University of Connecticut

School of Pharmacy

2011

Research Symposium

Wednesday, September 21, 2011

Morosko Student Lounge

School of Pharmacy

1:00 p.m. - 3:00 p.m.
This research symposium is part of the Society of Pharmacy Research’s larger mission designed to acquaint Pharm.D. and undergraduate students with research-oriented opportunities in the field of pharmacy. In collaboration with Rho Chi, it is our hope that this event will heighten student awareness of research conducted at the School of Pharmacy. Students will be able to discuss research, ask questions, and develop a greater understanding of recent past and current research endeavors.

The authors of the abstracts in these proceedings have attempted to summarize a great deal of research efforts in a few, short paragraphs. For many who are new to research, the material in the following abstracts may be difficult to understand. Perhaps the best way to approach this abstract booklet is to skim through it and find the subjects that interest you most. Then, go to the authors and ask them to explain their work. There are very few scientists who do not delight in talking about their research.

This event is made possible by a generous contribute from the Dean’s office and we wish to extend our sincere appreciation to Dean McCarthy and Associate Dean Hubbard for their continued support. Thanks goes to all of the faculty and students at the University of Connecticut School of Pharmacy who were able to participate in the 2011 School of Pharmacy Research Symposium.
# Proceedings of the 2011 School of Pharmacy Research Symposium

## Pharmaceutical Sciences

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Pharmaceutical Sciences

High Payload Dual Therapeutic-Imaging Nanocarriers for Triggered Tumor Delivery

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\textbf{Purpose}
To engineer high payload dual therapeutic-imaging dexamethasone palmitate (DEX-P) nanoparticles (NPs) and image their biodistribution and tumor uptake \textit{in vivo} using single photon emission computed tomography (SPECT).

\textbf{Methods}
High payload DEX-P NPs were prepared using the nanotemplate engineering technology. The prepared NPs were characterized in terms of particle size and drug deposition using gel permeation chromatography (GPC). The conversion of DEX-P to parent drug, DEX, and the release of NP components including drug, lipid and radioactive metal were investigated \textit{in vitro}. The uptake of DEX-P NPs was studied using human lung epithelial carcinoma A549 cells. \textit{In vivo} imaging of \textsuperscript{111}In-labeled NPs was conducted using SPECT, and a biodistribution study was performed.

\textbf{Results}
The prepared NPs were uniform in particle size and all compositions including drug, lipid and the radioactive metal. The high esterase activity in mouse plasma and esterase solution rapidly converted the prodrug DEX-P to DEX, while almost no degradation was observed in human plasma. SPECT/CT images showed significant tumor accumulation of NPs at 5 h post-injection. Although there was high liver uptake of the nanoparticles, no liver toxicity was observed based on histology and blood test. In carboxylesterase-deficient athymic mice (Es\textsuperscript{1+/1}/SCID), the pharmacokinetics of the drug was different from athymic nu/nu mice within 3 h after administration, but similar afterward which indicated that some esterase activity remained in these mice.

\textbf{Conclusion}
High payload nanoparticles containing an ester prodrug, DEX-P and an imaging agent, \textsuperscript{111}In, were developed for delivering DEX specifically to tumors triggered by high esterase activity and tracking the nanoparticles by SPECT. Radiolabeled drug-containing NPs may be used in image guided drug delivery and be applied to the development of personalized medicine through pharmacokinetic-pharmacodynamic modeling.
Predicting the Range of Absorption for Compounds that Precipitate in the GI Tract Using a Novel Biopharmaceutical Model

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PURPOSE: A biopharmaceutical model was developed to predict the range of absorption for compounds that precipitate in the GI tract. The model was utilized to investigate the influence of various factors (i.e., intestinal volume dose) on the extent of oral absorption and to determine the importance of each factor on the fraction absorbed.

METHODS: A mathematical model was constructed to relate a typical in vitro amorphous drug dissolution-time profile to absorption in vivo. The in vitro dissolution profile was sparingly parameterized using dissolution volume, plateau concentration, peak concentration and time to peak concentration. Dose, intestinal volume and first order absorption rate constant were also considered in the model. Equations for three in vivo cases were derived to consider concentration-dependent and time-dependent precipitation and for permeation-limited and dissolution-limited absorption. The in vivo absorption was calculated for several intestinal volumes, doses, first order absorption constants, in vitro peak concentrations and times to peak.

RESULTS: The use of the three different cases resulted in determination of an absorption range rather than a single value. As expected, the amount absorbed was influenced greatly by the absorption rate constant and the time at which in vitro peak concentration was reached. However, the in vitro peak to plateau concentration ratio did not correlate with fraction absorption. Instead, in vitro the peak concentration multiplied by time to peak correlated with the extent of absorption. Also, it was shown that the volume available for dissolution in the GI tract dramatically affected the amount absorbed. This is true particularly for low dose drugs in which the majority of the dose can dissolve and be absorbed before precipitation occurs.

CONCLUSIONS: A new biopharmaceutical model was used to estimate an absorption range for compounds that precipitation in the GI tract. The model allowed us to find that in vitro peak concentration, time to peak, dose and intestinal volume all influence the extent of absorption for amorphous compounds.
Biomarkers for Nasal Response to Naphthalene Vapor

Joseph Cichocki, Dr. John Morris, Dr. Laura Van Winkle, and Dr. Alan Buckpitt

Naphthalene (NA) is a nasal carcinogen in the rodent inducing significant increases in nasal olfactory neuroblastomas and nasal respiratory adenomas in rats chronically exposed to 30 ppm NA. The mode of action relative to carcinogenesis is unknown although activation by cytochrome P450 is thought to represent a critical step and regenerative cell proliferation following cytotoxicity is likely of importance. The current study is aimed at examining mechanistically relevant biomarkers for acute response to NA that can be applied to examine the regional (e.g. respiratory versus olfactory mucosa) nasal response to this agent. Towards these ends biomarker levels were examined in animals exposed for 1, 2 or 6 hours to 15 or 30 ppm NA. Oxidized and reduced glutathione (GSSG, GSH) levels were assessed to provide markers of oxidative stress and/or electrophile production in tissues dissected from specific regions of the rat nose. In a novel technique, nasal lavage was performed following NA exposure with fluid containing ethidium homodimer-1. Ethidium incorporation into nuclei provides an index of nasal cytotoxicity. Nasal GSH levels were rapidly depleted by naphthalene and reached steady state within 1 hour of exposure. At 30 ppm, nasal respiratory and olfactory mucosal GSH levels were depleted to 40% and 80% of control, respectively. GSSG/GSH ratios were not markedly altered. These results suggest NA is activated to an electrophile in both respiratory and olfactory epithelium, but that marked oxidative stress does not occur. Concentration dependent nuclear ethidium staining was observed in nasal epithelium of rats exposed to 15 or 30 ppm NA indicating a cytotoxic effect of NA. These biomarker methods provide region-specific assessment of nasal responses to NA. Regional tissue dissection and histochemical mapping of ethidium incorporation may provide useful tools to examine site selective responses to this carcinogenic vapor.
Effect of Formulation Parameters on siRNA Delivery using Anionic Lipoplexes

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ABSTRACT SUMMARY

The objective of this work was to prepare, evaluate and optimize anionic lipoplexes for efficient and safe delivery of siRNA to a breast cancer cell line (MDA-MB-231). Anionic liposomes (prepared using DOPG: 1,2-dioleoyl-sn-glycero-3-phospho-(1’-rac-glycerol), and the fusogenic lipid DOPE: 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine) were complexed with calcium and siRNA to prepare the anionic lipoplexes. Various formulation parameters (liposome composition, lipid concentration and calcium concentration) were evaluated and optimized. Lipoplexes with a composition of 1 µg/mL lipid (40:60 mol% DOPG:DOPE), 10 nM siRNA and 2.4 mM calcium showed high silencing efficiency (29.22 ± 5 % GFP expression) which was comparable to that obtained with cationic lipoplexes (Lipofectamine 2000, LF2000) (25.98 ± 2% GFP expression). Furthermore, anionic lipoplexes were far safer than LF2000 lipoplexes as determined by cell viability studies. The characterization studies indicated that particle size and surface charge were not critical factors in determining the silencing efficiency of anionic lipoplexes.

INTRODUCTION

siRNA discovery (1998) has accelerated the development of treatments for several genetic disorders such as respiratory syncytial virus, Huntington’s disease and cancer [1]. However, siRNA delivery has always been a key challenge due to its enzymatic instability, low cellular uptake and inability to escape from endosomes on its own. siRNA delivery has been enhanced using cationic liposomes that protect the siRNA against enzymatic degradation as well as facilitate cellular uptake and endosomal escape [2]. However, the toxicity of cationic liposomes remains an unresolved issue [3]. Anionic liposomes, on the other hand, are much safer due to the absence of positive charge (root cause of toxicity), and may be a suitable delivery vector for siRNA. In the present work, anionic lipoplexes were prepared using anionic liposomes (DOPG and DOPE) together with calcium and siRNA. Different formulation parameters were evaluated to optimize the lipoplexes for safe and efficient siRNA delivery. The lipoplexes were characterized for particle size and surface charge.

EXPERIMENTAL METHODS

Anionic liposomes were prepared with different DOPG/DOPE molar ratios using the film hydration method followed by extrusion to obtain small unilamellar vesicles with an approximate size of 100 nm. Lipoplexes were formulated by complexing these liposomes with siRNA (anti-eGFP, Ambion) using calcium chloride. Different liposome composition as well as lipid and calcium concentrations were investigated in the optimization studies. Experiments to determine silencing efficiency were performed on MDA-MB-231 cells stably transfected with eGFP, in the presence of serum (10%). GFP expression was obtained, using a microplate fluorimeter (488 nm/525 nm), 48h post-
incubation of the cells with the lipoplexes, The readout was normalized for protein content as obtained using standard BCA assay. Percentage GFP expression was obtained by considering untreated cells as 100%. Ca+siRNA mixture and siRNA alone were used as negative controls while LF2000 (Invitrogen) was used as the positive control. Cell viability studies were performed using Cell Titer-Blue assay (544 nm/590 nm) with 2 h incubation at 37°C. Percentage cell viability was obtained after normalizing by untreated cells. Particle size and zeta potential studies were performed using a Malvern Zetasizer ZS90. Samples were measured in triplicate following appropriate dilution.

RESULTS AND DISCUSSION

Transfection Studies

Transfection studies of anionic lipoplexes prepared with different liposome composition (DOPG:DOPE molar ratio) showed (Fig.1) increased protein knockdown (low GFP expression) with increase in DOPG content from 10 to 40 mol%. (2 µg/ml lipid, 2.4 – 3.3 mM Ca, 10 nM siRNA). There was no further increase in protein knockdown with increase in composition above 40 mol%, indicating that saturation had been reached. The Ca+siRNA control showed low knockdown efficiency (high GFP expression) for all calcium concentrations investigated.

![Graph showing effect of calcium concentration on GFP expression with different DOPG content.](image)

**Fig.1:** Effect of liposome composition (10-80 mol% DOPG) on silencing efficiency of anionic lipoplexes composed of 2µg/mL lipid and 10 nM siRNA with 2.4 to 3.3 mM Ca concentration, in breast cancer cells.(n=3)

When lipoplexes (40% DOPG, 2.4 mM Ca, 10 nM siRNA) prepared with different lipid concentrations (0.5-32 µg/mL) were evaluated, maximum silencing efficiency was observed at 0.5 µg/mL (Fig.2a). High lipid concentrations (such as, 32 µg/mL) slightly lowered the silencing efficiency (high GFP expression) and this is probably due to the formation of large aggregates. It is known that large lipoplex particles have low cellular uptake [4]. Particle size analysis (Fig.3b) indicated an increase in lipoplex size with lipid concentration which supports the above hypothesis. However, lipoplexes prepared at 0.5 µg/mL were extremely unstable showing rapid growth in particle size with time. Accordingly, a lipid concentration of 1 µg/mL was selected. In the case of LF2000 lipoplexes, the silencing efficiency increased as the concentration was increased from 0.5 to 1 µg/mL (lower GFP expression) but decreased at a concentration of 8 µg/mL.
Further increase in LF2000 concentration resulted in cell death due to extreme toxicity and therefore the experiment was terminated. The safety of the lipoplexes was further evaluated using Cell Titer-Blue assay. IC50 value for 50% cell viability was obtained as 22.9 for LF2000 lipoplexes but was greater than 100 µg/mL in case of anionic lipoplexes.

![Graph](a)

**Fig.2: (a)** Effect of lipid concentration on silencing efficiency of anionic lipoplexes compared to LF2000 lipoplexes. **(b)** Effect of calcium concentration in anionic lipoplexes compared to a Ca+siRNA mixture. (n=3)

According to **Fig.2b**, it was determined that the silencing efficiency of the lipoplexes increased with increase in calcium concentration up to 2.4 mM. The Ca+siRNA control also showed an increase in silencing with increase in calcium concentration. However, the silencing efficiency was low compared to that obtained with the anionic siRNA lipoplexes. The lipoplexes have additional features which improve silencing efficiency such as protection from enzymatic degradation and endosomal escape (facilitated through the presence of the fusogenic lipid DOPE).

The optimal lipoplex formulation (40 mol% DOPG, 1 µg/mL lipid concentration, 2.4 mM Ca and 10 nM siRNA) had a silencing efficiency similar to that of LF2000 of approximately 70% (29.22 ± 5 % and 25.98 ± 2% GFP expression, respectively) **(Fig.2).**

**Characterization Studies**

The particle size of the lipoplexes was almost three times (300 nm) that of the liposomes (100 nm) with a reduction in surface charge from -50 to -60 mV range down to -20 to -30 mV range following complexation. The liposome composition did not affect...
the particle size but there was a small change in the surface charge associated with a change in the DOPG content (Fig.3a). However, the lipid concentration did affect the particle size, increasing the lipoplex size from 300 nm at 0.5 µg/mL to as high as 1200 nm at 32 ug/mL. Interestingly, this change in particle size caused only a small reduction in silencing efficiency of approximately 10%.

![Graph (a)](image1)

**Fig.3:** Effects of: (a) liposome composition; and (b) lipid concentration on particle size and surface charge of anionic lipoplexes (n=3).

**CONCLUSION**

The optimized anionic lipoplex system resulted in high silencing efficiency with no cytotoxicity in a breast cancer cell culture model and shows promise as a potential delivery vector to safely and efficiently deliver therapeutic siRNA. Additionally, in these studies, particle size and surface charge were not determinants of silencing efficiency.

**REFERENCES**

Variation in Product Temperature and Drying Time within a Lyophilized Batch during Primary Drying

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It is current practice to develop a design space by defining the optimum operating conditions for primary drying and setting conservative operating ranges to assure “zero defects”. If, in fact, there are never any failures, the design space is probably set too conservatively. A six sigma strategy has 3.4 defects per million. When producing 10 billion units of a product over its lifetime, a six sigma strategy would predict 340,000 defective products. We aimed to determine the relationship between the design space for primary drying and the acceptable level of defects in a batch.

An in silico model has been developed to propagate the variances in several operating conditions (i.e., shelf temperature and fill volume) along with known variances in product resistance and heat transfer coefficient through to the variation in the time to complete primary drying and the maximum product temperature during primary drying.

As an example, the design space is defined here as the primary drying cycle time and mean shelf temperature that assure a certain level of dry product that does not exceed a temperature of -32.3°C. The area of the design space shrinks as (1) the acceptable level of defect is reduced and (2) the variances of input parameters increase.

Since the variance in product resistance, in particular, is known to change during scale-up, adjustments in the design space are required to achieve the same level of defect.
Opposite Effects of Polyols on Antibody Aggregation:
Thermal versus Mechanical Stresses

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Purpose: To investigate the effect of polyols on the physical stability of a MAb under thermal and mechanical stresses.

Methods: Thermal stability of MAb-U was analyzed using DSC in the presence of 10% w/v trehalose, glycerol, ethylene glycol and buffer solutions. High temperature accelerated stability studies were performed by incubating MAb-U in polyol and buffer solutions at 65°C for 5 days. Mechanical stress studies were conducted by shaking MAb-U in polyol and buffer solutions at 200 rpm for 5 days. SE-HPLC was used to calculate the percent aggregation obtained before and after the incubation and shaking periods. Surface pressure was determined using a Du-Nuoy ring surface tensiometer.

Results: Highest increase in the T_m of MAb-U was observed in trehalose, followed by glycerol, whereas ethylene glycol decreased the T_m. High temperature incubation results directly correlated with the trend in T_m of MAb-U. The trend observed in the order of increasing aggregation was trehalose < glycerol< buffer, consistent with the mechanism of preferential exclusion. However, higher surface pressure was observed for MAb-P in the presence of polyols than buffer, which implies an increase in the adsorption tendency of proteins in the presence of such polyols. Hence, an inverse correlation was observed between shaking and the T_m of MAb-U with addition of trehalose resulting in highest aggregation.

Conclusions: From the results of this study, it is deduced that polyols can have dual and opposite effects on the physical stability of proteins. Polyols increase the conformational stability of a protein by increasing its chemical potential upon preferential exclusion. An increase in the chemical potential of a protein also results in an increase in its propensity to adsorb at the air/water interface in order to reduce its chemical potential. This decreases the physical stability of proteins as interfacial adsorption can result in aggregation. Since proteins encounter different interfaces during the development process and the storage temperatures of proteins are much lower than their T_m, it is predicted that the use of polyols can be destabilizing for the aqueous protein-polyol formulations.
Role of Conformational and Solution Phase Stability in Physical Stabilization of Antibody-Polyol Formulations

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Purpose: To investigate the effect of polyols on the conformational stability of monoclonal antibodies and their tendency to adsorb onto the air/water interface. Methods: The effect of polyols on the solution phase stability of mAb-U and P upon agitation was investigated by shaking and stirring the solutions. SE-HPLC was used to determine the percent aggregation obtained upon shaking and stirring. The surface pressure of mAb-P and U in polyol solutions was determined using a surface tensiometer to mechanistically understand the effect of polyols on the tendency of mAbs to adsorb onto the air/water interface. Conformational stability of the mAbs in different polyols was analyzed by determining their T_m using DSC. The mechanism of conformational stabilization imparted by polyols was studied by calculating the polyol activity coefficients. Results: Upon shaking of mAb-U solutions, higher aggregation was observed in the presence of trehalose, sucrose and glycerol than either buffer or ethylene glycol. For mAb-P, trehalose, sucrose and glycerol showed lower aggregation than buffer and ethylene glycol. Since mAb-U is more hydrophobic than mAb-P, the opposite behavior highlighted the role of surface hydrophobicity of a protein affecting its solution phase stability. Upon stirring of mAb-P solutions, it was observed that thermal stabilizers, sucrose, trehalose and sorbitol cause higher aggregation than the thermal destabilizer, ethylene glycol. However, highest aggregation was observed in the solution without any polyol (buffer). This could be attributed to the two agitation methods exerting different type of stress on the mAb leading to different mechanisms of aggregation. Highest aggregation of mAb-P upon stirring was observed at pH 9.3 followed by pH 7.0 and least aggregation was seen at pH 5.0, pointing towards the contribution of protein surface charge and its solubility in the bulk affecting its adsorption onto the air/water interface. Surface pressure results showed a higher surface pressure of mAb-P and U in the presence of sucrose than buffer indicating an increase in the propensity of the mAb to adsorb onto the air/water interface in the presence of polyols. The trend of the calculated polyol activity coefficients correlated with the effect of the polyols on the thermal stability of mAb-P and U. Preferentially excluded polyols, trehalose and sucrose, showed a higher positive deviation from ideality (indicating stronger interactions with water than the protein) and ethylene glycol showed the least positive deviation amongst all the polyols studied. Conclusions: Physical stability of a protein is dependent on both its conformational stability and its tendency to remain in the solution phase. Polyols increase the conformational stability by decreasing the chemical potential of water. However, at the same time they also increase the chemical potential of proteins in the solution phase, which can be translated into an increase in its adsorption onto the air/water interface. The tendency of a protein to adsorb onto air/water interface is also determined by its surface hydrophobicity and the hydrophobicity of the polyol in solution.
Numerical Simulation and Optimization of Grinding in Hammer Mill

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Particle size reduction of dry material by mechanical means, such as milling, is an important operation for pharmaceutical, agricultural, food and paper industries. Size reduction is generally achieved by particle fracturing under the action of applied energy. Knowledge of particle flow, granular mixing and segregation, and size reduction in a hammer mill is thus critical to optimize the design and operation of such equipment.

Milling experiments were performed using sugar non pareils in Wiley Mill. We numerically model a pilot-plant scale hammer mill using a Discrete Element Method (DEM) to study the breakage and kinematics of the particle motion within the hammer mill. DEM based numerical simulation of particle dynamics was performed in a hopper configuration similar to our experiments. Simulations were carried out to study the effect of mill speed on kinetic energy of particles. In addition, parametric study was performed to understand the effect of hammer speed (rotational), feed rate, hammer-wall tolerance, and specific exit classification conditions on the final product size distribution. Below a critical hammer tip speed, a blending action rather than comminuting is observed. Increase in hammer tip speed causes higher frequency of impact of particles per unit time and higher specific energy of impact resulting in generation of much finer end product. With respect to feed rate, a narrow size distribution was obtained at lower feed rates. The feed rate determines the hold up of material in sizing chamber and hence energy required for size reduction. At low hold-up, longer path lengths are achieved by particles resulting in higher impact velocity and hence a finer size distribution. At higher hold up the number of collisions is high, but the kinetic energy per particle is low leading to poor breakage probability. Particle shape analysis revealed fragmentation to be the dominant mechanism of size reduction at higher speeds. We observe that both the specific kinetic and strain energy of the particles (colliding with hammer) increase as the impact point becomes closer to the hammer-tip. The net mill power is also derived from the hammer geometry, hammer tip velocities and impact forces. More simulation results will be carried out to study to describe powder flow in hopper, and estimate the induced impact stress and specific energy of fragmentation (impact).
High Shear Wet Granulation of fast flo lactose: Process Optimization

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A major concern of the pharmaceutical industry is to ensure content uniformity. Therefore, it is of utmost importance to find ways to produce drugs in large, uniform quantities. One of the mixing methods used to achieve this in the pharmaceutical industry is high shear wet granulation. In this method, fine powder particles agglomerate under influence of binder at high shear provided by action of impeller and chopper rotating at high speeds. Such size enlargement ensures uniform product flow with minimal losses and inhalational hazards. Different parameters that affect how well the product is mixed include: liquid addition rate impeller speed, chopper speed, fill volume, and viscosity of the liquid binder. Our research intends to optimize this process in a standard granulator (KG5, Key International Inc) in lab scale (1L and 5L vessel size). The performance of granulation is measured by recording the granule size distribution, moisture content and strength of the dried granules. Amperometric curves of granule strength against time were obtained for different parameters at 3 different levels. All parameters were found to affect the process significantly. A liquid addition rate of 6.5 mL/min is a setting that is ideal for adding water so that the product doesn't become too wet too fast and so that the process doesn't take too long. The impeller and chopper speeds found most useful are 250 rpm and 3000 rpm respectively. Higher speeds corresponded to higher adhesion, as measured by sharp deviations in the amperometric curves, while lower speeds increased the run time. At these speeds, the product is mixed without too much adhesion to the walls and lid of the compartment. Water is the main liquid binder used in the study but other solutions of a greater viscosity also yielded results where adhesion was reduced. The granule strength also increased for high viscosity binders. The ultimate goal is to build a theoretical model which fits the experimental data so that typical production cycles are optimized quickly saving both time and financial resources.
Triboelectrification, or electrostatic charging through frictional contact, of granular material is a well known concern in many industries. It can cause adhesion surfaces during powder flow, packing problems in industrial silos and hoppers and cause aggregation in dry powder inhalers. More importantly, such electrostatic charging is known to cause significant explosion hazards. The purpose of this study is to determine the influence of various factors affecting Triboelectrification and subsequently charge mitigation through various additives. The factors studied were particle type (lactose non-pareils and glass beads), particle size (50µm, 1mm, 3mm), particle mass (5g, 15g, 30g, 60g) surface type (polyvinyl chloride and aluminum chute and hopper), angle of inclination (15°, 25°, 30°, 45°) additive type (ascorbic acid, sodium bicarbonate, magnesium stearate and stearic acid) and additive concentration (0.5%, 1%, 2%, 5%, 10%, 15%). Particles were loaded onto the hopper and mixed with the excipient, deionized, then allowed to flow down the deionized chute at a fixed angle and the charge was measured in a Faraday’s cup under ambient conditions. We observed increase in charging on decreasing contact angles and lowering particle size. This is due to greater contact between particle and the surface. As mass increased, more charge was accumulated but variability also increased. Least variability occurred when 30g of particles of 1mm size was used at a 30° angle and these were used for charge mitigation studies. The particle tribocharging was in accordance with the calculated work functions. Maximum reduction was observed with compounds having high dipole moment (magnesium stearate>sodium bicarbonate>ascorbic acid>stearic acid). Also, charging of the powders decreased with increase in concentration of the excipients. This is explained due to a combination of effects arising out due to moisture adsorption by the excipients, which dampen charges; their intrinsic work function (calculated in silico) and their contact (determined by measurement of surface area using BET adsorption isotherm). The surface purity of the additives was characterized through XPS measurements.
Unraveling the mystery of ‘dynamic duo’: Src SH3 & Integrin β3 complex

Katyal Priya, Deshmukh Lalit, Vinogradova Olga

Src kinase is a member of Src tyrosine kinases family that plays an important role in integrin signaling, regulating cytoskeletal organization and modeling. Previous in-vivo studies have revealed that SH3 domain of Src directly interacts with the cytoplasmic tail (CT) of β3, particularly with the last four residues of its C-terminus (YRGT). In this study we have exploited biomolecular NMR in order to understand the underlying molecular interactions responsible to explain the interactions observed. Results from NMR titration experiments suggest that the two motifs, YRGT and the membrane proximal region of integrin β3 CT, bind to SH3 domain of Src under aqueous conditions. However, in membrane mimetic environment, hydrophobic interactions with membrane proximal region are prevented while binding with YRGT remains unaffected. An interesting observation found was that phosphorylated β3 did not bind and concluded that tyrosine phosphorylation is not required to realize binding. These are the initial results of the in-vitro studies, performed for the first time to demonstrate the direct interaction of integrin β3 with Src SH3. Further structural characterization of this interaction would help unravel the molecular details of the complex binding phenomena. This study has a lot of potential in designing novel therapeutics for treating neoplasia and thrombosis.
Identification and Characterization of Transcriptional Control Elements Regulating a Novel Receptor Mediated Signaling Regulator, TNIP1

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TNF alpha interacting protein 3 interacting protein 1 (TNIP1) is a novel nuclear receptor interacting protein, isolated and characterized as a corepressor of retinoic acid receptors and peroxisome proliferator-activated receptors in our lab. In addition to its role as a nuclear receptor coregulator, TNIP1 has been shown to regulate a variety of other receptor-mediated events as diverse as programmed cell death and cell cycling stemming from TNF and EGF signaling, respectively. Changes in TNIP1 expression levels are likely to impact the biological endpoints of these different pathways. As the importance of TNIP1 becomes more apparent, it is crucial to determine what controls its expression levels, as can be determined by a study of its promoter. We isolated ~6kb of the human TNIP1 promoter and examined it both in silico and experimentally for transcriptional control elements with an eye directed at constitutive and inducible elements. Sequence analysis by MatInspector predicted two specificity protein (Sp) sites in the proximal region of the promoter and multiple NF-κB sites in both the proximal and distal regions of the promoter. We predict the Sp family of transcription factors is responsible for much of TNIP1’s constitutive activity and NF-κB for its inducible expression. Transcriptional activation studies revealed NF-κB, Sp1 and Sp3 positively regulate TNIP1. Furthermore, EMSA and ChIP demonstrated the physical association between NF-κB, Sp1, Sp3 and specific regions of TNIP1 promoter. Decreased Sp1 protein via siRNA or Sp binding to cognate sites by mithramycin decreased TNIP1 mRNA while the potent NF-κB activator TNFα increased TNIP1 expression. In summary, we have demonstrated that Sp1 and Sp3 contribute to the constitutive regulation of TNIP1 promoter through two sites proximal to the transcription start site and that NF-κB contributes to the inducible regulation of TNIP1 via two distal sites. Changes in endogenous Sp or NF-κB levels or pharmacological control of their activity would be expected to affect TNIP1 expression, which, in turn, could ultimately regulate TNIP1-related biological endpoints such as cell death, proliferation, and inflammation, and more globally, diseases such as psoriasis and rheumatoid arthritis.
Identification of the Transcriptional Start Site(s) of the Human TNIP1 Gene

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TNFAIP3 interacting protein 1 (TNIP1) is involved in multiple cellular processes. Our laboratory characterized it as a nuclear receptor (NR) corepressor, where Peroxisome Proliferator Activated Receptor (PPAR) and Retinoic Acid Receptor (RAR) activity are repressed. These two NR's are involved in regulation of metabolism, development and skin homeostasis. Other groups have determined TNIP1 to inhibit NF-κB activation and TNF-α induced apoptosis, which are vital mediators in inflammation and programmed cell death. Since TNIP1 regulates various key processes in the cell, determining what regulates TNIP1 transcription levels is crucial.

Characterizing TNIP1’s promoter sequence is essential in determining what regulates its transcription. The TNIP1 promoter has binding sites for RAR, PPAR, NF-κB and Specificity Protein 1 (SP1) within the approximately 6 kB sequence upstream of the protein coding sequence. In addition to determining transcription factor response elements, characterizing the transcriptional start site (TSS) is also important in knowing how TNIP1 transcription is regulated.

TNIP1 mRNA consists of 18 exons with the coding sequence from exon 2 to 18. Exon 1 and part of 2 are untranslated. It has two alternative first exons due to splicing variations. The full TNIP1 gene sequence has been elucidated by NCBI's AceView online website using cDNA, mRNA and EST fragments. The TSS, however, has yet to be characterized for both alternative transcripts. Furthermore, the TNIP1 promoter lacks the canonical TATA box. Typically, genes lacking the TATA box have varying TSS.

Using the RNA ligase mediated rapid amplification of 5’ cDNA ends (5’ RLM-RACE) method, we determined that TNIP1 has two alternative mRNA splice variants, giving rise to two alternative first exons. Both alternative exon 1’s contains multiple TSS. Excluding the MCF7 breast cancer cell line, all TSS mapped upstream of the initiator codon methionine. Moreover, one splice variant is located upstream of our known promoter region, suggesting TNIP1 has an alternative promoter. Supported by NIH Grant AR04866 (BJA)
Pharmacy Practice

Removal of *Saccharomyces boulardii* from a hospital formulary and the impact on *Clostridium difficile*-associated diarrhea (CDAD).

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Background: Probiotics, such as *Saccharomyces boulardii*, have been used to prevent CDAD without definitive data to support its use. For several years, Hartford Hospital administered a protocol to give all patients receiving intravenous cefepime, ceftazidime, ceftriaxone, cefuroxime, clindamycin, ciprofloxacin, or levofloxacin *S. boulardii*. The protocol was discontinued in December 2009 and *S. boulardii* was removed from the formulary. This study compares the rate of in-patient acquired CDAD before and after the removal of *S. boulardii* from the formulary.

Methods: Patients were included if they had a positive toxin test for *C. difficile* during the 13 months before (control group) or during the 13 months after (study group) the removal of *S. boulardii* from the formulary. Patients were excluded if they had diarrhea within 48 hours of hospital admission or admitted during the month in which *S. boulardii* was removed from the formulary.

Results: Age, ethnicity, and place of residence prior to admission were similar between the two groups. There were 167 cases of CDAD in the control group and 191 in the study group resulting in a rate of CDAD of 0.999 cases per 1,000 patient days in the control group and 1.039 per 1,000 patient days in the study group (P=0.42). Mean time from admission to the first positive toxin test was also similar 12.2 days in the control and 10.2 days in the study group (P=0.32). Patients with CDAD had similar utilization of a *S. boulardii* linked antibiotic 65.3% in the control compared to 66.5% in the study group (P=0.9).

Conclusions: Removal of *S. boulardii* from the hospital formulary did not result in an increase in the rate of CDAD.
Intravenous Hydralazine for Blood Pressure Management in the Hospitalized Patient

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**Background:** Intravenous (IV) hydralazine has been approved for the treatment of hypertensive emergencies for 40 years. Due to the observation of increased use in the hospitalized patient, we assessed the rationale for its use and the effects of administration.

**Methods:** Patients (n = 94) were identified between April and October 2010 from a daily list of all hospitalized patients who had an order for IV hydralazine entered into the computerized physician order entry system. Prescribers were unaware that the study was being conducted. Demographic and clinical information, including pre-treatment blood pressure (BP), change in BP and heart rate (HR) within 2 hours post-administration of hydralazine, concurrent anti-hypertensive medications, and adverse events were obtained.

**Results:** Mean age was 69±18 years, 48% were female and 89% had a history of hypertension. Hydralazine IV was administered 201 times at a mean dose of 11.4 ± 4.3 mg. Only 4 (2%) of patients had any evidence of an urgent hypertensive condition (symptoms, target organ injury). Baseline BP was 175/82 ± 25/16 mmHg and reduced by 24/9 ± 29/15 mmHg while HR increased by 4 ± 13 beats/min. Changes from baseline in BP were evaluated according to quartiles of baseline BP. Minimal change in BP was observed in the lower quartile (-3 ± 20 mmHg) while marked changes were observed in those with the highest quartile of baseline blood pressure (-35 ± 25 mmHg). Seventeen patients experienced an adverse event, including hypotension in 11/17 (64%).

**Conclusions:** Intravenous hydralazine is a commonly prescribed agent for non-urgent cases of hypertension in the hospitalized patient. Changes in systolic BP, while related to baseline BP values, are nevertheless, highly unpredictable. These data suggest that this agent should not be used in the most hypertensive patients in the hospital setting.
Cost-Effectiveness of Apixaban Compared to Aspirin for Stroke Prevention in Atrial Fibrillation

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Background: Apixaban is a new direct factor Xa inhibitor that, when compared to aspirin, reduces the risk of stroke by 63% without significantly increasing the risk of major bleeding. The objective of this model was to estimate the costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness of apixaban compared to aspirin in patients with atrial fibrillation (AF).

Methods: On the basis of the results from Apixaban Versus Acetylsalicylic Acid to Prevent Stroke (AVERROES) trial and other published studies, we constructed a Markov model to evaluate the costs, QALYs, and the incremental cost-effectiveness of apixaban 5 mg twice daily compared to aspirin 81-325 mg daily in patients with AF from a societal perspective. We ran our Markov model in a hypothetical cohort of 65-year old patients with a CHADS2 score of 2 and a low risk of bleeding with AF over 35 years or until death. Evaluated outcomes included costs in 2011 US$, QALYs, and incremental cost-effectiveness ratios (ICERs). Costs and outcomes were discounted at 3% per annum. One-way sensitivity analysis and second order Monte Carlo simulation were performed to test the robustness of the model’s results.

Results: The base-case analysis revealed total life-time costs per patient were $92,087 and $109,654 for apixaban and aspirin, respectively. The corresponding quality-adjusted life-years (QALYs) were 9.94 and 8.86 for apixaban and aspirin, making apixaban a dominant strategy. One-way sensitivity analysis showed that results were sensitive to changes in the baseline rates of stroke, and the monthly cost of moderate to severe stroke. In patients with a low risk of stroke (CHADS2 score 0), apixaban was no longer cost-effective with the ICER of $64,998 per QALY; however, in patients with a moderate risk of stroke (CHADS2 score 1) apixaban remained dominant. Monte Carlo simulation revealed that apixaban dominated aspirin in 93% of 10,000 iterations, while 99% of the iterations were cost-effective at a willingness-to-pay threshold of $50,000 per QALY.

Conclusion: In AF patients aged 65 years or older with a CHADS2 score of 2 and a low risk of bleeding who are unsuitable for warfarin therapy, apixaban is likely an economically dominant alternative to aspirin.
Cost-Effectiveness of Rivaroxaban Compared to Warfarin for Stroke Prophylaxis in Atrial Fibrillation

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Background: Rivaroxaban, an oral Factor Xa inhibitor administered once daily without the need for anticoagulation monitoring, has demonstrated comparable efficacy to adjusted-dose warfarin for the prevention of stroke and a lower risk of intracranial hemorrhage (ICH) in patients with atrial fibrillation (AF).

Objective: To evaluate the cost-effectiveness of rivaroxaban compared to adjusted-dose warfarin for the prevention of stroke in patients with AF.

Methods: A Markov model was developed to estimate the cost-effectiveness of rivaroxaban 20 mg daily and adjusted-dose warfarin from the societal perspective using data from the Rivaroxaban Once daily, oral, direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation (ROCKET-AF) trial and other published studies of anticoagulation. For the base-case analysis, we assumed AF patients were 65-years of age and healthy, with a CHADS2 score of 2 and no contraindications to anticoagulation. Patients were followed for up to 35-years or until death, whichever came first. Evaluated outcomes included costs in 2011 US$, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). Costs and outcomes were discounted at 3% per annum. One-way and probabilistic sensitivity analyses were conducted.

Results: The base-case analysis revealed that rivaroxaban use resulted in more QALYs and was less costly than adjusted-dose warfarin, making it a dominant strategy. Rivaroxaban treatment resulted in 10.16 QALYs per patient, while adjusted-dose warfarin treatment resulted in 10.01 QALYs. Total lifetime costs per patient were $112,399 and $115,579 for rivaroxaban and adjusted-dose warfarin, respectively. One-way sensitivity analysis revealed our results were most sensitive to changes in the relative risk reduction of ICH with rivaroxaban, with the ICER varying from dominant to $191,000 per QALY. Monte Carlo simulation demonstrated that rivaroxaban was the dominant strategy in 55%, and cost-effective in 81% and 88% of 10,000 iterations at willingness-to-pay thresholds of $50,000 and $100,000 per QALY.

Conclusion: Our model suggests that rivaroxaban is likely an economically favorable alternative to adjusted-dose warfarin in patients with AF who have at least a CHADS2 score of 2 and no contraindications to anticoagulation.
Does Magnesium L-Lactate Improve Quality of Life in Patients with an Implantable Cardioverter Defibrillator?

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**Purpose:** The objective of this prespecified substudy of the Adjuvant Magnesium Trial was to evaluate the impact of oral magnesium L-lactate on quality of life (QoL) in patients with an implantable cardioverter defibrillator (ICD).

**Methods:** In this prospective, double-blind, placebo-controlled trial, 70 patients with an ICD were randomized to receive oral magnesium L-lactate (n=35) (6 tablets supplying a total of 504mg elemental magnesium daily) or matching placebo (n=35). Quality of life was measured using self-administered Ferrans & Powers QoL Index (Cardiac Version) questionnaires at baseline and at 3 and 6 months of therapy. This tool assesses QoL in persons with heart disease including satisfaction and health perception, functioning, socioeconomic factors, psychological and spiritual well-being, and family life. Participants rated their satisfaction over 35 questions with choices from 1 (“very dissatisfied”) to 6 (“very satisfied”). Total scores ranged from 0 to 30 points with higher scores indicating better QoL. Changes from baseline were compared between groups with the Mann-Whitney U or Student t-test (SPSS version 17.0, Chicago, IL).

**Results:** No significant differences in baseline characteristics, total QoL score or subscale QoL scores were seen. Due to the large number of tablets needed per day, long-term adherence was poor. Overall, 45 (64%) and 30 (43%) randomized patients completed questionnaires at 3 and six months. Magnesium L-lactate did not significantly impact the change from baseline in overall or subscale QoL scores versus placebo at 3 months. At 6-months, magnesium L-lactate did not significantly impact the change from baseline in overall QoL scores but significantly improved the health/functioning subscale score versus placebo (1.04 vs. -1.22, p=0.04).

**Conclusion:** *Overall, high dose magnesium L-lactate therapy does not appear to appreciably impact QoL in patients with an ICD over a 6-month period.*
An assessment of the available literature on the barriers to appropriate pain management in the community health care setting

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**Background:** Ineffective pain management may result from factors such as insufficient pain management knowledge base by healthcare providers, misunderstanding of the definitions for addiction, dependence and tolerance, misconceptions of upper limits for opioid dosing, fear of scrutiny by regulatory agencies regarding opioid prescribing and dispensing, and lack of opioid availability in pharmacies.

**Objectives:** The purpose of this research is to 1) identify studies that characterize the community pharmacists’ opinion, level of knowledge and comfort level with dispensing opioids for pain management, and 2) to assess, from the literature, the reasons for the barriers in the appropriate management of pain in the community setting.

**Method:** A thorough Pubmed search was performed using the search terms: community pharmacy, community pharmacists, pain, barriers, attitudes, knowledge and opioids to identify relevant studies. The bibliographies of the retrieved studies were also reviewed to identify further pertinent articles.

**Results:** Ten relevant articles published from 1992 to 2007 were identified. All studies were surveys and the focus of the studies were community pharmacists (2), community pharmacies (4), all licensed pharmacists within a state (2), and all health care professionals (2). The issues addressed in the studies include 1) the rationale for the lack of opioid availability in community pharmacies and 2) the knowledge and attitudes of the pharmacists and other health care professionals toward cancer pain management, opioid pain medications in relation to federal and state policies, opioid use in substance abusers, opioid adverse effects, and apprehension about dispensing/prescribing pain medications. The data showed that a majority of pharmacists were hesitant to dispense opioids for nonmalignant pain and to patients with a history of substance abuse due to fear of addiction. Forty-seven percent of health care providers were hesitant to provide opioid doses greater than that recommended in the Physican’s Desk reference. Forty-two to seventy nine percent of pharmacists were confused about definitions of addiction, tolerance, and psychological dependence. The percentage of pharmacists who believed the risk of addiction was high in cancer patients was 33.3% to 51%. While some community pharmacists were concerned about stocking opioids due to fear of robbery and federal agency scrutiny, a greater percentage of community pharmacists carried a low stock of opioids due to a lack of prescription demands.

**Conclusion:** Most of the survey data reflect information from at least ten years ago. Since then, the amount of pain management education in pharmacy school curriculums may have increased. Additionally, the implementation of Risk Evaluation Mitigation Strategy (REMS) for opioids may alter dispensing and prescribing habits. Based on the available data, it may be worthwhile to update the surveys and reassess the data in community pharmacists who have graduated in the last 10 years versus pharmacists who graduated more than ten years ago. The information would help to determine if further continuation education programs focused on pain management should be provided to improve the pharmacists’ knowledge base and comfort level with dispensing opioids.
Research in-progress: Characteristics optimal for residency candidates

Lisa Semancik, Dr. Girotto PharmD, BCPS

Purpose: The number of applicants to residency programs grow while the number of programs remains almost static it is important to determine characteristics that programs are looking for in future candidates. The goal of this study is obtain preliminary data to gain an understanding of what characteristics residency programs find optimal in candidates.

Methods: The study was given exempt status by the University of Connecticut's Institutional Review Board. ASHP's residency directory was used to identify PGY1 programs in the northeast United States (CT, MA, ME, NH, VT, NY, NJ, PA, RI). 133 programs were identified and the listed program directors have been invited via email to participate in the survey via Survey Monkey. The survey inquires about basic program factors: the numbers of applicants to the PGY1 program, available positions, and persons weighing in on the decision for an individual candidate. Then the survey seeks to obtain importance of criteria such as work experience, didactic grades, letters of recommendation, research experience, and interview characteristics (knowledge, critical thinking, communication, presentation, and personality attributes) for candidates applying to the programs. Program directors were also asked to provide additional data to expand if they felt additional data would be important. Descriptive statistics will be used to describe the data. Data will be collected and analyzed from the anonymous online-survey results.
Comparative Accuracy of SPECT and PET for the Diagnosis of Known or Suspected Coronary Artery Disease

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Background: Single photon emission computed tomography (SPECT) and positron emission tomography (PET) have evolved as competing alternatives to invasive coronary angiography in the diagnosis of coronary artery disease (CAD). At this time, the relative accuracy of these two nuclear imaging modalities is unclear.

Objective: To compare the diagnostic value of SPECT and PET to invasive coronary angiography for the detection of known or suspected CAD.

Methods: We conducted a systematic review of prospective studies evaluating the sensitivity and specificity of SPECT and/or PET with invasive coronary angiography as the reference standard. Two investigators independently performed MEDLINE and EMBASE searches through [insert dates], as well as a manual review of references of identified studies. Included studies were conducted prospectively, performed coronary angiography in all patients, reported sufficient data to calculate true and false positives and negatives and were published in English.

Results: One hundred seven and 8 studies assessing SPECT and PET, respectively, were identified. Bivariate meta-analysis demonstrated that PET had a significantly higher pooled mean sensitivity [93% (95% CI, 87% to 96%)] and specificity [85% (95% CI, 76% to 91%)] compared to SPECT [88% (95% CI, 86% to 90%) and 76% (95% CI, 73% to 80%)] (p=0.046 and 0.033, respectively).

Conclusions: PET imaging appears to be more accurate than SPECT in the detection of CAD.

Figure. Summary Receiver Operator Curves for Noninvasive SPECT and PET Imaging

Legend: Curves include a summary operating point for sensitivity and specificity on the curve and a 95% confidence ellipse.
Investigation of implementation practices for antimicrobial stewardship programs in children’s hospitals

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Dr. Jennifer Girotto, PharmD, BCPS

Purpose: Antimicrobial Stewardship Programs (ASPs) promote optimal antimicrobial use in hospitals to reduce cost, drug resistance and medication-related adverse events; however, problems can arise when proper safeguards are not in place to ensure necessary medications are available and/or reordered appropriately. The purpose of this project is to survey implementation strategies of ASPs at various children’s hospitals throughout the United States, with specific emphasis on restrictions and prior authorizations.

Methods: Hospitals were identified via searches of Children’s Healthcare of America and National Association of Children’s Hospitals and Related Institutes (NACHRI) found on the internet. A standard question set was developed to uniformly query children’s hospitals. The questions included inquiries about the current restrictions and prior authorizations, the length of time the program has been in place and the medications included in the intervention(s). For institutions where ASPs were not yet implemented, plans for future implementation were documented. Information was obtained from various Pharmacy Directors’ and Clinical Pharmacists via phone or, if requested, e-mail.

Results: Thirty-four out of seventy-four children’s hospitals responded. Of those, 71% have an ASP currently in place, 9% have plans to implement a program, while 21% do not have a program in place. Of those with current programs, 14 utilize prior authorizations, 5 restrictions on duration of use (3 with hard stops and 2 with soft stops) and 5 include both (2 with hard stops and 3 with soft stops). Just as importantly, 3 children’s hospitals had noted prior use of hard stop restrictions, but discontinued the practice due to concerns for patient safety.

Discussion/Conclusion: From these data, the vast majority of the hospitals include prior authorizations as a part of ASP implementation. Some hospitals also used restrictions to limit durations for various antibiotics. Soft stops are more common than hard stops. Since only a few hospitals have effective hard stop restrictions and others have moved away from this practice due to concerns regarding inadvertent stopping of the medication, proper safeguards need to be in place to ensure the success if this method is used. Further studies are needed to determine the most appropriate ASP implementations based on the individual hospital and computer systems.
Developing a New Integrated Dermatology Course for Pharmacy Students

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Objective: To design, implement, and evaluate an integrated basic and clinical science course on dermatology and assess its effect on pharmacy student’s perceptions, attitudes, and knowledge.

Methods: A novel one credit dermatology module was implemented in Spring 2010 as a part of the core curriculum offered to second year pharmacy students. The course was designed by faculty of Pharmacy Practice and Pharmaceutical Sciences such that students received the knowledge component of the course delivered via on-line lectures, readings, web based activities and a weekly on-line quiz to be completed prior to class meetings. Class time was utilized for case discussions and application of the material learned. A pre-and-post course comparison using a Likert-type scale (1=strongly agree, 5=strongly disagree) and descriptive statistics was used. The sample size was limited to the size of the enrollment in the course for 2 consecutive years. This study was approved by the University of Connecticut Institutional Review Board.

Results: A total of 141 students (73% of respondents) completed both the pre-and-post course questionnaires. Sixty-two percent of the respondents were female and 37.6% were male. Fifty-five percent were between 18 and 21 years and 41% between 22 and 24 years of age. Seventy-eight percent were currently employed in either a community or hospital pharmacy. At the start of the semester, students supported the inclusion of dermatology in the curriculum but did not feel competent in caring for patients with dermatologic conditions. Students also perceived that all the course topics offered in the course were relevant and applicable to their careers as pharmacists. At the end of the semester, students felt competent in achieving all the course objectives and strongly agreed that this course enhanced their knowledge of common dermatological conditions encountered in a community or ambulatory care setting.

Conclusion: Most student pharmacists believe that the inclusion of a dermatology course is useful and will enhance their roles as pharmacists.
The Society of Pharmacy Research (SPR) is a professional pharmacy organization in its third year at the University of Connecticut School of Pharmacy. The mission of SPR is to promote awareness and understanding in the area of pharmacy research. As the profession of pharmacy advances, the research opportunities for PharmDs grow and the importance of understanding research going on in the field of pharmacy is of increasing significance. Although by design the PharmD degree places emphasis on clinical competency, students may wish to enhance their education through clinical or scientific research.

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The Rho Chi, Alpha Gamma Chapter, advocates the pursuit of intellectual excellence and inquiry at the University of Connecticut School of Pharmacy. Rho Chi encourages outstanding scholarship and professional achievement. Through this Research Symposium, Rho Chi is proud to support student researchers in their own attainment of academic excellence.

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