# COVER SHEET FOR GRANT PROPOSALS

State Board of Education

| SBOE PROPOSAL NUMBER: (to be assigned by SBOE) | AMOUNT REQUESTED: $50,000 |
|---|---|

TITLE OF PROPOSED PROJECT:

Development of Cationic Prodrugs to Improve Topical Treatment of Musculoskeletal Disorders

SPECIFIC PROJECT FOCUS:

Synthesize and evaluate cationic prodrugs of nonsteroidal anti-inflammatory drugs for enhancing topical delivery of such prodrugs into local muscle and joint tissues for better treatment of musculoskeletal disorders.

| PROJECT START DATE: 7-1-2013 | PROJECT END DATE: 6-30-2014 |
|---|---|
| NAME OF INSTITUTION: Idaho State University | DEPARTMENT: Biomedical and Pharmaceutical Sciences |

ADDRESS: 921 S 8th Ave, Stop 8334, Pocatello, ID 83209 (Programmatic)

921 S 8th Ave, Stop 8046, Pocatello, ID 83209 (Administrative)

| E-MAIL ADDRESS: yanguan@isu.edu (Programmatic)<br>harrdave@isu.edu (Administrative) | PI PHONE NUMBER:<br>208-282-2681 (Prog)<br>208-282-2592 (Adm) |
|---|---|

| | NAME: | TITLE: | SIGNATURE: |
|---|---|---|---|
| PROJECT DIRECTOR | Guang Yan | Assistant Professor | |
| CO- INVESTIGATOR | | | |
| CO- INVESTIGATOR | | | |
| CO- INVESTIGATOR | | | |
| | | | |

| | NAME: | SIGNATURE: |
|---|---|---|
| Authorized Organizational Representative | Dr. Howard D. Grimes | 5.14.13 |
| | | |
| | | |

**SUMMARY PROPOSAL BUDGET**

Name of Institution: Idaho State University

Name of Project Director: Guang Yan

A. FACULTY AND STAFF

| Name/ Title | Rate of Pay | No. of Months CAL | ACA | SUM | Dollar Amount Requested |
|---|---|---|---|---|---|
| Guang Yan, Assistant Professor | $8400 / mo | | | 1.5 | $12,600 |
| | | | | | |
| | | | | | |
| | | | | | |
| **% OF TOTAL BUDGET:** 25.2% | | | | **SUBTOTAL:** | $12,600 |

B. VISITING PROFESSORS

| Name/ Title | Rate of Pay | No. of Months CAL | ACA | SUM | Dollar Amount Requested |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| **% OF TOTAL BUDGET:** | | | | **SUBTOTAL:** | |

C. POST DOCTORAL ASSOCIATES / OTHER PROFESSIONALS

| Name/ Title | Rate of Pay | No. of Months CAL | ACA | SUM | *Dollar Amount Requested* |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| **% OF TOTAL BUDGET:** | | | | **SUBTOTAL:** | |

D. GRADUATE / UNDERGRADUATE STUDENTS

| Name/ Title | Rate of Pay | No. of Months CAL | ACA | SUM | Dollar Amount Requested |
|---|---|---|---|---|---|
| Shabbir Lobo, doctoral student | $1,800 / mo | 6 | | | $10,800 |
| | | | | | |
| | | | | | |
| | | | | | |
| **% OF TOTAL BUDGET:** 21.6% | | | | **SUBTOTAL:** | $10,800 |

E. FRINGE BENEFITS

| Rate of Pay (%) | Salary Base | Dollar Amount Requested |
|---|---|---|
| 21% of salary | $12600 | $2,700 |
| 8.9% of salary | $10,800 | $1,000 |
| | | |
| | | |
| | | |
| | | |
| | | |
| | **SUBTOTAL:** | $3,700 |

F. EQUIPMENT: (List each item with a cost in excess of $1000.00.)

| Item/Description | Dollar Amount Requested |
|---|---|
| One syringe pump | $1,500 |
| One microdialysis sample collector | $2,000 |
| | |
| | |
| | |
| | |
| | |
| **SUBTOTAL:** | $3,500 |

G. TRAVEL:

| Dates of Travel (from/to) | No. of Persons | Total Days | Transportation | Lodging | Per Diem | Dollar Amount Requested |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | **SUBTOTAL:** | |

H. Participant Support Costs:

| | Dollar Amount Requested |
|---|---|
| 1. Stipends | |
| 2. Travel (other than listed in section G) | |
| 3. Subsistence | |
| 4. Other | |
| **SUBTOTAL:** | |

| I. Other Direct Costs: | | Dollar Amount Requested |
|---|---|---|
| 1. Materials and Supplies | | $13,100 |
| 2. Publication Costs/Page Charges | | |
| 3. Consultant Services (Include Travel Expenses) | | |
| 4. Computer Services | | |
| 5. Subcontracts | | |
| 6. Other (specify nature & breakdown if over $1000)<br>40 rats and the animal care fee<br>15 white rabbits and the animal care fee | | <br>$2,800<br>$3,500 |
| | **SUBTOTAL:** | $19,400 |
| J. Total Costs: (Add subtotals, sections A through I) | **TOTAL:** | $50,000 |
| | | |
| K. Amount Requested: | **TOTAL:** | $50,000 |
| | | |
| Project Director's Signature: | Date: | 5/15/13 |

**SBOE Idaho Incubation Fund Program Proposal**

# DEVELOPMENT OF CATIONIC PRODRUGS TO IMPROVE TOPICAL TREATMENT OF MUSCULOSKELETAL DISORDERS

**Name of Idaho Public Institution:** Idaho State University (ISU)

**Name of Faculty Member Directing Project:** Guang Yan, Ph.D., Assistant Professor

**Indicate If This Technology Been Proposed and/or Been Awarded:** No.

**Executive Summary:** Millions of Americans are suffering from musculoskeletal disorders (MSD) with severe pain and impaired mobility. The treatment of MSD is a multi-billion dollar market. Oral nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used as treatments but these are associated with high gastric and cardiovascular risks. Noninvasive topical treatment of MSD with low adverse effects is appealing. Currently available topical NSAIDs only show modest efficacy in treating MSD. The main reason is insufficient amount of drug delivered into the affected muscle and joint tissues (deep tissues) after topical application. Dr. Yan's group in ISU discovered that converting NSAIDs to cationic prodrugs and delivering them with iontophoresis (electric current assisted) topically can provide a much higher amount of drug in the local tissues including skin, subcutaneous, and muscle tissues. This could be a ground breaking technology in improving the efficacy in topical treatment of MSD. This technology is now in the process for a provisional patent filing. But additional research experiments are needed to develop a robust full patent application. Those include: to evaluate the cationic prodrugs penetration into joint tissues, and to synthesize some additional cationic NSAID prodrugs (to provide a more generalized chemical structure for patent protection) and to evaluate those prodrugs for their penetration into the deep tissues. With the promising experiment results from the preliminary study and from this proposed project, Dr. Yan and the ISU will actively engage in identifying commercialization partners for this technology. Overall,

this project will provide the needed information in developing a full patent and speed up the progress in commercialization of this promising technology for more effective topical treatments of MSD.

**Gap Project Objective and Total Amount Requested:** The objective of this project is to develop a technology to enhance topical delivery of NSAIDs into the muscle and joint tissues for better treatment of MSD. Dr. Yan's group has made good progress on this technology with some cationic NSAID prodrugs synthesized, tested them with rats in vivo and showed the prodrugs can greatly enhance the drug concentration in the local muscle tissues with great potential for better treating MSD. Additional experiments are needed to show that the prodrugs can also enhance the drug penetration into the joint tissues, and to synthesize additional NSAID prodrugs with some chemical structure variations to provide a more generalized chemical structure for the prodrugs in the patent filing. This incubation grant will speed up the progress of the project and advance the project to the next stage, which is to commercialize the technology. The total amount of the grant requested is $50,000.

**Resource Commitments Reflect the Priorities of the Home Institution(s):** Idaho State University has been granted the Carnegie Foundation's ranking of Research University-High status and is committed to reinforce its status by improving the research infrastructure in the University. Idaho State University is the leading university in health sciences education and research in Idaho. ISU's research priorities are to advance the state of knowledge in health sciences, invent novel intellectual properties, and create economically viable licensing and commercial spin-offs. ISU has recently formed the Division of Health Sciences to promote its mission in health sciences. The proposed project is directly related to the ISU health science research goals.

**Potential Impact to the Economy of Idaho:** This technology has great application in improving topical treatment of MSD for millions of Americans, which is a billion dollar market.

Commercialization of this technology is the ultimate goal of this project. The immediate economic impact to Idaho from this technology will be the royalties or licensing fees from commercialization of this technology, which will benefit the research and higher education in the Idaho State University.

**Market Opportunity:** Every year millions of people in the United States have been suffering with MSD such as osteoarthritis, rheumatoid arthritis, temporomandibular joint disorders, and ankle sprain. Oral NSAIDs have been used for treating those disorders but associated with high gastric ulceration/bleeding and cardiovascular adverse effects. Topical NSAIDs can greatly lower the incidence of those adverse effects but only show modest treatment efficacy. The current topical drugs can not sufficiently penetrate into deep tissues because the penetration process encounters multiple hurdles: the epidermis (especially the stratum corneum) barrier limits topical drug penetrating into the skin and the dermal blood circulation clears dermis drug into systemic circulation. To overcome these hurdles, our new technology employs an electric current (iontophoresis) to deliver a cationic prodrug of NSAIDs for enhancing the topical drug penetration into deep tissues.

The main application of this technology is for topical treatment of MSD. It was estimated that the sales of topical NSAID products were over $500 million in 2011, and the market was growing in double digits. In addition, the oral NSAID market was well over $8 billion. Within the foreseeable future, the topical NSAIDs will keep taking over the oral NSAID market shares.

This technology is targeting patients with localized muscle and joint pains such as arthritis and ankle sprain. It will compete with the topical NSAID products on the market. The new technology has the unique properties of faster and more localized delivery of drug to local tissues

for better topical treatment of MSD. The development of new products from this new technology would need to obtain FDA approval.

**The Technology and Path to Commercialization:**

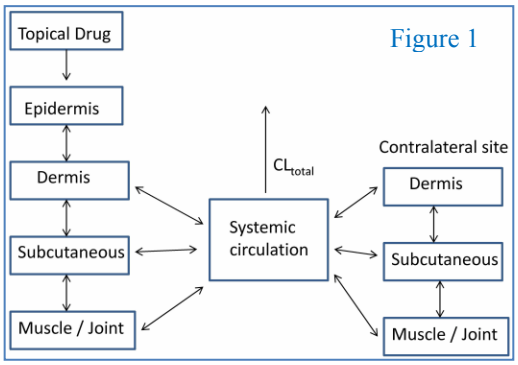


Figure 1

Topical drug penetration into deep tissues is a complicated process (Figure 1): topical drug delivery into epidermis, diffusion from epidermis into the dermis, drug exchange with systemic circulation, diffusion from dermis into subcutaneous tissue, drug exchange with systemic circulation, and diffusion from subcutaneous into muscle or joint tissue, the drug concentration in other tissues such as at the contralateral site is due to systemic drug redistribution. Based on this model, enhancing topical delivery into epidermis and lowering the drug clearance (exchange) from local tissue to systemic circulation will enhance topical drug penetration into deep tissues. Enhancing topical delivery into epidermis can be achieved by modifying the drug delivery method such as using iontophoresis. Lowering the drug clearance by systemic circulation can be achieved by lowering the blood flow into the tissue or lowering the capability of blood carrying the drug (lowering the drug plasma protein binding). Most NSAIDs have high plasma protein binding which leads to low drug retention in the local tissues after topical application.

The current technology is to use iontophoresis delivery of cationic NSAID prodrugs for enhancing the drug penetration into the muscle and joint tissues. Ketoprofen (Kt) was chosen as a representative NSAID. Dr. Yan's group has synthesized two cationic Kt prodrugs: Kt choline ester (KCE) and Kt methylcholine ester (KME) (Figure 2). Both prodrugs showed low plasma protein binding affinities (8%), which enable the prodrugs to retain in the local tissue for longer

time. Both KCE and KME can be converted back to the parent drug in the body.

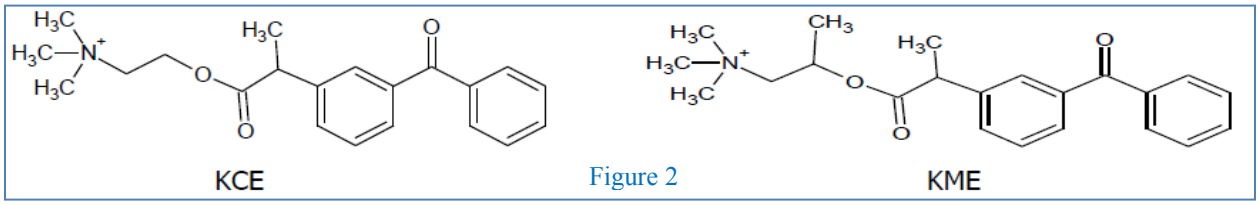



Figure 2

The iontophoresis of KCE was compared to the iontophoresis of ketoprofen (Kt) across human epidermis. The iontophoresis of KCE delivered 4 times more drug across the skin than that delivered by the iontophoresis of Kt. In addition, a rat study was conducted with the using of iontophoresis delivery of Kt, KCE, and KME from the rat back skin into the muscle tissues for six hours at two different electric currents (0.7 mA and 0.1 mA) and drug concentrations in each tissue layers (dermis, subcutaneous, shallow muscle, and deep muscle) and also in the plasma was determined with a HPLC. Iontophoresis of Kt showed much higher plasma concentration, iontophoresis of KCE showed almost zero plasma concentration at the initial two hours and then slowly increasing of the drug concentration in the plasma (only Kt was detected in plasma), iontophoresis of KME showed no detectable drug concentration in the plasma (means all drug was retained in the local tissues). The tissue drug concentration results are showed in Figure 3.

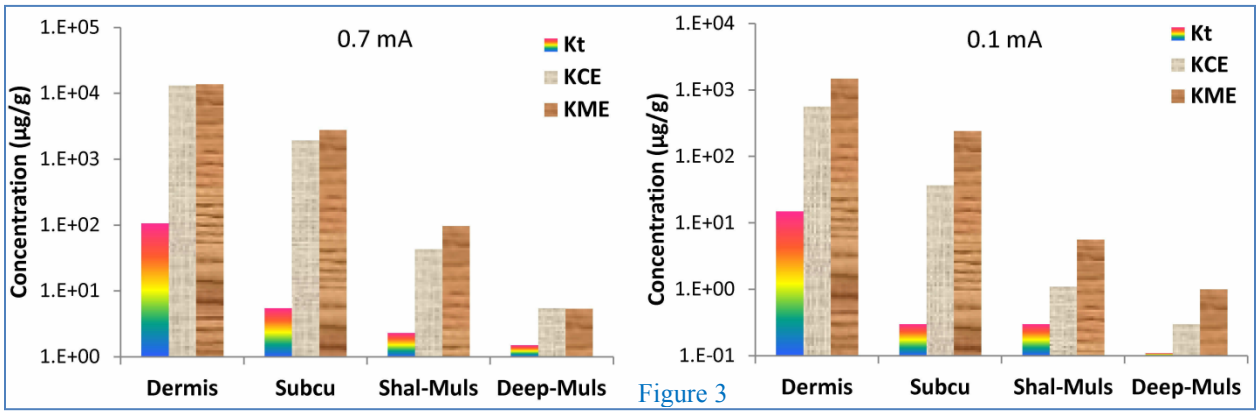



Figure 3

The two prodrugs showed much higher drug concentrations in the local tissues than that of the parent drug Kt under both electric current conditions, and the tissue drug concentrations under

the high current condition were higher. Thus the cationic prodrugs are more favorable in retaining in the local tissues which could provide better treatment of MSD.

The current technology will significantly improve the topical NSAID delivery into the deep tissues with higher tissue drug concentrations. And the iontophoresis method will also provide faster drug penetration into the body. Thus this technology will enable a faster and more effective treatment for MSD than the current topical NSAIDs on the market.

Dr. Yan has recently disclosed this technology to the Office of Research at the Idaho State University with an expectation that a provisional patent will be filed soon. It is expected that the prodrugs would also be advantageous in iontophoresis delivery into the joint tissues, but need to be confirmed with experiments. In addition, some additional cationic prodrugs are also needed to be synthesized by varying the cationic alcohol structure to establish a generalized chemical structure for the cationic NSAID prodrugs. These are the new tasks proposed in this project for filing a full patent.

This technology has been developed by Dr. Yan's group in ISU with his research startup fund and the INBRE research assistantship support.

The following steps will be taken to bring this technology to market. First, a provisional patent will be filed for this technology. Second, some additional experiments as proposed in this project will be carried out. Third, a full patent will be filed for this technology. Fourth, potential pharmaceutical companies or groups with interest in topical NSAID products will be contacted to engage talks in commercializing this technology or establishing partnership in co-development of the products.

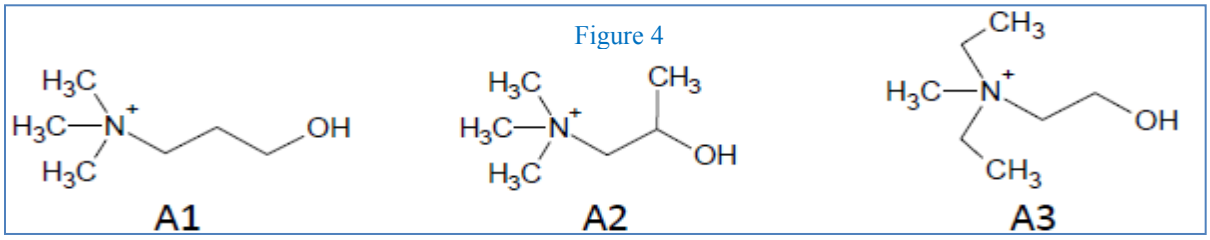
**Commercialization Partners:** There is no commercialization partner established for this technology right now. Identifying commercial partners will be initiated after the filing of the

provisional patent for this technology. The project director, Dr. Yan previously worked with pharmaceutical companies for more than four years in developing topical and transdermal drug products. He has wide connections in the pharmaceutical industry and will actively participate in the process of identifying the commercialization partners.

**Specific Project Plan and Detailed Use of Funds**

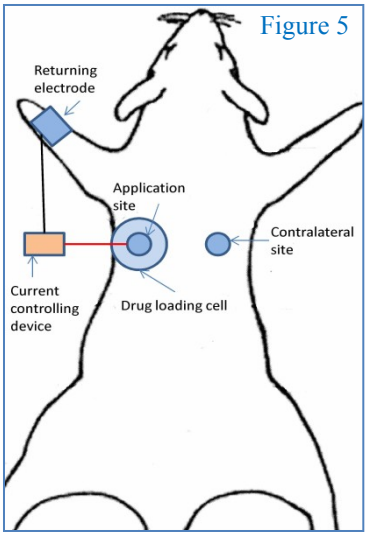
**1)** *Synthesis and characterization of the additional prodrugs*: Ketoprofen has a carboxyl group that can react with the hydroxyl group of a cationic alcohol to form cationic ester prodrug. Dr. Yan's group has synthesized KCE and KME by reaction with cationic alcohols choline and β-methylcholine. Three additional cationic prodrugs will be synthesized between ketoprofen and the cationic alcohols in Figure 4. The effects of longer chain (A1), α-methyl group (A2), and bulky quaternary ammonium group (A3) on the physicochemical properties of the prodrugs and also their penetration into deep tissues will be investigated. The protein binding affinity, the in vitro hydrolysis in water, the in vitro bioconversion rate in rat plasma, rabbit plasma, and also human plasma for the cationic prodrugs will be determined.

Figure 4

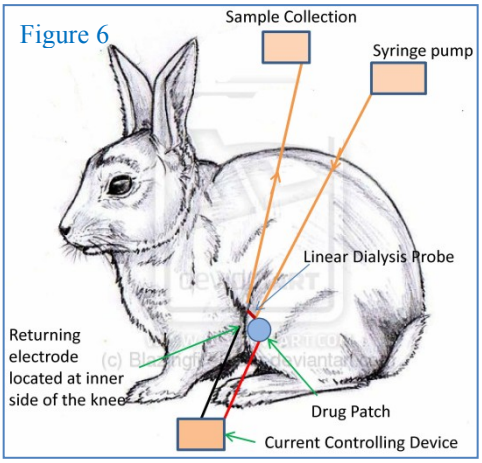



**2)** *In vivo rat study*: An in-vivo rat study will be used to determine the five cationic NSAID prodrugs penetration into the local muscle tissues after topical delivery with iontophoresis. This will determine whether the five prodrugs of different chemical structures show similar deep tissue penetration behavior or the drug retention in the deep tissues is dependent on the chemical structures, and what is the general chemical structure that contributes to the high drug retention in the local tissues. The experiment setup of the in-vivo rat study is demonstrated in Figure 5. A

constant current (0.1 mA or 0.7 mA) will be applied on the rats for 6 hours. At the end of the experiment, the rats will be euthanized. The skin of the application site will be washed and dissected with a biopsy punch for the tissue layers: epidermis and dermis layer (depth 0-2 mm), subcutaneous tissue and fascia layer (2-4mm), shallow muscle layer and fat pad layer (4-6 mm), and deep muscle (6-10 mm). The tissues from the contralateral site will be dissected with the same method. In addition, the plasma blood samples will also be obtained right before the experiment (time 0) and each hour during the experiment. The drug concentrations in the tissue and plasma samples will be analyzed with a HPLC.




**3)** *In vivo rabbit study*: This study is to demonstrate the cationic prodrugs are also more favorable in penetration into the joint tissues. Rat knee joint is too small for the evaluation of synovial fluid drug concentration in the joint. The rabbit knee joint has a size suitable for this evaluation. Three of the five prodrugs plus the parent drug will be evaluated for the drug penetration into the knee joint. The experiment setup is demonstrated in Figure 6. Rabbit will be maintained under anesthesia with isoflurane gas. One linear dialysis probe will be placed in each knee joint cavity of the two hind legs, one at the drug application site and one at the contralateral site. An iontophoresis drug patch will be placed on the skin of the outer side knee joint and the current returning electrode patch will be placed on the skin of the inner side knee joint. A 0.1 mA constant current will be applied to deliver the drug for 6 hours. Microdialysis samples will also be collected every 20 minutes. A blood sample



will be collected every hour. At the end of the experiment, the rabbit will be euthanized. The tissues at the knee joint area will be dissected. The drug concentrations in the plasma, tissues, and dialysate samples will be analyzed with a HPLC.

**4) Personnel.**

Dr. Guang Yan, project director, is an assistant professor in the Department of Biomedical and Pharmaceutical Sciences at the Idaho State University. He is an expert in transdermal drug delivery and product development. He has a Ph.D. in Pharmaceutics, with more than 14 publications and also one patent in a transdermal patch product. He also worked as scientist or senior scientists with several pharmaceutical companies in the drug product development including topical gels, patches, and also using electric current delivering drug into the eyes. He will coordinate all aspects of this project including experiment designing, prodrug synthesis and characterization, in vivo animal study, preparing patent filing, progress reporting and supervising Mr. Lobo in all aspects of the study. He will dedicate one and half summer months of his effort to this project and is available throughout the budget period for this project.

Mr. Shabbir Lobo is a fourth year Ph.D. student in the Department of Biomedical and Pharmaceutical Sciences under the direction of Dr. Yan. He has a M.S. degree in pharmaceutics and has been working on this project in the past year and will continue working on this project including the prodrug synthesis, in vivo animal evaluation of the prodrugs, and sample analysis. He will be in charge of the day-to-day experiment of this project. He will dedicate 6 calendar months of his effort to this project.

**5) Budget**

$50,000 is requested for this project, in which $27,100 is for salary and fringe benefits (please see summary of proposal budget for details). In addition, $6,300 was budgeted for about 40

Sprague Dawley rats and 15 New Zealand white rabbits with animal care fee, $1,500 for a syringe pump, $2,000 for a microdialysis sample collector, $2,500 for 40 linear microdialysis probes, $1,000 for HPLC vials, $1,800 for microdialysis sample collection vials, $1,000 for scintillation vials, $1,000 for HPLC solvents, $1,000 for HPLC column, $2,000 for chemicals for synthesis, and $2,800 for other lab supplies including gloves, kimwipes, isoflurane etc.

**6) Milestones.**

| Time line | Milestones |
|---|---|
| 1st Quarter | Finish the synthesis and characterization of the additional prodrugs. File a provisional patent for the current technology. |
| 2nd Quarter | Initiate the in vivo rat study of prodrugs penetration into the muscles tissues. Begin to identify potential commercialization partners. . |
| 3rd Quarter | Finish the in vivo rat study. Initial the rabbit study for penetration into joint tissue. |
| 4th Quarter | Finish the in-vivo rabbit study. File for a full patent. Initiate discussion with potential commercialization partners. Write summary report. |

**Institutional and Other Sector Support**

The project director, Dr. Yan, is an assistant professor in the ISU. He is under 9-month academic contract with full salary support from the University. He has been provided a research lab space and research startup fund. He has two graduate students working under his direction. He has previous been supported by the ISU Division of Health Sciences seed grant for his project of using prodrugs for enhancing topical methotrexate delivery, and was supported by the ISU research committee for his project of topical delivery of plasmid DNA nanoparticles into the skin. In addition, he also has a contract project supported by a private pharmaceutical company. Most of the instruments necessary for the proposed project are available in Dr. Yan's lab or in the shared equipment in his department.

**Note: we respectfully request that the confidential information disclosed here is not disseminated outside of the proposal review committee. Thanks.**

# Appendices

## FACILITIES & OTHER RESOURCES

### 1. Laboratory

Dr. Yan, project director, has a 600 sqft research laboratory dedicated for his research use. It is located in the second floor of the Pharmacy Building at the Idaho State University. The laboratory is well equipped with water, electricity, gas, hood, bench space, shelves, cabinets, and studying desks. The lab space is big enough to hold three research staff for running the proposed project. In addition, there are plenty of other common lab spaces available in the same floor of the building for the entire faculty in the Department such as instrument room with FTIR and dissolution apparatus, scintillation counter room, cell culture room, dark room, cold room, centrifuge room, microscopy room, and autoclave room. The research lab is located next to the Dr. Yan's office. Dr. Yan is available all year long supervising and running the research laboratory.

### 2. Office

The PI has office space of 120 sq ft located within the Department of Biomedical and Pharmaceutical Sciences, adjacent to his research laboratory.

### 3. Animal

The Sprague Dawley rats and New Zealand White Rabbits will be purchased from Charles River laboratory. They will be housed in the Idaho State University animal facilities. One of them is located in the basement of the College of Pharmacy building, the same building where the P.I.'s lab and office located. The IACUC is closely monitoring the animal facilities. The animal housing rooms are well controlled with temperature, humidity, and lighting system.

### 4. Computers

There are two desktop computers in the research laboratory. There is one desktop computer and one laptop in the PI's office. There are two IT technicians available in the PI's college for computer service.

### 5. Other Support

A secretary is available for helping the PI in accounting and ordering. A dedicated research statistician in the University is also available for helping the PI in designing the experiments and post-experiment data analysis. All instruments in the PI's University are available for use with limited usage fee.

**EQUIPMENTS**

**Dr. Yan's laboratory:**

Ventilation hood, a Fisher Scientific Isotemp – 20 $^{o}$C freezer, a Eppendorff Thermomixer, a Matrix portable isoflurane anesthesia system, a Precision reciprocal shaking bath, a Virsonic ultrasonic cell disruptor 100, a IKA T25 homogenizer, a Mettler AM 100 analytic balance, a BDC 2000 mixer, two Activa Dose II Iontophoresis delivery unit, a Thermo IEC bench top refrigerating centrifuge, a shaking incubator, Gaymer heating pump, and a HP-1050 HPLC system with chemstation software, an orbital shaker, multiple magnetic stirrers, in vitro diffusion console with 15 diffusion stations with Franz cells, rotary evaporator, patch casting knife, die cutter, flush column chromatography, vacuumed oven, oscilloscope, two side-by-side diffusion cell set.

**Department of Biomedical and Pharmaceutical Sciecnes (general use):**

Leica-DM IRB fluorescent Microscope with Leica DFC 300Fx camera in conjunction with LAS software, Vitris Unitop 400SL freezing dryer, Beckman Coulter Avanti J-26 XPI centrifuge, Beckman Coulter Optima L-100xp ultracentrifuge, Revco Ultima II -80 $^{o}$C Freezer, Hoshizaki ice maker, Steris Stage 3 Sterilizer, Millipore nanopure water purification system, Bio-Teck Synergy HT plate reader, Coulter DELSA 440 SX zeta potential analyzer, Coulter N4 plus dynamic light scattering particle size analyzer, two laminar flow biological hoods for cell culture, two incubation oven for cell culture, liquid nitrogen.

**Idaho State University (general use):**

JEOL 300 MHZ variable temperature NMR, GC-MS.

**CURRICULUM VITAE**

# GUANG YAN, PH.D.


Office Address: College of Pharmacy
Idaho State University
970 S. 5th Ave, Stop 8334
Pocatello, ID 83209

Phone: (208)282-2681
Email: yanguan@isu.edu


## Education:

Aug 1999 – Aug 2004, **Ph.D.**, Pharmaceutics and Pharmaceutical Chemistry
University of Utah, Salt Lake City, USA
Advisor: William Higuchi, Ph.D.

Aug 1996 – July 1999, **M.S.**, Pharmaceutics
Shenyang Pharmaceutical University, Shenyang, China

Aug 1992 – July 1996, **B.S.**, Pharmacy
Shenyang Pharmaceutical University, Shenyang, China

## Employments and Research History:

June 2009 – Present, Assistant Professor, Department of Biomedical and Pharmaceutical Sciences, Idaho State University, Pocatello, ID.

Feb 2009 – May 2009, Senior Scientist, Mylan Technologies Inc., Morgantown, WV

Nov 2006 – Dec 2009, Adjunct Assistant Professor, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah

July 2006 – Jan 2009, Senior Scientist, ZARS Pharma, Salt Lake City, Utah.

Nov 2005 – June 2006, Scientist, Aciont Inc., Salt Lake City, Utah.

Aug 2004 – June 2006, Post Doctoral Fellow, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah.

Aug 1999 – Aug 2004, Research Assistant, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah.

Aug 1996 – July 1999, Research Assistant, Department of Pharmaceutics, Shenyang Pharmaceutical University, China.

**Mentoring Experience**

Shabbir Lobo, Ph.D. student (Spring 2010 to Present)
Nashid Farhan, M.S. student (Spring 2010 to Summer 2012, Graduated)
Naresh Arelly, M.S. Student (Spring 2012 to Present)

**Training**

Preparing the CMC section for NDAs/INDs/CTDs. By Lynda Courville, Director of Education, CfPIE, 2008.

**University/College Service**

ISU College of Pharmacy Technology committee (Fall 2009 to Present)
ISU College of Pharmacy Faculty Affairs Committee (Fall 2010 to Present)
ISU Department of Pharmaceutical Sciences Curriculum Revision Committee (Fall 2011 to Present)

**Professional Service**

Reviewer for Journal of Controlled Release
Reviewer for Journal of Pharmaceutical Sciences
Reviewer for Drug Development and Industrial Pharmacy
Reviewer for Asian Journal of Pharmaceutics
Reviewer for AAPS Journal
Reviewer for Archives of Dermatology
Abstract Screener for AAPS annual meeting

**Professional Societies**

American Association of Pharmaceutical Scientist (AAPS)

**Teaching**

PHAR 9927 Dosage Form Design and Compounding (4 Credits)

PHAR 9926 Pharmaceutical Calculation (3 Credits)

PHAR 9905 Case Study (2 Credits)

PHAR 9906 Case Study (2 Credits)

**Research Support**

Co-investigator: **Guang Yan**, (PI: Sophie St-Hilaire). Improving the oral delivery of a DNA vaccine for rainbow trout. USDA subcontract. Budget period: 06/01/2010 – 12/31/2011. Funded: $85,000. Direct control: $25,000.

PI: **Guang Yan**. Methotrexate prodrugs for topical treatment of psoriasis. Idaho State University Division of Health Sciences Enhancement Grant. Budget period: 01/01/2011 – 06/31/2011. Funded: $10,000.

PI: **Guang Yan**, In Vitro Release Test of Drug Loaded Foley Catheters. Medcatheters, Inc. Budget period: 07/01/2011- 06/30/2012. Funded, $9,000.

PI: **Guang Yan**, (Co-PI: Henan Li). Topical Delivery of Plasmid DNA Nanoparticles into

Skin. Idaho State University Research Grant. Budget period: 01/01/2012 – 12/31/2012. Funded: $25,000.

**Publications**

1. Lobo S, Farhan N, Li H, **Yan G**. Evaluation of diclofenac prodrugs for enhancing transdermal delivery. Drug Dev Ind Pharm. In Press.
2. **Yan G**, Moribe K, Otsuka M, Papangkorn K, Higuchi WI. Quantitative determination of lattice fluoride effects on the solubility and crystallinity of carbonated apatites with incorporated fluoride. Caries Research. 47 (3):193–202 (2013).
3. Ding D, **Yan G**. A Convenient Method for the Synthesis of Aminomethyl-monoalkyl-phosphinate. Chin J Chem, 30: 1906-1908 (2012).
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**Patent**

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