First Annual UAMS College of Pharmacy Research Symposium

April 8 – 9, 2010

Discovery, Delivery, and Outcome: Pharmaceutical Care for the 21st Century
Keynote Speaker

Susan A. Rotenberg, Ph.D.
Professor of Biochemistry
Queens College of The City University of New York

“The Search for Substrates of Protein Kinase C”
Friday 12:00 pm
April 9, 2010
COPH 8/240
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IMPACT OF PHARMACIST COUNSELING ON PATIENT KNOWLEDGE OF EMERGENCY CONTRACEPTION.

Adam N. Pate, Nalin Payakachat, Denise Ragland

Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

Unintended pregnancy is a serious public health issue with significant physical, emotional, and economic costs to individuals, their families, and society as a whole. Currently, approximately one half of all pregnancies are unintended many of which could be prevented with safer sex practices or use of emergency contraception (EC). A previous study at the University of Arkansas for Medical Sciences (UAMS) University Women’s Clinic (UWC), found that 57% of surveyed women were unaware of emergency contraception and 73% of these women would be willing to use or consider using emergency contraception in the future. This environment presents an education need for which pharmacists are aptly suited to fulfill.

The purpose of this study is to assess patients’ awareness of emergency contraception, evaluate patients’ functional knowledge of emergency contraception, and determine the impact of pharmacist counseling on patients’ knowledge of EC.

This study is a pre- and post-test design (single group) with a convenience sampling method. Objectives will be assessed by a self-administered, 12-question survey as a pre-test and post-test before and after a 10-minute education session. Descriptive statistics and differences in knowledge scores will be assessed using the dependent t-test. Regression analysis will be used to explore factors that might relate to knowledge scores (e.g. age, race, education level, number of previous pregnancies, household income).

Results from this pilot project can be used to identify strategies to increase contraceptive knowledge and use while assessing education methods to decrease unintended pregnancies.
MEDICATION ADHERENCE IN ADOLESCENTS AND YOUNG ADULTS POST-LIVER AND RENAL TRANSPLANT: SELF-REPORTED BARRIERS AND STRATEGIES FOR IMPROVEMENT

Helyn S. McLain, PharmD, Catherine E. O’Brien, Pharm D, Holly D. Maples, Pharm D

Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

Research has shown that adherence to medications post transplant has been difficult in adolescents. Medications that are prescribed to patients who have undergone an organ transplant are important in the graft survival and the survival of the patient. The purpose of this study is to discover self-reported barriers to adherence as well as strategies for improvement in adolescents and young adults with renal and/or liver transplant.

This study assesses subjects’ level of adherence by the Multidimensional Adherence Classification System (MACS). This system bases the assessment of adherence on two things: patient- and parent-reported medication adherence and drug levels of tacrolimus or cyclosporine.

Subjects involved in the study include renal and/or liver transplant patients that are being followed in the outpatient clinics at Arkansas Children’s Hospital (ACH), currently taking tacrolimus or cyclosporine, 11-21 years of age, and transplanted at least 4 months prior to the study.

The primary outcome of the study is to determine barriers to adherence to transplant medications and ways that study subjects think adherence could be improved.

The two page survey consists of multiple choice and short answer questions and is given orally to the patients and their parent/caregiver. In addition to questions pertaining to adherence, subjects are asked for limited demographic data. Once the survey is collected we will collect the drug levels from the electronic medical record and place patients in one of four categories of the MACS. Subjects with drug levels of tacrolimus between 5-17 and cyclosporine levels 150-400 will be considered adherent. Subjects with levels outside of these ranges will be considered non-adherent.

We will utilize descriptive and inferential statistics to analyze the data.
EFFECT OF MULTI-DRUG RESISTANT GRAM-NEGATIVE ORGANISMS ON LUNG FUNCTION IN CYSTIC FIBROSIS PATIENTS.

Ashley S. Crumby, Pharm.D., Catherine E. O’Brien, Pharm.D., Holly D. Maples, Pharm.D.

Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

Research in the area of drug-resistant strains of Pseudomonas aeruginosa (PA) and Burkholderia cepacia (BC) is lacking, and no definitive correlation between the development of drug-resistant pathogens and a decline in pulmonary function has been identified. The purpose of this study is to evaluate the impact of multi-drug resistant organisms (MDROs) such as PA and BC on lung function, healthcare utilization, and overall health in cystic fibrosis (CF) patients.

A retrospective analysis is being conducted to evaluate the impact of MDROs in CF patients at Arkansas Children’s Hospital. Inclusion criteria are diagnosis of CF, positive PA or BC respiratory culture, and multi-drug resistance (MDR). MDR for PA is defined as PA isolates which are resistant to \( \geq 3 \) different antibiotic classes while MDR for BC is defined as isolates resistant to \( \geq 2 \) different classes of antibiotics. Exclusion criteria are ages < 1 year and > 18 years at the time of their first MDRO colonization. The estimated number of study participants is 46. Of this number, 37 patients have been colonized with PA, 9 have been colonized with BC, and 4 have been colonized with both organisms.

Each participant serves as his/her own control and will be included in the analysis from their first positive PA or BC culture. Impact on lung function is evaluated by comparing FEV\(_1\) percent predicted values prior to culture of MDROs with FEV\(_1\) percent predicted values following culture with these organisms. Impact on healthcare and antibiotic utilization is evaluated through analysis of the need for inpatient or outpatient antibiotic courses, prior to and after culture of MDROs. Impact on overall health is evaluated by comparison of BMI percentiles, fat-soluble vitamin levels, and depression diagnosis before and after culture of MDRO.

Descriptive statistics will be utilized to describe baseline characteristics and demographics. Appropriate inferential statistics will be used to compare endpoints before and after culture of MDROs. Analysis of variance will be used to compare across multiple groups or time points as appropriate. Chi-square analysis will be used to analyze qualitative data.
The objective of the study was to determine the pharmacokinetics and metabolism of hydrastine and berberine in human subjects after an oral dose of goldenseal supplement. Subjects (n=11) were given a single dose of goldenseal supplement (2.7 g), containing 78 mg hydrastine and 132 mg berberine. Serial serum (48 h) and urine samples were collected to assess the serum kinetics and urinary excretion. Hydrastine and berberine concentrations were determined using HPLC-MS/MS methodology. Metabolites of hydrastine and berberine were identified using liquid chromatography coupled to high-resolution mass spectrometry (LC-QToF). Pharmacokinetic parameters were calculated from serum concentration-time profiles using a model-independent approach.

For hydrastine, maximal serum concentration (C max ) was 225 ± 100 ng/ml, the time at which it occurred (t max ) was 1.5 ± 0.3 h, and AUC was 6.4 ± 4.1 ng*h/ml*kg. The elimination half-life was 4.8 ± 1.4 h. Corresponding values for berberine were 1.1 ± 1.2 ng/ml, 3.0 ± 3.3 h and 0.15 ± 0.09 ng*h/ml*kg, respectively. A berberine elimination phase was not evident from the serum concentration-time profile. Qualitative assessment of serum and urine showed rapid phase I and phase II metabolism of hydrastine and berberine. Phase I metabolites of hydrastine were found to undergo glucuronidation but not sulfation, while phase I metabolites of berberine were preferentially sulfated. The identities of different phase I and phase II metabolites were further confirmed by accurate mass measurement (<5 ppm).

Hydrastine and berberine absorption was extensive following oral administration of goldenseal supplement. Hydrastine serum AUC was considerably higher than that of berberine suggesting that hydrastine bioavailability was higher than berberine. Berberine serum and urine concentrations suggested enterohepatic recycling of berberine and a high volume of distribution for berberine. The project was funded by Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences.
DEVELOPMENT AND VALIDATION OF A LIQUID-CROMATOGRAPHY-MASS
SPECTROMETRY METHOD FOR DETERMINATION OF PHENCYCLIDINE IN
HUMAN SERUM AND ITS APPLICATION TO HUMAN DRUG ABUSE CASES

Krishna C. Chimalakonda1; Chris Hailey3; Ryan Black3; Allison Beekman3; Rebecca
Carlisle3; Elizabeth Lowman-Smith3; Heather Singletary3; S. Michael Owens2; and Howard P.
Hendrickson1

1Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for
Medical Sciences, Little Rock, AR 72205; 2Department of Pharmacology & Toxicology, College
of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR 72205; 3Arkansas
State Crime Laboratory, Little Rock, AR 72205

The objective of the study was to develop and validate an analytical method to quantitate drug of
abuse phencyclidine (PCP) in human serum and to apply this assay for the determination of PCP
in the blood and urine from five different abusers. PCP and internal standard (PCP-d5) were
isolated from sample matrix by solid-phase extraction using mixed-mode cation exchange. LC-
MS/MS analysis with positive electrospray-ionization (ESI) in the multiple reaction-monitoring
mode was used for quantitation of PCP. Analytical separation was achieved on a 3 µm C8 100 x
2.0 mm column preceded by a 10 x 2.0 mm C8 guard column, using a linear gradient. The
method was validated for accuracy, precision, linearity, and recovery by performing inter- and
intra-day validation. Validation studies consisted of calibration curves (1-1000 ng/ml) along with
quality controls at 1, 20, and 800 ng/ml, run on five different occasions. Matrix associated ion
effects were assessed by comparing calibration slopes generated from serum of five different
human subjects. The method was applied with minor modifications to determine the
concentrations of PCP in the blood and urine, obtained from five different abusers. The method
showed excellent accuracy and precision with error <14 % with CV <5.0 %, respectively. The
recovery of PCP was greater than 90% with the lower-limit-of-quantitation for PCP of 1.0 ng/ml.
The slopes of the calibration curves at 1, 300, and 1000 ng/ml using drug-free human serum from
five different donors were statistically similar, signifying negligible matrix-associated ion-
suppression. Application of the method to authentic PCP samples showed reasonable agreement
to results obtained by GC-FID when PCP concentrations were above 50 ng/ml. Blood-PCP
concentrations ranged from 3.2-80 ng/ml, while urine-PCP concentration ranged from 4.6-745
ng/ml. A rapid, accurate, and precise assay was developed and validated to quantitate PCP using
LC-MS/MS. The method was successfully applied to determine PCP in blood and urine from
current forensic methodology. Funding for this work was from NIDA/NIH (R42DA017596 and
R01DA007610) and the University of Arkansas for Medical Sciences College of Pharmacy.
QUANTUM MECHANICS AND MOLECULAR MODELING ANALYSIS OF THE BINDING OF VITAMIN E ANALOGUES TO THE ALPHA-TOCOPHEROL TRANSFER PROTEIN

Awantika Singh, Silvia Gonzalez, K. Sree Kumar, Martin Hauer-Jensen, Yadira F. Ordonez, and Cesar M. Compadre.

1Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, Little Rock, AR, 2Instituto de Química Aplicada, Universidad Técnica Particular de Loja, Loja Ecuador, 3Armed Forces Radiobiology Research Institute, Bethesda, MD, 4Department of Bioinformatics, University of Arkansas at Little Rock and University of Arkansas for Medical Sciences, Little Rock, AR

Vitamin E occurs in nature in eight different forms, \((\alpha, \beta, \delta, \text{ and } \delta)\) tocopherols and \((\alpha, \beta, \delta, \text{ and } \gamma)\) tocotrienols. The four forms of tocopherols and tocotrienols differ in the number and position of the methyl groups on the chromanol ring (\(\alpha\) has three, \(\beta\) and \(\gamma\) has two and \(\delta\) has one methyl group). Tocopherols and tocotrienols, which differ only in the degree of saturation of their hydrophobic phytol side chains, have significant differences in their biological activities and very large differences in their distribution and transport inside the human body. It is currently believed that these differences can be accounted by the differences in binding to the transport protein-\(\alpha\)-tocopherol Transfer Protein (TTP). This protein has recently been crystallized and the binding mode of \(\alpha\)-tocopherol to the protein has been described. In this paper we present the analysis of the binding of set of tocopherols, tocotrienols and tocol analogues to TTP using Quantum Mechanics and Molecular Modeling techniques. For the analyses, the geometrical structure and the molecular orbital description of the molecules were calculated theoretically. Calculations were carried out using a first principles density functional theory based method. In particular, we used the B3LYP hybrid functional as implemented in the Gaussian03 code. We used the 6-31 basis to obtain a first approximation of the geometry and it was refined using Alhrichs VTZ basis. The results of these analyses produce insights on the structural characteristics of these compounds and could be used as the basis to design analogues with improved transport properties.

The University of Arkansas for Medical Sciences, College of Pharmacy Research Fund, INBRE, and the Defense Threat Reduction Agency for their financial support.
SYNTHESIS OF BERBERINE PHASE I METABOLITES

Natalie N. Smith, Prem K. Gupta, E. Kim Fifer, and Howard P. Hendrickson

College of Pharmacy, Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, Little Rock, AR 72205

Demethyleneberberine and berberrubine are metabolites of the plant alkaloid, berberine. Berberine, isolated from Hydrastis Canadensis L., has been shown to be effective and safe in the treatment of type 2 diabetes and dyslipidemia. A description of the pharmacokinetics aids in the evaluation of the safety and functional dynamics of pharmacologically active compounds. Investigations of the pharmacokinetics of berberine require robust analytical methodologies and standards for berberine metabolites. Since these compounds are not commercially available, the chemical synthesis of these standards is described herein. Demethyleneberberine was synthesized by an acid catalyzed hydrolysis reaction using phloroglucinol and sulfuric acid. The product was purified using an OmniSpher C18 Column and a Sephadex LH-20 column with a methanol mobile phase. Berberrubine was synthesized using microwave irradiation and purified by separation on a Sephadex LH-20 column with a methanol mobile phase. The products were verified using an exact mass determination using Micromass Q TOF micro. This research was funded by UAMS College of Pharmacy, Pharmaceutical Sciences Student Research Fellowship.
This study aimed to determine if nonprescription emergency contraception (EC) availability impacted self-reported unintended pregnancy rates and to assess women’s knowledge and awareness of EC prior to and after nonprescription availability.

A survey regarding contraception use and knowledge was verbally administered to a cross-sectional, convenience sample of 272 pregnant women receiving prenatal care at a large urban community women’s clinic between August 2003 and October 2008. Demographic information was also collected. The Chi-square statistic and Fisher exact test (for categorical variables) and t-test (for continuous variables) were used to determine differences between two groups (before [BA] and after, [AA] nonprescription EC availability in the U.S. drug market) in terms of self-reported unintended pregnancy rates, knowledge and awareness of EC. The AA group reported higher incidence of unintended pregnancy when compared to the BA group (90.7% vs. 72.7%, P = 0.0172). The majority of both groups reported that they were not using any contraception at the time of conception (BA-84.4%; AA-83.3%). There was no significant difference in the participants’ awareness of EC between the two groups (BA-46.8% vs. AA-43.0%). Nor was there a significant difference between the two groups in the self-reported willingness to use EC in the future (BA-53.1% vs. AA-63.4%). However, among participants who were unaware of EC, 61% reported they would consider using it in the future after receiving brief EC counseling from a pharmacist or student pharmacist. Neither age nor pregnancy intention was associated with self-reported EC awareness but there was an association with income (P = 0.0410) and education (P = 0.0021). The change from prescription-only to non-prescription status of EC in the U.S. drug market did not impact the unintended pregnancy rate in this patient population. Lack of knowledge and awareness is still a major barrier to widespread EC use. This research was funded by UAMS College of Pharmacy, Pharmacy Practice Student Research Fellowship.
THE TEMPORAL ASSOCIATION BETWEEN PRESCRIBED OPIOIDS AND THE NATIONAL DEATH RATE DUE TO OPIOID POISONING

Mugdha N. Gokhale, B.Pharm., Bradley C. Martin Pharm.D., Ph.D.

Pharmaceutical Evaluation and Policy, Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

BACKGROUND: Deaths due to opioid overdosages have increased over the last decade and now represent the most frequent cause of death due to poisoning.

OBJECTIVES: To examine the relationship between prescription opioid use between 2000 and 2005 and the number of opioid related deaths.

METHODS: Data from two published sources were used for this study. The number of opioid poisoning deaths per year from 2000 to 2005 was obtained from the National Vital Statistics system multiple causes of injury mortality files (Warner 2009). Data for prescription opioid use was obtained from HealthCore Blue Cross and Blue Shield national commercial insurance plans (Sullivan 2008). The study population in these plans consisted of all enrollees which represented 2.7 and 3.8 million enrollees in 2000 and 2005 and those with at least one non-cancer pain diagnosis (NCPC: back/neck pain, headache joint pain) which corresponded to 485,794 individuals in 2000 that increased to 897,537 in 2005. Ordinary least square regression was used to study the temporal relationship between several opioid use measures and the number of opioid deaths per year.

RESULTS: Among all recipients, the cumulative opioid dose increased from 204.3 mgs morphine equivalents per enrollee per year to 371.4 mgs and among opioid users with a NCPC diagnosis the cumulative dose increased from 2473.5 mgs to 3406.9 mgs. Over the same time period, the number of yearly opioid deaths increased from 4,419 deaths in 2000 to 10,947 in 2005. There was a significant linear relationship observed between the cumulative yearly opioid dose per year per enrollee and the number of opioid related deaths ($\beta=39.65$, $R^2=0.99$, $p<0.0001$). A significant positive linear relationship was also observed between the number of annual opioid related deaths and opioid use measures of cumulative yearly opioid dose ($\beta=6.78$, $R^2=0.98$, $p<0.0001$), mean number of opioid prescriptions ($\beta=32640$, $R^2=0.67$, $p=0.04$), opioid dose per prescription ($\beta=166.7$, $R^2=0.88$, $p=0.005$) and mean days of opioid supply per year ($\beta=647.5$, $R^2=0.99$, $p<0.0001$). There was no significant relationship between the number of opioid related deaths and mean annual opioid dose per day ($R^2=0.02$, $p=0.77$). CONCLUSION: A strong linear relationship between opioid related deaths and several prescription opioid use measures over 2000 to 2005 was observed. This suggests that the acquisition of prescribed opioids through legal channels are associated with the national opioid death rate which calls for further vigilance on the part of prescribers and policy makers to ensure the safe use of opioid analgesics. Further research is warranted to confirm these correlations.
THE IMPACT OF PHARMACIST-PROVIDED HEALTH SCREENING AND EDUCATION PROGRAMS ON PARTICIPANTS’ KNOWLEDGE OF CORONARY HEART DISEASE RISK FACTORS AND HEALTH-PROMOTING BEHAVIORS

Leslie A. Mooney, Pharm.D. and Amy M. Franks, Pharm.D.

Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

Following informed consent, participants of free health screenings completed a pre-screening written questionnaire to determine baseline knowledge of coronary heart disease (CHD) risk factors. Pharmacists/student pharmacists conducted risk factor screening (lipid profile, blood glucose, body mass index, and blood pressure) and counseled participants about CHD risk factors. Four to eight weeks after the screening, a follow-up questionnaire was administered by telephone. Pre- and post-screening responses were compared to determine differences in participants’ knowledge of CHD risk factors and their participation in health-promoting behaviors. Changes in participants’ pre- and post-screening knowledge were determined by McNemar’s test and the Wilcoxon signed-rank test.

Of the 56 participants enrolled, 45 (80%) completed the post-screening telephone survey. The majority of participants were women (81%) and white (51%). Age ranged from 32 to 67 years (mean 45.8 years). Compared to pre-screening responses, participants showed significantly greater knowledge of “healthy” values for CHD risk factors, including blood pressure (p=0.02), fasting blood glucose (p=0.03), fasting total cholesterol (p<0.01), and body mass index (p<0.01), in post-screening responses. Following the screening, 20 (44%) participants had seen their primary care provider. Thirty-one of the 45 participants (69%) made at least one healthy behavior change.

Pharmacist-provided risk factor screening and education significantly increased participants’ knowledge of CHD risk factors and encouraged the majority of participants to seek medical care and/or make behavioral changes. These results demonstrate that screening and education programs may provide participants with the knowledge and motivation necessary to take a proactive role in their cardiovascular health and wellbeing.

The authors received no outside funding for the research described in this abstract.
THE ROLE OF DISCHARGE MEDICATION COUNSELING BY PHARMACISTS IN A RURAL HOSPITAL SETTING

Erin B. Hays, PharmD\textsuperscript{a,b}; Nalin Payakachat, BPharm, MSc, PhD\textsuperscript{b}; Tom Cummins, MD\textsuperscript{a};; and Maggie Miller, PharmD\textsuperscript{a}

\textsuperscript{a}White River Medical Center, Batesville, AR 72501; \textsuperscript{b}Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

The purpose of this study is to determine if discharge medication counseling by a pharmacist on new medications and/or changes of medications will improve quality of patient care as measured by readmission rates and patient satisfaction.

This study is a pilot, cohort study design using a convenience sample of patients at a rural community hospital. Inclusion criteria included (1) a discharged patient who is on new medications and/or with changes in medications and (2) medications will be managed in the home setting by the patient or their caregiver. The hospitalist referred the patient at discharge for medication counseling by a pharmacist. The pharmacist counseled the patient and/or caregiver and provided written instructions. A pharmacist contacted the patient and/or caregiver via telephone 48-72 hours after discharge for follow-up. Readmissions within 30 days were tracked. Patient satisfaction was evaluated through a patient satisfaction survey. Readmission rates were compared with the past six months using $t$-test statistic. Regression analysis was applied to explore relationships among continuous variables, and Chi-square and Fisher’s exact tests were used to investigate association among categorical variables.

Forty-eight patients participated in the study. It was observed that the greater the number of medications patients had at discharge was associated with more readmissions in 30-days ($p=0.013$). Of the completed patient satisfaction surveys, 87.5% said they would like the hospital to offer medication counseling by a pharmacist at discharge, and overall satisfaction was scored a 4.8 on a 5-point Likert scale. Pharmacist interventions included referring patients to a medication assistance program and providing medication help through hospital services.

This pilot study showed that more medications at discharge were associated with more readmissions. A pharmacist can help prevent these readmissions by offering discharge medication counseling for at risk patients. Patients were satisfied with the service and recommended that the service continue to be offered by the hospital.
IMPACT OF CHRONIC INHALED TOBRAMYCIN ON INCIDENCE OF TOBRAMYCIN RESISTANT PSEUDOMONAS AERUGINOSA IN CYSTIC FIBROSIS

Jonathan E. Barham, Catherine E. O’Brien, PharmD, Holly D. Maples, PharmD

Department of Pharmacy Practice, The University of Arkansas for Medical Sciences, Little Rock, AR 72205

Pseudomonas aeruginosa (PA) is the most prevalent bacteria that causes pulmonary infection in cystic fibrosis (CF) patients and has been linked to disease-related morbidity. Chronic, alternating monthly inhaled tobramycin (CIT) has become standard treatment for PA in CF patients. It has proven to be effective in improving lung function (FEV1) and weight (BMI) during the first 2 years of therapy. However, the development of tobramycin resistant PA due to this therapy has not been well characterized. This study aims to describe the long term impact of CIT on incidence of tobramycin resistant PA and the subsequent impact on pulmonary function in CF patients treated at Arkansas Children’s Hospital (ACH).

A retrospective chart review was conducted on CF patients colonized with PA and treated with CIT. Length of CIT therapy, total aminoglycoside exposure, PA cultures and susceptibilities, FEV1, and BMI data were collected 1 year prior to initiating CIT through May 2009.

Of 175 CF patients treated at ACH, 69 met selection criteria for this study. Tobramycin resistant PA was cultured from 25 patients (36%) after initiating CIT. Four patients cultured PA with intermediate susceptibility, and 3 patients cultured tobramycin resistant PA before exposure to CIT. At 5 years post-initiation of CIT, patients with tobramycin resistant PA showed lower lung function (FEV1) by 10% (p value = 0.02) compared to patients who did not culture tobramycin resistant PA.

Inhaled tobramycin is accepted as standard of care and has been shown to improve FEV1 and BMI, and decrease hospitalizations. In this study, 36% of CF patients developed tobramycin resistance while on inhaled tobramycin. This leaves limited future treatment options. A correlation was also found with PA resistance and decreasing pulmonary function. Further study is needed to assess whether long term inhaled tobramycin treatment is warranted in patients beyond the first few years of colonization as development of multi-drug resistance and decrease in pulmonary function places an increased risk for morbidity in the CF patient population.

This research was supported by the UAMS Pharmacy Practice Student Research Fellowship.
DISSOLUTION AND ANALYSIS OF THE MAJOR ALKALOIDS IN SIX COMMERCIAL PREPARATIONS OF GOLDENSEAL (HYDRASTIS CANADENSIS)

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Goldenseal is a dietary supplement derived from the roots of *Hydrastis canadensis*, a plant indigenous to the eastern part of North America. Historically, goldenseal has been used for the treatment of skin infections and gastrointestinal disorders, and for the enhancement of the immune system. Since the production and use of dietary supplements is not regulated by the U.S. Food and Drug Administration, the properties and pharmacological implications of these supplements have not been well-investigated. Previous studies have determined methods for the extraction and quantification of the major alkaloids in various brands of goldenseal preparations. These alkaloids, hydrastine and berberine, are thought to be the bioactive components of goldenseal. The purpose of this study was to evaluate the amount of these alkaloids obtained from the dissolution of six commercial preparations of goldenseal in order to determine any variability between preparations of the same type, in addition to the differences among the six preparations. Goldenseal capsules from six commercial suppliers were allowed to dissolve in HCl (pH 2.0) or citrate buffer (pH 6.0), with samples of the solutions taken at intervals from 0 to 120 minutes. The samples were analyzed for the presence and amount of hydrastine and berberine using liquid chromatography and UV detection to determine the dissolution of the alkaloids over time. Results from this study may be useful in making an *in vitro-in vivo* dissolution comparison to ascertain bioavailability and pharmacokinetics of goldenseal. *This research was supported by the UAMS Pharmaceutical Sciences Student Research Fellowship.*
The cytochrome P450 3A4 enzymes responsible for metabolizing a majority of pharmaceutical products pose significant drug-drug interactions when the enzymes are inhibited or induced by other drugs or herbal agents. In this research we have developed a model that uses Comparative Molecular Field Analysis (CoMFA) to correlate the \textit{in vitro} inhibitory series of compounds containing the benzodioxo-methylene moiety. Given that it would be impractical to test every naturally occurring compound in this class, this model can be used to screen for inhibitors to focus in the potentially more potent inhibitors for further testing.
A RETROSPECTIVE INVESTIGATION OF THE EMERGENCE OF LINEZOLID-RESISTANT STAPHYLOCOCCUS AUREUS INFECTIONS AT ARKANSAS CHILDREN’S HOSPITAL

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Linezolid was approved in 2000 to combat MRSA and improve treatment options for bone and pulmonary infections. However, in 2001, the first incidence of linezolid-resistant *S. aureus* was discovered. In 2006, three cystic fibrosis patients at Arkansas Children’s Hospital (ACH) were determined to have linezolid-resistant *S. aureus*. There has only been one other report of linezolid resistance in a patient with CF in the literature.

Our goal is to investigate how these patients developed linezolid resistance, whether it is from partial compliance, dosing, or from acquisition from each other by evaluating genetics of the strain, and to be able to give some insight towards appropriate dosing.

A chart review will be conducted to ascertain linezolid therapy including dosing and time periods, pulmonary function tests, and impact of linezolid resistance on hospitalizations. Confirmation that the strains obtained were linezolid resistant will be conducted through a variety of methods. The isolates will be sub-cultured onto blood agar (BAP), to ensure viability and purity. They will be retested on the BD Phoenix, E-test, and VITEK 2 to confirm linezolid resistance. Isolates will also be subjected to genetic testing using the multilocus sequence typing method (MLST).
Staphylococcus aureus is a devastating bacterial pathogen and the risk that it imposes to human populations is compounded by the emergence of antibiotic resistant strains. It is in this context that natural products offer an attractive pool of potential antimicrobial compounds. Gynoxys verrucosa, Wedd, is a shrub used in the Loja and Zamora-Chinchepe provinces of Ecuador for the treatment and healing of wounds, and it is commonly known as guangalo or balselicon.

We have identified dehydroleucodine (DHL) as potent agent against clinical isolates of methicillin-resistant S. aureus MRSA, methicillin-sensitive S. aureus (MSSA), methicillin-resistant Staphylococcus epidermidis (MRSE), and methicillin-sensitive S. epidermidis (MSSE). The hydrogenated compound leucodine, also present in this plant species was also tested and has very little activity. In this paper, we report the analysis of the structural features responsible for the activity of DHL. This analysis was performed in a comparative manner between DHL and leucodine, using X-ray crystallography, computational chemistry, using GAUSSIAN03, and molecular surface analysis, using SYBYL. The analysis reveals the exocyclic conjugated methylene in the lactone ring of DHL, and the presence of a secondary hydrogen binding point as necessary for the maximum antimicrobial activity.
DETERMINATION OF THE OCTANOL/WATER PARTITION COEFFICIENT OF α-TOCOPHEROL, THE MAIN COMPONENT OF VITAMIN E

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Hydrophobicity is a major factor in the absorption, transport, distribution, and binding to receptors of most bioactive molecules, and the logarithm of their octanol/water partition coefficient ($P_{ow}$) is considered the standard measurement of their hydrophobicity. α-Tocopherol is the most abundant component of vitamin E, and as such is an essential human nutrient. Unfortunately, its $P_{ow}$ has not been determined experimentally, and researchers had relied on its theoretically calculated $P_{ow}$ to explain its pharmacokinetic profile and its structure-activity relationships. The previously reported theoretically $P_{ow}$ values are in the range between 9.6 and 11.9 that would suggest that α-tocopherol is practically insoluble in water. In this investigation we have developed and validated an analytical method for the determination of α-tocopherol, sensitive enough to determine its $P_{ow}$. This method is based on the analysis of the silylated derivative of α-tocopherol using gas chromatography/mass spectrometry and β-tocopherol as internal standard. The experimentally determined octanol/water partition coefficient for α-tocopherol was 6.6, that is between 1,000 and 1,000,000 more soluble in water than previously reported.
DELETION OF PROTEIN KINASE Cε PREVENTS MITOCHONDRIAL DYSFUNCTION AND AMELIORATES ISCHEMIC KIDNEY INJURY.

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Previously, we have shown that activation of PKCε is involved in mitochondrial dysfunction caused by hypoxia/reoxygenation injury in renal proximal tubular cells in primary cultures. Blocking PKCε activation prior to hypoxia ameliorated hypoxia-induced decreases in mitochondrial respiration, complex I activity, and ATP production in vitro. This study tested the hypothesis that deletion of the PKCε gene decreases mitochondrial injury in renal proximal tubules and improves kidney function after renal ischemia in mice. Wild type (WT) C57BL/6J and homozygous mice carrying a deletion of the PKCε gene (KO) were used to induce renal bilateral ischemia (50 min). At 24 hr after ischemia, blood and kidneys were collected for assessment of renal functions and morphology, and mitochondria were isolated from renal cortices to determine their functions. State 3 respiration in mitochondria energized by substrates oxidized via complex I was reduced 44% in WT, but unchanged in KO mice. State 3 respiration coupled to complex II decreased by 27% in WT, but did not change in KO mice. Ischemia decreased mitochondrial respiratory control ratio (RCR) by 50% in WT but only 17% in KO mice. Activities of respiratory complexes I, III, and IV were decreased 59, 89, and 61%, respectively, in mitochondria isolated from WT ischemic kidneys. PKCε deletion prevented ischemia-induced decreases in activities of respiratory complexes. Ischemia increased plasma creatinine levels 12-fold in WT, but only 3-fold in KO mice. PKCε deletion reduced morphological damage in ischemic kidneys including 50% decrease in tubular necrosis (only individual/small groups of necrotic tubules in the corticomedullary junction) and decreased tubular dilatation, loss of brush border, and distal segment damage. We conclude that PKCε deletion: 1) prevents decreases in mitochondrial respiration and activities of complexes I, III, and IV, 2) improves mitochondrial coupling, and 3) decreases morphological damage and improves renal function after ischemia/reperfusion.

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