

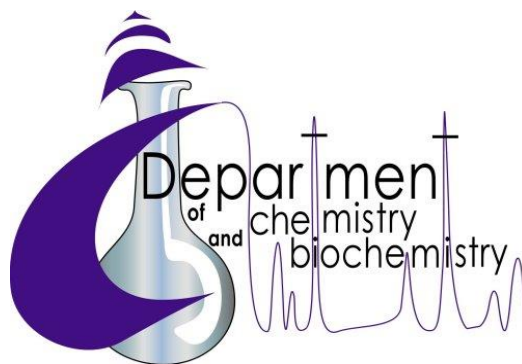
4-21-2015

## Department of Chemistry and Biochemistry Seminar

Michelle Schmidt



Department of Chemistry & Biochemistry



19<sup>th</sup> Annual Petersheim Academic Exposition



Tuesday April 21, 2015

5:30-9:00 PM

Science and Technology Center

Seton Hall University

South Orange NJ 07079

**Department of Chemistry and Biochemistry Seminar**

**5:45 – 7:00 PM**

**The Helen Lerner Amphitheater, SC101**

**McNulty Hall Science Complex**

**Michelle Schmidt**

**Ph.D. Seminar**

**Mentor: Dr. Nicholas Snow**

**QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) Extraction with Gas  
Chromatography for Drug Analysis**

## **Student Poster Presentations**

**7:00 – 9:00 PM**

**McNulty Atrium**

### **List of Faculty Mentors**

<b><u>Mentor</u></b>	<b><u>Page</u></b>
Dr. Cosimo Antonacci (Biochemistry)	4
Fr. Gerald Buonopane (Food Chemistry)	5
Professor Alexander Fadeev (Surface Chemistry)	9
Professor Sergiu Gorun (Materials Chemistry)	12
Professor Yuri Kazakevich (Separations Chemistry)	14
Professor Stephen Kelty (Computational Chemistry)	17
Professor Joseph Maloy (Analytical Chemistry)	20
Professor Cecilia Marzabadi (Carbohydrate Chemistry)	21
Professor Wyatt Murphy (Inorganic Chemistry)	25
Professor Monika Raj (Bio-organic Chemistry)	33
Professor David Sabatino (Chemical Biology)	37
Professor Nicholas Snow (Analytical Chemistry)	39

# **DEVELOPING A MAMMALIAN CELL PROMOTER ASSAY TO TEST FOR CRITICAL STRUCTURAL ELEMENTS REQUIRED FOR PROTEIN OVEREXPRESSION IN ACUTE LYMPHOBLASTIC LEUKEMIA**

Taryn Heiser and Dr. Cosimo Antonacci

*Department of Chemistry and Biochemistry, Seton Hall University South Orange, NJ*

Acute Lymphoblastic Leukemia (ALL) is a type of cancer that is most prevalent in children. It is a disease that progresses rapidly and results in the overpopulation of abnormal white blood cells in the bloodstream. Protein overexpression may be linked to the development of this cancer. In particular, one protein of interest has been recognized to be overexpressed possibly driven by unique DNA sequences. These sequences adopt structures that have been implicated in a variety of oncogenic promoter regions. The long-term goal of this research project is to develop therapeutics for the treatment of this cancer, which are aimed to target these DNA structures. To achieve this goal, a reporter plasmid has been created. We report here the progress towards the implementation of this unique promoter assay.

# EXAMINATION OF THE ANTIOXIDANT PROPERTIES OF ESSENTIAL OILS

Scott McAfee and Fr. Gerald Buonopane

*Department of Chemistry and Biochemistry, Seton Hall University South Orange, NJ*

The synthetic antioxidants BHT and BHA are used in the food industry to prevent or slow down lipid oxidation in a given food system. These have both been found to be minor carcinogens, so finding a safer and preferably more natural antioxidant that still has the same strength as its synthetic counterparts is important. Essential oils could be the solution to this issue because certain oils have noted antioxidant properties that could theoretically be used to replace BHT and BHA. The idea of this research is to test the antioxidant capabilities of various essential oils and other additives against BHT and BHA. The oils being tested include Clove Bud, Clove Leaf, Eugenol, Geranium, and Geraniol. Vitamin E is the only other additive being tested.

The first step in testing the antioxidant properties is running a DPPH assay. This entails recording the fluorescence spectrum of dilutions of the oils in ethanol with 1ml of 0.3mM DPPH added. The dilutions used are 300, 150, 50, 15, 10, and 5 ug/mL in ethanol to a volume of 2.5 mL, a blank containing 2.5mL of ethanol is also included. Using the spectrum percent inhibition (assessment of free radical scavenging activity) can be calculated showing the antioxidant properties and allowing for easy comparisons.

My research is focused on Vitamin E and I am in the process of completing the DPPH assay. The next step is a model food system that will be evaluated using the TBARS assay (thiobarbituric acid reactive species). Each model system will be set up the same way with the different antioxidants. My model system will include a source of lipids (ex. Linoleic acid), Vitamin E (the antioxidant), and a pro-oxidant (ex. Lipoxygenase). These systems will be stored in an incubation oven at constant conditions and checked once a day for a yet to be determined time period. Ideally the results of the DPPH assay and the model food systems will provide a suitable natural antioxidant that could be used in the food industry.

1. Riccardo Amorati, Mario C. Foti, and Luca Valgimigli *Journal of Agricultural and Food Chemistry* 2013 61 (46), 10835-10847.
2. Leopold Jirovetz, Gerhard Buchbauer, Ivanka Stoilova, Albena Stoyanova, Albert Krastanov and Erich Schmidt *Journal of Agricultural and Food Chemistry* 2006 54 (17), 6303-6307.
3. Seema Farhath, M. S.; Vijaya, P. P.; Mumtaj, P.; Vimal, M. *Journal of Chemical & Pharmaceutical Research*; 2013, Vol. 5 Issue 9, p219.

## THE ANTIOXIDATIVE PROPERTIES OF ESSENTIAL OILS

Adam Kmeck and Fr. Gerald Buonopane

*Department of Chemistry and Biochemistry, Seton Hall University South Orange NJ*

Research was performed with Fr. Buonopane on the antioxidative properties of essential oils. The oils from certain plants, clove in the case of this research, produce antioxidants, which can prevent oxidation in food. A DPPH assay was performed with varying concentrations of clove leaf oil and clove bud oil. According to analysis, the essential oils do present antioxidative properties as the absorbance values at 518 nm vary as the concentration of oil changes. Some of the data from the spectrophotometer did not transfer. Because of this, a definitive conclusion cannot be proclaimed. More trials need to be performed before definitive conclusions can be states. With the newly acquired data, the equation

$$\text{Antioxidant Activity \%} = \left| \frac{Abs_{sample} - Abs_{blank}}{Abs_{blank}} \right| \times 100\% .^1$$
 Then, the oils, including mine, that produced satisfactory results will continue in research, but will take place on a linoleic acid model. This is used to simulate lipid oxidation in the human body and will provide results on whether these essential oils have antioxidative properties that could be useful.

- 1) Mensor, L.; Menezes, F.; Leitao, G.; Reis, A.; Dos Santos, T.; Coube, C.; Leitao, S. Screening of Brazillian Plant Extracts for Antioxidant Activity by the Use of DPPH Free Radical Method. *Phytother. Res.* **2001**, 15, 127-130.

## ANTI-OXIDATIVE PROPERTIES OF ESSENTIAL OILS INVESTIGATED AS POSSIBLE NATURAL FOOD PRESERVERS

Jack Bowman and Fr. Gerald J. Buonopane

*Department of Chemistry, Seton Hall University, South Orange NJ 07079*

The central focus of this study is to research new non-carcinogenic avenues for food preservation; in the hopes of replacing the current artificial standards with alternative organically based preservatives. The desired objective is to acquire an innocuous and naturally synthesized chemical that still effectively acts as an antioxidant or food preserver. The data from this research strongly suggests essential oils of aromatic plants as this alternate safe option. The research conducted essentially tested the hypothesis that these essential oils, in particular the plant extract geranium, possessed the necessary properties to inhibit oxidation or the decomposition of food. The research group then developed a standard set of procedures that involved incorporating an oxidizing agent, a composite substance that decomposes organic compounds, into various concentrations of the geranium oil within an ethanol based solution. The process was then run through a UV-VIS spectrophotometer that determined the effectiveness of the oil to inhibit the properties of the oxidizing agent through the derived formula. Although the results proved mildly inconclusive, further testing is currently being done to reveal promising results. Moreover, other procedures in the future using linoleic acid, a common fatty acid that would serve as a substrate in which an oxidizing agent and the geranium oil could interact, should also point to the potential use of essential oils as prospective food preservers. In conclusion, more testing is obviously needed in order to solidify the claim that some essential oils could be used as natural preservatives. However, future research should reveal rather optimistic results.

1. Farhath, M. S. Seema, P. P. Vijaya , P. Mumtaj and M. Vimal. "A comparative study on antioxidant activity of essential oils and curcumin using thiobarbituric acid reactive substances." *Journal of Chemical and Pharmaceutical Research*. 2013; 5(9): 219-221.



## A MORE NATURAL WAY TO PRESERVE FOOD

Adam Kmeck, Jack Bowman, Scott McAfee and Fr. Gerald Buonopane

*Department of Chemistry and Biochemistry, Seton Hall University South Orange, NJ*

Throughout the semester I have been working with the essential oil Ginger Grass, in order to see if it would work better as an antioxidant than using the preservatives we have now. In order for Ginger Grass to be considered an antioxidant it would have to be a “chain-breaking” antioxidant.

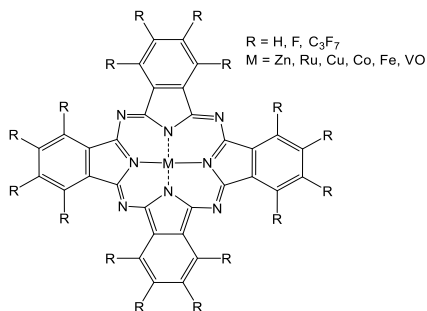
To begin the experiment, we had to make a 1M solution of the oil. Next I had to make a different concentration of ginger grass, by combining ginger grass and ethanol, to obtain a 2.5 mL solution. Then we had to combine 1 mL of 2,2-diphenyl-1-picrylhydrazyl (DPPH), with each mixture of ethanol and ginger grass, and created a negative control that consisted of 1 mL of DPPH and 2.5 mL of ethanol. The next step was to use the UV-Vis spectrophotometer and find the absorbance values at 518nm. Then we subtracted the concentrated solution from the blank and divided by the blank. This gave us the percent inhibition, allowing us to determine the free radical scavenging activity. Next we are moving into the assessing the antioxidant activity using the linoleic acid model system, by using the TBARS assay. This method uses the MDA formed from the split product on an unsaturated fatty acid, which was created by the oxidation of a lipid substrate.<sup>1</sup>

<sup>1</sup>UC Davis. Methods for Testing Antioxidant Activity. <http://ucce.ucdavis.edu/files/datastore/608-46.pdf> (accessed April 8, 2015)

## SOLUTION ADSORPTION OF PHTHALOCYANINES ON SOLID SURFACES

Gabriel C. Graffius, Dr. Alexander Y. Fadeev, and Dr. Sergiu M. Gorun

*Department of Chemistry and Biochemistry, Seton Hall University*



In our current work, we have undertaken a systematic study of the Langmuir solution adsorption isotherms of phthalocyanines on several solid surfaces. Quantitation of the adsorption was obtained by solution UV, reflectance UV, NMR, and CHN analyses. The initial work focused on adsorption of Zinc phthalocyanines in acetone on several metal-oxide surfaces. Strong physisorption or potentially chemisorption occurred on the surface of alumina,

which plateaued at a theoretical monolayer. Subsequent studies of modified silica surfaces evaluated additional adsorbate-adsorbent interactions. The adsorption, in the order of quantity adsorbed, was alumina  $\geq$  aminated silica  $\gg$  silica  $>$  hydrophobic silica.

Porous alumina and aminated silica were selected for additional studies in acetone due to a strong adsorption interaction. We first studied adsorption on acidic and basic activated aluminas to investigate the trend of strong adsorption to electron donating surfaces. Basic aluminas showed very strong adsorption while the acidic alumina showed very little. Next, several zinc phthalocyanines with different levels of fluorination were evaluated. Perfluoroalkyl phthalocyanines containing different transition metals were also studied. Finally, parallel studies were also completed in methylene chloride (CH<sub>2</sub>Cl<sub>2</sub>), a non-polar solvent. Adsorption from CH<sub>2</sub>Cl<sub>2</sub> occurred on all metal oxide surfaces, but it could be removed by washing with acetone.

We have shown that the solution adsorption of fluorinated phthalocyanines is a valid technique for making solid supported phthalocyanine materials. Initial conclusions are that a strong adsorption occurs via Lewis acid/base interactions between the metal center and the adsorbate with a weak contribution from hydrogen bonding. Future work will focus on understanding the mechanism of the adsorption interaction and studying the orientation of the phthalocyanines on the solid surface.

## **REDUCED WETTING OF NITROCELLULOSE WITH ENERGETIC PLASTICIZER**

Henry Grau and Dr. Alexander Y. Fadeev

*Department of Chemistry & Biochemistry, Seton Hall University*

The present study involves a continuation of work involving a surface chemistry project with the primary goal of creating a phobic interface on the surface of nitrocellulose (NC). The functionality of the phobic surface will be intended to inhibit liquid components such as energetic plasticizers from diffusing and migrating through a nitrocellulose based propellant formulation. The work performed involves the surface functionalization of NC. The reacted nitrocellulose was characterized to determine the degree of surface functionality and to determine if the performance of NC was changed due to modification. The H<sub>2</sub>O sink tests were performed and showed that the functionalized nitrocellulose remained buoyant compared to neat nitrocellulose which sinks immediately when exposed to a water bath. Size exclusion chromatography was utilized to show an increase of molecular weight distribution for the functionalized NC versus the neat NC. Contact angle measurements with hexadecane, water, and nitroglycerin as probe fluids revealed a degree of functionalization on the material's surface. Elemental analysis showed the presence of increased surface atom concentrations for the functionalized NC. Differential Scanning Calorimetry (DSC) was utilized to confirm onset temperatures of decomposition in relation to baseline NC. Future work will involve modifying the reaction to further enhance the non-wetting properties of the functionalized NC.

## DEVELOPING TECHNIQUES FOR ENCAPSULATION OF TARGET MOLECULES INTO METAL OXIDE PORES

Karthik Jayaraman and Dr. Alexander Y. Fadeev

*Department of Chemistry and Biochemistry, Seton Hall University South Orange NJ*

In this study we propose a “bottle-around-a-ship” strategy to encapsulate novel molecules inside the pores of metal oxide surfaces (adsorbent). The essence of “bottle-around-a-ship” strategy lies in the use of nanoparticles to build an enclosure around the pores loaded with target molecules. Several “adsorbent-nanoparticle” model systems were tried to demonstrate the “bottle-around-a-ship” strategy. The model systems that we tested include “Porous Alumina-Colloidal Silica”, “Porous Aluminated Silica-Colloidal Silica” and “Porous Silica-Colloidal Alumina”. The charge driven attraction between adsorbent and nanoparticles is being exploited to build a nanoparticle enclosure around the pores. For example, the negatively charged silica adsorbent would attract the positively charged alumina nanoparticles, resulting in capping or closure of pores.

We propose to create a catalyst material by encapsulating metal phthalocyanines inside the pores of metal oxides. The encapsulation supposedly acts as a barrier to liquid solvent, while enabling the pores to be accessible to gas molecules. The loading of phthalocyanines onto the pores is done by repeated addition of certain volume (equal to pore volume of adsorbent) of ruthenium phthalocyanine in acetone and eventually evaporating the acetone. The encapsulation was done by reacting the loaded adsorbent with the nanoparticles in aqueous medium using an in-house procedure.

Thermo gravimetric analysis and nitrogen adsorption were performed to demonstrate the loading of phthalocyanines inside the pores. The nitrogen desorption measurements were used to demonstrate that the encapsulated pores were still accessible to gas molecules. Future work will involve optimizing the encapsulation technique and identifying the most suitable adsorbent-nanoparticle system.

# SYNTHESIS AND CHARACTERIZATION OF FLUORINATED PHTHALOCYANINES

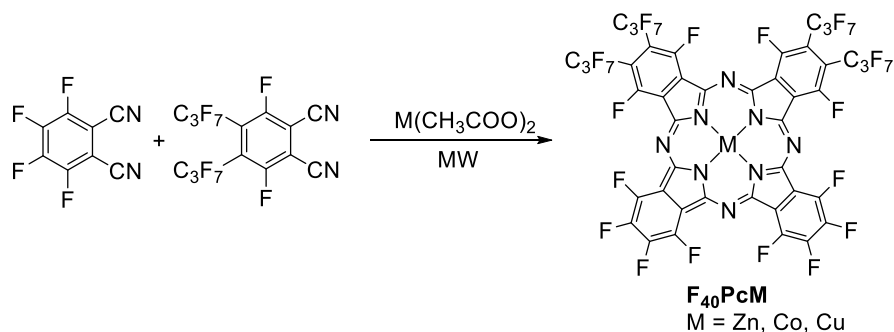
Patrick Heintz and Dr. Sergiu Gorun

*Department of Chemistry and Biochemistry, Seton Hall University South Orange NJ*

Fluorinated phthalocyanines exhibit significant electronic deficiency and, as a result, their metal complexes are likely to exhibit enhanced binding to atoms and molecules containing lone pairs of electrons. The more common binding mode of metal complexes is to molecules in solution, but solid-state binding is equally important. Specifically, metal surfaces contain oxygen atoms. For example those of oxides and hydroxides that form when metals are exposed to environmental conditions. The surface oxidation process is an early stage of the onset of corrosion.

The goal of this project proposes is to take advantage of incipient corrosion, i.e. to coverage of a metal surface by oxygen containing species and use these species as anchoring points for hydrophobic, electron deficient metal complexes that, once bonded, could arrest further oxidation. The ultimate goal is the preservation of metal surfaces of hardware used in industry.

Candidates for the proposed binding are fluorinated phthalocyanines with intermediate steric hindrance, such as  $F_{40}PcM$ ,  $M$  = metal, Figure 1.



## PHTHALOCYANINE BIOCONJUGATES AND THEIR APPLICATIONS IN PHOTODYNAMIC THERAPY

Carrion E.<sup>#\*</sup> Kozuch, S.<sup>#</sup>, Patel, M.<sup>#</sup>, Patel, H.<sup>#\*</sup>, Sabatino D.<sup>#</sup>, Gorun S.M.<sup>#\*</sup>  
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Phthalocyanines (Pcs) form an important class of photosensitizers that are being considered for photodynamic therapy (PDT) of malignant tumors. Despite their favorable PDT properties, they lack clinical utility due to poor stability in the presence of the reactive oxygen species (ROS) they produce as well as poor pharmacological properties and poor selectivity. To address these limitations, a novel class of cancer-targeting fluoroalkyl metal phthalocyanines is being developed. The fluoroalkyl metal phthalocyanines are functionalized with a carboxylic acid group (F<sub>48</sub>H<sub>7</sub>COOHPcM; M = divalent metal) which allows for bioconjugation with either a cancer cell targeting peptide (Pep42) or an oncogene targeting oligonucleotide (asDNA). In this context, the cell surface GRP78 receptor has been selected as a bio-marker for our tumor-targeting PDT approaches. In this presentation, we illustrate the synthesis, characterization and bioconjugation of these F<sub>48</sub>H<sub>7</sub>COOHPcMs with cancer targeting biomolecules.

1. Patel, P.; Patel, H.H.; Borland, E.; Gorun, S.M.; Sabatino, D. *Chem. Commun. (Camb)*. **2014**, 50, 6309-6311.

# **THE CONCEPT OF STANDARD ADSORPTION ISOTHERMS: COMPARISON OF EXCESS ADSORPTION OF BINARY AQUEOUS ORGANIC MIXTURES ON CLASSICAL PACKING MATERIAL AND CORE-SHELL SBA-15 MODIFIED WITH ALKYLATED LIGANDS**

M. Figus, Y.V. Kazakevich, and Dr. A. Y. Fadeev

*Department of Chemistry and Biochemistry, Seton Hall University South Orange, NJ*

The excess adsorption isotherms of acetonitrile from water were measured on four in-house packed columns with different adsorbent geometry. A classical 10  $\mu\text{m}$  porous silica particle and SBA -15 10  $\mu\text{m}$  nonporous spherical particle that was prepared using polymer-templated sol-gel synthesis and were well characterized via low temperature nitrogen adsorption, TGA, and STEM. The adsorbent's surface was chemically modified via solution phase reaction of  $\text{C}_n\text{H}_{2n+1}\text{Si}(\text{CH}_3)_2\text{N}(\text{CH}_3)_2$  where  $n = 1, 4, 8, 18$ . The energies of adsorption, surface area, and pore volumes of modified substrates were calculated using nitrogen adsorption isotherm. Grafting density of bonded ligands was determined from the weight percent of carbon. Comparison of the excess adsorption isotherms measured on these columns, and expressed in surface specific form demonstrates significant similarity of the adsorption properties for all columns. This allows us to introduce the "standard adsorption isotherm" for reversed-phase alkane type columns and suggests that adsorption depends on the type of ligands and bonding density of the ligands and it is independent on the adsorbent geometric morphology, pore shape, and distribution.

# STUDY OF THE EFFECT OF SURFACE, ORGANIC MODIFIER NATURE AND COMPOSITION ON THE HPLC RETENTION OF FLUORINATED PHTHALOCYANINES AND OTHER MODEL COMPOUNDS

Sauvelson Auguste, Mathias Kant and Dr. Yuri Kazakevich

*Department of Chemistry and Biochemistry, Seton Hall University South Orange, NJ*

Compounds with significant number of conjugated  $\pi$ -electrons are usually demonstrate unusual retention behavior in HPLC as mobile phase organic content varies. Fluorinated phthalocyanines are showing an extreme case of these effects. We compare their retention on regular C18-type (Halo-C18) surface with more  $\pi$ -active surfaces like perfluorophenyl (Kinetex-PFP) and cyano (Ascentis-CN).

The effect of the variation of eluent composition was studied on all these adsorbents for MeOH/water and THF/water mobile phases. Simple aromatic compounds such as benzene, toluene, hexafluorobenzene were also used for comparison with fluorinated phthalocyanines (F-Pc's) as well as polynuclear aromatic compounds (anthracene, coronene).

Cyano-type surface demonstrated specific retention pattern for F-Pc's showing reversed elution order as compared with the retention on regular C18 column in MeOH/water mobile phase.

The most dramatic is the difference in F-Pc's retention in MeOH and THF modifier used. The selectivity as a function of the number of fluorine atoms significantly improves with the substitution of MeOH with THF while the selectivity for regular aromatic and PNA's did not change as much.



# INVESTIGATION OF H<sub>2</sub>O INTERMOLECULAR INTERACTIONS WITH HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Mathias E. Kant and Dr. Yuri Kazakevich

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While water is one of the most abundant molecules on earth many of its intermolecular interactions with other compounds are still very much a mystery. The research is aimed at understanding some of the interactions that to date have gone uninvestigated. Among other factors the research was focused on determining compounds hydrophobicity, or if they have extended interactions with water and other surfaces. This research was conducted via High Performance Liquid Chromatography, which is a highly controlled process of inputting very precise amounts and concentrations of a solution and recording various data such as retention time, and influences on pressure. Collected data is graphed in the form of retention factors and  $k'$  in order to extrapolate y-intercepts and other important information from the data. The research was very successful in determining how water interacts with a variety of chemical compounds. The hope is that the research will be useful in the future understanding of how H<sub>2</sub>O behaves, and have practical real world applications. Which include but are not limited to, how water as a solvent interacts with the solute, how to better predict which interactions might take place, and to understand in what time frame these interactions take place. This type of information is incredibly important in the pharmaceutical industry, kinetics in chemistry, and simple academia for the pursuit of knowledge.

## Reference:

Y.V. Kazakevich Low-Energy Interactions in High-Performance Liquid Chromatography, The Journal of Chromatography A. 1999, 872, 49-59

## **CHEMICALLY ROBUST PHTHALOCYANINES: PHOTSENSITIZER AND ELECTRON SHUTTLE IN SOLID STATE DYE SENSITIZED SOLAR CELLS**

Patrick J. Dwyer, Rory J. Vander Valk, and Dr. Stephen P. Kelty

*Center for Computational Research, Department of Chemistry and Biochemistry, Seton Hall University, South Orange, New Jersey 07079, U.S.A*

A completely solid state dye sensitized solar cell (DSSSC) is proposed in which chemically robust phthalocyanine (Pc) sensitizers,  $F_{16}ZnPc$  and  $F_{40}ZnPc$ , are sandwiched between n-TiO<sub>2</sub> and p-NiO. While the energy conversion efficiencies of conventional Grätzel cells are continually increasing, the DSSSC design effectively solves the long term stability issues of the volatile liquid electrolyte. Through analysis of the electronic structure of the Pc|semiconductor systems, the free energy associated with hole injection into the valence band of NiO upon photoexcitation of the sensitizer and electron injection into the conduction band of TiO<sub>2</sub> from the reduced form of the sensitizer as well as the competing charge recombination processes are calculated. Thermodynamically, the charge injection processes are found to be favored over the undesired charge recombination processes. These findings suggest promising energy conversion for the NiO|Pc|TiO<sub>2</sub> DSSSC.

## MITIGATION OF SURFACE AGGREGATION IN MODIFIED PHTHALOCYANINES AS POTENTIAL PHOTSENSITIZERS

Rory J Vander Valk, Patrick J. Dwyer, and Dr. Stephen P. Kelty  
*Center for Computational Research, Department of Chemistry and Biochemistry, Seton  
Hall University*

Important to the development of dye-sensitized solar cells is the longevity and photo-conversion efficiency of the dye. To improve cost effectiveness, dyes of superior thermal and chemical stability are desirable to extend device performance. In this study, we examine a series of peripherally fluorinated Zinc-Phthalocyanines (FxZnPc). Introduction of chemically inert fluorine and isopropyl fluoroalkyl groups on the periphery of the Pc improve the dye stability and allow for tunable photo-physical properties. Additionally, introduction of the bulky isopropyl fluoroalkyl groups help mitigate molecular aggregation in thin films which is known to be detrimental to maintaining the desired photo-physical properties of the surface coating. Using molecular dynamics and first principles modeling, various substituent effects on surface adhesion and aggregation over TiO<sub>2</sub> surfaces are characterized for both symmetric and asymmetric substitution.

## MOLECULAR MODELING OF TRANSIENT RECEPTOR POTENTIAL VANILLOID TYPE 1 ION CHANNEL (TRPV1)

Kelly Raymond, Yufeng Wei, PhD and Stephen Kelty, PhD

*Center for Computational Research, Department of Chemistry and Biochemistry, Seton  
Hall University*

The Transient Receptor Potential (TRP) family of ion channels encompasses more than 30 members, which are expressed in many different tissues and cell types.<sup>1</sup> Molecular modeling will be used in order obtain structural and functional data on Transient Receptor Potential Vanilloid Type 1 (TRPV1) ion channel in its membrane bound environment. In particular, the transmembrane and C-terminal domain regions of TRPV1 are of particular interest. TRPV1 is part of the TRP family gated by vanilloids, heat and protons.<sup>2</sup> The S1-S4 region of the channel is the putative ligand-binding segment, while the C-terminal domain is suggested to respond to temperature and is regulated by phosphatidylinositides (PIP<sub>2</sub>). Despite the crucial roles in mediating signal transductions at both peripheral and central nervous systems, TRP channels are poorly understood in the context of structures and mechanisms.<sup>4</sup> A molecular model of the published transmembrane section of TRPV1 along with the putative, unstructured C-terminal domain was created using their respective homology models and inserted into their membranes.<sup>5</sup> Simulations are currently being performed using both a lipid membrane containing PIP<sub>2</sub> and one without PIP<sub>2</sub> in order to determine its on TRPV1. Molecular dynamics simulations could provide pivotal information about ligand binding, voltage sensing, interaction with heat/cold and proton binding for TRPV1. A greater understanding of the structure of TRPV1 could provide important details on how to alleviate certain diseases such as pain, asthma and diabetes.

### References:

1. Jara-Oseguera, A., Nieto-Posadas A., et al. (2010) Molecular Mechanisms of TRPV1 Channel Activation. *The Open Pain Journal*. **3**: 68-81.
2. Clapham, D. E. (2003). TRP channels as cellular sensors. *Nature*. **426** (6966): 517-524.
3. Frenandez-Ballester, G.; Ferrer-Montiel, A. (2008) Molecular Modeling of the Full-length Human TRPV1 Channel in Closed and Desensitized States. *J. Membrane Biology*. **223**: 161-172.
4. Raymond, K.A.; Twomey, E.C.; Wei, Y. (2014) Characterization of Temperature-Sensing and PIP<sub>2</sub>-Regulation of TRPV1 Ion Channel at the C-terminal domain using NMR Spectroscopy and Molecular Dynamics Simulations. *J. of Integrated Omics*. **4** (2): 79-86.

# FINITE DIFFERENCE SIMULATION OF CONCENTRATION EFFECTS ON PEAK TAILING AND RETENTION FACTORS IN ADSORPTION CHROMATOGRAPHY

Nicole Charles, Antonio Macaluso and Dr. Joseph Maloy  
*Department of Chemistry and Biochemistry, Seton Hall University*

Finite difference simulations have been used previously to model surface adsorption effects in partition chromatography. This VBA has been developed in-house] to run in Excel. Rather than treating the mobile phase fraction as a fixed quantity as in partition chromatography, this software computes a variable, concentration-dependent mobile phase fraction for each and every theoretical transfer using the dimensionless input parameters. It thereby generates a numerical representation of the peak resulting from a set of four input parameters. These parameters represent: the mobile phase partitioning fraction ( $X$ ); the adsorption equilibrium constant ( $K_{ad}C_o$ ); the relative molar surface adsorption site density ( $\Gamma_o A$ )/( $C_o V_m$ ); and the number of theoretical plates ( $N_o$ ). The VBA software generates a numerical representation of each peak and computes its characteristics such as retention time,  $t_R$ , and retention factor,  $k'$ , using statistical moment analysis; the USP peak tailing factor is also computed.

This work examines the effect of concentration variation on peak tailing factor and retention factor. In order to have only concentration-dependent input parameter (note that both ( $K_{ad}C_o$ ) and ( $\Gamma_o A$ )/( $C_o V_m$ ) are concentration-dependent), ( $\Gamma_o A$ )/( $C_o V_m$ ) may be multiplied by ( $K_{ad}C_o$ ) to produce ( $K_{ad}\Gamma_o A/V_m$ ), a concentration independent input parameter. At fixed values of ( $K_{ad}\Gamma_o A/V_m$ ) then, variation in ( $K_{ad}C_o$ ) produces the desired effect on peak tailing and retention.

In this study, tailing factors for adsorption were modelled in the absence of partition. (Note that the software allows partition and adsorption to be modelled simultaneously.) This was accomplished by setting the fraction of the mobile phase  $X = 0.9999$ .

The results of these simulations show that the tailing factor and the retention factor for an adsorption peak will vary with concentration. The purpose of this research is to correlate experimental results with the results of these simulations. Chromatograms were obtained for caffeine and phenol on two different C-18 columns. Since these two compounds are known to exhibit tailing, values for their tailing factors at different concentrations may be compared with those predicted by the simulation in order to establish whether the tailing factor variation and retention factor variation with concentration is consistent with that predicted by the simulation.

## IMPROVED SYNTHESIS OF CNS-ACTIVE GLYCAL-BASED BENZYLIDENE DERIVATIVES

Emi Hanawa, Jamie Talisman and Dr. Cecilia Marzabadi

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Epilepsy is one of the most common central nervous system (CNS) disorder, affecting 65 million people worldwide. Like other CNS disorders, epilepsy is chronic and cannot be fully cured. There are many antiepileptic drugs (AEDs) available to control seizures. The first generation of antiepileptic drugs (AEDs) control seizures by manipulating  $\text{Na}^+$  channels,  $\text{Ca}^{2+}$  channels or GABAergic neurotransmission. Unfortunately, more than a third of epileptics have seizures that are not effectively controlled with existing AEDs. To treat seizures that are resistant to those AEDs a second generation of AEDs has been developed. The second generation is designed to act simultaneously by several different mechanisms.

Previously, we prepared a sugar-based benzylidene compound with the general structure. This lead compound was tested in receptor-based CNS assays and showed nanomolar affinity for  $\text{GABA}_A$  and  $\text{mGluR}_2$  receptors. It was also tested in rodent models of epilepsy and gave satisfactory results. Overall yields of the lead compound are low due to the lability of the compound under the reaction conditions of acetal formation. We have set out to further optimize anticonvulsant activity of our lead compound by modifying one or more functional group(s) and also improving the yield. Several modifications have been done and the overall yields were significantly improved. Despite the improved yields, some of the derivatives did not show expected biological activity and others are yet to be tested.

## **CARBOHYDRATE-BASED DRUGS IN TREATING CENTRAL NERVOUS SYSTEM DISEASES**

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The blood-brain barrier (BBB) prevents a variety of pharmaceutical drugs from gaining entry into the brain. The low permeability function of the BBB is brought about by the epithelial-like tight junctions that is found within the brain capillary endothelium. This particular property of the BBB causes difficulty in the treatment of central nervous system diseases (CNS). However, the brain does allow glucose, its main energy source, to cross the protective barrier. Thus it appears that carbohydrate-based drugs have the ability to cross this BBB. Furthermore, these drugs could have the potential in treating CNS diseases. As such, carbohydrate-based drugs could be developed to lessen the symptoms of various CNS disorders. The starting compound, tri-O-acetyl-D-glucal, underwent oxidation of the primary hydroxyl to the aldehyde. With further research, it will undergo Wittig olefination followed by a hydroboration oxidation reaction to bring the compound closer to the conversion of the desired bicyclic analog. The bicyclic analog is expected to have a better half-life than the original parent compound.

## ACETALATION OF 1,5-ANHYDRO-2-DEOXY-3,4-O-ISOPROPYLIDENE-D-LYXO-HEX-1-ENITOL (GALACTAL)

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Carbohydrates are known to be digested by cancer cells, and because of this, the possibility to destroy cancer cells through the use of carbohydrate-based drugs is a therapeutic strategy. Our approach utilizes the carbohydrate D-galactal as a starting material. To a suspension of 1,5-anhydro-2-deoxy-D-lyxo-1-enitol (D-galactal) and 2,2-dimethoxypropane,  $\text{TsOH} \cdot \text{H}_2\text{O}$  was added causing a reaction to take place. The mixture was diluted with  $\text{NaHCO}_3$  then extracted with  $\text{CH}_2\text{Cl}_2$ . It was further washed with brine and dried with  $\text{Na}_2\text{SO}_4$ . A yellow syrup was obtained. This reaction between the galactal, 2,2-dimethoxy propane and  $\text{TsOH} \cdot \text{H}_2\text{O}$  removed water from the starting sugar and an acetylation was able to occur. A TLC was performed and the sample was then placed on a rotary evaporator to remove any residual solvent. An NMR was taken to further determine that the contents of the sample were in fact the compound of interest. Column chromatography in a 9:1 hexane: ethyl acetate solvent system was performed and fractions were obtained. Further TLCs were run on the fractions to determine the location of the intended compound.



## **CARBOHYDRATE CONJUGATES FOR CANCER METABOLISM-TARGETING THERAPIES AND MULTIDRUG RESISTANCE**

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The Warburg effect is the observation that most cancer cells produce an enhanced amount of ATP by a high rate of glycolysis followed by lactic acid fermentation in the cytosol to promote metastasis. In non-cancerous cells a comparatively low rate of glycolysis is followed by the oxidation of pyruvate in the mitochondria. The latter process is aerobic as opposed to the earlier process that is anaerobic. Typical malignant tumor cells have glycolytic rates up to 200 times higher than those of their normal tissues of origin; even if oxygen is plentiful. The mission of this project is to develop a library of molecules consisting of carbohydrate conjugates with the properties of biological specificity and lipophilicity to compromise ATP production novel to cancer cell glycolysis and multidrug resistance. These prospective compounds will address a dual purpose, either to promote apoptosis or to diminish cancer cell multidrug resistance as adjuvants so as to enhance the traditional modes of treatment via chemotherapy or radiotherapy. The advantage of such an approach will improve long term patient survival rates and quality of life, even with immune compromising diseases such as diabetics and lupus that are known to traditionally impede treatment. Currently work is underway in developing 2-deoxy based carbohydrates containing analogs of cholesterol or alkyl chains of varying lengths and bifurcations. Additional work is to include coupling marker specific peptides to the various glycolipids. Bioactivity testing will encompass measuring the oxygen consumption rate and the extracellular acidification rate as indicators of mitochondrial respiration and glycolysis.

## MEASUREMENTS OF THE EFFECT OF HCL AND NAOH CONCENTRATION ON THE FLUORESCENT LIFETIMES OF HYDROXYPYRENE

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There has been intense interest in the fluorescence properties of polyaromatic hydrocarbons such as pyrene as biomarkers for petroleum contamination in fish. Polyaromatic hydrocarbons consists of hydrogen and carbon arranged in the form of two or more fused benzene rings and occur in high concentrations in crude oil. Prior work in our laboratory has shown that the fish menhaden rapidly metabolizes pyrene to hydroxypyrene. This derivative has different excited state properties from pyrene, including different excitation and emission spectra, and excited state lifetimes. There is also the complication of ground and excited state proton transfer. Measurement of the excitation and emission spectra, and the associated lifetimes of hydroxypyrene in 75% ethanol with varying amounts of HCl and NaOH have been made and will be reported. A tentative analysis of the equilibria, energetics and kinetics of the hydroxypyrene ground and excited states will be discussed.

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## FLUORESCENCE INVESTIGATION THE ACID-BASE BEHAVIOR OF 1- AND 2-NAPHTHOL IN 75% ETHANOL

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This report will focus on the adaptation of the original analysis by Bentivegna, et. al. from traditional excitation spectroscopy to excitation-emission spectra (EEMs), providing a complete profile of the steady state fluorescence process. The metabolites of interest are 1- and 2-hydroxynaphthalene. Both are in the category of polyaromatic hydrocarbons (PAHs) and their metabolites, also known as polynuclear aromatic hydrocarbons (PNAs) and polycyclic organic matter (POM). They are composed of hydrogen and carbon arranged in the form of two or more fused benzene rings in linear, angular, or cluster arrangements, which may or may not have substituted groups attached to one or more rings (Sims and Overcash 1983). To determine the spectroscopic behavior of these two compounds, the acid (HCl) and base (NaOH) content varied in each sample, determining the effect on the intensity and energy of the absorption and emission properties of both metabolites. The samples were be examined by UV-Vis, excitation and emission spectroscopy. UV-Vis spectra was first obtained on a Hewlett-Packard 8452A diode array spectrometer upgraded by OLIS. Then, the fluorescence spectra was collected on a Horiba Fluorolog 3.

## THE EFFECTS OF BSA ON THE FLUORESCENCE OF 1-PYRENOL

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In 2010, the Gulf Oil Spill caused the fish in the general area to ingest toxic components of crude oil, thus potentially resulting in diseases for the fish and the people who consumed said fish. Since the spill, Seton Hall University has been attempting to discover methods in which polyaromatic hydrocarbons (PAHs), which are carcinogenic components of petroleum<sup>1</sup>, can be safely extracted from the fish. One such method being tested is the binding of the PAHs, which become hydroxylated in the fish, to common proteins, such as bovine serum albumin (BSA), and then the extraction of the protein-bound molecules using known solutions. When the PAHs bind with another substance, their fluorescence properties are altered; this property was used in order to determine if any of the BSA bound to the PAH. Two stock solutions were made of the two amino acids that fluoresce from BSA, tyrosine and tryptophan; 15 mg/mL of tryptophan was diluted to 100 mL with 75% EtOH, and 10 mg/mL of tyrosine was diluted to 100 mL with the same solvent. Then, the EEMS (excitation emission spectra)<sup>2</sup> were measured for the two solutions; afterwards, the EEMS of the hydroxylated PAH, 1-pyrenol, were taken. Then, multiple 4 mL solutions containing varying amounts of either tyrosine and 1-pyrenol or tryptophan and 1-pyrenol were made in order to observe under what concentrations, if any, the two substances would bind. EEMS of each of these samples were then measured in order to see if the spectra showed alterations from the spectra taken from the original solutions, thus showing if the two substances bound together.

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## FLUORESCENCE INVESTIGATION OF THE ACID-BASE BEHAVIOR OF 9-PHENANTHROL

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When the Deep Water Horizon of the Mississippi Canyon Site 252 exploded on April 20, 2010, oil spillage had a huge impact on the Gulf of Mexico's fish population. This is particularly important as the fishing industry is a major part of the Gulf of Mexico's economy. In order to identify and quantitate petroleum contamination in fish, specifically menhaden, methods to rapidly analyze for petroleum markers is needed. The compounds of interest are polycyclic aromatic hydrocarbons (PAHs) and their metabolites. One potential metabolite is 9-phenanthrol. In order to determine the spectroscopic behavior of this compounds, the acid-base behavior of the ground and excited state forms of 9-phenanthrol were investigated by varying amounts of either HCl or NaOH in 75% ethanol to solutions of 9-phenanthrol and measuring the absorption, emission and excitation spectra. Prepared samples was examined by UV-Vis, excitation and emission spectroscopy. Analysis of this data will lend insight into the best conditions for identifying and quantitating 9-phenanthrol.

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## FLUORESCENCE ANALYSIS OF VITAMIN E IN 75% ETHANOL

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After the 2010 BP Oil Spill, menhaden fish were collected to determine whether oil components were absorbed, and if so, what physiological effects might have occurred. Fluorescence analysis of tissue extracts showed that hydroxylated derivatives of polycyclic aromatic hydrocarbons were observed, along with fluorescence vitamins such as E and A. In order to quantitate the amount of vitamin E present, spectroscopic studies were initiated to determine the fluorescence properties of vitamin E in the 75% ethanol extraction solvent. Initial measurements show that vitamin E exhibits non-Beer's Law behavior in both absorption and emission spectroscopy. The results will be presented and discussed.

## **FLUORESCENCE SPECTROSCOPY OF TRYPTOPHAN AND TYROSINE AS A FUNCTION OF HCL AND NAOH CONCENTRATION IN 75% ETHANOL**

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Studies have shown that fluorescence excitation spectroscopy is a useful technique for detecting polyaromatic hydrocarbons (PAH) and fluorescent vitamins in 75% ethanol extraction samples of menhaden organs. One complicating issue of concern is that many of the hydroxy compounds are photoacids. That is, upon optical excitation, they deprotonate. This has the effect of quenching the fluorescence of some, but not all, hydroxyfluorophores. Other hydroxylfluorophores have their fluorescence enhanced as a result of high or low pH. By modifying the solution pH, we can effectively “turn on” or “turn off” various classes of hydroxyfluorophores. This has the advantage of increasing the sensitivity of the technique, and proving corroborating evidence for the identity of the fluorophore. This research project determined the amounts of hydrochloric acid and sodium hydroxide that can be added to cause the change in fluorescence spectra. The emission spectra of tryptophan and tyrosine in 75% ethanol and known aliquots of hydrochloric acid and sodium hydroxide solution were studied.

**ASSESSMENT OF THE VIABILITY OF MICROWELL PLATES AS SAMPLE  
HOLDERS FOR ANALYTICAL EXCITATION-EMISSION SPECTROSCOPY  
MEASUREMENTS OF POLYAROMATIC HYDROCARBONS IN 75%  
ETHANOL: WELL FILL DEPTH EFFECTS**

Lauren Ridley and Dr. Wyatt R. Murphy

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Polyaromatic hydrocarbons (PAHs) in the environment are a significant concern as many compounds in this class are potential carcinogens. PAHs resulting from petroleum spills<sup>1-4</sup> can contaminate natural waters and the products obtain from them (fish and fish products in particular). Previous studies by Bentivegna, et. al.<sup>5</sup> on ethanolic extracts of organs from menhaden captured in the vicinity of the Deepwater Horizon (Macondo oil well) spill have shown that fluorescence excitation spectroscopy is a useful technique for detecting the presence of PAH metabolites and fluorescent vitamins. In order to address the issue of the large number of samples taken from the menhaden, the first goal for this project is to develop the techniques to obtain EEMS (excitation emission matrices) spectra in a microwell with any artifacts associated with the plate reader optics removed via correction factors. There are a number of optical compromises present in microwells that do not exist in normal cuvette-based measurements. First, the excitation and emission light must be passed through an optical fiber bundle, which is not as efficient as transmitting the light.<sup>3</sup> Second, the optical geometry of the microwell depends on the focus of the optical fiber bundle and the depth of the sample (determined by the microwell geometry and fill depth). Third, substantial scattering from the bottom of the well can be an issue and is highly dependent on the placement of the fiber bundle. The current study is focused on the fill depth of the microwell to optimize conditions for measuring EEMS.

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## MODERNIZATION OF THE GENERAL CHEMISTRY LABORATORY AT SETON HALL UNIVERSITY

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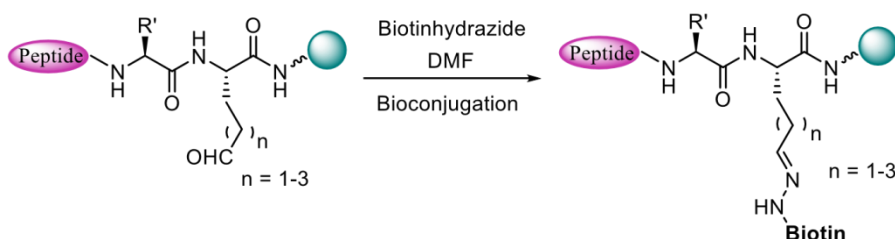
The Department of Chemistry and Biochemistry recently acquired two new sets of computer controlled equipment and software from Vernier Software and Technology: a SpectroVis Plus Spectrophotometer and a Lab Quest Mini including pH, temperature, and voltage probes. The SpectroVis Plus allows the collection of absorption or emission spectra in the visible region. The Lab Quest Mini and probes permit the collection in real time of the pH, temperature and/or voltage of a solution. The goal of this project was to develop new general chemistry laboratory exercises that will incorporate this new equipment. These labs are unique to the instrumentation as well as Seton Hall. Three of the labs that will be highlighted in this research are: the determination of food dye concentrations in commercial Kool-Aid, the determination of the Stern-Volmer relationship by the fluorescence quenching of quinine, and the determination of thermodynamic values of cobalt (II) chloride. The research also will discuss the advantages and the disadvantages of the new equipment as well as the labor associated with designing laboratory procedures.

## RAPID BIOCONJUGATION OF PEPTIDES USING ALDEHYDE AS AN ANCHOR ON THE SOLID SUPPORT

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Bioconjugation is a very useful technology for labeling of biomolecules such as peptides or proteins with fluorescent probes, affinity tags, or isotope labels.<sup>1</sup> The labeled biomolecules can be used to study the function and to track the path of a biomolecule. Various techniques are known for the bioconjugation, but most widely used are Cu-catalyzed click reactions<sup>2</sup> or the addition of thiols to electrophiles.<sup>3</sup> Limitations of these methods include the presence of toxic reagents and relatively slow reaction rates. Our method involves synthesis of peptide bioconjugates on solid support by utilizing well-known reactions of the aldehyde group. The key activation step involves the formation of aldehyde linker on a peptide chain by using FmocSPPS. The resulting aldehyde containing peptide can be further functionalized by reaction with oximes, hydroxyamines and hydrazides.<sup>4</sup> This methodology is highly chemoselective and has a potential of synthesizing peptide bioconjugates on solid support at a much faster rate with high yields.



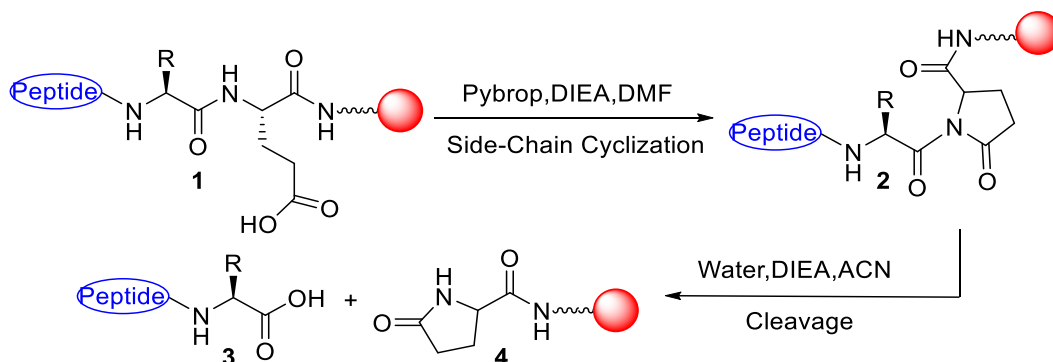
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# GLUTAMIC ACID-SELECTIVE CHEMICAL CLEAVAGE OF PEPTIDES

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Numerous enzymatic methods for site-specific cleavage of peptide bonds are used for determining the primary structure of proteins. However, enzymes are limited in their cleavage capability due to the inability to interact with un-natural amino acid residues.<sup>1</sup> We propose a chemical method for site-specific peptide cleavage that does share the limitations of enzymes. In the first key step, strong activation of the carboxyl group of glutamic acid residue would lead to the novel formation of the backbone imide moiety (**2**). In the second key step, hydrolysis at the imide moiety (**2**) would lead to cleavage of the peptide chain into the N-terminal fragment (**3**) and cyclic imide-containing C-terminal fragment (**4**). Importantly, the key activation step utilizes the most robust reaction: the condensation of an amine and carboxyl group. As a result, the method is compatible with amino acid side chains and protecting groups commonly used in peptide synthesis.



**Scheme 1.** Methodology for selective cleavage of peptides at glutamic acid

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## **FMOC SOLID-PHASE SYNTHESIS OF C-TERMINAL PEPTIDE THIOESTERS BY FORMATION OF BACKBONE 2-OXAZOLIDINONE MOIETY**

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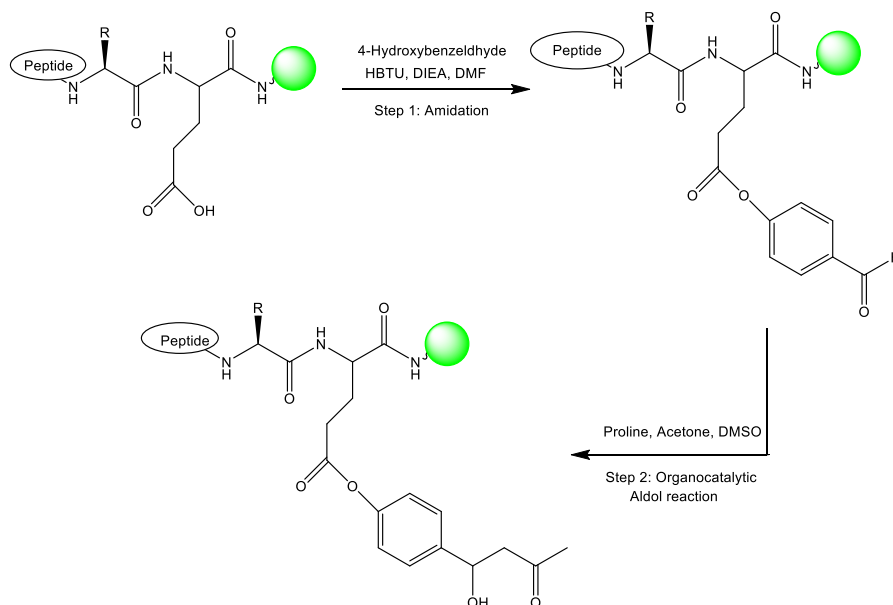
The chemical synthesis of proteins has been a landmark in the field of chemical biology. It enables the preparation of complex proteins with both natural and unnatural amino acid residues. Among various methods, Native Chemical Ligation is the most effective. It involves the coupling of C-terminal peptide thioester with another peptide containing N-terminal cysteine residue. We are interested in developing a methodology that will allow the synthesis of C-terminal peptide thioesters on solid support by using Fmoc-SPPS approach. This novel approach will be based on the formation of C-terminal 2-oxazolidinone as a result of the activation of a backbone amide in the peptide. Such 2-oxazolidinone are obtained from serine or threonine residues and have previously been explored in the synthesis of constrained peptidomimetics and foldamers by Luca Gentilucci. Inspired by this work, we developed a method for the activation of a backbone amide in a peptide by formation of a backbone 2-oxazolidinone, which, after displacement by a thiol, provides the peptide thioester.

## CATALYTIC METHOD OF DEVELOPING BIOCONJUGATION REACTIONS

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Bioconjugation consists of adding one molecule to another to create a complex molecule where at least one molecule is of biological origin. Synthesis of bioconjugates relies on chemoselective reactions that allows the creation of covalent bonds between two chemically stable groups under mild and aqueous conditions. Current methodologies exist, but the current most common method utilizes is a Cu-catalyzed click reaction of azides and alkynes. As novel approaches are tested, we begin to look at new methodologies for synthesizing bioconjugates by replacing the need for toxic metal catalysts with organocatalysts, such as proline. Organocatalysts have the potential for saving both time and money, and require only simple operation, and both reduce overall waste for bioconjugate production. As a substitution for toxic catalyst, we propose using proline, an organocatalyst, the bioconjugation reaction to initiate an aldol reaction. We rely on the use of this organocatalytic aldol reaction to produce the desired conjugation of the biomolecules (Scheme 1). This reaction allows for further development into selective conjugation of larger molecules while still utilizing an organocatalyst.



Scheme 1: Organocatalytic Approach for Bioconjugate Synthesis

## SYNTHESIS AND CIRCULAR DICHROISM STRUCTURAL ANALYSES OF THE CYTOTOXIC D-(KLAKLAK)<sub>2</sub> PEPTIDE SEQUENCE

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The apoptosis inducing (pro-apoptotic) peptide sequence, D-(KLAKLAK)<sub>2</sub>, has been shown to disrupt mitochondrial structure and activity, ultimately leading to cell death in bacteria.<sup>1</sup> Considering the amphiphilic nature of this sequence, this peptide may prove to be a synthetic challenge by conventional Merrifield peptide synthesis. Our work describes an optimized Fmoc-based solid phase peptide synthesis (SPPS) of the cytotoxic D-(KLAKLAK)<sub>2</sub> peptide sequence on a polar poly (ethylene) glycol resin. The peptide was synthesized in good crude purities (98%) and isolated in acceptable yields (40%) following RP-HPLC. Peptide identity was confirmed by molecular weight following LC/MS analyses. Peptide structure and stability properties were next evaluated. Circular Dichroism (CD) spectroscopy of the peptide (60-200  $\mu$ M) in water, phosphate buffered saline (PBS) and 2,2,2-trifluoroethanol (TFE) validated the anticipated  $\alpha$ -helix peptide secondary structure. Peptide structural stability was evaluated as a function of temperature (25-80 °C) and with the addition of surfactant (SDS) and lipid formulations. These results demonstrated a versatile peptide secondary structure that is highly influenced by the solvent conditions. This presentation will thus showcase the synthesis and structural properties of this important bio-active peptide sequence.

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## B7H6: A NOVEL LIGAND IN CANCER-BASED IMMUNOTHERAPY APPROACHES

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The B7H6 ligand is a cellular membrane expressed protein that binds specifically to the NKp30 receptor ( $K_D = 1.0 \pm 0.2 \times 10^{-6}$  M) through stable hydrophobic, H-bonding and salt bridge interactions.<sup>3,4</sup> Binding of B7H6 to NKp30, triggers association of NKp30 to an ITAM bearing protein, such as CD3 $\zeta$ , leading to a signaling cascade that results in the reorganization of the NK cells' cytoskeleton and initiation of Ca<sup>2+</sup> flux that ultimately leads to the secretion of inflammatory cytokines which triggers tumor cell lysis and death.<sup>1,2,5</sup> Interestingly, B7H6 was found to be constitutively expressed on the surface of tumors but not on healthy cells, making it a valuable tumor bio-marker. Thus, the discovery of the B7H6-NKp30 binding interaction offers an opportunity in the development of novel cancer-based immunotherapy approaches. Towards this effect, we've confirmed the binding affinity and specificity of B7-H6 with NKp30 overexpressed constitutively on the surface of NK92-MI cells by flow cytometry. This binding interaction resulted in the release of TNF $\alpha$  and IFN- $\gamma$  according to an ELISA. Taken altogether, this presentation will highlight our most recent efforts in validating B7H6 as a lead protein biologic in cancer therapy.

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# **THE USE OF QuEChERS AND IL-SDME FOR THE EXTRACTION OF DRUGS OF ABUSE FROM URINE USING GAS CHROMATOGRAPHY- MASS SPECTROMETRY**

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Extraction techniques are plentiful; however, determining which technique to implement for analysis can be difficult. Percent recovery, selectivity, ease of extraction, and ruggedness, must all be considered. It is the goal of this study to investigate three different extraction methods: QuEChERS (Quick, Easy, Cheap, Effective, Rugged, Safe), IL-SDME (ionic liquid single drop microextraction), and SPME (solid phase microextraction). In this discussion, the use of QuEChERS will be emphasized. QuEChERS is a liquid-liquid microextraction combined with a dispersive solid phase extraction cleanup. Primarily used for the extraction of pesticides from food products, QuEChERS has not yet been thoroughly investigated for forensic samples. This study will serve to determine if QuEChERS is a viable extraction method for the analysis of drugs in urine as well as compare this extraction method to the use of IL-SDME and SPME. In IL-SDME an ionic liquid drop is suspended above the sample until such a time that equilibrium has been reached. The drop is then desorbed in the GC inlet. This method is very similar to that of SPME except for the use of an ionic liquid drop rather than a coated fiber as the extraction media. The optimization of these techniques for the extraction of amphetamine, methamphetamine, morphine, benzoylecgonine, methadone, oxazepam, secobarbital, phencyclidine, and nortriptyline from urine will be discussed as well as the sensitivity and selectivity of the method via gas chromatography-mass spectrometry (GC-MS).



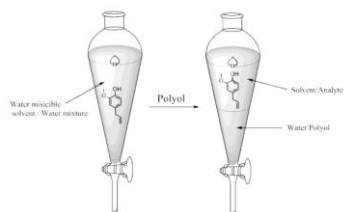
# POLYOL INDUCED EXTRACTION (PIE) OF ESSENTIAL OILS FROM WATER / ORGANIC SOLVENT MIXTURES

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In this work, it is shown that the novel extraction technique of Polyol Induced Extraction (PIE) can be applied to the extraction of essential oils. By employing the use of a polyol mass separating agent (MSA) in aqueous solvent mixtures, two immiscible phases are able to be generated. For this study, glycerol as a mass separating agent, is employed in acetonitrile / aqueous solvent systems. The applicability of this technique as an alternative extraction technique was assessed by the extraction of the main flavor and fragrance compounds that comprise six essential oils. In the extraction of eugenol (4-allyl-2-methoxy phenol) from clove buds, we were able to determine the partition coefficients and from them calculate percent recovery data and thermodynamic data in the temperature range of -20°C to 20°C. Furthermore, we were able to identify the main components present in each essential oil via gas chromatography/mass spectrometry and compare the compositional profile to that of traditional extraction techniques. The optimized extraction conditions (-10°C, 1:1 ACN/water (v/v), 20% glycerol) for eugenol at -10°C led to a partition coefficient (KEO) of 86 and an extraction efficiency of 97% in the acetonitrile-rich phase. The eugenol migration to the organic phase is a spontaneous process ( $\Delta G^\circ = -9.6$  kJ/mol) and a combination of endothermic and exothermic processes ( $\Delta H^\circ = 0.009$  kJ/mol) with entropy being the driving force behind the reaction ( $\Delta S^\circ = 0.07$  J/K,  $T\Delta S^\circ = 0.018$  kJ/mol). The same technique was repeated on five other essential oils (cinnamon bark oil, caraway seed oil, spearmint leaf oil, peppermint leaf oil and anise seed oil) with the same trend in results, which demonstrates this novel process can be used for the extraction and recovery of the main compounds of interest present in essential oils.



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## ANALYSIS OF NSAIDs RESIDUES IN WATER BY SPME-GCxGC-TOF-MS

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Recently, the residues of non-steroidal anti-inflammatory drugs (NSAIDs) are studied as emerging pollutants in water which enter the environment while they are manufactured, during improper disposal of expired or unused drugs and also through human and animal excretion. Mostly the analysis of NSAIDs using gas chromatography (GC) is done by incorporating derivatization techniques such as methylation and other methods to make them volatile and heat resistant. In this work, the selectivity of various solid phase micro extraction (SPME) fibers to extract NSAIDs without derivatization was studied. The extracted NSAIDs were then analyzed by GCxGC coupled to time of flight mass spectrometer (TOF-MS) to study the chromatographic selectivity of GCxGC which separates the analytes in two dimensions where a different combination of columns will be evaluated. The NSAIDs will be separated using the selectivity and high sensitivity of GCxGC-TOF-MS. Upon analysis, this method can also be applied to determine the NSAIDs in complex matrices such as urine, blood for clinical toxicology for trace level analysis.

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## THE EXTRACTION OF STEROIDS FROM WATER USING QUECHERS AND SPME SAMPLE PREPARATION WITH GC-MS/MS ANALYSIS

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Extraction techniques are plentiful; however, determining which technique to implement for analysis can be difficult. It was the goal of this study to briefly investigate and compare the extraction of steroids from water using QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) and SPME (solid phase microextraction). QuEChERS is a liquid-liquid extraction combined with a dispersive solid phase extraction (d-SPE) cleanup, removing matrix interferences that may be present. The QuEChERS literature QuEChERS is primarily focused on the extraction of pesticides from food products using liquid chromatography (LC). This study looked to expand the application of QuEChERS using GC for 7 steroids: diethylstilbestrol, praesterone, methandriol, estrone, estradiol, mesterolone, and boldenone.

The QuEChERS results were compared to those using SPME, a comparison that is not present in the literature. For QuEChERS, the pH (6.0), salt amount (500mg NaCl and MgSO<sub>4</sub>), and organic solvent type (acetonitrile) were all optimized. In using SPME, the pH (8.0), salt amount (2.15g NaCl), water amount (8.5mL), and extraction time (60 minutes) were all optimized using a PDMS/DVB fiber [1]. An optimized multi-reaction monitoring method using GC-MS/MS was prepared for the 7 steroids and used in comparing the detection levels of each extraction method. The lowest level detected for QuEChERS was 5ppm; whereas SPME was able to detect much lower levels, down to 500 ppt. The reason for these detection differences will be discussed as will future work to be performed.

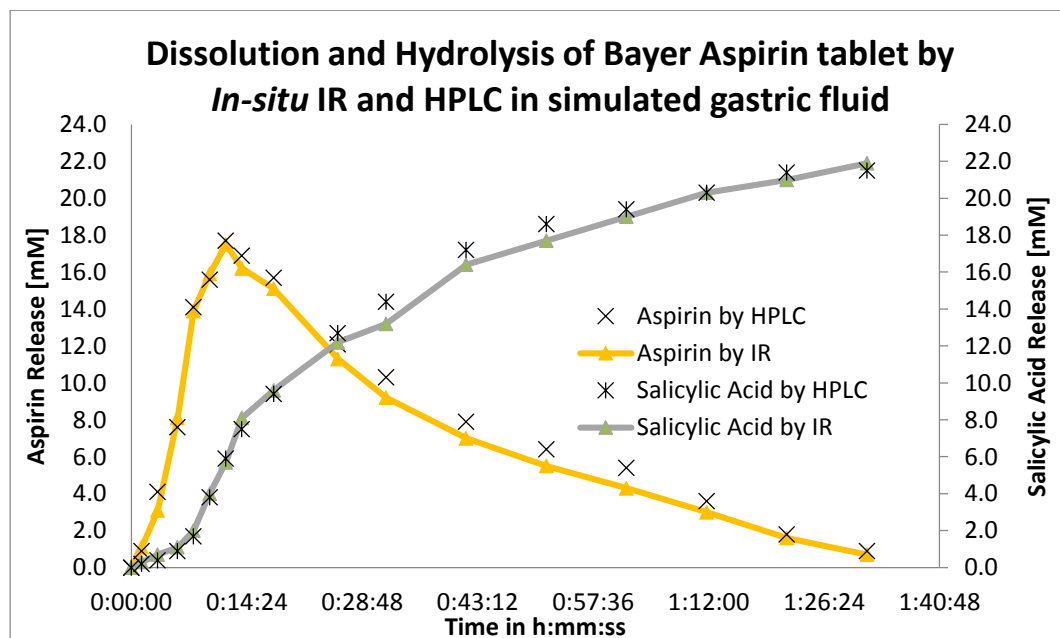
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## UNDERSTANDING THE DYNAMIC PROCESS OF DISSOLUTION AND HYDROLYSIS OF ASPIRIN BY ATR-FTIR

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Dissolution studies are critical tests for measuring the performance of a drug product. In the past few years, the importance of the dissolution test has increased. Using in-situ ATR/FTIR spectroscopy we developed a methodology of analyzing and monitoring dissolutions of pharmaceutical APIs. The accuracy of this technique was found to be  $\pm 3\%$  relative to HPLC and UV. In this presentation we discuss a dynamic analysis of the dissolution and subsequent hydrolysis of aspirin by ATR/FTIR. This technique allows real time analysis of the behavior of aspirin under simulated physiological conditions (pH 1.2, 4.5, 6.8) as aspirin ( $1205\text{ cm}^{-1}$ ) and salicylic acid ( $1388\text{ cm}^{-1}$ ) are detected as separate and distinct peaks in the IR. An example of the analysis is shown in figure below where 325 mg aspirin is dissolved/ hydrolyzed in 100 mL of pH 1.2 simulated gastric fluid in a period of 2 hr. This technique suggests a future potential for real-time studies of dissolution and hydrolysis of other pro-drugs.



## **APPLICATION OF IONIC LIQUID COLUMNS TO THE ANALYSIS OF FLAVOR AND FRAGRANCE COMPOUNDS**

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Traditional, polar (polyethylene glycol/wax) stationary phase gas chromatography columns pose challenges for flavor and fragrance analysis: thermal instability at high temperatures, unchanging selectivity, and short shelf life. Recently, capillary columns using ionic liquids as stationary phases have become available. Ionic liquid columns offer a potential combination of high polarity and high temperature stability. Performance of an SLB-IL60 column will be compared to a traditional wax column, with focus on elution pattern, resolution, and thermal stability, demonstrating the applicability of ionic liquid columns to the flavor and fragrance industry, specifically by comparing the retention behavior of flavor and fragrance compounds on ionic liquid and wax stationary phases. In addition, a unique natural product extract analyzed using GCxGC-TOF-MS equipped with an ionic liquid column in the first dimension will be demonstrated. Extraction methods will be compared to obtain an extract with an odor profile comparable to the natural product.

## SEPARATION OF ETHANOL- WATER MIXTURES USING MASS SEPARATING AGENTS

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Ethanol is a very popular alcohol used in many industries such as alcohol-consumers and biofuels. Although ethanol is a very high demand, its production is limited and it is easily miscible with other liquids, such as water, causing ethanol to become impure. Since ethanol that is used in the industries is desired to be greater than 97% pure, it is crucial to purify ethanol using most efficient method. Because ethanol easily mixes with water, ethanol-water mixture was chosen to conduct the studies of ethanol separation. One of the popular separation methods is separation using mass separating agents (MSAs). Although  $K_2CO_3$  is one of the popular MSAs used to separate ethanol-water mixture, it does not purify ethanol completely and therefore another MSA should be used in order to separate ethanol from water. Newly discovered MSA – Potassium Sodium Tartrate (PST), separates ethanol and water into two separate layers after it is added to the mixture and solution is at 60°C. The kinetic study of the process is crucial in order to determine the effectiveness of the reaction and determining whether the given MSA can be potentially used in industry. Therefore determining thermodynamic parameters such as the rate constant, Gibbs' free energy, enthalpy, and entropy will show the behavior of the overall reaction.

## DISSOLUTION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS USING INFRARED SPECTROSCOPY

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A comparison study was conducted to look at the formulation of three brands of naproxen sodium. These brands included Bayer Aleve®, CVS All Day Pain Relief and Walgreens All Day Pain Relief. The active and inactive ingredients were the same yet the size and shape of the tablets differ among the three brands. S-naproxen was extracted from the tablets and evaluated by GC-MS to determine the purity of naproxen in the tablets. Dissolution was monitored by an IR probe for eight hours while using 0.1M phosphate buffer pH 7.4, 0.05M phosphate buffer pH 4.5 and simulated gastric fluid pH 1.2 as the medium. The percent dissolved was calculated for each brand and times vary depending on the pH level. All three brands dissolved one hundred percent in an eight hour period. A kinetic study was completed for each brand at all three pH levels. It cannot be determined if a first order process took place at the beginning of the dissolution process. However as time evolved the dissolution profile resembled a zero-order process.

