AABPS 2017

Quality as a Competitive Edge

4th CONVENTION

Marriott Courtyard Newark

Newark, Delaware

July 21-22, 2017

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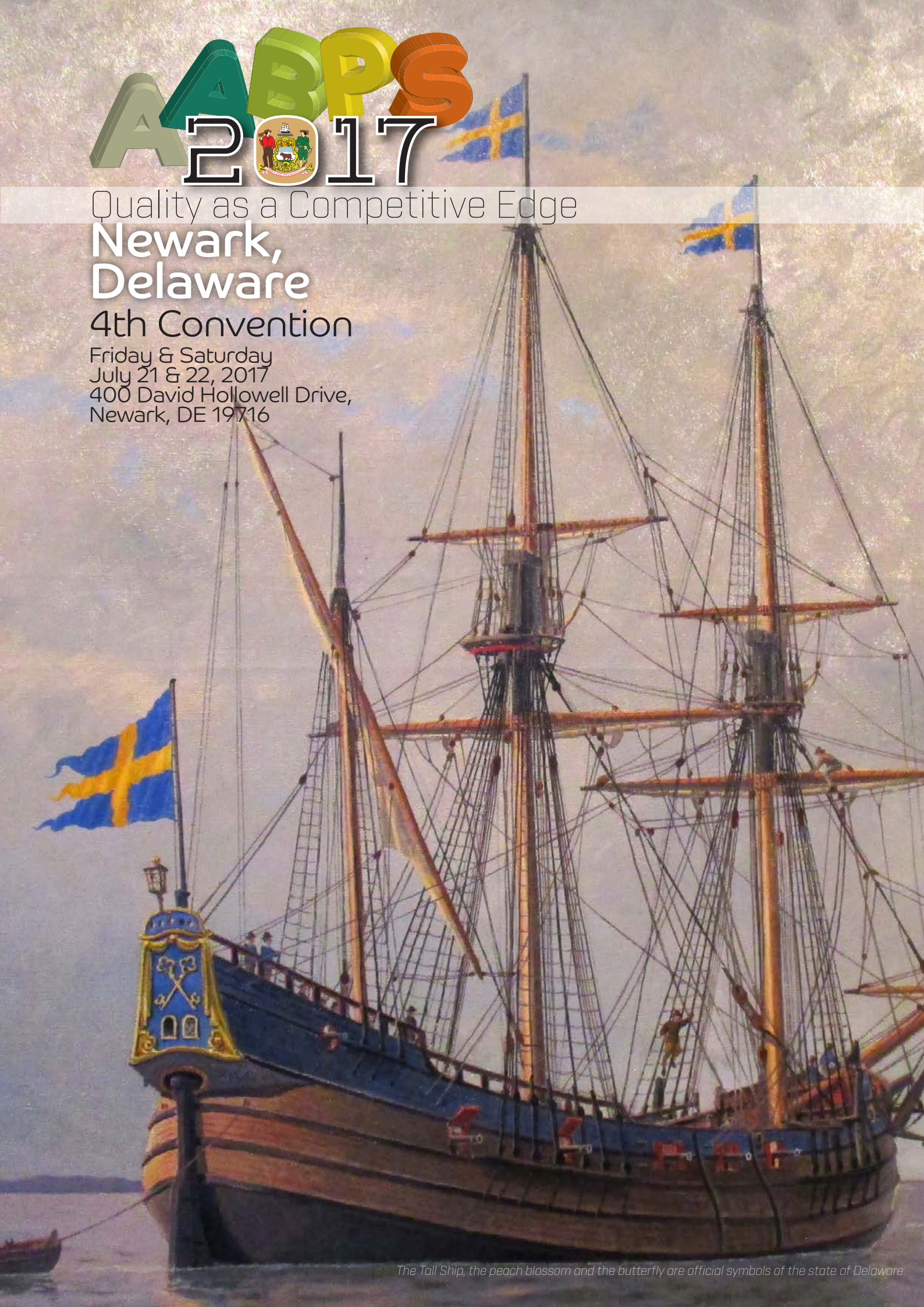
AABPS 2017

Quality as a Competitive Edge

Newark, Delaware

4th Convention

Friday & Saturday
July 21 & 22, 2017
400 David Hollowell Drive,
Newark, DE 19716



The Tall Ship, the peach blossom and the butterfly are official symbols of the state of Delaware.

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Quality as a Competitive Edge

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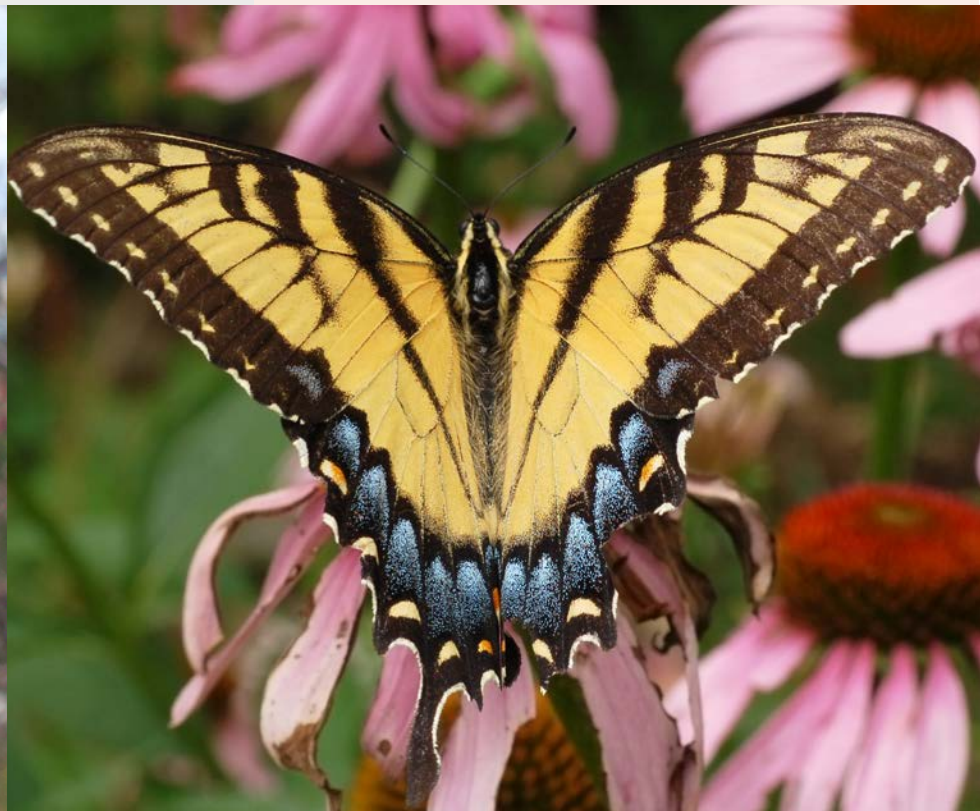

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MESSAGE

I am delighted that the American Association of Bangladeshi Pharmaceutical Scientists (AABPS) is holding its 4th Annual Convention in Newark City, Delaware from July 21-22, 2017. I am also pleased that the AABPS has been increasingly collaborating with the growing Bangladeshi Pharmaceutical industry, which is among our most technologically advanced sectors.

At present, Bangladesh imports only 3% of the drugs it needs, and the local pharmaceutical industry meets the rest 97%. Moreover, the industry exports medicines to about 90 countries in Asia, Africa, Latin America and even in Europe. Recently, some Bangladeshi companies have passed the US FDA inspections paving way for exports of its medicines to the USA.

A significant development for Bangladesh has been the WTO-TRIPS Council granting the country exemption from obligations to implement patents and data protection for pharmaceuticals products until 2033. This waiver provides the industry to manufacture and deliver low cost medicines to the local market as well as to export their products globally.

In fact, prudent government policies, favorable investment climate, skilled and knowledgeable professionals and innovative ideas have been the driving force for such phenomenal developments of Bangladesh's pharmaceutical industry.

The AABPS members could support this progress by sharing their expertise in pharmaceutical research and development with their counterparts in Bangladesh. This could help in making Bangladeshi pharmaceutical products visible in the USA. In this way, they could give back something to their country of origin, Bangladesh.

Once again, my warmest congratulations to all the members of the American Association of Bangladeshi pharmaceutical Scientists (AABPS) and best wishes for the grand success of the event.

(Ambassador Mohammad Ziauddin)

Welcome Note

Message from AABPS President and Executive Committee

On behalf of American Association of Bangladeshi Pharmaceutical Scientists (AABPS), I am very delighted to welcome our members, speakers, guests, sponsors, volunteers, and family members to the 4th AABPS Convention at Newark, Delaware. We are extremely happy to see your overwhelming enthusiasm to learn about innovative research, and an opportunity to network with meeting attendees and mutual exchange of ideas. Like our previous events, the 4th AABPS convention is a continuation of building a stronger AABPS and achieving its mission.

The AABPS executive committee firmly believes that the commitment and dedication of our members have made AABPS advance into a highly visible and successful professional organization. With the help of our members, AABPS has put increased efforts on professional enrichment, enhanced collaboration, leadership and career development, mentor-mentee program and graduate/professional education. AABPS members with their expertise and innovations, are greatly contributing for a better global human health and well-being. In this regard the theme of this year's convention "Quality as a Competitive Edge" is very applicable to our efforts.

The combination of great professional programs, internationally recognized experts and speakers, networking opportunities, finest hospitality and excellent entertainment program during this convention are results of strong commitments of the convener, Dr. Imran Ahmed, and all the convention committee members listed in the convention magazine. We are honored to recognize all of them for their dedication and meticulous work for executing the convention in a very short time span. Also, we would like to specially acknowledge and thank our sponsors, volunteers and families for their support in organizing the convention.

The 4th convention will provide ample opportunities for scientific and professional exchange, collaboration, catching up with old friends or make new friends. Each of the executive members of AABPS are eager to meet you during the convention. If you have any questions or suggestion about AABPS and the convention, please let us know. I hope you will have a very productive and exciting time at the convention surrounded by peers, family and friends.

Best Wishes and Cheers!

Muhammad Delwar Hussain, M.Pharm., Ph.D.
President, AABPS

Message from the Convention Committee Chair

It is my pleasure to welcome our members and guests to the 4th Convention of the American Association of Bangladeshi Pharmaceutical Scientists (AABPS) in Newark, Delaware, the home of the University of Delaware Fightin' Blue Hens.

This year we are delighted to offer an assortment of high quality scientific presentations from experts and thought leaders from the FDA, academia and industry. We are also providing networking opportunities to dialogue with fellow pharmaceutical scientists to share lessons learned and best practices.

The theme for this convention is "Quality as a Competitive Edge". For pharmaceutical scientists life is our life's work. We must constantly remind ourselves that the patient is waiting for our products and breakthroughs. It is a tremendous responsibility that that we embrace with passion and pride. Working in a highly regulated and competitive industry we may be inclined to view quality in terms of rules, regulations, cost and compliance. However, in our profession we must adopt quality as a core value that defines the essence of who we are. Our commitment to quality builds public trust and reputation in our products and services which in turn is what sets us apart from our competition. So, indeed, quality is a competitive edge. Today you will hear insightful and informative talks on end-to-end quality in all aspects encompassing pharmaceutical research, development, supply chain and access to medicine.

An important mission of the AABPS is to inspire our next generation of pharmaceutical scientists to higher education and training as well as to help them with their career development decisions. Previously, we created a mentor-mentee program to pair up our graduate students and post-docs with veterans in the field as well as provide a forum for graduate students to present their research work for peer review and recognition. Due to its popularity and high level of interest from students, we will continue this initiative at this convention. We encourage our experts and senior members of the Association to participate in this mentorship program. Also, we are offering an open session on opportunities for enhancing collaboration and leveraging the expatriate expertise to enhance and strengthen the pharmaceutical and health sector in Bangladesh.

I would like to recognize the many individuals who volunteered their time, talent and treasure to make this convention possible. My special thanks goes to the organizing committee chairs who worked tirelessly under tight timelines, the donors and sponsors without whose financial support this convention would not be possible, and finally the executive committee of the AABPS for their leadership and direction. I would like to recognize our young talent- Rajib Paul and Jahidur Rashid- who energized and motivated us with their action-oriented and laser focus abilities. Last but not the least, I would like to extend my personal thank you to two "old timers" whose wisdom, experience and calm was invaluable- Delwar Hussain, our AABPS President who experienced a personal loss but still supported us without interruption and our advisor- Zahur Islam, whose expert advice calmed us down in difficult times.

Finally, the AABPS is not all work and no play. We conclude convention with a fun-filled entertainment with an inspirational talk on entrepreneurism, dinner and a cultural program with Bangla song and music by well-known artists. Please enjoy the convention and let's get started...

Imran Ahmed, Ph.D.
Convention Convener, AABPS

AABPS 2017

Message from Newark City Mayor, Delaware

July 13, 2017

Dear Participants:

It is my great pleasure to welcome you to the City of Newark. We are delighted our wonderful City was chosen to host the 4th Annual Convention of the American Association of Bangladeshi Pharmaceutical Scientists on July 21-22, 2017. We hope you feel at home during your stay!

Newark is a wonderful place to live, work, and play. As you know, we are the home of the University of Delaware that offers students a great education, and much culture, including the arts, music and sports. Newark has made a commitment to preserving our downtown that hosts a variety of restaurants and shops, and we encourage you to leisurely walk our vibrant Main Street, located just a few blocks from the Courtyard by Marriott. While Newark has grown into a bustling small city, it continues to maintain its college town charm and commercial diversity.

On behalf of the Newark City Council and Administration, I hope you enjoy your stay and again welcome you to our city.

Sincerely,

Polly Sierer

Mayor

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Imran Ahmed, PhD
Vice-President

Mohammad Hossain, PhD
General Secretary

Abdus Salam, MS
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AABPS **4th Convention Committee**

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-Imran Ahmed
-Rajib K Paul

Logistics
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-Mohammad Hossain

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-Abdus Salam
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- Jahidur Rashid
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-Mohammad Hossain
-Muhammad Jamil Habib

Graduate Students Affairs
-Jahidur Rashid
-Utpal Mondal

Graduate Student Award
-Mohammad Hossain
-Zahur Islam
-Jahidur Rashid
-Muhammad Jamil Habib
-Muhammad Delwar Hussain

Convention Program

Marriott Courtyard Newark- University of Delaware, Newark, Delaware
Friday & Saturday, July 21-22, 2017
Program Theme: ***Quality as a Competitive Edge***

FRIDAY, JULY 21, 2017 – CONVENTION KICK-OFF AND WELCOME RECEPTION

TIME	TITLE	MODERATOR	ROOM
6:00 pm – 8:00 pm	**Set-up and Registration**	Abdus Salam, MS	Foyer
6:15 pm – 7:15 pm	**Meeting of the Convention Committee Team**	Imran Ahmed, PhD	Board Room
7:15 pm – 8:15 PM	**Student Forum- Research Presentation & Mentor-Mentee Career Consultation**	Jahidur Rashid, PhD	Salon A/B/C
8:30 pm – 10:30 pm	**Dinner reception** **Sponsored by and compliments of AABPS**	Muhammad Delwar Hussain, PhD and Imran Ahmed, PhD	Salon A/B/C

SATURDAY, JULY 22, 2017

TIME	TITLE	MODERATOR	ROOM
8:00 am – 6:00 pm	R E G I S T R A T I O N	Abdus Salam, MS	Foyer
8:00 am – 8:45 pm	**Breakfast and Networking**		Salon A/B/C Patio
MORNING SESSION			
9:00 am to 9:15 am	**Session 1: Welcome**	Moderator/Speaker	Salon A/B/C
9:00 am–9:10 am	Welcome Address	Muhammad Delwar Hussain, PhD *PRESIDENT, AABPS*	
9:10 am-9:15 am	Opening Remarks	Imran Ahmed, PhD *CONVENER, 4TH CONVENTION*	
9:20 am -10:30 am	**Session 2: Plenary Session I- Quality Systems**	Session Moderator: Muhammad Jamil Habib, PhD *HOWARD UNIVERSITY*	Salon A/B/C
9:20 am-9:50 am	**Regulatory Quality & Compliance Systems:** Clinical Pharmacology Considerations for Assessment of Biosimilarity	Ping Ji, PhD *SENIOR CLINICAL PHARMACOLOGIST, OCP, FDA*	
9:50 am-10:20 am	**Quality Medicine and Affordable Healthcare:** Prescription Practices and the Role of Pharmaceutical Industry in Strengthening the Health Care System	M. Hafizur Rahman, MBBS, MPH DrPH; *JOHNS HOPKINS UNIVERSITY BLOOMBERG SCHOOL OF PUBLIC HEALTH*	
10:20 am-10:30 am	Brief Question & Answer	Moderated by Muhammad Jamil Habib, PhD	
10.30 AM - 10.50 AM: MORNING REFRESHMENT BREAK (Salon A/B/C Patio)			
10:55 am – 11:45 am	**Session 3: Keynote Speech I**	Session Moderator: Rajib Paul, PhD; *FDA*	Salon A/B/C
10:55 am- 11:25 am	**CMC Quality Expectations:** "Pharmaceutical Quality Throughout the Drug Product Lifecycle – A Regulatory Perspective from FDA/CDER's Office of Pharmaceutical Quality (OPQ)"	Susan Rosencrance, PhD *DIRECTOR, OFFICE OF LIFECYCLE DRUG PRODUCTS (OLDP), FDA*	
11:25 am-11:45 am	Combined Moderated Panel Discussion with Speakers from Sessions 2 & 3	Co moderated by Muhammad Jamil Habib, PhD & Rajib Paul, PhD	
11.45 AM - 12.55 PM: GROUP LUNCH BUFFET (Salon A/B/C Patio)			

Convention Program

TIME	TITLE	MODERATOR	ROOM
1:00 pm -1:55 pm	**Session 4: Plenary Session II- Quality Right First Time**	Session Moderator: Jahidur Rashid, PhD *UNIVERSITY OF UTAH*	Salon A/B/C
1:00 pm –1:30 pm	**Quality Decision-** Bioequivalence Studies with CMC Implications	Professor James E. Polli, PhD *UNIVERSITY OF MARYLAND*	
1:30 pm –2:00 pm	**Quality Formulations for Success:** Developing Drug Product According to Biopharmaceutical Risk Assessment Roadmap	Professor Abu T. Serajuddin, PhD *ST. JOHN'S UNIVERSITY*	
2:00 pm- 2:10 pm	Brief Question & Answer	Moderated by Jahidur Rashid, PhD	
2.10 PM - 2.30 PM: AFTERNOON REFRESHMENT BREAK (Salon A/B/C Patio)			
2:35 pm – 3:25 pm	**Session 5: Keynote Speech II**	Session Moderator: Tazin Mahnaj, PhD, *FDA*	Salon A/B/C
2:35 pm – 3:05 pm	**Quality Generic Drug Development:** Opportunity and Challenges for Professionals in Pharmaceutical Arena	Salah U. Ahmed, PhD; *PRESIDENT AND CEO, ABON PHARMACEUTICALS*	
3:05 pm – 3:25 pm	Combined Moderated Panel Discussion with Speakers from Sessions 4 & 5	Co-moderated by Jahidur Rashid, PhD and Tazin Mahnaj, PhD	
3:30 pm – 4:30 pm	**Session 6: Graduate and Post Graduate Forum**		Salon A/B/C
3:30pm - 4:15pm	Postgraduate Options and Guidance	Muhammad Jamil Habib, PhD *HOWARD UNIVERSITY*	
4:15 pm – 4:30 pm	Research Presentations		
4:35 pm – 5:20 pm	**Session 7: Forum Discussion**	Moderator: Shamim Ahmed, PhD *SENIOR DIRECTOR DEVELOPMENT OPERATIONS, R&D, PFIZER*	Salon A/B/C
4:35 pm – 5:20 pm	Enhancing Pharmaceutical Sector Collaboration with Bangladesh	Forum Discussion	
5:25 pm - 5:55 pm	**Session 8: AABPS Business**		Salon A/B/C
5:25 pm – 5:45 pm	Future Plans for AABPS	Muhammad Delwar Hussain, PhD	
5:45 pm – 5:55 pm	Financial Report	Abdus Salam, MS	
6:00 pm – 6:10 pm	**Session 9: Closing Remarks**	Muhammad Delwar Hussain, PhD	Salon A/B/C

EVENING SESSION

6.30 PM : GROUP DINNER BUFFET (Salon A/B/C Patio)			
	Dinner Speech	Salah U. Ahmed, PhD	Salon A/B/C
	Awards and Recognitions	Muhammad Delwar Hussain, PhD *PRESIDENT, AABPS*	Salon A/B/C
7.30 pm	E N T E R T A I N M E N T	Program Director & Emcee: Rajib Paul, PhD	Salon A/B/C
10:00 pm	Closing		Salon A/B/C

Invited Speaker

Ping Ji, PhD,
Senior Clinical Pharmacologist, OCP, FDA

Dr. Ping Ji is lead biologics and master reviewer in the Office of Clinical Pharmacology Division 2 in FDA. She joined FDA in 2008. Before that, she was working in Bristol-Myers Squibb for 5 years working on Drug Development and Clinical Research. She got her PhD in Pharmaceutical Sciences from University of Minnesota and BS in Pharmacy from Beijing Medical University. She is the Chair of PKPD subcommittee in National Biotechnology Conference and has also coauthored many manuscripts and abstracts.

Abstract:

Biosimilars are a category of biologic products that are licensed in the United States through a pathway created under the Biologics Price Competition and Innovation Act of 2009 (BPCI Act). FDA recommends a stepwise approach in developing evidence to support a demonstration of biosimilarity. The demonstration of biosimilarity should consider the totality of the data and information, including structural and functional characterization, nonclinical evaluation, human PK/PD data, and clinical data, including immunogenicity data. The purpose of the presentation is to present clinical pharmacology consideration of biosimilars. The objective and study design aspect of a well-designed clinical PK and/or PD study in a biosimilar development program will be covered in the presentation.

M. Hafizur Rahman, MBBS, MPH DrPH.
Johns Hopkins Bloomberg School of Public Health

Title of the presentation:

Medicine and Affordable Healthcare: Prescription Practices and the Role of the Pharmaceutical Industry in Strengthening the Health Care System

Synopsis:

Irrational use of medicine is prevalent in Low and Middle Income countries (LMIC). People's use of medicine is governed by social, cultural, political and economic conditions. We have analyzed factors leading to irrational medicine prescription, including socio-cultural factors associated with drug prescription practices, factors associated with government policies and regulatory structures, and factors related to pharmaceutical companies. Suggested comprehensive framework to promote rational use of medicine in LMIC illustrates how these factors operate and influence drug prescription practices of formal and informal health care providers in LMIC.

To promote and practice rational use of medicine, understanding the pharmaceutical market and its key players that affect the delivery of pharmaceuticals is critical. A framework will identify and understand the role of key stakeholders, specifically pharmaceutical companies and drug detailers, in ensuring safe and affordable access to pharmaceuticals by the poor in Bangladesh. Findings from a pilot study conducted in Chakaria, Bangladesh are used to fill in the knowledge gaps.

Biography:

M Hafizur Rahman, MBBS, MPH, DrPH, a faculty member at the Johns Hopkins University Bloomberg School of Public Health, USA, is a public health physician having more than 15 years of experience in directing health systems research and training programs in low and middle income countries. Dr. Rahman's research objectives/interests focus on improving health systems performance for the poor, protecting the poor and vulnerable against the impact of health-related shocks, developing innovations in health service provision, and accessibility and utilization of health services for the poor and vulnerable. Major areas of his research include mortality and morbidity measures in maternal, neonatal and child health, program impact evaluation, health care seeking behavior, and access to pharmaceuticals and drug markets. While conducting research and intervention studies on health systems in general, and effective health service delivery in particular in a number of Asian and African countries, Dr. Rahman has offered courses on health systems in low and middle income countries to the graduate students at Hopkins. He has been engaged in teaching/training in strategic leadership and management course for the health care providers in low and middle income countries. He has also been engaged in teaching health systems research methodology in other research and academic universities/institutions in Asia and Africa. As a faculty of Johns Hopkins School of Medicine (joint responsibility), Dr. Rahman has been involved in clinical research with the colleagues from Johns Hopkins School of Medicine. Dr. Rahman served as an Advisor and a Consultant at the international organizations including the World Health Organization (WHO) and the World Bank, Washington DC. Dr. Rahman has published his research work in leading peer-reviewed scientific journals.

Key Note Speaker

Susan Rosencrance, Ph.D.
Director, Office of Lifecycle Drug Products, Office of Pharmaceutical Quality
Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Dr. Susan Rosencrance currently serves as the Director for the Office of Lifecycle Drug Products in the Office of Pharmaceutical Quality (OPQ). In this capacity, she directs procedures and processes for evaluating and assessing drug product quality during the lifecycle of both brand name and generic drug products. Prior to joining the FDA, Susan worked at Merck & Co.'s R&D Laboratories in Rahway, New Jersey. She joined the Office of Generic Drugs (OGD) in 1991 and spent the majority of her tenure in CDER working on generic drug products. She held various roles within OGD including senior chemistry reviewer, team leader, deputy division director, and OGD Deputy Director for Chemistry. Susan also served as the Deputy Director for Generic Drug Chemistry in the Office of Pharmaceutical Science prior to the formation of OPQ. Susan holds a Ph.D. in Chemistry from American University and completed her dissertation research at the NIH Laboratory of Biophysical Chemistry conducting a molecular dynamics study on hydrophobic interactions in alpha-helical coiled coils found in proteins. She received her bachelor's degree in Biochemistry from Hood College and also completed studies at the University of Strasbourg in Strasbourg, France in the Institute Internationale D'Etudes Française – Université Louis-Pasteur.

Key Note Speaker

Salah U. Ahmed, PhD

Dr. Salah U. Ahmed is the Founding President & CEO of Abon Pharmaceuticals, LLC, a Specialty Pharmaceuticals, engaged in the development of high barrier to entry generic products as well as brand products following 505(b)(2) pathway. Started in 2009, Abon established itself as having the expertise to develop drug products with significant formulation challenges. Abon's current portfolio has an estimated market cap of about $ 2.5 billion. A team of high caliber scientists, and supporting management personnel are key to Abon's competent competitiveness. In addition to a broad range of oral and injectable products, Abon has multiple brand products in the pipeline based on its patented technology, covering route of administration otherwise not possible for the specific drugs under development.

Prior to the establishment of Abon, Dr. Ahmed was the Executive Vice President, Global Head of Research and Development and Chief Scientific Officer at Barr Pharmaceuticals, Inc. Dr. Ahmed led diverse R&D operations in the USA and several countries in Europe developing generics, proprietary pharmaceuticals, API and biotechnology products. He managed a portfolio with a broad range of Drug Delivery Systems (DDS) including parenteral, nasal, ocular, oral, transmucosal, transdermal, and intrauterine routes of administration.

Dr. Ahmed received his B. Pharm (Hons) and M. Pharm from University of Dhaka, Bangladesh, prior to earning his MS in Industrial Pharmacy and PhD in Pharmaceutical Sciences from St. Johns University, New York. He has about four decade of pharmaceutical experience in academia and industry. During his tenure at Barr Labs, his leadership role in product development significantly contributed to Barr's transformation to a specialty pharmaceutical company and a world leader in the generic pharmaceuticals industry.

Dr. Ahmed has a notable track record in pharmaceutical research involving special DDS, solid-state interactions, statistical design and mathematical modeling in product development, in-vitro/in-vivo performance of dosage forms. His interests extended to cGMP facility design and mentored individuals to achieve professional excellence. His research work in drug development originated more than 30 patents. He authored or co-authored more than 70 research papers, abstracts and book chapters. He has been a distinguished speaker in many pharmaceutical conferences/workshops in the USA and in Europe.

Dr. Ahmed currently advises academic committees in two of the largest Universities offering Pharmaceutical education in the New York metropolitan area. He is a member of the Overseers Council with Long Island University and is an advisor to the faculty for the Graduate program in College of Pharmacy and Health Science St. John's University.

The present topic would discuss the trend and challenges in the industry and the role one can play to benefit his/her Organization. Since significant number of Bangladeshis are in leadership position in industry, an overview of opportunities and challenges impacting industries is expected to benefit us in today's competitive environment.

James Polli, PhD
Professor of Pharmaceutical Sciences at University of Maryland Baltimore
University of Maryland Baltimore

Title: Bioequivalence Studies with CMC Implications

Abstract

Contributors to on-going pharmaceutical quality are formulation science and well-designed bioequivalence methods/standards. The goal of this lecture is to review three recently completed bioequivalence studies that inform about the performance of a generic tablet in patients, as well as the impact of tablet/capsule excipients on bioequivalence. The average bioequivalence standard will be discussed in the context of patient sub-populations. After completion of this activity, the participant will be able to:

- Discuss results from a randomized, double-blind, multiple-dose, steady-state, fully replicated bioequivalence study comparing generic to brand in "generic-brittle" epilepsy patients
- Explain average bioequivalence in the context of a patient sub-population
- Describe the impact of several common excipients on oral Biopharmaceutics Classification System (BCS) class 3 drug bioequivalence

Biography:

Dr. James E. Polli is Professor and Ralph F. Shangraw/Noxell Endowed Professor in Industrial Pharmacy and Pharmaceutics at the University of Maryland School of Pharmacy. He received a B.S. in Pharmacy from the Philadelphia College of Pharmacy and Science and a Ph.D. (pharmaceutics) from the University of Michigan. He is also co-Director of the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI; www.cersi.umd.edu), an FDA-funded collaborative agreement with the Agency, and Director of the online MS in Regulatory Science program (www.pharmacy.umaryland.edu/regulatoryscience). His two main research interests are 1) maximizing oral bioavailability through formulation and chemical approaches and 2) developing public quality standards for oral dosage forms. He has published in the areas of dissolution, drug intestinal permeability, transporter substrate requirements, prodrug design, oral bioavailability, in vitro - in vivo correlation, and bioequivalence. Dr. Polli is a fellow of the American Association of Pharmaceutical Scientists, an Editorial Board member of several journals, an Editor of Pharmaceutical Research, and a member of the FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee. He teaches professional pharmacy students and graduate students, and has served as advisor to 19 Ph.D. graduates.

Abu Serajuddin, PhD. Professor, St. John's University

Dr. Abu Serajuddin is Professor of Industrial Pharmacy at St. John's University, Queens, NY. Prior to joining St. John's in September 2008 as a Full Professor, he worked for over 32 years in the pharmaceutical industry in scientific and managerial positions. In his latest position in the pharmaceutical industry, he served as Executive Director of Research and Development for Novartis Pharmaceuticals Corp. from 2003 to 2008. Novartis Pharmaceuticals named him Novartis Leading Scientist, which is a top honor bestowed by the company for extraordinary contribution to the development and growth of the company through scientific excellence. Dr. Abu Serajuddin authored over 100 research papers, book chapters and patents, having 6400 citations, and he made over 125 invited presentations in major scientific conferences in the USA and other parts of the world. For his research achievements, he received three of the most distinguished awards given by the American Association of Pharmaceutical Scientists (AAPS): AAPS Research Achievement Award for Formulation Design and Development (FDD) in 2010, AAPS Research Achievement Award for Manufacturing Science and Engineering (MSE) in 2014, and AAPS Lipid-Based Drug Delivery Outstanding Research Award in 2015. More recently, in 2016, he was the recipient of the IPEC Ralph Shangraw Memorial Award, the highest scientific recognition given by the International Pharmaceutical Excipients Council (IPEC) for research on pharmaceutical excipients and excipient-related technologies. Additionally, Dr. Serajuddin attained Fellow status in American Association of Pharmaceutical Scientists (AAPS) and American Pharmacists Association (APhA).

Infliximab (Remicade®): from bench to clinical practice. A paradigm shift in the management of Rheumatoid Arthritis

Mahboob U. Rahman, MD PhD
Vice President Therapeutic Area Head, Autoimmunity & Skeletal Diseases, Global Clinical Development
Immunology & Dermatology Franchise, Novartis Pharmaceuticals Corpoartion

Adapted from:

Hsia et al. Infliximab (Remicade®): from bench to clinical practice. A paradigm shift in rheumatology practice. *APLAR Journal of Rheumatology 2006; 9: 107– 118*

ABSTRACT:

Rheumatoid Arthritis (RA) is a serious debilitating disease. Until early 1990s management of RA involved symptomatic relief only. Even after Disease Modifying Anti-Rheumatic Disease Drugs (DMARDs) like methotrexate became standard of care in mid-1990s the RA disease activity could not be fully controlled and structural damage and eventual physical disability remained common. In addition, toxicities of these conventional DMARDs prevented their effective use. Infliximab (an anti-TNFα monoclonal antibody) being the first targeted biologic therapy brought in a paradigm shift in the way RA is managed, by providing not only dramatic improvement of signs and symptoms but also inhibition of structural damage progression. The development of infliximab from bench to clinical practice and how it and subsequent other biologic therapies changed the way RA is managed will be discussed.

CONVENTIONAL THERAPIES FOR RA (Rheumatoid Arthritis)

RA is a chronic, progressive systemic immune-mediated inflammatory disease manifesting primarily as inflammation (pain, swelling, and stiffness) and destruction of synovial joints leading to severe disabilities. RA being a systemic disease also affects rest of the body with characteristic extra-articular manifestations including but not limited to increased incidence of cardiovascular disease and malignancy, leading to substantial morbidity and increased mortality. By the early and mid-1990s several conventional therapies became available which included corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), and disease-modifying antirheumatic drugs (DMARDs). DMARDS (methotrexate, cyclosoporine, hydroxychloroquine, sulfasalazine, gold salts, and penicillamine) were often administered if other non-steroidal anti- inflammatory drugs were unsuccessful.[1,2] However, due to their lack of adequate efficacy or due to toxic effects, most patients could not be sustained on DMARDs for long.[3,4] By the mid 1990s, methotrexate emerged as the DMARD of choice for long-term use in RA patients.[1,2,5] However, methotrexate is not able to adequately control signs in symptoms in most patients and also could not adequately inhibit the structural damage progression.[6,7] Given the suboptimal benefits achieved with DMARDs and corticosteroids for the treatment of RA, an unmet medical need still existed.

Development of Infliximab

Infliximab (Remicade®) is a monoclonal antibody that binds and neutralizes the cytokine tumor necrosis factor-α (TNF-α) (see Figure 1). TNF-α was first detected as an endotoxin-

induced serum factor that lysed murine tumor cells, and this biologic activity provided its name, TNF.[8] Once the gene for TNF-α was cloned and the re-combinant protein was purified numerous additional biologic functions became apparent, including the critical role of TNF in the pathogenesis of a number of immune-mediated inflammatory diseases (IMIDs).[9] Infliximab has been approved by the FDA for reducing the signs and symptoms of many IMIDs including rheumatoid arthritis (RA), Crohn's disease (CD), ankylosing spondylitis (AS), ulcerative colitis (UC), and psoriatic arthritis (PsA).

It all began in the mid 1970s, when researchers at the Laboratory for Molecular Biology in Cambridge, UK successfully fused a myeloma cancer cell with an immune cell to create a hybridoma, and the scientific field of monoclonal antibodies (mAbs) was born, which led to the Biotech revolution.

On May 16, 1979, Centocor, Inc. was founded by Hubert Schumacher and his associates, and was incorporated in Pennsylvania, USA. At the time, endotoxins were known to induce the production of TNF-α, and it was also known from animal models that conditions such as sepsis could be induced by TNF-α. Researchers believed that inhibiting TNF-α could be a viable approach to prevent and manage sepsis. Centocor started developing a TNF-α inhibitor (a new class of molecules at the time) initially for the treatment of sepsis in the mid to late 1980s. One of the candidate molecules was 'cA2', which was later generically named 'infliximab'. This chimeric monoclonal antibody against TNF-α was developed from a murine monoclonal antibody, 'A2', that was made by Dr. Jan Vilcek and Jumming Le of New York University,[10] while Drs. Peter Daddona, Scott Siegel, and David Knight, under the leadership of Dr. John Ghrayeb at Centocor, completed the chimerization and characterization of cA2.[11]

Meanwhile, in England, Drs. Ravinder Maini (a rheumatologist) and Marc Feldmann (an immunologist) had joined efforts to examine the role of specific cytokines in inflammatory pathways leading to RA. Feldmann and Maini's interests and approach to studying human tissue at the height of the disease, rather than animal models, proved to be critical to the identification of TNF-α as a key regulator of the inflammatory and tissue-destructive pathways in RA. Feldmann's laboratory studied the total cell mixture, reflecting the complex interactions of all cells present in vivo in synovium, rather than the monolayers of adherent synoviocytes that were passaged for several weeks before being studied. Dr. Fionula Brennan, a colleague of Marc Feldmann, used this total cell mixture system developed by disaggregating synovium obtained from patients with RA who were undergoing joint surgery in experiments to study the ability of various anti-cytokine antibodies to interfere with interleukin (IL)-1 production. At that time, IL-1 was considered to be of major importance in the pathogenesis of inflammatory arthritis. Dr. Brennan showed that a mouse monoclonal antihuman TNF-α antibody blocked the production of IL-1. This unexpected outcome, as well as that of other experiments showing TNF-α blockade, resulted in down-regulation of several other inflammatory cytokines including macrophage colony stimulating factor (M-CSF), IL-6, and IL-8, lead to the concepts of TNF-α being a 'master regulator' and the 'TNF-dependent cytokine cascade', which were soon shown to be over-simplistic.

Another view of the success of anti-cytokine intervention in RA at that time was the existence of a tilt in the balance between pro- and anti-inflammatory factors that favor inflammation, and that the disruption of any of these factors reversing the tilt of balance toward anti-inflammatory factors, could result in disease improvement. This view led to the exploration and development of antirheumatic and anti-IMID therapies that have since targeted different cytokines and different components of the immune system. These therapies included rituximab (anti-B-cell),[12,13] anakinra (anti-IL-1 agent),[14] tocilizumab (anti-

IL-6 agent),[15] and abatacept (anti-T-cell activation).[16] These studies contradicted the long-held belief that blocking cytokines individually or in combination was not practical. Most research in RA at this time focused on T-cells as a target, including CD4+ T-cells. In the 1990s, several clinical trials were conducted using anti-CD4 mAbs as treatment for patients with RA.[17–19] Treatment with anti-CD4 mAbs was shown to decrease circulating CD4+ T-cell counts; however, clinical efficacy was inadequate.[17–19] Similarly, a humanized anti-lymphocyte monoclonal antibody, CAMPATH-1H was studied in RA clinical trials.[20–21] The results of these studies showed that CAMPATH-1H reduced lymphocyte counts; however, clinical efficacy was not maintained over time. Despite much focus on the involvement of T-cells and CD4+ cells, some investigators did not overlook the role of TNF-α in RA.

The importance of TNF-α in RA was further established in Dr. Maini's laboratory, where the immunohistology of rapidly frozen rheumatoid biopsies demonstrated the presence of TNF-α and the up-regulation of TNF-α receptors. It was also shown that TNF-α blockade by a mouse anti-TNF-α antibody ameliorated collagen-induced arthritis in mice. However, anti-TNF-α therapy in chronic inflammation was still considered by many to be a high-risk strategy, given the potential redundancy in the immune system (multiplicity of cytokines with similar actions and other cytokines emerging to restore the activity of a blocked cytokine). There were also concerns about the high costs, safety, immunogenecity, and the inconvenience of injections, which would make TNF-α inhibitors impractical therapeutic agents.[22]

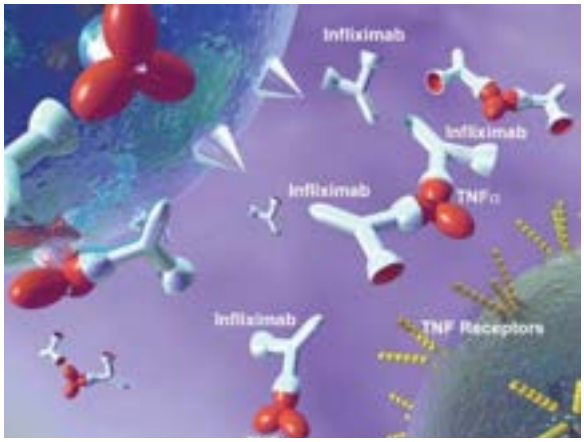

Figure 1: Infliximab binds and neutralizes the biological activity of TNF-α by blocking TNF-α from binding to its receptors.

Despite general concerns about TNF-α inhibitors, cA2 (later named infliximab) research continued and eventually led to the first human trial of infliximab conducted in 10, and subsequently, 20 RA patients under the direction of Drs. Michael Elliot, Marc Feldmann, and Ravinder Maini at the Kennedy Institute.[23] Treatment with cA2 resulted in significant, and is some cases dramatic (documented in videos at the Kennedy Institute), clinical improvement of RA for these patients.[24–26] The results of these small, exploratory studies led to full clinical investigation of anti-TNF-α in a pivotal phase III study, Anti-TNF Therapy in RA with Concomitant Therapy (ATTRACT).[26] Dr. Harlan Weissman, who led Centocor's Clinical Research and Development at the time, directed the development of infliximab as a therapeutic agent for RA. Dr. Weissman along with Drs. Thomas Schaible (clinical scientist) and Kimberly DeWoody (biostatistician) played a crucial role in the development and execution of the ATTRACT protocol, which led to the FDA's approval of infliximab for the treatment of RA.[26] While Drs. Feldmann and Maini were the first investigators to treat patients with cA2, the first publication was a case report describing the use of a TNF-α blocking agent in a patient with CD.[27] Five years later, in August 1998, the FDA approved infliximab, later registered as Remicade®, for the short-term treatment of CD, representing the first approval for a monoclonal antibody directed against TNF-α in any indication by a regulatory authority worldwide. This initial approval was followed approximately one year later by the FDA's approval of infliximab plus methotrexate (MTX) for the treatment of the signs and symptoms of RA in patients who had an inadequate response to MTX alone.

Conclusion

In the late 1990s the introduction of infliximab (a targeted anti-cytokine therapy), as well as other TNF-α inhibitors, offered a dramatically better treatment option for patients with RA in terms of controlling signs and symptoms, preventing structural damage, and being reasonably safe and well-tolerated, and thereby changing the RA treatment paradigm. Now many other targeted anti-cytokine therapies have emerged which has made a dramatic difference in the lives of not only patients with RA but several other rheumatologic disease.

Infliximab was quickly followed by several other anti-TNF-α agents as well as other biologic and small molecule therapies for RA. Etanercept (another anti-TNF-α agent) was almost simultaneously marketed along with Infliximab (in 1998). 3 other anti-TNF-α agents, adalimumab, golimumab and certolizumab were approved by 2010. In addition to the anti-TNF-α agents other biologics including abatacept (a co-stimulation inhibitor), rituximab (anti-CD20) and tocilizumab (anti-IL-6) are part of the armamentarium against RA. These agents are however, not completely safe, and are not oral (injectable) and expensive.

The development of oral agents like the JAK-inhibitors (tofacitinib and baricitinib) has provided similar efficacy as the biologics with the convenience of oral administration. Biosimilars of the biologic agents are arriving and may lower the cost to some degree. Safety remains a concern with all these agents.

Before the advent of infliximab the focus was on providing symptom (pain, swelling, and stiffness) relief and managing the toxicities of the conventional DMARDs. With the arrival of infliximab and other biologics not only the RA patients have dramatically better symptom relief but they are now maintaining the structural integrity of their joints, reduced cardiovascular morbidity/mortality and better quality of life. Even remission and cure are being discussed-a paradigm shift in the management of RA.

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Pegylated Liposomes for BBB-GLUT Transporter Targeting

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***Introduction*:**

Blood brain barrier (BBB) is a complex structure of endothelial cells and tight junctions that restrict the permeability of wide array of drug molecules[1]. Due to the restricted nature of the BBB, delivery of active therapeutics in efficient amount across this barrier became a major challenge. Several biological based and chemical based approaches have been implemented by the researchers to overcome this obstacle. However, transporting of encapsulated active therapeutics such are pegylated liposomes with targeting ligand by utilizing the BBB transporter is getting more attentions. Therefore, the main objective of the current research study was to investigate glucose transporter (GLUT) targeting of Citalopram-HBr (Cit-HBr) for increased permeability across the BBB. Our previous study demonstrated that optimized N-Acetyl Glucosamine (NAG) coated pegylated formulation was able to target the rat endothelial BBB at low cytotoxicity[2]. Hence, the objective of the current study was to investigate the effects of particle size, entrapment efficiency and drug release characteristics of pegylated multilamellar liposomal formulations on Citalopram Cit-HBr permeability across the rat endothelial BBB cell culture.

***Methods*:**

Five NAG coated pegylated multilamellar liposomal formulations were prepared shown in table-1 by the thin film method as described by Evjen et al. (2011)[3] The entrapped drug within liposomal vesical was quantitated after centrifugation. The particle size, the polydispersity index (PDI), Zeta potential were determined by using Malvern multiple light scattering technique. Float-A-Lyzer dialysis tubes (cellulose ester dialysis tube, 1 ml, molecular cutoff 50kD, Spectrum Laboratories, Los Angeles, CA) were used to determine the in-vitro leakage of Cit-HBr from the liposomal formulations. The initial burst effect and the delayed release characteristics of the released drug from the liposomal vesicles were represented by selecting the percentage of drug release from 2 and 24 hours. Primary rat brain microvascular endothelial cells (RBMECs) were used for cytotoxicity analysis and drug permeability testing. Cytotoxicity assay was performed with the CellTox Green Cytotoxicity test kit [4]. Apical-Basal transport of the five liposomal formulations was evaluated across the RBMECs monolayer as described by Vernon et al., 2011[5].

Results and discussion:

The results revealed that particle size, entrapment efficiency, zeta potential and PDI values of the five liposomal formulations ranged from 13 - 2003 nm, 50 - 75%, -0.126 to -29.6mV and 0.02 - 1, respectively (Fig 1). Two release time points, namely 2 hours and 24 hours, were selected to understand the initial burst effect followed by sustained release characteristics of the formulations, respectively. As shown in Figure 1, all five liposomal formulations showed sustained release characteristics. The in vitro RBMECs

permeation models were developed. Cytotoxicity results indicated a cell viability of more than 90% for all five formulations over a drug concentration range of 0.312 –0.625 mg/ml and more than 49% over a concentration range of 1.25-2.5 mg/ml (Fig-2). TEER of the monolayer was ≥ 200 Ωcm^2 and Lucifer Yellow (LY) transport was less than 1% before and after the transport study in RPBMECs (data not shown). Apparent drug permeability (Papp) values for five formulations ranged from 5.01×10^4 cm/min to 15×10^4 cm/min (Fig 3). As shown in Figure 4 and 5 more than 90% of the entrapped Cit-HBr was transported across the RBMECs by the formulation F2 that achieved 53.86% of entrapment efficiency and exhibited particle size of 1153 nm, PDI of 0.13 and Zeta potential of -1.09 (Fig-1).

Table 1: Composition and processing variables of five liposomal Cit-HBr formulations

Batch	Phospholipon (mg)	Cholesterol (mg)	Dicetyl phosphate*	PEG*	NAG*	Drug** concentration	Hydration volume, ml
F- 1	200	100	6	10	12	5	10
F- 2	100	50	3	5	4	5	10
F- 3	200	100	6	10	4	5	10
F- 4	200	100	6	10	8	20	10
F- 5	200	100	6	10	8	10	30

* The amounts were added as percentages of the total lipid in the formulation.
** Drug concentration mg/mL in the hydration medium.

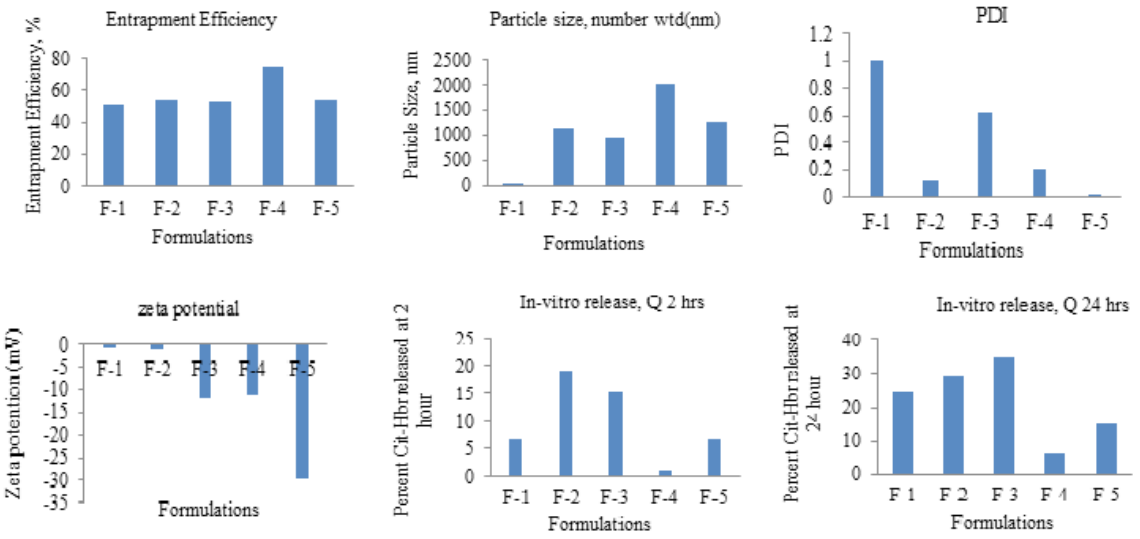

Figure-1: % of Entrapment Efficiency, number weighted particle size (nm), PDI, Zeta potential(s^{-1}) and In-vitro percentage of drug release at 2 hour and 24 hour of the five liposomal formulations.

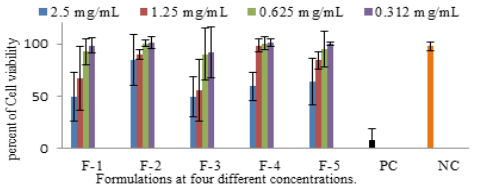

Figure 2: Represent the Percentage of RPBEME Cells viability for the five formulations at 2.5, 1.25, 0.625 and 0.312 mg/mL respectively. Each data point represents the mean ± SD of four determinations.

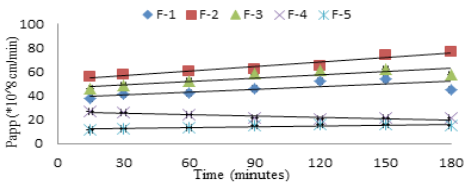

Figure-3: Unidirectional (A-B) transport study through the rat brain endothelial cells monolayer represents Papp (cm/min) of the five liposomal formulations (at 2.5 mg/ml conc.) from 15 mins to 180 minutes. Each data point represents the mean± SD of four determinations.

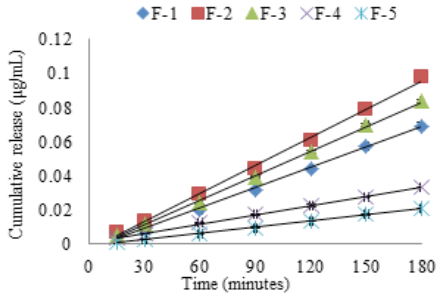

Figure 4: Unidirectional (A-B) Cumulative release (µg/ml) of the five liposomal formulations (2.5 mg/ml) at different time intervals. Each data point represents the mean ± SD of four determinations.

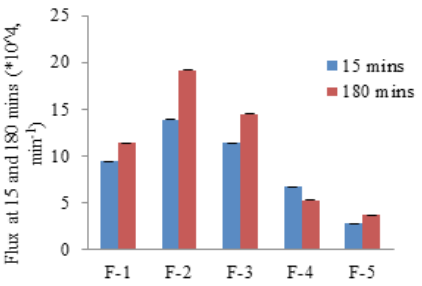

Figure 5: Unidirectional (A-B) flux (min^{-1}) of the five liposomal formulations (2.5 mg/ml) at 15 and 180 mins. Each data point represents the mean ± SD of four determinations.

Conclusion:

The study demonstrated successful formulation of NAG-coated pegylated multilamellar liposomes greater than 50% drug entrapment efficiency. Cytotoxicity results indicated that the formulations were well tolerated by the cells up to a concentration of 0.625 mg/ml. The Papp values provided a preliminarily proof that NAG coated liposomes could be considered a potential delivery vector of medications to the brain.

Disclaimer: The views expressed are those of authors and do not necessarily represent the official position of the Agency (FDA).

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Innovative Drug Delivery Approach for Treatment of Brain Cancer

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Introduction:

Central Nervous System (CNS) is the most complex system of the human body with unique anatomical and physiological characteristics. Brain and spinal cord are two major parts of CNS but brain has more complex pathophysiological mechanism and most of CNS disorders are because of abnormalities in anatomy and physiology of the brain. Although we can see many advancements in our understanding of CNS pathophysiological mechanisms, there are not absolute treatment for CNS abnormalities and disorders. Alzheimer's disease, Parkinson disease, and brain cancer are main CNS disorders that there is no cure for them. Brain cancer is very broad CNS disorder which contains many different types of brain tumors. The main barrier to the treatment of these disorders is the blood-brain barrier (BBB). BBB has very unique molecular structure which protects the brain against endogenous and exogenous toxic particles. Scientists have been investigating BBB molecular structure to develop new formulations of the drugs with ability to pass BBB and target the brain. Multiple innovative drug-delivery approaches have been developed such as colloidal drug-carrier systems (e.g. nanoparticles), biodegradable wafers, breaching the wall using ultrasound and microbubbles, osmotic (chemical or hypertonic shock) BBB disruption, and biochemical BBB disruption.

Brain Tumors:

There are more than 120 types of brain and CNS tumors [1]. Today, most medical institutions use the World Health Organization (WHO) classification system to identify brain tumors. The WHO classifies brain tumors by cell origin and how the cells behave, from the least aggressive (benign) to the most aggressive (malignant). Some tumor types are assigned a grade, ranging from Grade I (least malignant) to Grade IV (most malignant), which signifies the rate of growth. Glioma is a broad term includes all tumors of supportive tissue of the brain that represent 74.6% of all malignant tumors. Glioblastoma represent 14.9% of all primary brain tumors, and 55.4% of all gliomas. Glioblastoma has the highest number of cases of all malignant tumors, with an estimated 12,390 new cases predicted in 2017. Astrocytomas, including glioblastoma, represent approximately 75% of all gliomas. Astrocytoma has been categorized in four categories: Grade I – Pilocytic Astrocytoma, Grade II – Low-grade Astrocytoma, Grade III – Anaplastic Astrocytoma, Grade IV – Glioblastoma Multiforme (GBM) [2].

Glioblastoma Multiforme (GBM):

Glioblastoma Multiforme, which is one of a group of tumors referred to as gliomas, is the most common and deadliest of malignant primary brain tumors in adults. Glioblastoma has been classified as a Grade IV (most serious) astrocytoma. GBM develops from the lineage of star-shaped glial cells, called astrocytes that support nerve cells. Astrocytes are the star-shaped cells that make up the glue-like or supportive tissue of the brain.

GBM develops primarily in the cerebral hemispheres but can develop in other parts of the brain, brainstem, or spinal cord. GBM can be composed of several different cell types and it can develop directly or evolve from lower grade astrocytoma. It is most common brain cancer in older individuals and more common in men than women. This type of brain cancer is less common in the children. Median survival rate is about 15 months, and its 5-year survival rate is 4% [2]. The cause is unknown, but increasingly research is pointing toward genetic mutations.

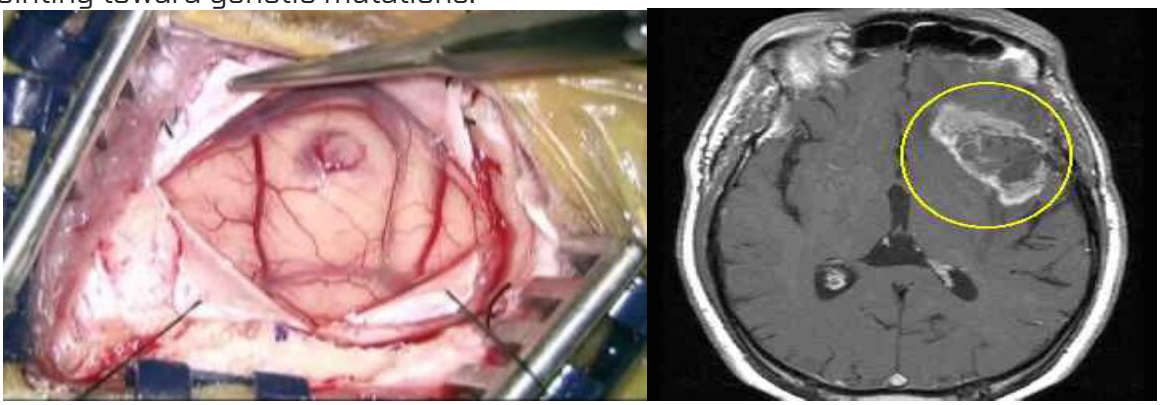

Figure 1. Glioblastoma during surgery (left), Glioblastoma seen in MRI (Right) (Source: http://www.aboutcancer.com/mri_gbm.htm)

These tumors are usually highly cancerous since the cells reproduce quickly and they are supported by a large network of blood vessels. Because these tumors come from normal brain cells, it is easy for them to invade and live within normal brain tissue. However, glioblastoma rarely spreads elsewhere in the body.

Types of Glioblastoma:

There are two types of glioblastomas: Primary, and Secondary Glioblastoma. Primary, or de novo glioblastoma is the most common form of glioblastoma that tends to form quickly, and it is very aggressive. In secondary glioblastoma, tumors have a longer and slower growth, but still are very aggressive. They may begin as lower-grade tumors which eventually become higher grade. They tend to be found in people 45 and younger, and represent about 10% of glioblastomas [2].

Symptoms of Glioblastoma:

Because glioblastomas can grow rapidly, the most common symptoms are usually caused by increased pressure in the brain. These symptoms can include headache, nausea, vomiting, and drowsiness. Depending on the location of the tumor, patients can develop a variety of other symptoms such as weakness on one side of the body, memory and/or speech difficulties, and visual changes [2].

Treatment of Glioblastoma:

Glioblastoma can be difficult to treat because the tumors contain so many different types of cells. Some cells may respond well to certain therapies, while others may not be affected at all. This is why the treatment plan for glioblastoma may combine several approaches. The first step in treatment is diagnosis and relieving the pressure on the brain with safely removing as much tumor as possible through surgery. Surgery is commonly the initial therapeutic approach for tumor de-bulking and obtaining tissue for diagnosis. Tumor resection is of prognostic value; it may be beneficial to attempt maximal tumor resection provided that neurological function is not compromised by the extent of resection. Chemotherapy and radiation are other options for treatment [2]. Based on American Society of Clinical Oncology (ASCO) Guideline recommendations, Partial-

brain fractionated radiotherapy with concurrent and adjuvant temozolomide (TMZ) is the standard of care after biopsy or resection of newly diagnosed glioblastoma in patients up to 70 years of age [3].

Hypo-fractionated radiotherapy for elderly patients with fair to good performance status is appropriate. The addition of concurrent and adjuvant temozolomide to hypo-fractionated radiotherapy seems to be safe and efficacious without impairing quality of life for elderly patients with good performance status. Reasonable options for patients with poor performance status include hypo-fractionated radiotherapy alone, temozolomide alone, or best supportive care. Concomitant and adjuvant temozolomide (TMZ) chemotherapy in addition to radiotherapy(RT) significantly improved median, 2- and 5-year survival in a large randomized trial, and is the current standard of care for patients with GBM up to age 70 or fit elderly patients older than 70 years. TMZ is administered daily (7 days a week) during radiotherapy and for 5 days every 4 weeks for six cycles as maintenance (adjuvant) treatment after the end of radiation [3]. European Society for Medical Oncology also recommends TMZ or TMZ/RT as treatment option for primary and secondary Glioblastoma [4].

Innovative Drug Delivery to Brain:

Colloidal drug-carrier systems/nanoparticles:

Nanoparticles (NPs) are colloidal carriers that can have a natural or synthetic origin and can vary from 1 to 1000 nm in size. Beside the polymeric nanoparticles, there are other types of colloidal carriers, for example liposomes and micelles that have been extensively studied for drug delivery to the brain [5]. Schematic illustration of Polymeric nanoparticles, liposomes, and micelles shown in figure 2. The physico-chemical properties of NPs, determine the passage mechanism across the BBB: i) Some NPs open tight junctions between endothelial cells or induce local toxic effects which leads to increase permeability of the BBB. ii) NPs can be transported through endothelial cells by transcytosis. iii) Some NPs also can be transported through endothelial cells by endocytosis. There are several parameters that affect the efficiency of NP systemic circulation, BBB passage and cellular delivery. Composition, size, shape, and type of ligand are main nanoparticle (NP) features influencing systemic delivery and blood brain barrier (BBB) passage [5].

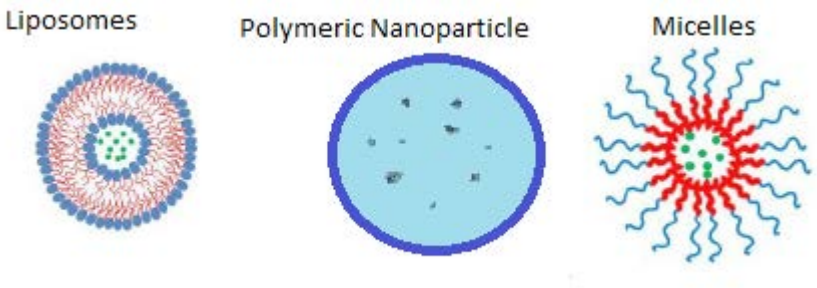

Figure 2. Schematic illustration of liposomes, polymeric nanoparticles, micelles (Source: Safety and Toxicity of Nanoparticles in Medicine, Muhammad Delwar Hussain and Matthew Ogbuehi. In: Sethi R, Kolli C and Hussain D eds. Toxicology: The Past, Present, and Future of Basic, Clinical and Forensic Medicine. Vol. 1; Nova Science Publishers, Inc., New York, NY, 2015; 45-67.)

NPs can be classified into natural, when molecules such as proteins (albumin), and polysaccharides are used, or synthetic. Synthetic NPs can be made of very common polymers such as poly (lactic-co-glycolic acid) (PLGA), poly (ethylenimine) (PEI), or from inorganic agents like gold, silica or alumina. NPs can vary in their size (1–1000 nm) and are able to deliver drugs into cells by entrapping, adsorbing or covalently bounding

them. Several trials have been shown a clear inverse correlation among NP size and BBB penetration. In particular, most of the studies for brain disorders which performed on animal models have used NPs with diameters between 50 nm to 100 nm [5]. Also the size of nanoparticles is one of the main factors in their toxicity. Nanoparticles because of their nanoscale dimensions have potential for interaction to specific cells and organelles of the cells, and interference with cellular functions. NPs can assume different shapes such as spherical, cubic, and rod-like shapes. Although most of the studies have been performed with spherical NPs since they are relatively easy to prepare, in vitro studies have demonstrated that rod-like coated with specific antibodies have higher adhesion propensity than their spherical counterparts [5]. Specifically, polysterene NPs with a rod shape (501 ± 43.6 × 123.6 ± 13.3 nm) coated with an antibody against the transferrin receptor showed in vivo a 7-fold increase in brain accumulation when compared to their spherical NP counterpart. Shape of NPS also have important role in their toxicities. NPS can have different charges such as negative, zwitterionic, and positive, but negatively charged spheres are widely used in intravenous applications. In other words, Zeta potential is another important parameter that affects the passage of NPs through the BBB. It has been shown that NPs with high zeta potential (high positive charge) cause immediate toxicity to the BBB [5]. Therefore, most of the NP formulations described in the literature for brain delivery have moderate (between – 1 to – 15 mV) or high (between – 15 to – 45 mV) negative zeta potentials. Another important feature of NPs is the possibility of functionalization with different types of ligands. Ligands are distributed into four major categories: i) Capable of mediating protein adsorption (e.g. polysorbate 80), ii) Able to interact directly with the BBB (e.g. transferrin proteins, antibody or peptides), iii) Capable of increasing hydrophobicity (e.g. amphiphilic peptides), and iv) Able to improve blood circulation (e.g. polyethylene glycol or PEG) [5].

Biodegradable Wafer:

Carmustine, Gliadel wafer, is the only approved polymeric system by the US Food and Drug Administration for the treatment of brain tumors [6]. Carmustine is an alkylating agent that is used for the patients who are undergoing surgery for Glioblastoma. Implantation of chemotherapy-impregnated wafers (carmustine polymers) into the resection cavity before radiotherapy has been shown to marginally improve median survival compared with radiotherapy alone [7]. Convulsions, infections, abnormal wound healing, and swelling of the brain are the complications of implanted biodegradable Gliadel wafer [6,8]. Also if Gliadel is not implanted properly, the wafer could block the flow of CSF and might cause obstructive hydrocephalus or abnormal accumulation of fluid in the brain. The Gliadel wafer is not recommended in pregnant women as carmustine can cause harm to the fetus, and also it cannot be used for patient who has allergy to carmustine [8]. Up to 8 wafers (7.7 mg each) may be placed to cover as much of the resection cavity as possible. Slight overlapping of wafers is acceptable, and wafers broken in half may be used, but wafers broken in more than 2 pieces should be discarded [7].

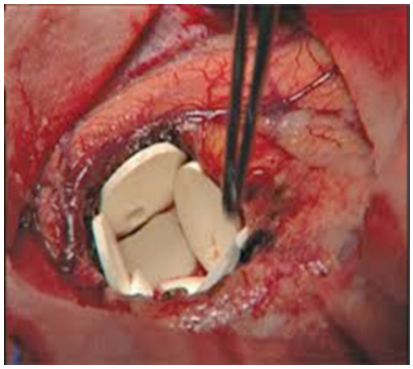

Figure 3. Implantation of Gliadel wafer (source: http://www.nature.com/nrd/journal/v3/n6/fig_tab/nrd1414_F4.html)

Breaching the wall using ultrasound and microbubbles:

In this approach, focused ultrasound (FUS or FU), sonication, is used in combination

with microbubbles. In this non-invasive method FUS disrupts the brain tissue to deliver CNS therapeutics to localized target sites [6,9]. Microbubbles, 1–10 micrometer, consist of a semi-solid gas (perfluorocarbon) [6,10]. Microbubbles are injected into the blood and ultrasound vibrate these microbubbles which can force apart endothelial cell which leads to increased permeability of endothelial cells. This procedure enables drug targeting to brain by breach of BBB. Duration of sonication, concentration of microbubbles, frequency of pulse, pulse length, and influence of standing waves and pressure are parameters that should be considered for efficacy and safety [6]. Although no neurotoxicity issue has been reported with this method, the clinical application of this approach should be studied for more details [6,10].

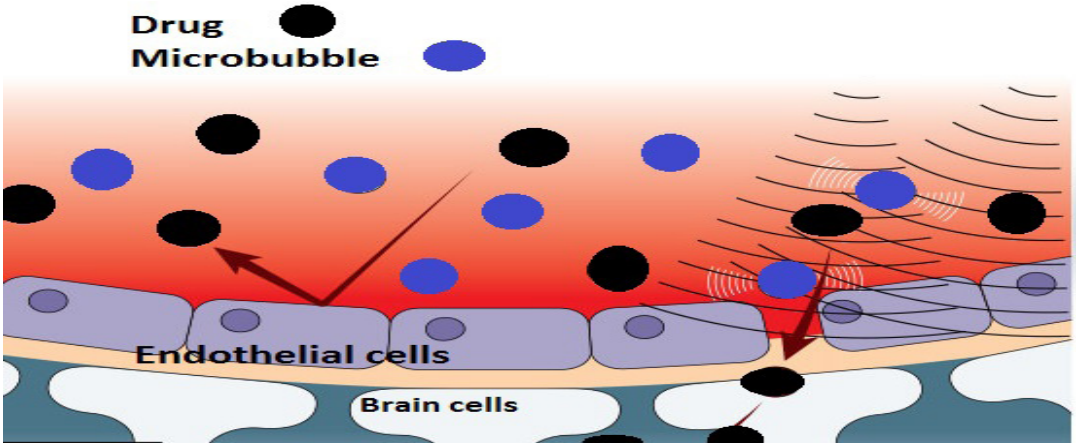

Figure4. BBB Disruption by FUS (source: https://www.newscientist.com/article/mg22229742-400-human-brains-ultimate-barrier-to-open-for-first-time/*)*

Osmotic (chemical or hypertonic shock) BBB disruption:

This type of drug delivery to brain has been used in combination with nanoparticles, gene delivery, and peptides delivery. In this type of drug delivery, osmotic pressure across the BBB is the main concept for drug delivery to brain so osmotic agents such as mannitol can be used for this approach. Osmotic agents shrink the endothelial cells hyper-osmotically, and then open endothelial tight junction, which lead to passive diffusion of large molecules across the BBB. Structural brain damage, micro-embolisms, altered neuronal function, and passage of plasma proteins are complications and risk factors of this type of drug delivery to the brain [6,7].

Biochemical BBB disruption:

In this type of drug delivery that have been studied in animal models, vasoactive amines such as bradykinin and its analog RMP-7 has been used. These vasoactive substances act on B2 receptor of endothelial cells and increase permeability of endothelial tight junction which leads to passage of large molecules across the BBB [6,7]. In addition to bradykinin, histamine, and adenosine are other vasoactive substances that have been used to increased permeability of BBB. Adenosine increases permeability of endothelial tight junction by acting on 2A receptors [6,7].

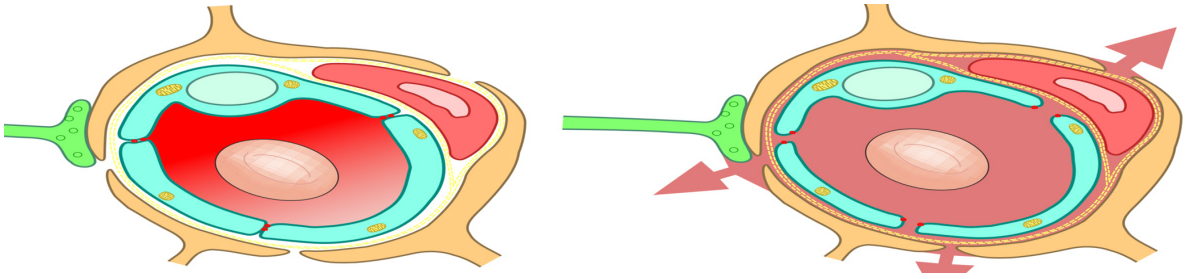

Figure 5. Normal endothelial cells (left), Osmotic shrinkage of endothelial cells (right) (Source: http://www.tandfonline.com/doi/abs/10.1517/13543784.10.10.1809)

Conclusion and Future Perspectives:

Successfully treating CNS disorders, in particular brain tumors, has been very difficult because of natural defense mechanism of brain by BBB. Achieving an appropriate drug delivery to brain has been greatest challenge for drug formulation scientists since not only developed drug formulation should be able to pass the BBB but also should have less toxicity and high safety margin. Future studies should be focused on developing a drug delivery with fewer side effects such as biodegradable wafers and nanoparticles since they affect locally on brain tissue and they have less systemic side effects. Non-Invasive methods such as FUS are other drug delivery approaches that may have high potential for future clinical applications.

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Abstracts

Evaluation of film dosage form of epinephrine drug

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Purpose:

Epinephrine, also known as adrenalin or adrenaline, is a hormone, neurotransmitter and medication that is used for the treatment of a number of disease conditions such as anaphylaxis, cardiac arrest, and superficial bleeding. The drug is available as an intramuscular injection which can have some limitations such as patient compliance, cost, side effects etc. The purpose of this study is to evaluate an oral film dosage form of epinephrine for buccal administration. The oral film dosage form has several advantages over other dosage forms of epinephrine. Oral films are applied mainly in buccal and sublingual route of administration, both of which are systemic. This administration provides consistency of drug concentration levels in the blood, have an immediate onset of action, and can avoid the first pass effect. The specific goals are to develop an oral film dosage form of epinephrine, determine the stability of the film and evaluate the disintegration time.

Methods:

The film was prepared using the appropriate biodegradable polymers and applying an evaporation method. The polymers were selected after conducting an extensive screening study based on the stability in different conditions. These conditions include: the pH of the solvent, temperature, and disintegration time. The selected polymers were then used to form the epinephrine containing film. We then tested the disintegration and stability of the drug containing film in different conditions such as in saliva, saliva substitute, DI water, high pH solvent, low pH solvent, room temperature, refrigerated, and freezer conditions.

Results:

The polymers Kollidon 90, Kollidon 30, Kollidon VA 64 and Kollicoat IR were found most suitable for the epinephrine drug. The film dosage form of the drug using these polymers were obtained in nice smooth form of the film with thickness of approximately 5-200 µm and with desired tensile strength. The stability study shows the film was stable at both room temperature and refrigerated conditions. The disintegration study shows the films were disintegrated in the saliva solution in less than 30 seconds, in water in less than 30 seconds and in a saliva substitute in less than 1 min.

Conclusion:

After an extensive screening process, 3 out of 4 films tested were stable in room temperature and refrigerated conditions and the disintegration time was less than 1 minute. The future direction of this project will include content analysis and quantification of epinephrine in the film.

Chronic Oral And Intraperitoneal Glucose Loading Causes Hyperglycemia-Mediated Hypertension Through Increased Na+-Retention In The Kidney Proximal Tubule

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Purpose:

Hyperglycemia in glucose-fed animals can promote hypertension, the mechanism of which is not clear. Though some studies ascribed the elevated blood pressure (BP) to increased sympathetic activity, there was no significant increment in blood glucose when animals were fed glucose only with drinking water. In contrast, our model demonstrated a very high level of blood glucose, which was progressively sustained throughout the study period. Moreover, there is no data available in literature as to renal impairment in response to chronic glucose feeding to animals till date. Therefore, we hypothesized that sustained blood glucose levels developed in our rat model can increase the exposure of proximal tubule to high glucose through increased glucose filtration. This can induce proximal tubule-specific dysregulation in renin-angiotensin system and oxidative stress that may promote expression and activity of Na+-K+-ATPase (NKA) through which increased Na+-retention may occur.

Methods:

In this study, we used 4 groups of Sprague Dawley rats: control, glucose-treated, tempol-treated, and captopril-treated groups for two weeks. In addition, we microdissected proximal tubule (PT) from heterogenous tissue environment of the kidney cortex employing laser capture microdissection (LCM) technique to explore for the expression of NKA α1 in PT.

Results:

Our study demonstrated progressively sustained blood glucose levels throughout the study in glucose-treated animals. However, tempol- and captopril-treated groups showed significantly high glucose levels in only second week. Plasma insulin level, and BP were significantly increased in glucose-treated animals. Increased BP can be attributed to significantly increased oxidative stress, and Ang II levels (increased from 46.67 pg/ml to 99 pg/ml) in the kidney cortex of glucose-treated animals. Our results also showed significantly decreased urine flow, urinary sodium excretion, implying increased sodium reabsorption followed by increased blood volume. Interestingly, increased sodium reabsorption may occur through upregulation of PT-specific α-subunit of Na+-K+-ATPase (NKA α1), which is signigicantly overexpressed in glucose group. Moreover, phosphorylation at Ser-18 residue of NKA α1 is depleted in the glucose group leading to an increase in ratio of NKA α1 to phosphorylated-NKA α1 (Ser-18), implying higher activity of NKA resulting in increased sodium reabsorption. All these events are reversed in captopril- and tempol-treated animals

Conclusion:

In summary, it is evident that hyperglycemia induced by chronic oral and intraperitoneal glucose loading promotes hypertension through increased upregulation of Ang II, oxidative stress, which enhance Na+-reabsorption through increasing the expression and activity of Na+-K+-ATPase in the proximal tubule, leading to increased blood volume and eventual blood pressure.

Targeting the cell cycle in Lung Cancer using miRNAs and the development of a new delivery carrier

A K M Nawshad Hossian and George Mattheolabakis
Basic Pharmaceutical Sciences, School of Pharmacy, University of Louisiana Monroe

Lung cancer (LC) is the primary cause of cancer related deaths in the world, with >80% of the cases being non-small cell lung cancer. Downregulation of CDK1 and 4 proteins, key regulators of cell cycle progression, correlates with decreased LC cell proliferation. Enforced expression of miRNAs is a promising approach to regulate genes, but unfortunately nucleic acid delivery poses formidable challenges. We studied a combinatorial miRNA treatment to target the CDK1/4 genes. In parallel, we develop a carrier for the co-delivery of miRNAs and chemotherapeutics. We investigated the effects of transfecting A549 cells with miR-143-3p and miR-506-3p, and analyzed the differential expression of the CDK1/4 genes, targets of the two miRNAs respectively, by qPCR. Furthermore, we evaluated any changes in the cell cycle distribution, apoptosis and protein expression following transfection. We developed a novel polymer composed of α-Tocopherol (TC), Polyethyleneimine (PEI) and Polyethylene glycol (PEG), by the direct conjugation of PEG to PEI, and subsequent conjugation of TC. By adjusting the TC to PEG-PEI ratio, formation of nanosized micelles of ~180nm diameter takes place. Furthermore, the nanocarrier successfully complexed with miRNAs. Following cell transfection with the two miRNAs, we detected a significant downregulation in the mRNA levels of the CDK1 and CDK4 genes, an effect most pronounced through the combinatorial treatment with both miRNAs. Analysis of transfected cells clearly demonstrated a shift of the cell cycle populations. Downregulation of the protein expression resembled an evident representation of targeting cell cycle. The combinatorial effect of micro RNA in cell cycle arrest become more obvious when we found the clear shift of cell population to late apoptosis in flow cytometry technique. On the other hand, MTT assay with polymer showed low toxicity to cell A549. Our data clearly demonstrate that the dual miRNA treatment regulates the cell cycle progression and our polymer can entrap miRNAs.

Structure-Activity And Structure-Fluorescence Property Relationships In A Series Of Carbonic Anhydrase Inhibitors As Potential Colon Cancer Theranostic Agents.

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Background:

Carbonic anhydrase (CA, EC 4.2.1.1) is a zinc enzyme responsible for the reversible hydration of carbon dioxide to bicarbonate, being involved in respiration and CO2 transport between the metabolizing tissues and the lungs, pH and CO2 homeostasis, electrolyte secretion, aqueous humor secretion, biosynthetic reactions, etc. In mammals 16 isozyme or CA-related proteins have been described to date, with different catalytic activity, sub-cellular localization, and tissue distribution. Over the last decade a connection was established between cancer and the expression of certain carbonic anhydrase isozymes. Recent studies have shown that membrane bound carbonic anhydrases CA IX and CA XII are over-expressed in many tumor cells. Pharmaceutical agents that can selectively inhibit CA IX and CA XII may have therapeutic value for detection, imaging and treatment of a large variety of hypoxic tumors.

Objective:

The purpose of the current study was to develop a series of membrane-impermeant low molecular weight CA inhibitors that can have theranostic potential for colon cancers.
Methods: A series of CA inhibitors obtained through conjugation of potent CA inhibitor benzolamide with positively charged pyridinium moieties. The new compounds were purified by standard chromatographic methods and characterized by 1H- and 13C-NMR, LC-MS and HRMS. They were tested for their inhibition properties against several isozymes of carbonic anhydrase (CA) - CA I, CA II, CA VII CAIX, CAXII. Their lipophilicity was calculated with ChemDraw®. Fluorescence properties of these compounds were determined using UV-Vis and Fluorescence Spectroscopy.

Results and discussion:

This new series of compounds were obtained in fair yields and the spectroscopic techniques confirmed their proposed structures. Several representatives displayed good CA inhibition properties, which was correlated with the structure and the lipophilicity of the compounds and the structure-fluorescence properties relationships belonging to this new set of compounds were established.

Conclusions:

This new series of compounds displayed good CA inhibition properties, selectivity and fluorescence properties which recommend them as theranostic probes with potential CA inhibition effect in the early detection and treatment of hypoxic tumors such as colon cancer.

Acknowledgment:

A grant from Seattle Foundation

Nano-engineered particles for oral small molecules and biologics delivery

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Background:

In recent years small molecular therapeutics and biologics, which are non-oral administrable, are tremendously increasing due to their effectiveness of treating many chronic diseases. However, oral dosage forms are market dominant that shares about 50% of total pharmaceutical market because of prominent demand of the pharmaceutical companies. Stability of the small molecules and biologics in stomach, and absorption inability are the major barriers that barred them from oral delivery. Therefore, there is a huge scope of research and development for making these small molecules and biologics oral administrable.

Objective:

The main objective is developing a platform technology with biocompatible and biodegradable polymeric carrier that will solve stability and absorption issues.

Methods:

Layer-by-layer coating with polysaccharide and enhancing absorption through bile acid transporter of small intestinal membrane by incorporating bile acids.

Results and Discussion:

Deoxycholic acid conjugated heparin forms a self-assembly micelles, that were used for loading fluorescence quantum dots and orally administered to mouse in order to imaging GI tract. The results led us to oral delivering of small molecules anticancer drug Docetaxel for cancer treatment and imaging noninvasively. We have further modified the systems for oral delivering of biologic for diabetes treatment which show a single dose can maintain blood glucose for a week and multiple dose helps to regenerate pancreatic cells. We have also observed feasibility of this system for oral antigen delivery.

Conclusions:

Polysaccharide linked bile acid mediated particulate delivery systems enhance stability as well as absorption followed by bioavailability of the orally administered small molecules and biologics.

Acknowledgement:

NRF-2015R1A2A1A05001832, NRF-2015R1D1A1A09060567, and NRF-2014R1A2A2A03004802

Formulation and Evaluation of Polymeric Mixed Micelles of Quercetin for Management of Ovarian Cancer

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Background:

Quercetin, a flavonoid, has wide range of pharmacological properties including antioxidant, anti-inflammatory, and anti-proliferative activities. The application of quercetin as a therapeutic agent is greatly restricted due to its low water solubility and poor bioavailability. Polymeric micelles have been emerged as an effective drug delivery system owing to their small particle size, sustained release of drug, enhanced cellular uptake and increased biological activity.

Objectives:

The objective of this study was to develop mixed micelles for enhanced anticancer effect of quercetin.

Methods:

Micelles composed of polymers in different proportion and different concentration of quercetin were prepared by thin film hydration method. The micelles were characterized for their physicochemical properties. In vitro cytotoxicity of the micelles was studied in SKOV-3, ovarian cancer cell line.

Results and discussion:

The best formulations were obtained with Pluronic polymers composed of P123 and P407 in the molar ratio of 7:3 (A16); and P123, P407 and TPGS in the molar ratio of 7:2:1 (A22). The particle size of quercetin-loaded micelles was 24.83±0.44 and 37.10±4.23 nm before and after lyophilization, respectively for A16. The drug loading was 8.75±0.41% with 87.48±4.15% encapsulation efficiency for A16. For A22, the particle size before lyophilisation and after lyophilisation; drug loading; and encapsulation efficiency were 26.37±2.19 and 45.88±13.80 nm; 9.01±0.11%; and 90.07±1.09%, respectively. Micelles exhibited sustained release of quercetin compared to free quercetin. The solubility of quercetin was significantly increased (1161 and 1025 fold higher in A16 and A22 respectively) than pure quercetin. The micelles have low critical micelle concentration indicating their stability in aqueous media. The IC50 value of both the micellar preparations in SKOV-3 cells was twofold less than the free drug. Conclusions: The mixed micelles of P123/P407 (7:3 molar ratio) and P123/P407/TPGS (7:2:1 molar ratio) can effectively deliver quercetin for treatment of ovarian cancer.

Extra-virgin olive oil Met inhibitor oleocanthal-lapatinib: A novel synergistic combination for HER2-dependent breast malignancies

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Receptor tyrosine kinases (RTKs) are key regulators of normal cellular growth and proliferation. Dysregulation of RTKs, particularly in the EGFR/HER2 family, is a hallmark of aggressive breast and other malignancies profile. Small-molecule tyrosine kinase inhibitors (TKIs) are among the most effective cancer targeted treatments. (-)-Oleocanthal (OC) is a naturally occurring phenolic secoiridoid from extra-virgin olive oil which showed significant activity against invasive breast cancer via c-Met inhibition. The dual EGFR/HER2 inhibitor lapatinib (LP) is approved for treatment of HER2-amplified breast cancer. Currently strong evidences are available for the involvement of c-Met overexpression and/or dysregulated activation of its signaling pathway in the development of resistance to breast cancer targeted therapies already in clinical use, specifically those targeting members of the EGFR family. Therefore, combined treatment of OC and LP was hypothesized to be mechanistically synergistic in suppressing growth, migration, and invasion of HER2-overexpressing breast cancer. Results revealed that combined treatment of sub-effective OC and LP doses resulted in synergistic antiproliferative effects against BT-474 and SKBR-3 HER2-positive breast cancer cells both in vitro and in vivo. Protein microarray and Western blot analyses showed that combined treatment of OC and LP inhibited the phosphorylation of EGFR, HER2, and c-Met RTKs. This effect was also associated with inhibition of multiple mitogenic signaling pathways including Ras/MAPK, PI3K/Akt, and JAK/STAT. Antimigratory effects of combined OC and LP treatment was associated with reduced activation of FAK, Brk, and Paxillins. Animal studies showed that combined OC 5 or 10 mg/kg with LP 50 or 12.5 mg/kg treatments, respectively, showed more than 90%, each, inhibition of BT-474 tumor cells growth in nude mice xenograft models via suppression of Met-EGFR-HER2 RTKs activation and downstream pathways. In conclusion, this study supports the translational use of OC as a dietary supplement to synergize the chemotherapeutic effects of LP for effective control of HER2-dependent breast cancers.

CYP2E1 Enzyme Kinetics And In Vitro Toxicological Evaluation Of Diallyl Sulfide (DAS) Analogs For The Prevention Of Alcohol- And Acetaminophen-Induced Toxicity

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Purpose:

Cytochrome P450 2E1 (CYP2E1) is involved in the metabolism of more than 85 xenobiotics along with various endogenous substrates. In high dose alcohol use (binge/chronic drinking) and acetaminophen abuse/overdose, CYP2E1 plays the major role in causing severe hepatic and extra-hepatic injury. Through the production of toxic metabolites and reactive oxygen species, CYP2E1 potentiates adverse cellular and biochemical reactions. The induction of CYP2E1 by ethanol (ETH) further worsens the outcome. In addition, acetaminophen (APAP)-induced liver injury is the number one cause of overdose-related liver failure in the United States. The crucial role of CYP2E1 has been well documented in APAP-mediated toxicity (production of the toxic metabolite, N-acetyl-p-benzoquinone imine). However, there is no approved selective CYP2E1 inhibitor available in the market that can be used specifically in these scenarios to counteract the toxic effects. Diallyl sulfide (DAS), a chemical found in garlic, is a selective inhibitor of CYP2E1 and has shown beneficial effects against ethanol- and other xenobiotic-induced hepatoxicity in numerous studies. However, DAS is also a CYP2E1 substrate that upon metabolism produces the toxic metabolites- diallyl sulfoxide and diallyl sulfone. These metabolites cause toxicity especially in high doses and with long-term usage of DAS. Therefore, the objective of this study was to find a potent CYP2E1 inhibitor with low/negligible toxicity even with high dose and chronic use. This can be achieved with appropriate structural modifications to DAS.

Methods:

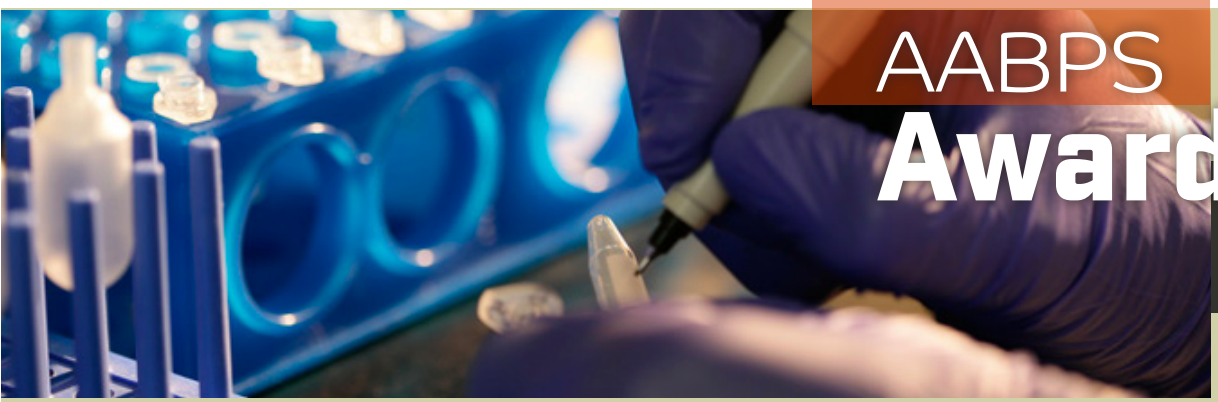
We studied eight commercially available analogs of DAS in this study, which were selected based on computational docking studies. We determined CYP2E1 inhibition kinetics using the standard para nitro-phenol hydroxylation assay. We analyzed the data using GraphPad Prism 5 software. We evaluated in vitro cytotoxicity of these analogs in three clinically relevant CYP2E1 expressing cells (hepatocytes, monocytes, and astrocytes). We used flow cytometry, XTT cell viability assay, LDH activity assay, and caspase-3 activity assay to determine the cytotoxicity. For this study, we pre/co-treated the cells with these analogs and ethanol/ acetaminophen, and determined the efficacy of these analogs in preventing cellular toxicity.

Results:

Of the eight analogs, we found that thiophene (TP), allyl methyl sulfide (AMS), diallyl ether (DE), 2-(prop-2en-1-yloxy) ethan-1-amine (PEA), and 2-prop-2-enoxyacetamide (PEXA) were significantly less cytotoxic than DAS, even at higher concentrations. DE, TP, and AMS showed similar/better CYP2E1 inhibition capacity than DAS. All of the analogs are reversible inhibitors (mostly competitive in nature) of CYP2E1. DE and TP had lower IC50 values at saturating and sub-saturating substrate concentrations and DE had the lowest Ki value (3.1 μM), relative to DAS (6.3 μM). The most crucial observation from our study is that TP, AMS, DE, PEA, and PEXA were able to prevent ethanol- and acetaminophen- mediated toxicity in primary hepatocytes.

Conclusions:

These results are very promising in the search for a novel CYP2E1 inhibitor that can be used as a therapeutic tool for preventing ethanol and acetaminophen-induced hepatotoxicity. Moreover, we are the first to report the extensive enzyme kinetics with CYP2E1 for DAS and its analogs.



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Criteria for the selection of the Award:

1. Cumulative GPA.
2. Publications: Peer reviewed, Published, Accepted or Submitted, Research Articles, Book Chapters, Review Articles, Communications, Letter to the Editor or Miscellaneous.
3. Patent Applications: Submitted, Accepted or Awarded.
4. Research Presentations: Published/Accepted Research/Conference Abstracts/Oral presentations.
5. Meritorious Achievements: Submitted Grant Applications (As a Student PI or Co-PI) Funded Grant Application (As a Student PI or Co-PI) Recipient of Prestigious Awards (External).
6. Service Activities: Significant contributions to AABPS activities, student organizations (as an officer),community outreach, scientific, or college/graduate school/university level services as committee members or officers.
7. Teaching Experience: As a Teaching Assistant in the classroom, laboratory or small group teaching.

Recipients

Mohammad Arifur Rahman, Graduate Student, University of Tennessee Health Sciences Center

AKM Nawshad Hossian, Graduate Student, University of Louisiana at Monroe

Utpal Kumar Mondal, Graduate Student, Temple University

Abu Bakar Siddique, Graduate Student, University of Louisiana at Monroe

Selim Fakhruddin, Graduate Student, University of Louisiana at Monroe

Cultural **Performers**

Krishna Tithi Khan

Ms. Krishna Tithi Khan is an enlisted singer in Bangaladesh Radio and Television. Her father Tapash Kumar Khan, an enlisted singer in Bangladesh Radio and Television, trained her at three years old for singing. Later, she started learning music in “Chayanot” and “National Nazrul Academy” renowned musical academies in Bangladesh. Since 1997, she has been performing in many national and international cultural competitions and programs.

She has been awarded “National Children Competition” in 1997, “Bangladesh Children Academy Musical Competition” in 1997, “National Primary Education and Cultural Week Competition” in 1997, “Annual Sports and Cultural Competition” in 1998 and 1999, “National Children Academy Competition” in 1999, ‘Ummesh Cultural Society’ in 1999, “National Children Academy” in 2000, “Dhaka Intercity Educational and Cultural Week Competition” in 2000 and 2001, “ Ispahani Girls High School” in 2000, “Dhaka Intercity Cultural Forum” in 2000 and 2001, “National Natun Kuri - 2002”, “Viqarunnisa Noon College” in 2005, “Inter University Cultural Competition” in 2008, top four in “Channel I Shera Kontho -2009”, “Channel I Sherader Mohajuddho” in 2010; National Shilpokola Academy” as a “Best Young rising singer” in 2011, “National Film and Cultural Award Ceremony as a “Best Rising Star” Female category in 2012, “International music festival-2012” in Qatar, “Meryl Prothom-Alo star Award” performance in 2013. Perform[illegible] different international cultural shows in USA since 2013, including “FOBANA conventi[illegible]5” in New York and “FOBANA convention -2016” in Washington DC; “Bangl[illegible] Society of North America” in 2015; “Best Promising Singer in North America” - 2015; “I[illegible]onal music festival in Florida-2016”; “Best Female Singer-2016” arranged by “[illegible]” a p[illegible]ar magazine in North Am[illegible].

Solo album Named “MIX SALAD” featuring by Fuad in 2010.

Kamruzzaman Bakul

Vocalist of green x band (Bangladesh); Singing in North America since late 90’s; Performed in different cultural shows all over the United States. Got 3 times dallywood film and music award, jemini music award, awarded by FOBANA, NABC and others.

Registrants

- Abir Absar
- Imran Ahmed
- Maliha Ahmed
- Nadira Ahmed
- Sarah Ahmed
- Mahibah Ahmed
- Ayat Ahmed
- Sharif Ahmed
- Salah Ahmed
- Shamim Ahmed
- Tashrik Ahmed
- Qamrul Ahsan
- Tasnia Aktar
- Selina Akter
- Hasina Akter
- Parveen Aktet
- Shahid Alam
- Sabiha Alam
- Ishrak Alam
- Eram Alam
- Muhammad Ali
- Asif Ali
- Ping Ji
- Abul Azad
- Monira Azad
- Alea Begum
- Miraz Chowdhury
- Shimina Chowdhury
- Swapan Das
- Selim Fakhruddin
- Muhammad Jamil Habib
- Maniza Habib
- Mahnaz Habib
- Shamim Hasan
- Shayaan Hasan
- Sarah Hasan
- Raquibul Hasan
- Mohammad Iqbal Hossain
- Muhammed Anwar Hossain
- Meher Hossain
- Yanah Hossain
- Yarah Hossain
- Ajmain Hossain
- Rumana Hossain
- Mohammad Hossain
- Rabeya Hossain
- AKM Nawshad Hossian
- Muhammad Delwar Hussain
- Md Rafiqul Islam
- Rebecca Islam
- Zahur Islam
- Muhammad Islam
- Mahmudul Huq Khan
- Leilani Khan
- Fadi Khan
- Aneeqa Khan
- Oliza Khanam
- Tazin Mahnaj
- Quamrul H Majumder
- Mohammad Hasan Miah
- Md Mohiuddin
- Utpal Mondal
- Tanzir Mortuza
- Begum Naher
- Mohammed Nooruzzaman
- Md Nurunnabi
- Rajib Paul
- James Polli
- Rafeza Rashid Poly
- Md Bodruddoza Rafique
- Mohammad Hafizur Rahman
- Mohammad Nadim Rahman
- Mohammad Arifur Rahman
- Md Ashequr Rahman
- Ashfiha Rahman
- Ahnaf Rahman
- Raek Rahman
- Jahidur Rashid
- Susan Rosencrance
- Warda Salah
- Abdus Salam
- Raed Salam
- Shafkat Salam
- Abu Serajuddin
- Syed Shahriyar
- Shahzeen Shahriyar
- Abu Siddique
- Shahinoor Taleb
- Ayman Taleb
- Amreen Taleb
- Mohammed Taleb
- Afsana Bahar Trini
- Mohammad Uddin
- AKM Nasir Uddin
- Brity Ullah
- Albirr Ullah
- Mohammad BarkatUllah
- Abu Hasnat Zulfiker

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Food Menu

Morning Refresher – 7:45am

- Sliced assorted fruits,
- Assorted muffins, danishes & pastries
- Freshly brewed coffee, decaf, & herbal teas
- Fresh squeezed orange, apple & cranberry juice

12:10pm Lunch

- Assortment of Freshly Baked Breads and Rolls
- Soup of the day
- Homemade pasta salad
- Red, white, & bleu coleslaw
- Deli Meat Platter
- Roast Beef (HALAL), Chicken Breast (HALAL)
- Tuna Salad
- Assorted Domestic Cheese Display
- Deli Tray Condiments
- Herbed Mayo
- Whole Grain Mustard
- Dijon Mustard
- Horseradish
- Individual Bag of Chips
- Chef's Selection of Assorted Desserts
- Freshly Brewed Coffee
- Decaffeinated Coffee, Taylors Teas & Iced Tea

Afternoon Refresher -2:45pm Coffee Break

- Assorted cookie & brownie tray
- Fresh whole fruit
- Granola & Nutri-Grain® bars
- Party mix
- Assorted sodas

Dinner Buffet- 6:00pm

- Fresh baked rolls & butter
- Spring Green – Crisp spring green lettuce, wedge tomatoes, sliced cucumbers & shaved onions unite to create this classic, delicious salad. Served with a creamy ranch & homemade balsamic vinaigrette.
- Grilled Chicken Breast - Halal
- Fish: Grilled Atlantic Salmon
- Penne Pasta - Marinara
- Seasonal Vegetable
- Rice Pilaf
- Chef's Selection of Dessert
- Coffee & Decaf, Herbal Teas, Iced Tea

American Association of Bangladeshi Pharmaceutical Scientists (AABPS)

Purpose:

The primary purpose of the AABPS, is to serve its membership, and, in specific- the pharmaceutical professionals of Bangladeshi origin residing in North America and working in academia, industry, hospitals, health insurance companies, pharmacies, government or other research institutions- by providing a forum for the interchange of knowledge. AABPS is a non-political, non-religious, not-for-profit, US tax exempt educational organization.

Objectives:

1. To foster communication and collaboration among pharmaceutical scientists and professionals of Bangladeshi origin and residing in North America.
2. To support its members in achieving their highest level of professional career through collaboration, consultation, mentoring, education and exchange of knowledge.
3. To provide timely scientific programs, ongoing education, publications and networking opportunities for the scientists and professionals involved in discovery, development, manufacture and marketing of pharmaceutical products and services.
4. To facilitate communication and contacts between the Association Members and interested personnel in Bangladeshi pharmaceutical industry, government regulatory agency, and academic institutions regarding transfer of knowledge and consulting services on pharmaceutical sciences.
5. To promote fraternity and solidarity among the pharmaceutical scientists and professionals.

Become a member of AABPS; achieve your career goals and enjoy collaboration and friendship of people with similar background and interest.

Please support AABPS with your tax-deductible donations and advertisement.

AABPS Upcoming Events

(Tentative)

- AABPS Meeting 2017: November 13, 2017 (San Diego, CA)
- AABPS Picnic: July 2018 (New Jersey)
- AABPS Executive Committee election by December 2018
- 5th AABPS Convention: July 2019 (Maryland)

www.aabps.org

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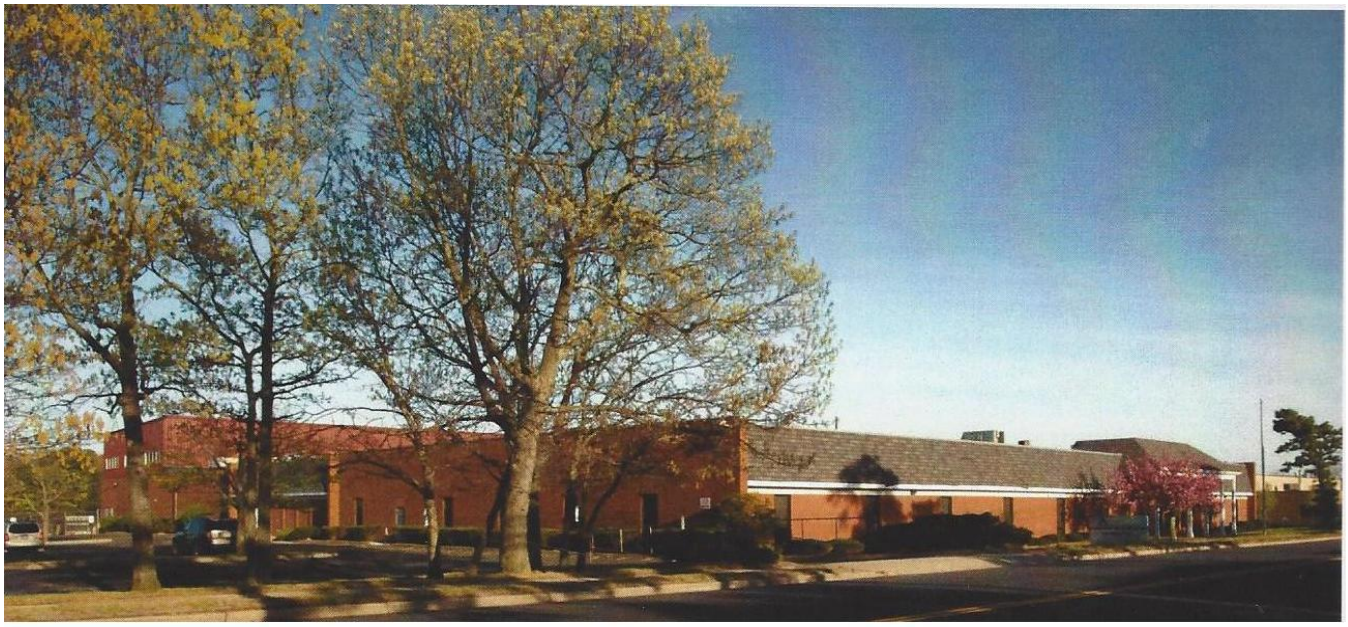

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