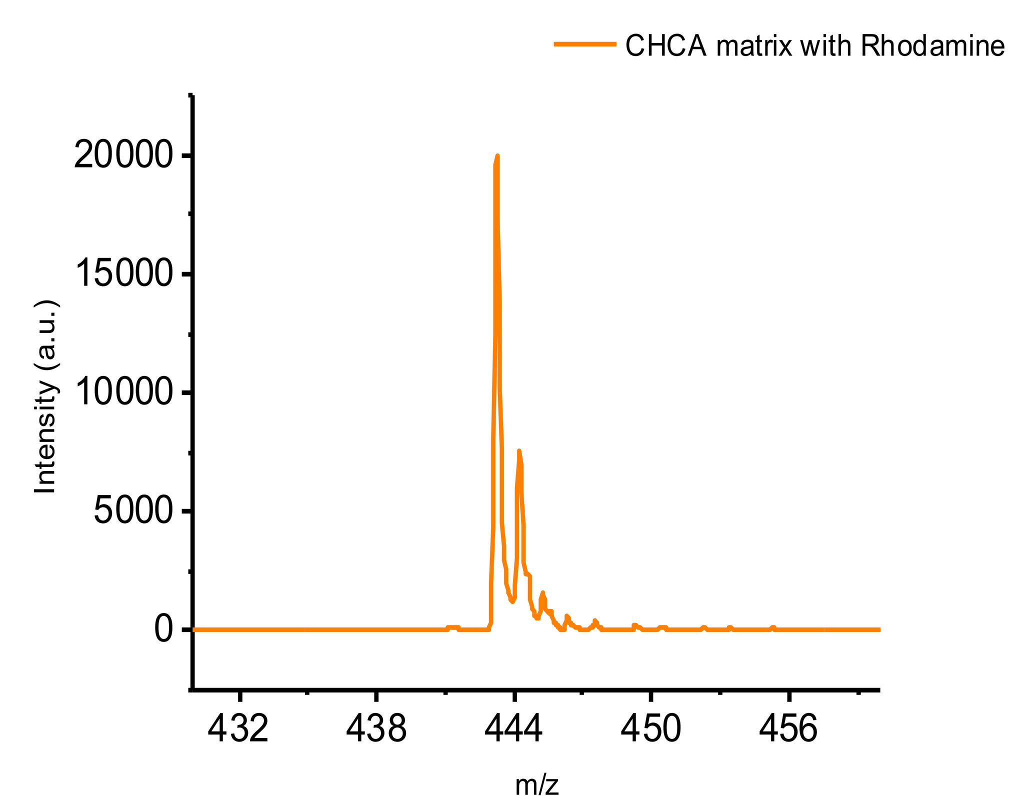

Figure 4. MALDI mass spectrum of rhodamine using CHCA matrix

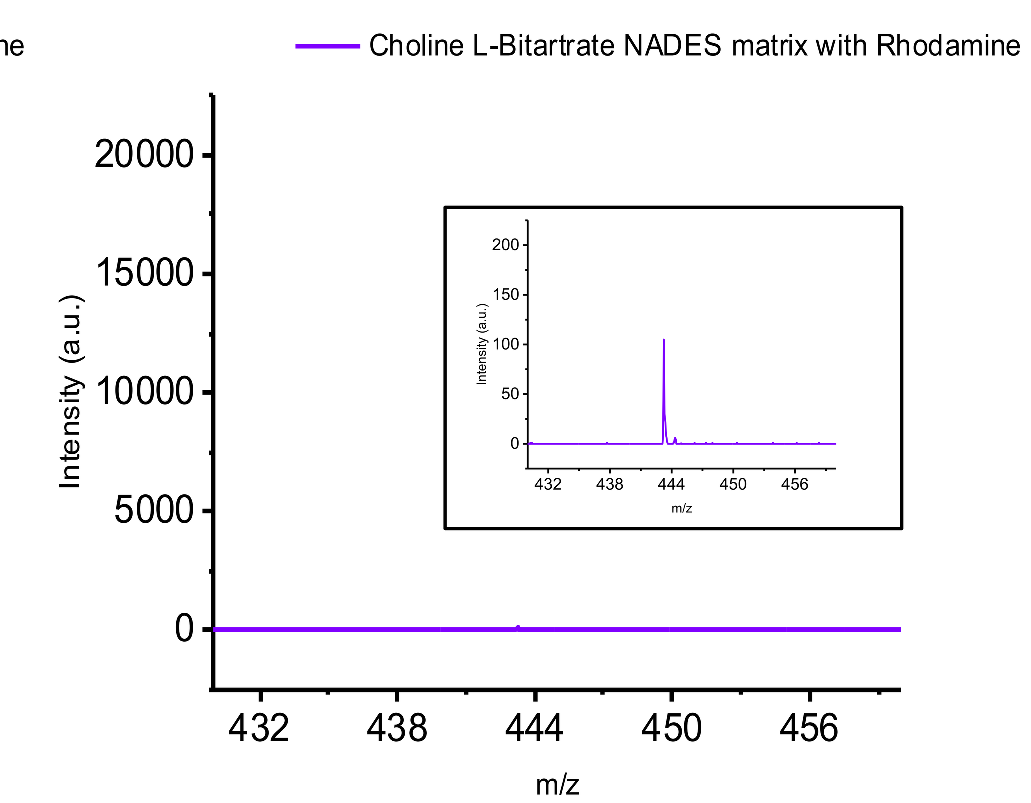

Figure 5. MALDI mass spectrum of rhodamine using NADES IV matrix

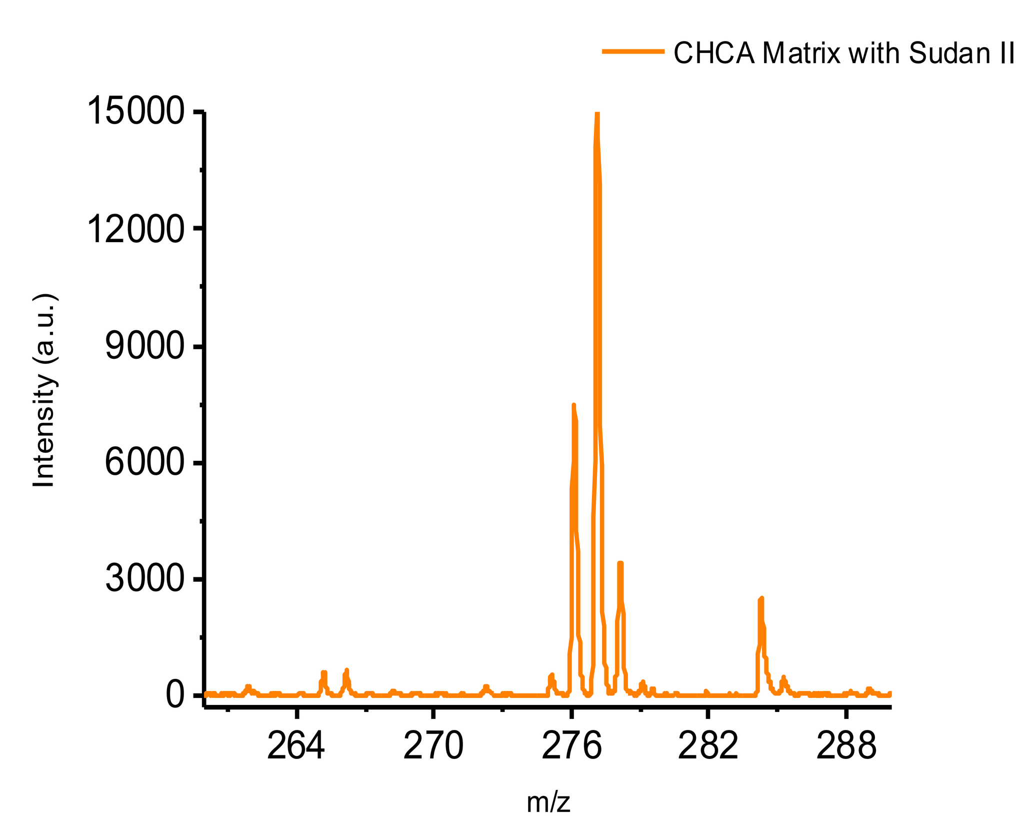

Figure 6. MALDI mass spectrum of sudan dye II using CHCA matrix

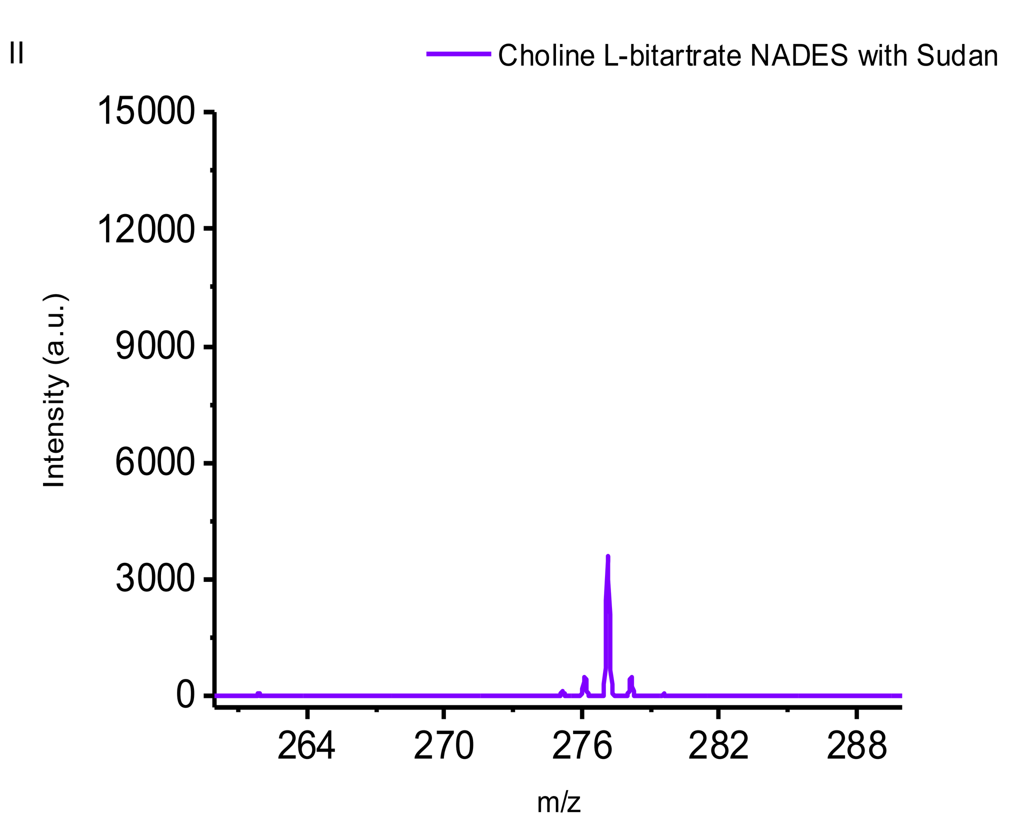

Figure 7. MALDI mass spectrum of sudan dye II using NADES IV matrix

Conclusions

From our spectral dynamics investigation, NADES containing quinine consistently shifted approximately 15 nm to the left, confirming a desired peak range around 337 nm. While our spectral shift data indicated that our NADES formulations should be compatible as a MALDI matrix, we only obtained an analyte signal a minimal number of times using a MALDI matrix. The data presented represents the few instances where the matrix was successful, in which the intensity of the analyte signal from the MALDI matrix was substantially lower than the analyte signal obtained from the standard CHCA matrix. Overall, while the spectral shift of the NADES indicated promise for use in the MALDI, there seems to be other variables within the NADES preventing its use as a successful MALDI matrix. While NADES matrices hold future potential, CHCA still remains the most consistently effective matrix for the detection of small analytes in MALDI-TOF.

Future Work

Going forward, it is important to gain a greater understanding of the variables at play within NADES, including viscosity and hydrogen bonding network, in order to better understand the unpredictable performance of NADES within the MALDI. Additionally, we believe that the power of the laser within the MALDI at Clemson may not be strong enough for this investigation. Therefore, we would like to perform this same project on a MALDI-TOF with a stronger laser in order to confirm our hypothesis or eliminate laser power as a possible limiting variable.

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