مجلس قطر للبحوث والتطوير والابتكار
QRDI COUNCIL

الصندوق القطري لرعاية البحث العلمي
Qatar National Research Fund

جامعة الدوحة للعلوم والتكنولوجيا
UNIVERSITY OF DOHA FOR SCIENCE & TECHNOLOGY

كتاب الملخصات
المؤتمر الدولي حول أحدث طرق السيليكو في اكتشاف الأدوية وتطويرها

Book of Abstracts of the International Conference on *in silico* Trends and Approaches in Drug Discovery and Development

22 - 24 أكتوبر 2023

22 - 24 October 2023

Welcome Message from University of Doha for Science and Technology

Welcome to the International Conference on *in Silico* Trends & Approaches in Drug Discovery and Development. This conference represents a significant milestone for Qatar, uniting a diverse community of researchers, educators, and students who share a deep interest in the dynamic fields of computational pharmacology and drug discovery within the realm of bioinformatics.

The conference has several key objectives, including showcasing cutting-edge computational techniques employed in exploring protein-ligand interactions, presenting advancements in in-silico approaches related to drug delivery systems, and implementing these innovations in translational research protocols within Qatar. These efforts aim to bolster research in areas such as cancer, diabetes, infectious diseases, and genetic disorders. Furthermore, we are proud to announce that the conference has received funding support from QRDI, contributing to the elevation of *in Silico* pharmacology's study and application in drug discovery and development research and education. This significant support aims to position Qatar as a leader in these vital fields.

We extend our warmest welcome and sincere thanks for your participation in this groundbreaking conference, where innovation, education, and inclusivity converge to shape a brighter and more promising future.

Best wishes,

Prof. Michael Phillips
Conference Vice Chair
Director, Applied Research, Innovation and Economic Development
UNESCO Chair on TVET and Sustainable Development
QAPCO Professional Chair in Vocational Studies
UNESCO-UNEVOC Centre Coordinator

Welcome Message from Qatar Research, Development, and Innovation (QRDI) Council

We, as QNRF programs, part of Qatar Research, Development, and Innovation (QRDI) Council, are honored to sponsor the International Conference on *in Silico* Trends & Approaches in Drug Discovery and Development at the University of Doha for Science and Technology (UDST) in Doha, Qatar, from October 22 to 24, 2023. This conference marks a significant milestone in Qatar, bringing together a diverse community of researchers, academics, and students who share a profound interest in the dynamic realms of *in Silico* pharmacology and drug discovery & development.

Together, we are elevating the study and application of *in Silico* pharmacology in drug discovery and development research and education to unprecedented levels, positioning Qatar as a leader in these critical fields. We thank you for participating in this groundbreaking conference, where innovation, education, and inclusivity converge to shape a brighter and more promising future. Your presence is a testament to the collaborative spirit and dedication that drives our shared pursuit of knowledge and progress.

Sincerely

Dr. Hisham M. Sabir

Executive Director,

Qatar National Research Fund Programs Office

Qatar Research Development and Innovation Council

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Preface

Welcome to the International Conference on *in silico* Trends & Approaches in Drug Discovery and Development, which was hosted at the University of Doha for Science & Technology in Doha, Qatar, from October 22 to 24, 2023. This conference marked as a pioneering event in the region, bringing together researchers, academics, and students who shared interest in the dynamic field of *in silico* pharmacology, with a central focus on drug discovery and development. The overarching goal of the conference was to promote scientific knowledge and showcase frontiers of innovation within the realms of drug discovery and development through the application of *in silico* pharmacology methods.

The event was guided by the following primary objectives:
Advance Computational Techniques: Cutting-edge computational techniques employed in the investigation of critical protein-ligand interactions.
Innovations in Drug Delivery Systems: Recent developments in *in silico* approaches and methods to drug delivery systems.
Translational Research in Qatar: Advances in translational research protocols in Qatar, with a focus on critical healthcare challenges, such as cancer, diabetes, infectious diseases, and genetic diseases.
Harnessing Artificial Intelligence: The transformative potential of the integration of artificial intelligence into drug discovery processes.
Enriching Education: Integration of computational approaches into various pharmacy and biomedical education programs.
Fostering Inclusivity: Inspire and encourage students and researchers, including those with disabilities, to actively engage in the world of *in silico* pharmacology and drug discovery.

The primary objectives of the conference were delivered in the form of three distinct thematic areas:
1) **Computation and Protein-Ligand Interactions**: Delved into fundamental concepts, such as protein-ligand interactions, sequence analysis, fold recognition, artificial intelligence, molecular dynamics, molecular docking, network pharmacology, and *in silico* design and synthesis of novel molecules.
2) **Computation and Drug Delivery**: Revolved around biopharmaceutics and pharmacokinetics, with advances that streamline research and development in the pharmaceutical industry and beyond.
3) **Computation and Science in the Pharmacy Curriculum**: Addressed the implementation of computational techniques in the curriculum of various pharmacy and biomedical programs, allowing the early exposure of students to such techniques, which is inevitable in this era.

The event was illuminated by distinguished invited keynote speakers:

- Ian Haworth (University of Southern California, USA),
- Pornchai Rojsitthisak (Center of Excellence in Natural Products for Ageing and Chronic Diseases, Thailand),
- Chris Cunningham (Concordia University/AACP, USA),
- Mona Minkara (Northeastern University, USA),
- Bhumika Patel (Nirma University, India), and
- Puthen Veettil (Hamad Bin Khalifa University, Qatar)

The said esteemed experts in the field of *in silico* pharmacology research and education are committed to fostering collaboration with Qatar's universities and industries. The partnership aims to initiate international initiatives in research and education, bridging the gap between cutting-edge research and effective teaching methods, ultimately positioning Qatar as a leader in the field of *in silico* pharmacology and advancing the educational landscape. Additionally, the conference uniquely emphasized the paramount importance of diversity and inclusivity in science education, particularly for students with disabilities. This was epitomized by our honored guest, Dr. Mona Minkara, whose remarkable journey as a blind scholar serves as a testament to the limitless potential of human determination and innovation.

We extend our heartfelt gratitude to the Qatar National Research Fund (QNRF) and Qatar Research, Development, and Innovation Council (QRDI) for their indispensable financial assistance. Our appreciation also extends to the Scientific Planning Committee for their meticulous reviews, and we are grateful of the diligent efforts of the local organizing committee. We offer our thanks to all authors for their active participation, and recognize the invaluable contributions made by all individuals who played a role in the conference's success. Together, we made significant strides in advancing the agenda for *in silico* pharmacology in drug discovery and development, through both research and education, paving the way to position Qatar at the forefront of these critical fields.

We thank you for joining us at this groundbreaking conference, where innovation, education, and inclusivity converged to illuminate the path toward a brighter future.

Asma El-Magboub & Mohammad Asif Khan - Conference Chairs
October, 2023

About the Conference

This international conference is a forum for researchers, academia, students, and industry to explore new ideas, techniques, and tools with a specific focus on "*In-silico* pharmacology and drug development: trends in research and education". This conference aims to achieve the following goals and objectives:

- To demonstrate the state-of-the-art computational techniques used to investigate protein-ligand interactions.
- To compile advances in the *in-silico* approaches related to drug delivery systems.
- To explore GastroPlus®, the physiologically based pharmacokinetic modeling program used to predict pharmacokinetics in different patient populations.
- To implement the advances in the translational research protocols in Qatar, to support research in cancer, diabetes, infectious disease, and genetic disease.
- To explore the assimilation of artificial intelligence in drug discovery as well as science education.
- To integrate computational approaches to different pharmacy education programs, as well as other related biomedical education programs.
- To inspire and encourage disabled students and researchers, through world-renowned Scientist – Dr. Mona Minkara, who believes Vision is more than Sight.

Focused sessions:

The computation and protein-ligand interactions
Protein-Ligand Interactions | Sequence Analysis | Fold Recognition | Artificial Intelligence

Protein Dynamics | Molecular Dynamics | Molecular Docking | Network Pharmacology |

In silico Design and Synthesis of Novel Molecule

The computation and drug delivery
Biopharmaceutics And Pharmacokinetics | Gastroplus® | BCS | Molecular Conformation | Ophthalmic Devices.

The computation and science in the pharmacy curriculum
Translation Of Pharmaceutical Science and Drug Discovery into Practice | Artificial Intelligence in Science Education, Molecular Modeling in A Pharmacy Curriculum | Computer-Aided Drug Design in A Graduate Curriculum | International Education in Pharmacy, And Disability in Science Education.

Local Conference Organizing Committee Members

Advisors:
Dr. Salem Al-Naemi, President, UDST
Prof. Rachid Benlamri, Vice President of Academic, UDST
Dr. Mohammed H. Jarrar, RDI Senior Scientific Expert, Qatar Research, Development and Innovation (QRDI)

Conference Co-Chairs:

Dr. Asma El-Magboub
Assistant Professor, College of Health Sciences, UDST

Prof. Mohammad Asif Khan
Associate Dean, College of Computing and IT, UDST
President, Asia Pacific Bioinformatics Network (APBioNET)

Conference Vice Chair:
Prof. Michael Phillips
Director, Applied Research, Innovation and Economic Development, UDST
UNESCO Chair on TVET and Sustainable Development
QAPCO Professional Chair in Vocational Studies
UNESCO-UNEVOC Centre Coordinator

Scientific Program Committee:
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Dr. Ravi Rangarajan, College of Health Sciences, UDST
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Deputy Lead: Nayla Higazy, Applied Research, Innovation and Economic Development, UDST
Assistant Lead: Jennifer Macahia, Applied Research, Innovation and Economic Development, UDST
Editorial Assistant: Hasna Ashraf *(Research Student)*

Published, 2023

About the University of Doha for Science and Technology

University of Doha for Science and Technology (UDST) was officially established by the Emiri Decision No13 of 2022, and it is the first national university that specializes in applied academic, technical, and professional education in the State of Qatar. UDST offers over 60 bachelor's and master's degree programs, diplomas, and certificates. The University houses five (5) colleges, namely the College of Business, the College of Computing and Information Technology, the College of Engineering and Technology, the College of Health Sciences, and the College of General Education. Additionally, there are specialized science and technology training centers catering to the growing needs of both the academia and industry. UDST is recognized for its student-centered learning and state-of-the-art facilities. Its world-renowned faculty and researchers work on developing students' skills and help nurture graduates who are well-equipped to proudly serve different sectors of the economy and contribute to the development of human, social and economic goals, both nationally and internationally.

Scientific Program Schedule

Sunday, 22 October 2023

Master of ceremony: Nayla Higazy

Time	Session	Speaker	Venue
1:00-2:00	**Registration and Poster Set-up**		**Building 1 Lobby**
2:10-2:20	**Welcome Note** Flash Talk Presentation and Judging Guidelines	**Dr. Mohammad Asif Khan** CCIT, UDST President, Asia Pacific Bioinformatics Network (APBioNET)	**Theater 1**
2:20-4:30	**Flash Talk Presentations**	**All Participants**	**Theater 1**
4:30-4:35	**Closing Remarks**	**Dr. Asma S. El-Magboub** Conference Chair Assistant Professor, UDST	**Theater 1**
4:35-5:00	**Coffee Break and Networking**		**Building 1 Lobby**

Monday, 23 October 2023 | Venue: Auditorium

Master of ceremony: Dr. Shannan MacNevin

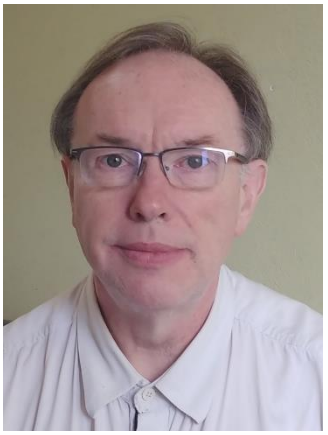
Time	Session	Speaker
8:00-9:00	**Registration | Welcome Refreshments**	**Building 1**
9:00-9:05	Welcome Speech	**Dr. Salem bin Nasser Al-Naemi** President, UDST
9:05-9:10	Opening Speech	**Dr. Mohammed H. Jarrar** Qatar Research Development and Innovation Council
9:10-9:15	Ministry of Public Health	**Dr. Ahmed Hussein Babiker** Ministry of Public Health, Qatar
9:15-10:00	***Session Chair: Dr. Mohammad Asif Khan*** **Opening Keynote** Principles of *in silico* Approaches in Research	**Dr. Ian Haworth** University of Southern California, USA
10:00-10:15	Appreciation and Awards	**Dr. Salem bin Nasser Al-Naemi** President, UDST
10:15-10:45	**Group Photo | VIP Poster Tour | Coffee Break**	**Building 1 Lobby & VIP Lobby**
10:45-11:15	***Session Chair: Dr. Asma S. El-Magboub*** Deciphering the Enhanced Antiviral Activity of Double Mutant Surfactant Protein−D Binding with Trimannose on Influenza A: Insights from Molecular Dynamics Studies	**Dr. Mona Minkara** Northeastern University, USA
11:15-11:45	Multi−omics and AI in the era of precision medicine	**Dr. Souhaila Al Khodor** Sidra Medicine
11:45-12:15	Computational Approaches in Drug Discovery: Integrating Molecular Docking and Network Pharmacology	**Dr. Pornchai Rojsitthisak** Chulalongkorn University, Thailand
12:15-1:30	**Lunch | Prayer**	**Building 1 and Atrium 1**
	Poster Display & Networking	**VIP Lobby**
1:30-2:00	***Session Chair: Dr. Asma S. El-Magboub*** Translation of pharmaceutical science and drug discovery into practice: 10 years of a molecular modeling project in a pharmacy curriculum	**Prof. Christopher W. Cunningham** Concordia University, USA
2:00-2:30	Lead identification through *in silico* ligand−based pharmacophore modeling and virtual screening: A case study on selective PARP1 inhibitors	**Dr. Bhumika Patel** Nirma University, India
2:30-3:00	**Coffee Break | Poster Display**	**Building 1 & VIP Lobby**
3:00-3:30	***Session Chair: Dr. Asma S. El-Magboub*** Human ACE2 orthologous peptide sequences show better binding affinity to SARS−CoV−2 RBD domain: Implications for drug design	**Dr. Mohammad Asif Khan** CCIT, UDST President, Asia Pacific Bioinformatics Network (APBioNET)
3:30-3:50	*Experiences from in silico drug discovery and pharmacogenomics*	**Dr. Puthen Veettil Jithesh** Hamad Bin Khalifa University, Qatar
3:50-4:15	***Session Chair: Dr. Mohammad Asif Khan*** Conference Survey | Closing Remarks	**Dr. Michael Phillips** Director, ARIED, UDST, Qatar

Tuesday, 24 October 2023 | Venue: Auditorium

Master of ceremony: Mr. Abdulla Ansari

Time	Session	Speaker
8:00-9:00	**Welcome Coffee | Poster Display**	**Building 1**
9:00-9:05	Welcome speech	**Dr. Shahriar Siddiq** **Department Head, Pharmacy**
9:05-9:30	"Tightening the loose ends"	**Dr. Mohammad Asif Khan** CCIT, UDST President, Asia Pacific Bioinformatics Network (APBioNET)
9:35-10:20	Uncapping Your Potential: The Unseen Advantage	**Dr. Mona Minkara** Northeastern University, USA
10:25-10:30	UDST, Industry and Community Engagement	**Dr. Michael Phillips** Director, Applied Research, Innovation and Economic Development, UDST
10:35-10:45	Conference Video: Closing Remarks	**Dr. Asma S. El-Magboub** Assistant Professor, UDST

Keynote and Invited Speakers



Dr. Ian S. Haworth
Associate Professor and Vice Chair of Pharmacology and Pharmaceutical Sciences
University of Southern California, California, USA

Biography

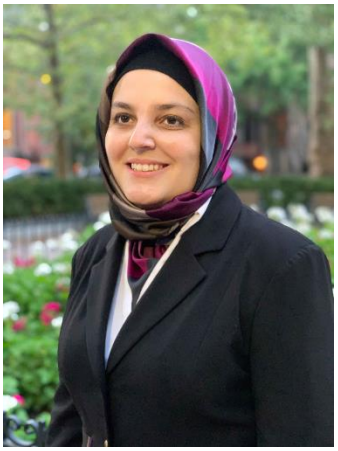
Dr. Ian Haworth is an Associate Professor and Vice Chair of the Department of Pharmacology & Pharmaceutical Sciences in the Mann School of Pharmacy & Pharmaceutical Sciences at the University of Southern California. He received his Ph.D. in Physical Organic Chemistry from the University of Liverpool, UK, and then spent three years as a Postdoctoral Fellow at the University of Oxford, UK before joining USC. His research work lies at the interfaces of chemistry, biochemistry, and computation. This work involves development and utilization of algorithms for prediction of drug-protein molecular interactions and simulation of ADME properties of drugs. Dr. Haworth's laboratory has published more than 100 scientific articles on this work. Current projects include examining the relationship of affinity with solvation at drug-protein interfaces; physiologically based pharmacokinetic (PBPK) modeling aimed at mechanistic understanding of drug disposition; and use of cheminformatics and machine learning in prediction of molecular association. Dr. Haworth also has a major role in teaching of medicinal chemistry and biopharmaceutics at USC, and he has lectured and taught courses on this content worldwide. He is also currently co-Director of the International Summer Program in the USC Mann School of Pharmacy. Dr. Haworth has utilized problem-based learning in teaching of science courses for many years, and he has published and presented widely on these educational approaches. He is also interested in utilization of computational methods in evaluation of educational outcomes, including new approaches to curriculum mapping and assessment.

Principles of *in-silico* Approaches in Pharmacology Research

In silico methods are increasingly important in drug discovery and development. These methods include molecular-based computational approaches using molecular modeling and docking; simulation of pharmacokinetics using compartmental and physiologically based pharmacokinetic (PBPK) modeling, and use of machine learning to build complex models of molecular events and use these models for prediction. In this talk, examples of these three areas will be discussed based on recent work in our laboratory. First, modeling approaches using explicit solvation can improve understanding of the role of water at molecular interfaces. We have developed Solvate/Watgen as an algorithm for prediction of interface solvation, as a basis for ligand design incorporating solvent retention and exclusion. Second, compartmental and PBPK methods will be described for prediction of environmental toxicological effects and for detailed understanding of molecular events modulating drug disposition, using GastroPlus software. Finally, a machine learning approach using molecular descriptors will be discussed for prediction of inhibitors of tau fibril formation, using the KNIME software platform.

Dr. Mona Minkara
Assistant Professor of Bioengineering
Northeastern University, Massachusetts, USA

Biography



Dr. Mona Minkara is an Assistant Professor in the Department of Bioengineering and an Affiliate Faculty in the Department of Chemistry and Chemical Biology at Northeastern University. She received her Bachelor of Arts from Wellesley College and her Ph.D. in Chemistry from the University of Florida. Dr. Minkara is the head of the COMBINE (Computational Modeling for Biointerface Engineering) Lab, which focuses on the study of pulmonary surfactant, a complex protein-lipid substance secreted by the alveoli in the lungs and its potential therapeutic applications in the medical field. Dr. Minkara specializes in using an array of computational tools to apply to biomolecular problems, and her laboratory is developing innovative approaches that combine protein and surfactant modeling to investigate the PS system computationally. As a blind scientist, she is committed to making science more accessible and inclusive through engineering new tools for blind and partially sighted scientists, and she is involved in several projects dedicated to promoting accessibility in STEM fields. The importance of interdisciplinary research is emphasized in her work, which highlights the efficacy of computational methods in drug discovery and elucidating the complexities of the pulmonary surfactant (PS) system.

Deciphering the Enhanced Antiviral Activity of Double Mutant Surfactant Protein-D Binding with Trimannose on Influenza A: Insights from Molecular Dynamics Studies

Deciphering the Enhanced Antiviral Activity of Double Mutant Surfactant Protein D Binding with Trimannose on the Influenza A Virus: Insights from Molecular Dynamics Studies Surfactant Protein D (SP-D) is a member of the collectins, collagen-containing lectin proteins that belong to a broader category of pattern recognition receptors, fundamental to the primary immune defense. SP-D serves as a barrier against pathogens, including bacteria, fungi, and viruses. While wild-type SP-D binds these pathogens, previous studies have shown its antiviral activity against Influenza A Virus is limited; however, a double mutant SP-D, with mutations Asp325Ala and Arg343Val, shows enhanced inhibitory effects. The molecular basis for this enhanced binding to viral glycans is not fully understood. In our research, we employ microsecond-scale molecular dynamics simulations, paired with free energy perturbation and quantum mechanics. Using trimannose as a model and considering over twelve different glycan binding poses and point mutation models, we seek to understand the mutant SP-D's heightened antiviral properties. Our findings pave the way for designing optimized SP-D variants for improved pathogen specificity.

Dr. Souhaila Al Khodor
A/ Executive Director- Translational Medicine Department,
Director-Maternal and Child Health Division, Sidra Medicine

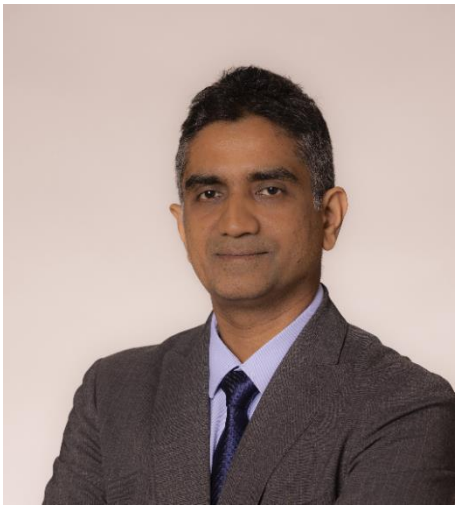
Biography

Dr. Al Khodor is the Acting Executive Director of Translational Medicine Department and the Director of Maternal and Child Health Division in the Research Branch at Sidra Medicine, Qatar. Dr. Al Khodor received her bachelor's degree in medical Lab. technology from the Faculty of Public Health at the Lebanese University in 2001. Soon after, she started her master's degree in microbiology and Immunology at the American University of Beirut (2002-2004). Dr. Al Khodor received her second master's degree and PhD in Microbiology and Immunology from the University of Louisville, Louisville, KY, USA (2005-2008). Before joining Sidra, Dr. Al Khodor worked as a postdoctoral fellow in the Signaling systems Unit, laboratory of Systems Biology, at the National Institute of Allergy and infectious Diseases (NIAID), National Institutes of Health (NIH) in Maryland, USA. Dr. Al Khodor's laboratory in Sidra focuses on characterizing the role of the microbiome in health and disease, with a particular emphasis on maternal and child health and the integration of metagenomics with other omics aiming to identify predictive markers for various diseases and pathological conditions. Dr. Al Khodor is an adjunct Faculty at the College of Health & Life Science in Hamad Bin Khalifa University, and an Adjunct Assistant Professor at the Department of Biomedical Sciences, College of Health Sciences in Qatar University. Dr. Al Khodor has over 67 peer-reviewed publications. She currently serves as an Assistant Specialty Chief Editor for Frontiers in Cellular and Infection Microbiology and is the Section Editor for Metagenomics in the Journal of Translational Medicine.

Multi-omics and AI in the era of precision medicine

Recent advances in the field of omics, bioinformatics and artificial intelligence have empowered us with novel ways to understand disease pathogenesis and improve patient outcomes. Systems level characterization of biological data including genomics, epigenomics, metabolomics, metagenomics and proteomics is becoming not only feasible, but also essential for unraveling the complex interactions in health and disease. Using machine learning tools and algorithms, it is possible to integrate multiomics data with clinical information to develop predictive models that identify risk before the disease is clinically apparent, thus facilitating early interventions to improve patients' health. During my presentation, I will cover some of the recent research performed in my laboratory at Sidra Medicine, where the integration of multi-omics and AI has been instrumental in identifying biomarkers of various diseases affecting maternal and child health. These advancements are propelling us closer to the forefront of precision medicine and the transformation of healthcare.

Dr. Mohammad Asif Khan
Professor and Associate Dean, CCIT, UDST
President, Asia Pacific Bioinformatics Network (APBioNET)



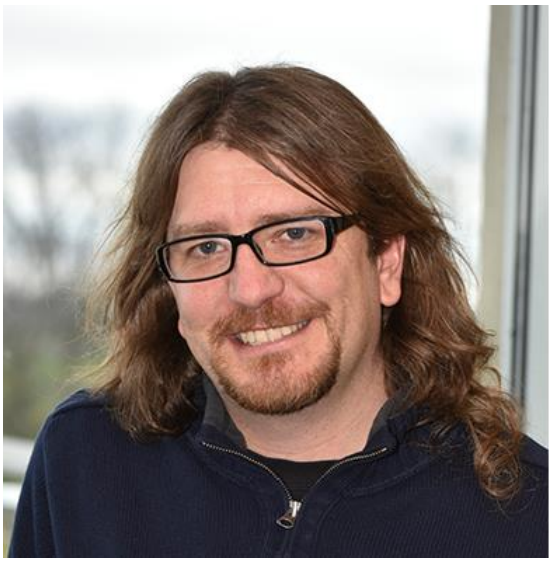
Biography

Dr. Mohammad Asif KHAN joined the University of Doha for Science and Technology (UDST) as a Professor and Associate Dean at the College of Computing and Information Technology. He holds a PhD from the National University of Singapore. Dr. Khan was then recruited as a faculty member at the Johns Hopkins University (JHU) in the United States. Shortly thereafter, he was selected to be part of a pioneering team from JHU tasked with establishing a presence in Malaysia as part of a collaboration with the newly established Perdana University (PU), which operated under the auspices of the Malaysia Prime Minister's office. At PU, Dr. Khan played a pivotal role in its foundation, serving as the Founding Director of the Centre for Bioinformatics and later as the Founding Dean of the School of Data Sciences. In addition to his contributions to PU, Dr. Khan's expertise led to his appointment as a Professor at Bezmialem Vakif University in Istanbul, Turkey, where he was seconded through the prestigious "International Fellowship for Outstanding Researchers" awarded by the Scientific and Technological Research Council of Turkey. Dr. Khan's extensive academic and entrepreneurial journey demonstrate his commitment to advancing education and research in the fields of computing, information technology, and data sciences on a global scale.

Human ACE2 orthologous peptide sequences show better binding affinity to SARS-CoV-2 RBD domain: Implications for drug design.

Computational methods coupled with experimental validation play a critical role in the identification of novel inhibitory peptides that interact with viral antigenic determinants. The interaction between the receptor binding domain (RBD) of SARS-CoV-2 spike protein and the helical peptide of human angiotensin-converting enzyme-2 (ACE2) is a necessity for the initiation of viral infection. Herein, natural orthologs of human ACE2 helical peptide were evaluated for competitive inhibitory binding to the viral RBD by use of a computational approach, which was experimentally validated. A total of 624 natural ACE2 orthologous 32-amino acid long peptides were identified through a similarity search. Molecular docking was used to virtually screen and rank the peptides based on binding affinity metrics, benchmarked against human ACE2 peptide docked to the RBD. Molecular dynamics (MD) simulations were done for the human reference and the *Nipponia nippon* peptide as it exhibited the highest binding affinity (Gibbs free energy; −14 kcal/mol) predicted from the docking results. The MD simulation confirmed the stability of the assessed peptide in the complex (−12.3 kcal/mol). The top three docked-peptides (from *Chitinophaga sancti*, *Nipponia nippon*, and *Mus musculus*) and the human reference were experimentally validated by use of surface plasmon resonance technology. The human reference exhibited the weakest binding affinity (Kd of 318–441 pM) among the peptides tested, in agreement with the docking prediction, while the peptide from *Nipponia nippon* was the best, with 267–538-fold higher affinity than the reference. The validated peptides merit further investigation. This work showcases that the approach herein can aid in the identification of inhibitory biosimilar peptides for other viruses.

Dr. Christopher W. Cunningham
Chair of Chemistry Section
American Association of Colleges of Pharmacy (AACP)
Associate Professor of Pharmaceutical Sciences
School of Pharmacy, Concordia University, Wisconsin, USA



Biography

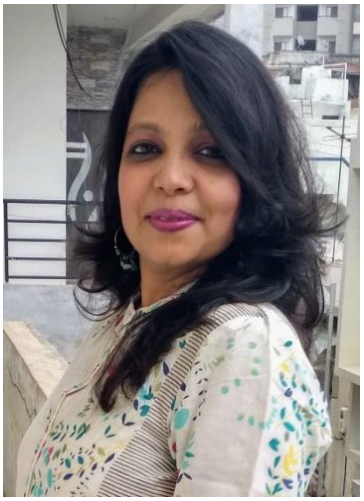
Dr. Cunningham is an Associate Professor of Pharmaceutical Sciences at Concordia University Wisconsin (CUW) School of Pharmacy. He received his B.S. in Chemistry and Germanic Studies (*cum laude*) from the University of Maryland, College Park (2002), and his Ph.D. in Pharmaceutical Sciences from the University of Maryland, Baltimore School of Pharmacy (2008). His training was supported by a Ruth L. Kirschstein predoctoral fellowship. He completed postdoctoral training in Medicinal Chemistry as a member of the Specialized Chemistry Center at the University of Kansas (2008–2011). At CUW, he has been Director of the Center for Structure-Based Drug Discovery and Development since 2014. His research program focuses on developing tools to study the role of endogenous opioid and cannabinoid neutoransmitter systems in diseases like pain, stress and anxiety, and substance use disorders.

Translation of pharmaceutical science and drug discovery into practice: 10 years of a molecular modeling project in a pharmacy curriculum

As pharmacists are the medications experts on the healthcare team, they are frequently called upon to communicate the basic science underpinnings of drug action to broad audiences. The traditional lecture format often used in higher education is often inadequate to prepare students for this task. Increasingly, pharmacy educators are called upon to use more tactile methods that allow students to explore complex concepts more deeply and practice communicating basic science to fellow practitioners and patients. Since opening in 2010, the Concordia University Wisconsin School of Pharmacy have incorporated a molecular modeling project into a Pharmacology and Medicinal Chemistry course sequence. What began as a professor-guided, “static” simulation has transformed over the years into a student-driven drug discovery project. An overview of the evolution of the project will be presented, as will some preliminary evidence supporting the value of the project to student success.

Dr. Bhumika D. Patel
Assistant Professor of Pharmaceutical Sciences
UG Research Council at Institute of Pharmacy
Nirma University, India

Biography



Dr. Bhumika Patel is working as an Assistant Professor in the Department of Pharmaceutical Chemistry and Coordinator of UG Research Council at the Institute of Pharmacy, Nirma University, Ahmedabad. She has 16 years of teaching and 13 years of research experience. Her area of research includes drug repurposing using in-silico techniques, rational design and synthesis of different heterocyclic compounds under various therapeutic classes like diabetes, cancer, TB etc. She has a sound knowledge of computer aided drug design techniques like pharmacophore modeling, QSAR, Virtual Screening, Molecular docking and MD simulation, Homology modeling etc. and has worked on software like Sybyl, Discovery Studio, Gold, Schrodinger, etc. She received Best Assistant Professor Award 2018-19 for the Overall Performance in Teaching, Co-Curricular Activities and Research from Nirma University. She is a member of professional bodies like American Chemical Society, APTI, IPA, ISCB (Indian Society of Chemists and Biologists), RSSDI (Research Society for the Study of Diabetes in India), ISTE (Indian Society for Technical Education), etc.

Lead Identification through In-Silico Ligand-Based Pharmacophore Modeling and Virtual Screening: A Case Study on Selective Poly (ADP-Ribose) Polymerase1 (PARP1) Inhibitors

One of the most significant members of the Poly (ADP-Ribose) Polymerase (PARP) enzyme family, PARP1, is essential for DNA damage repair, gene transcription, and the apoptosis of cancer cells. Therefore, PARP1 inhibitors are crucial in the treatment of solid tumors in patients with either germline BRCA mutations or with homologous recombination repair deficiency. All marketed PARP1 inhibitors; Olaparib, Rucaparib, Niraparib, Talazoparib etc. are nonselective and mediate their antitumor effect through catalytic inhibition of both, PARP1/2 which end up into have many hematological side effects. To circumvent this problem, there is a need to develop next generation selective PARP1 inhibitors. In this study, we developed and validated ligand-based pharmacophore model, ADHRR_3, using known selective PARP1 inhibitors using the PHASE module of the software, Schrodinger LLC, New York, USA. Pharmacophore based virtual screening was performed against the Chemdiv anticancer compound library (61538) and Lead like screening compound library of Life chemicals (32439). The top 1000 hits were further refined through docking based high throughput virtual screening in Schrodinger and then resulted hit were further redocked using standard precision (SP) and extra precision (XP) modes to achieve high accuracy. Identified top 3 hits showed interactions with crucial amino acids in the catalytic site as well as with the amino acids in allosteric site which may govern the selectivity towards PARP1. XP docking of these 3 hits into the PARP2 structure also showed low docking score and weak interactions in comparison to marketed non-selective drug, Olaparib. The outcome of this in-silico study definitely supports the application of computer-aided techniques to the discovery of novel and selective PARP1 inhibitors.

Dr. Pornchai Rojsitthisak
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Biography

Dr. Pornchai Rojsitthisak is an Associate Professor at the Faculty of Pharmaceutical Sciences and also serves as the head of the Center of Excellence in Natural Products for Ageing and Chronic Diseases at Chulalongkorn University, Bangkok, Thailand. After obtaining his B.Sc. and M.Sc. from Chulalongkorn University, he earned his Ph.D. from the University of Southern California in 2002. His research emphasizes the enhancement of physicochemical and biopharmaceutical properties of drug candidates derived from natural products using methods like prodrug design and nanoformulations. Additionally, his lab develops analytical methods for identifying bioactive compounds in various matrices using techniques such as HPLC and LC-MS/MS.

Computational Approaches in Drug Discovery: Integrating Molecular Docking and Network Pharmacology

Drug discovery and development processes, though expensive and time-intensive, are seeing promising advancements with omics technologies and computational tools. An emerging synergy in this domain is the integration of molecular docking and network pharmacology. Molecular docking predicts the binding affinity of molecules to target proteins, aiding in potential drug candidate identification. Network pharmacology, in contrast, delves into the intricate interactions within biological systems, spotlighting various targets and disease-relevant pathways. This amalgamation offers a richer understanding of drug-target interactions, supporting the potential for polypharmacology. We recently applied these methods to plant-derived compounds, prodrugs, and drug combinations. For example, we investigated the therapeutic potential of (−)-dendroparishiol for bacterial meningitis. Docking displayed its affinity for iNOS and COX-2, whereas network pharmacology emphasized its involvement in oxidative stress and neuroinflammation. Our study on curcumin diethyl γ-aminobutyrate (Cur-2GE) suggested its potential analgesic properties due to its favorable binding to GABAA receptors. Additionally, we identified potential synergistic interactions between curcumin and metformin for anti-inflammatory effects. Importantly, *in vitro* and *in vivo* models validated our computational predictions, underscoring their reliability. In summary, combining molecular docking and network pharmacology can revolutionize drug discovery, enriching our understanding of drug interactions and pushing forward the pharmacology and therapeutics field.

Dr. Puthen Veettil Jithesh
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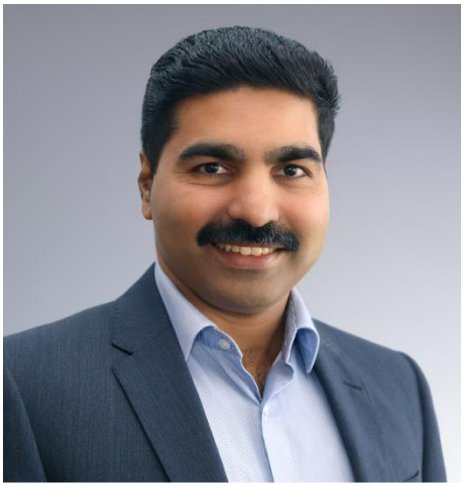

Biography

Dr. Puthen Veettil Jithesh, FRSB is an Associate Professor at the College of Health and Life Sciences at Hamad Bin Khalifa University Qatar. Dr. Jithesh holds a PhD in Bioinformatics from Queen's University Belfast, United Kingdom. He has over 25 years of research in Bioinformatics and Computational Biology at several prestigious institutes in India, Qatar, and Russell Group research universities in the United Kingdom. His research focuses on bioinformatics and computational biology tool development and applications in translational research, pharmacogenomics for the prediction of effectiveness and toxicity to drugs, identification of causal variants in rare genetic diseases, and machine learning and data science toward the implementation of precision medicine. He leads the pharmacogenomics stream of the Qatar Genome Program Research Consortium. He was also the Head of Bioinformatics for the Oxford Translational Molecular Diagnostic Centre at the University of Oxford and held honorary appointments with the Wellcome Centre for Human Genetics and the Oxford University Hospitals NHS Trust.

Experiences from *in Silico* drug discovery and pharmacogenomics

Virtual screening, molecular modeling, docking, and dynamic simulations are potent tools *in Silico* drug discovery. In this presentation, I will showcase instances where these techniques were applied to identify potential drugs targeting SARS-CoV-2 and its variants. In one such study, we selected 200 reported antiviral peptides of different species from the antimicrobial peptide database (APD). Molecular docking identified one natural antimicrobial peptide, Protegrin-2, with high binding affinity and stable interactions with the main protease Mpro of SARS-Cov-2. Subsequent free energy calculations and molecular dynamics simulations illustrated a high affinity interaction between the two. Further study on the impact of the binding of Protegrin-2 to Mpro using a Bioluminescence Resonance Energy Transfer (BRET)-based assay showed that it inhibits the proteolytic cleavage activity of Mpro. Pharmacogenomics (PGx) studies the influence of genetic variants on drug response so that efficacy can be maximized, and toxicity can be minimized. PGx provides one of the best opportunities for precision medicine implementation, which can improve health outcomes and reduce costs. We developed a bioinformatics tool for the analysis of population genomics data to identify clinically important pharmacogenetic variants and predict phenotypes such as response and adverse reactions to drugs. Further, we analyzed the actionable pharmacogenomic landscape of the Qatari population from 6218 whole genome sequencing data generated by the Qatar Genome Program, and compared these frequencies with other world populations, revealing important differences in distribution. For example, the actionable frequency of SLCO1B1 was twice as compared to other populations, suggesting higher risk of myopathy when taking simvastatin. These findings underscore the need for tailoring drug treatments based on population-specific pharmacogenomic insights, promising better health outcomes and reduced healthcare costs.

Abstracts

Mebendazole Loaded Nanoparticles for Lung Cancer Therapy

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Lung cancer is the most common cause of cancer death. Upon their microscopic appearance, lung cancers are categorized into two following categories: Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Many patients are only diagnosed at stage III or IV with poor Prognosis. Advanced-stage lung cancer represents a fatal and incurable disease, People with non-small cell lung cancer can be treated with surgery, chemotherapy, radiation therapy, targeted therapy, or a combination of treatments. Targeted therapy focused on specific abnormalities present within cancer cell including EGFR mutation. the T790M mutation in the tyrosine kinase domain of the EGFR leads to acquired resistance to first generation EGFR TKIs. Therefore, a combination of various targeted therapeutic agents not only enhance the treatment outcome but can also be more effective preventor overcome the improvement of acquired resistance. Loaded drug Nanoparticles (ZSM-5 AND SBA-16) were used as targeted therapy and detected their stability and loading percentage by several approaches: infrared, X-Ray Diffraction, TGA, and HPLC. The treatment was applied on cell culture in-vitro experiments including MMT assay, colony and migration assay. The result found that the loaded drug nanoparticles IC50 less than free drug (MELT-2015) we used and that indicate the nanoparticles enhance treatment and decreased the dose of drug.

Exploring Potential Anti-Neurodegenerative Activity of New Proaporphine Alkaloids from *Cissampelos Capensis* L.f.: Pharmacokinetic and Molecular Docking Investigations

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Current treatments for Alzheimer's disease (AD) and Parkinson's disease (PD) have been found to possess limited efficacy along with various side effects. Natural products are recognized as vital resources for neurological disorders treatment. *Cissampelos capensis* L.f., a medicinal plant, is renowned for its healing properties. Recently, three new proaporphine alkaloids (cissamaline, cissamanine, and cissamdine) were isolated from *C. capensis*. As the biological targets of these alkaloids remain unknown, this study aims to serve as a starting point to explore the potential of these alkaloids in treating neurodegenerative disorders. In this study, *in Silico* studies of eight human protein targets were conducted to determine the inhibitory potential of the new proaporphine alkaloids as a potential treatment of PD and AD. Drug likeness and ADMET analyses indicate that cissamaline, cissamanine, and cissamdine are safe with favorable ADMET profiles, making them suitable for central nervous system targeting. Furthermore, molecular docking studies reveal these alkaloids' binding interactions with AD and PD-related protein targets are comparable or superior to established drugs, except for COMT, for which binding interactions were weaker. The *in-silico* findings of this study provide promising evidence for the potential use of these proaporphine alkaloids as neuroprotective agents.

Targeting PAD4: Computational repurposing strategy of some FDA-approved drugs for the treatment of rheumatoid arthritis

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Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder that is still unknown in its cause. It is more common in females than males. There are several therapeutic options available for RA, including DMARDS, biological DMARDS, T and B cells targeted therapy, Interleukin targeted therapy, and RANKL inhibitors. Peptidyl arginine-deiminase IV (PAD4) are enzymes that are abundant in neutrophils and are believed to drive citrullination under inflammatory conditions. Citrullination can alter the protein structure, creating a new epitope that is recognized by the immune system. PADs catalytic activity requires high calcium concentrations, and hyperactivation of PAD4, which is overproduced in RA, can cause overproduction of deiminated proteins, leading to immune attack on joint tissues. Halo amidines and GSK199 are compounds that can block PAD4 activity but have metabolic and membrane permeability drawbacks, and there is no FDA-approved drug for PAD4. Therefore, our goal is to repurpose some FDA-approved drugs to target PAD4 using a computational drug repurposing strategy. A total of 1650 FDA-approved drugs were retrieved from the Zinc 15 database and were then prepared and filtered using Maestro software, resulting in 1590 unique compounds. Molecular docking was performed on the crystal structure of the human PAD4 protein in the antagonist state, which was obtained from the Protein data bank (PDB code: 4X8G). 263 drugs that can bind to PAD4 were identified using High Throughput Virtual Screening (HTVS), and after further Standard-precision (SP) and extra-precision (XP), 5 drugs were obtained (Ioversol, Pemetrexed, Leucoverin, Chlordiazepoxide, Chlorthalidone), which were then subjected to Shape Screening, and Induced Fit Docking to validate the binding. The findings of this study suggest that these hits could have potential therapeutic benefits for RA treatment. Further research will be conducted to examine the efficacy of these hits on PAD4 through molecular dynamics and in vitro studies.

In-Vitro In-Silico PBPK Modeling Approach for The Prediction of In-Vivo Pharmacokinetics of Ciprofloxacin HCl Containing Gastro-Retentive Drug Delivery System

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Pharmaceutical research is currently focused on developing precise drug delivery methods and using computer software, such as PBPK modeling, to simulate conditions within the human body. This study aimed to formulate a gastro-retentive tablet containing Ciprofloxacin HCl by using an in-silico approach to estimate how the prepared formulations would perform in vivo in the human body. The tablets were prepared using HPMC K4M polymer as the primary component, which demonstrated sustained and extended floating capabilities for up to 24 hours. This prolonged the stay of the formulation in the stomach, leading to the complete and enhanced release of Ciprofloxacin HCl. The floating and slow-release behaviors of HPMC K4M were evaluated to confirm its gastro-retentive properties. The pharmacokinetic profile of the selected tablets, exhibiting gastro-retentive properties, was predicted *in Silico* based on in-vitro release and floating duration data, utilizing physiological-based pharmacokinetic modeling tools. The plasma drug concentration over time profile and pharmacokinetic parameters were derived from the in-vitro dissolution profile through a convolution method, and the data were analyzed using PKSolver. This model successfully anticipated sustained and prolonged-release tablets containing 500 mg of Ciprofloxacin HCl, demonstrating significant retention of the drug in the stomach for extended periods.

In silico and _in vivo_ based characterization of potential inhibitors that target the C- Terminal domain of Aha1 protein.

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Tau aggregation is a hallmark of numerous neurodegenerative disorders known as tauopathies such as Alzheimer's disease (AD). In tauopathies, tau becomes hyperphosphorylated which leads to the aggregate's formation. Several emerged studies have linked Tau aggregation to the Hsp90 ATPase activity. The Hsp90's ATPase activity is regulated by a group of cochaperones including Aha1. Thus, inhibiting the Hsp90-ATP cycle by inactivating Aha1 might be an effective therapeutic solution. In this work, a combination of *in Silico* and *in vitro* approaches was utilized to identify a drug-like small molecule that targets Aha1. Molecular docking and NMR spectroscopy were used to investigate the interaction between Aha1, and a set of potential inhibitors designed to target its activity. The findings of this study demonstrated that among these potential inhibitors, KU-1357 binds to the Aha1's C-terminal domain of the Aha-1 (C-Aha1). This interaction is promoted by hydrophobic and electrostatic interaction driven by a subset of residues residing in the C-Aha1.

Design and Optimization of Sustained Release Tablets of Axitinib-A DoE based Approach

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Objective: The objective of this research was to design sustained-release formulations of Axitinib (AXB), a tyrosine kinase inhibitor used to treat renal cancer patients, using the Quality by Design (QbD) method.

Significance: Currently, no sustained-release tablets of AXB have been documented using the QbD method. Developing such formulations is of significant importance as they could enhance treatment efficacy, reduce dosing frequency, and improve patient compliance by providing a controlled and prolonged release of the drug.

Methods: We have employed the Box-Behnken statistical design (BBD) with the wet granulation technique, investigating drug-release retardant polymers: HPMC K4M (X1), HPMC K15M (X2), and Polyvinyl pyrrolidone (PVP) (X3). In vitro cumulative percentage releases in 0–24 h (R1 to R10) were used as dependent variables. In-vitro release tests and kinetic equations were employed to analyze the improved formulations.

Results: Utilizing response surface graphs, the study analyzed the impacts of each factor and achieved an optimized sustained-release formulation with a desirability function of 0.793. Among the kinetic release models evaluated, the Peppas model exhibited the highest correlation (R = 0.9978) and determination coefficient (R2 = 0.9955), indicating a strong fit for the release profile.

Conclusions: The research findings demonstrate the significance of using the Box-Behnken statistical design (BBD) to enhance sustained-release formulations and assess the impacts of formulation factors. The developed sustained-release formulation, with a promising fit to the Peppas kinetic model, holds great potential for improved treatment outcomes and long-term release, offering a potential advancement in cancer therapy.

Keywords: Axitinib, Hydrophilic matrix tablets, Box-Behnken statistical design, Dissolution, Sustained release and stability.

Descriptors to Classifiers and Predictor: A Machine Learning Approach to Predict Small Molecule Binders of Pantothenate synthetase of Mycobacterium Tuberculosis

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The discovery of new drug molecules after high throughput screening depends on experimental assessment of ADMET and related physiochemical properties of small molecules. The process itself is costly, time and labor intensive. Computational approaches, such as virtual screening, docking, and machine learning represent an effective alternative to predict these properties with less cost as well as time efficient. The current study used the true active and inactive drug candidates to train a Machine Learned (ML) model against one of the potent drug targets used to treat Mycobacterium tuberculosis (Mtb) i.e., Pantothenate synthetase (PS). The PS catalyzes amide bond formation of pantothenate from D-pantoate and β-alanine followed by Mg-ATP hydrolysis into Mg-PPi and AMP. The pantothenate is a key precursor of coenzyme A and ACP, and essential for fatty acid metabolism, cell signaling, synthesis of polyketides and non-ribosomal peptides. Initially, 20 descriptors were shortlisted based on their significant Pearson's correlation with logIC50 values. Unique combination of 20 descriptors were obtained. As a result, six descriptors are found to be most significant based on their significant r2 value. The binary classification models with six different algorithms named LR, LDA, CART, NB, KNN and SVM were trained using obtained descriptor dataset to classify molecules as active and inactive. This ML based method can be used to screen libraries containing millions of drug-like compounds to classify them as either drug-like or non-drug-like against PS of Mtb.

Computational Evaluation of *Azadirachta indica*-Derived Bioactive Compounds as Potential Inhibitors of NLRP3 in the Treatment of Alzheimer's Disease

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Background: The development of therapeutic agents against Alzheimer's disease (AD) has stalled recently. Drug candidates targeting amyloid-ß (Aß) deposition have often failed clinical trials at different stages, prompting the search for novel targets for AD therapy. The NLRP3 inflammasome is an integral part of innate immunity, contributing to neuroinflammation and AD pathophysiology. Thus, it has become a promising new target for AD therapy.

Objective: The study sought to investigate the potential of bioactive compounds derived from *Azadirachta indica* to inhibit the NLRP3 protein implicated in the pathophysiology of AD.

Methods: Structural bioinformatics via molecular docking and density functional theory (DFT) analysis was utilized for the identification of novel NLRP3 inhibitors from A. indica bioactive compounds. The compounds were further subjected to pharmacokinetic and drug-likeness analysis. Results obtained from the compounds were compared against that of oridonin, a known NLRP3 inhibitor.

Results: The studied compounds optimally saturated the binding site of the NLRP3 NACHT domain, forming principal interactions with the different amino acids at its binding site. The studied compounds also demonstrated better bioactivity and chemical reactivity as ascertained by DFT analysis and all the compounds except 7-desacetyl-7-benzoylazadiradione, which had two violations, conformed to Lipinski's rule of five.

Conclusion: *In silico* studies show that A. indica derived compounds have better inhibitory potential against NLRP3 and better pharmacokinetic profiles when compared with the reference ligand (oridonin). These compounds are thus proposed as novel NLRP3 inhibitors for the treatment of AD. Further wet-lab studies are needed to confirm the potency of the studied compounds.

Discovery of Potent natural Analogue to overcome Off-target Toxicity of RNA: An integrated Machine Learning and Chemoinformatics Approach

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The adverse toxicological effect caused by interaction between the drug and the unintended target is termed as off-target toxicity, often unknown which may lead to preclinical and clinical toxic events. This inadvertent off-target interaction causes various toxic effects including hepatotoxicity, cardiotoxicity, retinal toxicity, skin toxicity, nephrotoxicity, etc. Finding non-toxic or low-toxic substances that could potentially replace or substitute for the current drugs that would otherwise have adverse effects is therefore urgently needed. Researchers are looking to natural chemicals, which are thought to possess the therapeutic effect but have a wide range of structural variety and less harmful effects, to address this challenging situation. Chemoinformatics and machine learning can be used to compute the binding of potent natural analogues to different macromolecules, which may help in the development of a viable therapeutic. This report aims to provide theoretical information about how a variety of drugs bind to many unintended targets and cause toxicity, with particular emphasis placed on the antiretroviral agent, Zidovudine. A massive data of 7, 23,878 natural compounds were collected by exploring the available databases including Natural Product Activity and Species Source Database (NPASS), Phenol-Explorer, LOTUS, Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT), and others. Afterward, the compounds were narrowed down based on their ADMET profiles and drug- likeness characteristics. The Tanimoto Coefficient under a specified similarity index of 64% was used to screen for structural similarity among the 75,803 shortlisted compounds with better pharmacokinetic properties. This resulted in a screened list of 54 compounds, which were then docked with the drug in article's specified target and off-target to perform comparative analysis. Three naturally occurring analogues of the drug were selected as potential therapeutic compounds that fall into the drug likelihood category well, have superior absorption, distribution, metabolism, and excretion (ADME) profiles, and have better anticipated toxicity profiles as compared to the synthetic drug.

Targeting Glycogen Synthase Kinase-3β (GSK-3β) in Breast Cancer by harnessing Cyperus Esculentus Compounds- A Computational Approach

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Cancer remains a primary cause of mortality in developed regions, while globally it ranks second, with breast cancer being a prevalent diagnosis in women. In an endeavor to explore novel inhibitory approaches, this research focuses on potential bioactive compounds derived from the Cyperus esculentus plant, screening their capacity to inhibit Glycogen Synthase Kinase-3β (GSK-3β) through *in Silico* methods. Procuring the 3D structure of the receptor protein and 28 bioactive compounds from the Protein Data Bank (PDB) and PubChem server, a comprehensive drug-likeness screening was conducted. AutoDock Vina software was utilized for the molecular docking process, targeting GSK-3β. The subsequent analysis unveiled seven bioactive compounds exhibiting notable inhibitory activity, with binding energies spanning from -8.3 to -9.2 kcal/mol. When evaluated for their Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) properties, epicatechin and catechin emerged as promising compounds due to their comparatively lower toxicity. Thus, these findings accentuate the potential of C. esculentus-derived compounds in inhibiting GSK-3β, a key enzyme associated with breast cancer, positioning epicatechin as a paramount candidate for subsequent investigation.

Keywords: Glycogen Synthase Kinase- 3β enzyme, Cancer, Breast cancer, Estrogens, Receptors, Molecular docking, Phytocompounds.

Computer-Aided Drug Discovery from Some Plant Compounds against Chronic Myeloid Leukemia: c-Abl Kinase Inhibitors in-focus

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Chronic myeloid leukemia (CML) is a hematological malignancy characterized by neoplastic transformation of hematopoietic stem cells, followed by a cytogenetic marker that derives from a translocation involving chromosomes 9 and 22. This results in the formation of the Philadelphia (Ph) chromosome, housing fused breakpoint cluster region (BCR) and the Abelson (ABL) oncogene (BCR-ABL1). Tyrosine kinase activity of BCR-ABL1 is reported as the initiator and maintainer of CML through c-Abl kinase, therefore needs to be put in check. Despite the advent of three generations of TK inhibitors, efficacy, safety, and recurrent drug resistance are still a challenge. The focus here is to identify potential inhibitors of Abelson kinase (c-Abl) from compounds in plants with anti-leukemic potentials using drug-likeness, molecular docking, molecular dynamics simulations (MDS), density function theory (DFT), and *in Silico* pharmacokinetics (ADMET) screening. 58 compounds were screened for drug-likeness, out of which 44 compounds were docked against c-Abl kinase using Maestro 12.5, and the top hit compound and nilotinib (control drug) was subjected to MDS for 100 ns in Desmond, ADMET through AI drug Lab server and DFT with Spartan software. Isovitexin (-15.492 kcal/mol) was identified to have a closer binding value with nilotinib (-16.826 kcal/mol), a similar binding pose, and showed superior structural stability and chemical reactivity properties. From the findings here, isovitexin may be a potential inhibitor of c-Abl kinase. However, *in vitro* and *in vivo* experiments are required urgently to validate the findings here, as this may produce an alternative to rescue the challenges in CML treatment/management.

Keywords: Chronic myeloid leukemia; Anti-leukemic plants; Plant compounds; c-Abl kinase; Tyrosine kinase inhibitors

Proteomic Insight Towards Key Modulating Proteins Regulated by the Aryl Hydrocarbon Receptor Involved in Ovarian Cancer Carcinogenesis and Chemoresistance

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Background: Gynecological malignancies pose a severe threat to female lives. Ovarian cancer (OC), the most lethal gynecological malignancy, is clinically presented with chemoresistance and a higher relapse rate. Several studies have highly correlated the incidence of OC to exposure to environmental pollutants, such as 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), a process mainly mediated through activating the aryl hydrocarbon receptor (AhR).

Rationale and Objectives: We have previously reported that exposure of ovarian cancer cells to TCDD, an AhR activator, significantly modulated the expression of several genes that play roles in stemness and chemoresistance. However, the effect of AhR activation on the whole ovarian cancer cell proteome aiming at identifying novel druggable targets for both prevention and treatment intervention purposes remains unrevealed.

Methods: We conducted a comparative proteomic analysis of OC cells A2780 untreated/treated with TCDD for 24 h using a mass spectrometry-based label-free shotgun proteomics approach.

Results: Upon AhR activation, we found that out of 2598 proteins identified, 795 proteins were upregulated, and 611 were downregulated. String interaction analysis and KEGG-Reactome pathway analysis approaches identified several significantly dysregulated proteins that were categorized to be involved in chemoresistance, cancer progression, invasion and metastasis, apoptosis inhibition, survival, and worse prognosis in OC. Our study helped us to identify the cross-talk between AhR and several other molecular signaling pathways and their involvement in the carcinogenesis and chemoresistance of OC.

Conclusions: This study provides a better idea about the role and involvement of AhR in ovarian carcinogenesis and chemoresistance. Moreover, the study suggests that AhR is a potential therapeutic target for OC prevention and maintenance.

Bioactive Compounds from *Ocimum tenuiflorum* and *Poria cocos*: A Novel Natural Compound for Insomnia Treatment Based on A Computational Approach

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Insomnia, a widespread public health issue, is associated with substantial distress and daytime functionality impairments and can predispose to depression and cardiovascular disease. Cognitive Behavioral Anti-insomnia therapies including benzodiazepines often face limitations due to patient adherence or potential adverse effects. This study focused on identifying novel bioactive compounds from medicinal plants, aiming to discover and develop new therapeutic agents with low risk-to-benefit ratios using computational drug discovery methods. Through a systematic framework involving compound library preparation, evaluation of drug-likeness and pharmacokinetics, toxicity prediction, molecular docking, and molecular dynamic simulations, two natural compounds such as 2-(4-hydroxy-3-methoxyphenyl)-8-methoxy-6-prop-2-enyl-3,4-dihydro-2H-chromen-3-ol from *Ocimum tenuiflorum* and 7-(2-hydroxypropan-2-yl)-1,4a-dimethyl-9-oxo-3,4,10,10a-tetrahydro-2H-phenanthrene-1-carboxylic acid from *Poria cocos* exhibited high binding affinity with orexin receptor type 1 (OX1R) and type 2 (OX2R), surpassing commercial drugs used in insomnia treatment. Additionally, they showed interactions with critical amino acid residues within the receptors that play crucial roles in competitive inhibitor activity, like commercial drugs such as suvorexant, lemborexant, and daridorexant. Further, molecular dynamics simulations of the protein-ligand complexes under conditions that mimic the *in vivo* environment revealed both compounds' sustained and robust interactions with the OX1R and OX2R, reinforcing their potential as effective therapeutic candidates. Furthermore, upon evaluating both compounds' drug-likeness, pharmacokinetics, and toxicity profiles, it was discerned that they displayed considerable drug-like properties and favorable pharmacokinetics, along with diminished toxicity. The research provides a solid foundation for further exploring and validating these compounds as potential anti-insomnia therapeutics.

Keywords: Insomnia, orexin receptors, computational drug discovery, molecular docking, molecular dynamic simulations, medicinal plants, bioactive Compounds.

Unraveling the action mechanism of *Coffea arabica* for the treatment of Cervical Cancer: Network pharmacology and molecular docking analysis

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Herein, we employed an integrated network pharmacology approach to identify the bioactive components and potential pharmacological mechanisms of *C. arabica* for cervical cancer (CC) treatment**.** In total, 7 potential active compounds, and 55 shared targets for CC treatment were obtained. Eleven targets from protein-protein interaction analysis (EGFR, SRC, and MDM2) with a degree, betweenness and closeness centrality values was higher than average were strongly associated with CC. These targets were mainly focused on the biological processes' regulation of the apoptotic process. KEGG enrichment analysis revealed that the potential target genes were associated with pathways in cancer which might activate highly enriched cancer signaling pathways including PI3K-Akt and MAPK1 signaling pathways to halt the progression of CC cell proliferation. Molecular docking analysis showed the treatment of CC by *C. arabica* might occur through the interaction of stigmasterol with SRC and EGFR. This finding provides a new basis and great support for emerging research on CC.

Integrating In-Silico Approaches into an Undergraduate Pharmacy Degree: Analysis of the Opportunities within the UDST Research and Statistics Course

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The research and statistics (RSST) course is mandatory for third year students and is delivered by the College of General Education in UDST. The integration of molecular dynamics (MD) simulations into a modified RSST course, for pharmacy technology students, would provide opportunities for hands on understanding of MD and its use in drug design whilst also providing opportunities for meaningful data analysis and reporting. Taking a transformative approach to the RSST curriculum design would support students to see the interdisciplinary nature of pharmacy, by drawing on topics from their introductory chemistry, physics, mathematics courses whilst also preparing them for their Year 4 modules. The presentation seeks to outline, by way of an exploratory case study, the steps needed to align RSST with the pharmacy technology course and opportunities that this modified course would present. It is presented from the viewpoint of an instructor.

The successful use of MD in undergraduate courses has been documented in several papers. However, little literature exists describing how MD can be used to provide a holistic view of drug discovery process and research. Opportunities for use of education research tools to gather quantitative data on students' perceptions of the learning environment after using MD will also be discussed. Overall, this presentation is intended to act as a vehicle to start conversations on using MD in undergraduate pharmacy courses by highlighting opportunities, key considerations and potential measures of success.

Sixteen Novel Autism Candidate Genes Identified in 35 Trio Simplex Families in Qatar by Genome Sequencing

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Autism spectrum disorder (ASD) is a complex neurodevelopmental condition with a strong genetic component. Despite substantial advances in ASD research globally, there remains a significant underrepresentation of genetic studies focusing on ASD in the Middle East, including Qatar. In this study, we aimed to address this gap by conducting genome sequencing of autism families from Qatar to identify candidate autism genes. The study cohort consisted of 35 trios, each comprising an affected child with autism and their unaffected parents. By leveraging genome sequencing, we identified 16 novel candidate genes showing significant association with autism in the Qatari population. Twenty genes have been previously implicated in neurodevelopmental disorders (NDDs) in other populations, underscoring the conserved genetic basis of autism across different ethnicities. These variants included three splicing, five nonsense, one frameshift and 23 missense changes. Our analysis provided a molecular aetiological diagnosis and demonstrated significant association between ASD and fundamental cellular processes, such as neuron migration, the ubiquitin pathway, ion transport, and transcription activity essential for proper cognitive development. The scarcity of genetic studies on autism in the Arabian Peninsula has impeded our understanding of the unique genetic landscape of ASD in this region. The results of our study contribute significantly to filling this knowledge gap and provide valuable insights into the genetic architecture of autism in Qatar. The identification of candidate autism genes offers valuable insights into the complex genetic makeup of autism in this population, with potential implications for the development of tailored interventions and improved healthcare outcomes.

Kaur-16-ene found in *Vernonia amygdalina* inhibited multiple trypanosome brucei drug targets in docking studies

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African trypanosomiasis is a vector-borne parasitic disease-causing serious risks to the lives of about 60 million people and 48 million cattle globally. Nigerian medicinal plants are known to contain a wide variety of phytochemicals and some of these plant extracts have been screened for anti-trypanosomal activity. Vernonia *amygdalina* is used in Nupe land for the management of sleeping sickness by the local traditional healers. Molecular docking involves the use of computational tools to study the binding affinity between a protein and a drug candidate within the binding site of the protein followed by measurement of their interactions. This study docked the compounds present in *Vernonia amygdalina* into the active site of multiple trypanosome brucei drug targets (trypanosome brucei farnesyl phosphate, trypanosome brucei trypanosothione reductase, trypanosome brucei Rhodesiense piperazine carboxamide and trypanosome brucei triosephosphate isomerase) followed by assessment of binding affinity, ligand receptor integration of the hit compound and finally, determined some selected ADME properties. The result showed kaur-16-ene had better inhibition of trypanosome brucei multiple enzymes, the superior binding affinity of kaur-16-ene is believed to be as a result of the presence of pi-alkyl and alkyl bonds between kaur-16-ene and the bonding amino acids present within the active site of the respective target protein. However, kaur-16-ene possess inferior ADME properties when compared to berenil. This study shows the anti-trypanosomal potential of kaur-16-ene and could be explored in the management of trypanosomiasis.

Keywords: Trypanosome brucei, *Vernonia amygdalina*, Molecular docking, ADME evaluation

Exploring Inhibition of ASK1 by Phytochemicals from *Momordica charantia* (Linn.) for Pancreatic Cancer: An *in silico* Investigation

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The utilization of *Momordica Charantia* (Linn) for diverse human ailments has been well-documented, with a range of biological activities attributed to it. This study aims to uncover anti-cancer compounds from M. charantia targeting ASK-1, shedding light on the underlying molecular interactions. A selection of 77 compounds sourced from the PubChem database underwent molecular docking analysis as facilitated by the Schrödinger Maestro tool. Predictions of drug-like characteristics were achieved through the Qikprop module and the AdmetSar webserver. Our investigation reveals that the phytoconstituents from *M. charantia* exhibit superior binding affinity and a comparable MM-GBSA score to the reference drug, Camptosar. Moreover, advanced ADMET projections affirm the non-carcinogenic nature of these compounds, aligned with Lipinski's rule. The implications of these phytocompounds are promising within contemporary medicinal strategies harnessing natural origins. These findings spotlight these identified substances as prospective anti-cancer agents. Nevertheless, preclinical and clinical evaluations are imperative to gauge their efficacy in addressing pancreatic cancer.

Computational study of meclizine as anti-eczema

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Meclizine is antihistamine used to treat motion sickness. The computer-aided prediction was done to meclizine by using PASS software and molecular docking. The in-silico Study of Meclizine prediction showed that Meclizine has anti-eczema activity with possible activity 95%. Therefore, the study has designed to explore the anti-eczema activity of Meclizine and five formulations of meclizine ointment have been prepared using different bases. The efficiency of meclizine ointment has been evaluated by testing the physical compatibility and stability, homogeneity and irritant effect, absorbance and spread ability, chemical identification, calibration curve, drug content (assay), and dissolution test. This is followed by evaluating the ointment's effectiveness on volunteers and molecular docking. Five creams trials have been prepared, and two formulas (F3, and F5) have been selected for further evaluation. The formulas three and five have passed the physical and chemical tests and showed compatibility, homogenous, absorbed, non-irritant, and stable with calibration curve (R= 0.9999). then, F5 showed more efficient activity as anti-eczema patients than F3. These results has been correlated to the molecular docking where the meclizine showed binding to protein ID; 1a3f (phospholipase a2 (PLA2) from naja venom), protein ID; 2nru crystal structure inhibitor=Interleukin-1 (IL-1) and receptor associated kinase-4 (IRAK-4). The molecular docking against the four targeted proteins and comparing with ibuprofen as a standard drug ensure that Meclizine has anti-inflammatory drugs that could be used further. The combined power of Meclizine as an antihistamine and anti-inflammatory play a role in the relief of eczemic patients in 90% of the tested patients

An In-silico Approach based designed multi-epitope vaccine against Hepatitis A Virus (HAV)

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Background: This study aimed to design a novel vaccine construct against Hepatitis A virus (HAV) from the polyprotein using various insilico tools. The vaccine was designed from the conserved epitopes interacted against B and T lymphocytes by mixing of highly immunogenic, nonallergic and nontoxic epitopes with suitable adjuvant and linkers.

Method: Multi-epitope vaccine was designed from polyprotein of Hepatitis A virus (HAV) with an immunoinformatics approach, validated *in Silico* to be stable, non-allergic and antigenic. Cytotoxic T-cell, helper T-cell, and B-cell epitopes were computationally predicted from polyprotein sequence. The T-cell epitopes, overlapping with the B-cell epitopes, were included in the vaccine construct to assure the humoral and cell-mediated immunity. The mycobacterium tuberculosis 50S ribosomal protein L7/L12 was added as an adjuvant at the N-terminal of the construct to increase immunogenicity. Molecular docking performed with toll-like receptor 4 (TLR 4) using the HDOCK server. The efficient translation of the vaccine in an expression vector was assured utilizing *in Silico* cloning approach.

Results: The aimed vaccine composed of 460 amino acids and was shown to be antigenic in Vaxijen server (0.6194) and nonallergenic in Allertop server. The physiochemical properties of the vaccine presented isoelectric point of 9.71. The instability index (II) was 21.74 categorizing the vaccine as stable. Aliphatic index was 82.15 and the grand average of hydropathicity (GRAVY) was - 0.110 categorizing the vaccine as hydrophilic. Prediction of vaccine 3D structure was predicted, refined and validated to assess the stability of the vaccine via Ramachandran plot and ProSA-web servers. Solubility of the vaccine construct was greater than the average solubility provided by proteinsol and SOLpro servers representing the solubility of the vaccine construct. The disulfide engineering was done to reduce the high mobile regions in the vaccine to improve stability. Docking of the vaccine construct with TLR4 verified efficient binding energy with attractive binding energy of -333.86 kcal/ mol and -318.33 kcal/ mol for TLR4 chain A and chain B respectively. In cloning, the vaccine protein was reverse transcribed into DNA sequence and cloned into pET-30a (+) vector to confirm translational potency and microbial expression.

Conclusion: A unique vaccine construct from polyprotein against B and T lymphocytes was generated with potential protection against the epidemic. The present study might assist in developing a suitable therapeutics protocol to combat HAV infection.

Keywords: HAV, polyprotein, Multiepitopes vaccine, B-lymphocytes, T-lymphocytes

Probing the potential of Dehydrozingerone in Diabetic Wound Healing via Network Pharmacology and Molecular Docking studies

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Network pharmacology was established based on systems biology and multi-directional pharmacology. Instead of the conventional "single-ligand-single-target" process, network pharmacology emphasizes the drug's multi-target mode of action. Network pharmacology is an approach which can be used to identify disease- causing network rather than disease-causing genes. Drug discovery is significantly affected by interactions, networks and inherent robustness, which is an underlying characteristic. Dehydrozingerone [DHZ] may be an effective therapy for diabetic wounds by accelerating through the modulation of different markers involved in the phases of wound healing. Present study focussed on understanding the mechanism of DHZ based on Network Pharmacology and Molecular Docking studies. The aim of the study was to elucidate the mechanism of DHZ through network pharmacology and molecular docking. Targets of DHZ were identified using databases like Swiss Target Prediction, BindingDb and SuperPred and the targets of the Diabetic wound healing were identified with the help of DisGeNet and GeneCards database with the keyword "Diabetic wounds" and "Diabetic wound healing". In conclusion, the comprehensive approach integrating network pharmacology, GO, KEGG analysis, and molecular docking with MM/GBSA calculations has provided valuable insights into dehydrozingerone's potential for diabetic wound healing- Target Identification: Network pharmacology identified key protein targets and associated mechanisms, Biological Processes and Pathways: GO and KEGG analysis projected relevant biological processes, functions, cellular components, and pathways, Molecular Docking and Binding Affinity: Molecular docking studies, along with MM/GBSA calculations, revealed strong ligand-protein interactions, supporting the therapeutic potential of DHZ. This holistic approach facilitates our understanding of therapeutic action of dehydrozingerone, paving the way for future experimental investigations in diabetic wound care.

Artificial Intelligence in Drug Development: Implications and prospects in pharmacy curriculum

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Background: Pharmaceutical sciences as a discipline deals with discovering and developing drugs to treat various diseases and ailments. The development of drugs is a complex and, time and resource intensive process. These new drugs and therapies are crucial in the overall healthcare system for improving quality of life of people and provide timely medical treatment to those that need it.

Objective: The objective of this study was to identify role of Artificial Intelligence (AI) in revolutionizing drug development and its potential to reduce time to market of a new drug.

Methods: Secondary literature search was carried out to understand the role of AI in drug discovery and development. Data from PubMed was accessed using keyword search. The keywords used were "Artificial Intelligence" and "Drug Development". The search was restricted to published literature in the last one year.

Discussion: AI has been increasingly seen by pharmaceutical companies as a tool to improve and reduce time for drug discovery and development. The application of AI in pharmaceutical industry is manifold that includes entire value chain; from drug discovery to post marketing surveillance. The application of AI specifically in the field of drug development include improving efficiency through finding molecular pathways, identification of lead compounds, protein-structures, synthesis drug like compounds, establishing Mechanism of Action of chemical moieties and drug re-purposing to name a few. It is also believed that the role of AI can substantially reduce the time of bringing a new drug to market thereby offering early advantage of therapy to patients that need it. Training of pharmacy graduates in this emerging field is paramount and these topics shall be part of curriculum keeping in sync with changing times and requirements.

Conclusion: Translation of pharmaceutical science into practice is multifaceted. Including newer technologies such as Artificial Intelligence can be game changes and inclusion of such subjects in pharmacy curriculum can expand the understanding about translation of pharmaceutical sciences and enhance skills of pharmacy graduates improving their employability.

Network Construction and Molecular Docking of *Cynamoruim coccinum* and *Cistanche tubulosa* for the Treatment of Huntington's Disease.

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Huntington's disease is caused by a mutation in the huntingtin gene that subsequently leads to a deformed protein with a polyQ tail. The mutation occurs mainly in neuron cells of the brain, interrupting natural processes in cells and inducing progressive degeneration of patient's health. Currently, Huntington's disease has no known cure, but drugs are given to alleviate the symptoms. In this research, the ability of naturally occurring compounds was investigated as factors that can alleviate oxidative and neurological symptoms associated with this disease. *Cynamoruim coccinum* and *Cistanche tubulosa* are parasitic plants that have been extensively utilized in medicinal applications due to their many active phytochemicals. 5 randomly selected phytochemicals from *C. coccinum* and *C. tubulosa* were screened for drug likeness and ADMET properties. Salidresol had the greatest drug likeness score (0.55) while Mussaenosidic acid showed the lowest score (0.32). When it comes to oral bioavailability, Medicagenic acid scored the greatest (0.56) while Mussaenosidic acid scored the lowest (0.11). A network of genes implicated as targets for protein and phytochemicals was constructed and explored. Enrichment pathway analysis revealed the involvement of Adenosinergic A2A receptor (ADORA2A) in all the phytochemical analysis which has been shown to be closely related to Huntington's disease age of onset. Qualitative (structural) and quantitative docking of all phytochemicals against huntingtin proteins most active binding pocket yielded varying binding scores: Ajugol=-5.9, Medicagenic acid= -8.5, Quercitin= -9.2, Salidresol= -9.2, Mussaenosidic acid =-9.7 kcal/mol). The variation in binding scores reflected the stability of the protein ligand complex. In conclusion, Mussaenosidic acid shows great potential in binding to the mutated huntingtin protein, however the low drug likeness score and oral bioavailability must be overcome to consider it as a possible drug.

Identification of an unusual combination of actionable mutations through genomic profiling in a child with an aggressive sarcoma.

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A 3-year-old male child was diagnosed at Sidra Medicine with embryonal rhabdomyosarcoma (ERMS) of the neck, which is a rare and aggressive childhood cancer. Initial stage-based chemotherapy resulted in tumor progression. The expedited Genomic Oncology Profiling (eGOP) procedure was activated, and deep whole-exome sequencing (300X on tumor and 100X on germline DNA) was performed. Unexpectedly, we identified somatic mutations in two genes of the RAS/MAPK pathway (BRAF and HRAS), which are classically mutually exclusive. A clinical-grade NGS was performed that confirmed both mutations. The identified BRAF mutation (N581I) is a non-classical (Class III) hot-spot mutation, that has not been previously reported in ERMS. Class III BRAF mutations are a novel group of mutations characterized by the induction of a low tyrosine kinase activity and require coexistent mechanisms for maintaining RAS activation through feedback mechanisms. This observation explains the presence of HRAS mutation in our case (HRAS is an upstream modulator of BRAF). We then analyzed publicly available somatic mutation data from 65853 patients across different cancer types. Overall, only 4% of patients bearing BRAF V600E (class I) mutations co-expressed RAS mutations. Conversely, BRAF N581I mutation co-occurred with RAS mutations in around half of the cases carrying N581I mutation. Overall, these results suggest that the double HRAS/BRAF mutation was the driver oncogenic event in this patient. Tumors with Class III BRAF mutations are resistant to classic BRAF inhibitors, and drugs (or combinations) specifically targeting Class III BRAF mutated tumors are currently in clinical trials. While our patient has subsequently achieved complete remission following intensified treatment, the risk of relapse remains high and this information might be considered for therapeutic decision at further relapse/progression.

Deciphering the binding mechanism of SARS-CoV-2 NSP6-TBK1 and Identification of Small Molecule Inhibitors for instigating the Host Immune Response

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SARS-CoV-2, responsible for COVID-19, employs various mechanisms to invade the host. The NSP6 protein plays a critical role in evading the human immune system by interacting with the TANK-binding kinase (TBK1) receptor, suppressing IFNβ production. We used structural biophysical approaches to analyze the effect of newly annotated mutations with potential impact on the binding of NSP6 and TBK1. Among the identified mutations, four (F35G, L37F, L125F, and I162T) were found to significantly destabilize the structure of NSP6. Furthermore, molecular docking analysis highlighted that the mutant NSP6 displayed its highest binding affinity with TBK1, exhibiting docking scores of -1436.2 for the wildtype and -1723.2, -1788.6, -1510.2, and -1551.7 for the F35G, L37F, L125F, and I162T mutants, respectively. This suggests the potential for an enhanced immune system evasion capability of NSP6. Particularly, the F35G mutation exhibited the strongest binding affinity, supported by a calculated binding free energy of -172.19 kcal/mol. To disrupt the binding between NSP6 and TBK1, we conducted virtual drug screening to develop a novel inhibitor derived from natural products; we identified 5 hit compounds as the most promising candidates with a docking score of -6.59 kcal/mol, -6.52 kcal/mol, -6.32 kcal/mol, -6.22 kcal/mol and -6.21 kcal/mol. The molecular dynamic simulation of top 3 hits further verified the dynamic stability of drugs-NSP6 complexes. In conclusion, this study provides a valuable insight into the higher infectivity of the SARS-CoV-2 new variants and a strong rationale for the development of novel drugs against NSP6.

Network Pharmacology Approach and Molecular Docking of *Prosopis cineraria* β-Sitosterol in Treating Diabetes Mellitus Bioinformatically

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Diabetes mellitus, a globally spread disease targeting human health, contributes to many side effects and complications. The increasing incidence through the decades requires optimum drug viability and increasing awareness to combat disease progression. *Prosopis cineraria*, known as the wonder tree, is a traditional medicinal plant that originated in India and spread to the dry regions. It has an effective therapeutic effect on multiple diseases. Certain experimental studies investigated the effectiveness of different *P. cineraria* plant extracts against diabetes mellitus. This study uses network pharmacology and molecular docking approaches to shed light on *P. cineraria* phytochemicals' effects in treating diabetes mellitus. The bioactive constituents of β-Sitosterol in targeting diabetes mellitus progression were determined by multiple pathways by triggering SRC and PPARα activity. Using molecular docking, the stability of the protein-ligand binding interaction is verified in the active binding pockets for further experimental studies. Study findings demonstrated stable and successful bindings of SRC and PPARα diabetic targets with the β-Sitosterol compound presented in *P. cineraria*. Multiple gene oncology enrichments and signaling pathways evaluated the effectiveness of *P. cineraria* as part of diabetes-related pathways. Maintaining PPARα and SRC activity influences the treatment of diabetes mellitus by triggering pancreatic cells for insulin secretion. Accordingly, the anti-diabetic evidence of *P. cineraria* functional pathways was assessed by network pharmacology and molecular docking strategies.

Network Pharmacology and Molecular Docking Approach to the Screening of Active Components and Mechanisms of Basil on Alzheimer's Disease

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Alzheimer's disease (AD) accounts for most of the dementia cases. It results in loss of memory and the inability to perform daily functions independently. The annual herb *Ocimum basilicum* has six active compounds that are recently being studied to test for their affectivity in treating conditions like anxiety, high blood pressure, inflammation, and memory loss. In this study, bioinformatics tools were utilized to determine the mechanisms of eugenol (one of basil's active compounds) on Alzheimer's disease. After obtaining the common targets between AD and eugenol, active protein-protein interactions (PPI) and network construction were done. Furthermore, one gene from the active compounds, AKT1 gene, was used for molecular docking which resulted in revealing that AKT1 can be a potential agent in the treatment of AD.

Role of Ascorbic Acid Compound from Capparis Spinosa Fruits on colorectal cancer: *In silico* Investigation

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Colorectal cancer (CRC), a frequently occurring cancer, has become the third leading cause of mortality. The Capparis spinosa is a type of wild plant from the *Capparidaceae* family extracted from the fruit of the Capparis spinosa plant that had anti-proliferative effects on colorectal cancer cells. In this study, the network pharmacology technique was utilized to characterize the mechanism of Ascorbic Acid on CRC. Furthermore, the active ingredient-target-pathway network uncovered that Ascorbic Acid conclusively contributed to the development of CRC by affecting the STAT3, followed by JUN, PRKCA, PRKCD, PTGS2, PRKCB, GSK3B, AR, PPARG, and PRKCE gene. After that, molecular docking was used to verify the practical activity of the active ingredients against the prospective targets. Molecular docking results predicted that several critical targets of CRC (along with STAT3 and PRKCD) bind stably with the corresponding active ingredient of Ascorbic Acid. It concluded through network pharmacology methods that multiple biological processes and signaling pathways involved in Ascorbic Acid exerted a preventing effect in treating CRC for further experiments. The molecular docking results provide us with sound direction for further experiments. In the Analysis study, network pharmacology integrated with docking analysis revealed that Ascorbic Acid exerted an excellent preventive effect on CRC by acting on cancer pathways. Finally, this enables us to understand the biological mechanism of the anti-cancer activity of Ascorbic Acid.

Molecular Mechanism of Prosopis cineraria Against Chronic Kidney Disease Using Network Pharmacology and Molecular Docking Approaches

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The chronic kidney disease (CKD) and its associated complications, emphasizing the importance of early detection and management. Plant-based compounds offer promising potential due to their diverse chemical structures and pharmacological actions. The study highlights *P. cineraria* as a promising candidate for CKD treatment, considering its long history in traditional medicine and the presence of bioactive substances with antioxidant, anti-inflammatory, and nephroprotective properties. In this study network pharmacology followed by molecular docking was utilized to evaluate the potential treatment of CKD by *P. cineraria*. The study identifies β-sitosterol from *P. cineraria* as a key compound affecting the PPAR-α gene. Molecular docking confirms the stable binding of the compound to its target, further supporting its potential as a drug candidate. The PPAR signaling pathway, particularly PPAR-α, is highlighted as crucial in CKD, controlling lipid metabolism, inflammation, oxidative stress, and renal repair. Modulating this pathway with specific agonists or modulators shows promise in CKD treatment. However, further experimental research and clinical trials are required to validate the efficacy and safety of *P. cineraria* and its compounds in CKD management. The study underscores the potential of network pharmacology in identifying and exploring new therapeutic options for CKD.

Uncovering Potential Drug Candidates for Autism-Associated SSBP3 Protein: A Ligand-Based Pharmacophore Modeling Study

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Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disorders characterized by two core features namely deficits in social communication and interaction, and repetitive and restricted patterns of behavior and interests. About one in hundred children is estimated to have ASD, and genetic and environmental factors have been shown to contribute to its etiology. Currently, there is no known remedy for ASD rather the treatments focus on minimizing the symptoms and maximizing the abilities through behavioral therapies and interventions. Among genetic factors, copy number variations are considered to be the leading cause of ASD. Several studies have shown that mutations in single-stranded DNA binding protein (SSBP3) are associated with neurodevelopmental and neuropsychiatric disorders. Our recent study showed that the Drosophila melanogaster ortholog, Ssdp, is a dosage-sensitive gene and plays a crucial role in the regulation of neurodevelopment and ASD-associated behaviors in the fruit fly model. Thus, the goal of the study is to target SSBP3 and identify potential drug candidates using computer-aided drug design. The process initiates with ligand-based pharmacophore modeling, followed by virtual screening of ZINC database against the validated pharmacophore model. The hits obtained from virtual screening were screened based on their binding affinities to SSBP3. The target SSBP3 protein structure was identified using the homology modeling technique, which was also validated through different procedures to ensure its accuracy and reliability. The top-ranked hits identified from molecular docking were furthered screened based on ADME and toxicity properties. Additionally, molecular dynamics simulations were used to assess their stability and binding interactions with SSBP3. The study paves a way for introducing personalized medicine for the treatment of individuals with copy number variations in the SSBP3 gene. This will allow to provide treatment options that focus on the cause of the disorder, rather than merely managing the symptoms.

The NeurOmics Project of Pakistan

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Neurological disorders have become a major public health problem in Pakistan in recent years. Its treatment and management strategies are a daunting problem in Pakistan due to lack of funding, poorly developed primary and basic health care facilities and weak political processes. This increasing rate depends upon certain rare, neglected and often difficult to understand neurological conditions. These disorders therefore require special attention, particularly in rural areas where these disorders remain unexplored. Identifying specific genetic markers may provide a useful explanation for disease etiology, molecular characterization, and pathogenesis. We used Next generation sequencing to investigate the novel causative gene(s) in hundreds of families and understand the role in order to develop effective treatments for neurological and neuro-developmental disorders. Using exome sequencing of more than 50 families, the causative genetic variants were clarified in the families, and 20 convincing candidate genes were identified. We aim to provide insights into the processes that have modeled the extant genetic diversity in the Pakistani populations as well as the consequences of the diversity observed, including their relation to disease susceptibility. Our goal is to pursue this mission by emphasizing individual and collaborative faculty investigations in confluence with this genetic research cycle paradigm. This conference would be a nice platform for us to showcase our research projects.

In silico Characterization of the Novel SDR42E1: Insights from Evolutionary Conservation and Molecular Dynamics

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Background: The short-chain dehydrogenase/reductase (SDR) superfamily encompasses enzymes that play essential roles in vital biological processes, including the metabolism of steroid hormones and lipids. Recent genetic studies have linked the novel short-chain dehydrogenase/reductase 42 extended-1 (*SDR42E1*) gene, which encodes the SDR42E1 protein, to 25-hydroxyvitamin D levels. However, the precise function of this gene and its associated protein remains enigmatic.

Methods: We investigated the SDR42E1 protein and its potential interactions with Vitamin D compounds using various bioinformatic approaches. Additionally, molecular docking combined with molecular dynamics were conducted to explore binding conformations and interactions with various Vitamin D substrates.

Results: The phylogenetic analysis unveiled that the nucleotide sequences of human SDR42E1 exhibit high evolutionary conservation across nematodes and fruit flies. Through molecular docking analysis, we identified strong binding affinities between SDR42E1 and its orthologs with Vitamin D3 and essential precursors, 8-dehydrocholesterol, followed by 7-dehydrocholesterol and 25-hydroxyvitamin D. The hydrophobic interactions observed between the protein residues and Vitamin D compounds supported the predicted transmembrane localization of SDR42E1. Notably, the conservation of critical residues, such as tyrosine 142 and glutamine 131, facilitate these binding affinities, suggesting their functional significance in Vitamin D pathways throughout different species.

Conclusion: Our investigation provides valuable insights into the potential role of SDR42E1 in Vitamin D metabolism. We establish a foundation for future characterization research and the exploration of targeted therapies for Vitamin D deficiency and related health conditions.

Keywords: SDR42E1; Vitamin D compounds; Bioinformatics analysis; Evolutionary conservation; Molecular docking simulations

Exploring D-Glucosazone as a Quorum Sensing Inhibitor to Attenuate Virulence factors and Biofilm Formation in *Pseudomonas aeruginosa*

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Background: *Pseudomonas aeruginosa*, a Gram-negative bacterium, poses a significant threat in healthcare settings, primarily affecting immunocompromised individuals, burn victims, and those with comorbidities such as tuberculosis and cystic fibrosis. Its resistance mechanisms to antibiotics underscore the need for alternative treatment strategies.

Methods: In this study, we explored the potential of D-Glucosazone as a quorum sensing inhibitor targeting the LasR receptor in P. aeruginosa. Molecular docking was employed to assess binding affinity, utilizing a LasR-based pharmacophore. Molecular dynamics simulations (MD) were conducted for 1000 ns using the Desmond simulation package to evaluate stability. Quorum quenching properties were assessed by inhibiting violacein pigment production in *Chromobacterium violaceum*. Additionally, *in-vitro* assays examined the impact on virulence factors and biofilm formation in P. aeruginosa.

Results: D-Glucosazone demonstrated promising inhibitory potential against LasR, as indicated by favorable docking scores and binding energies compared to the natural ligand. MD simulations further supported the stability of the ligand-receptor complex. Quorum quenching was confirmed through the inhibition of violacein production. In-vitro experiments revealed a significant reduction in virulence factors and biofilm formation in P. aeruginosa.

Conclusion: The findings suggest that D-Glucosazone holds promise as an antibiofilm agent, offering an alternative approach to attenuate P. aeruginosa virulence by interfering with bacterial cell-to-cell communication. This research contributes to the development of innovative strategies to combat biofilm-related infections and addresses the urgent need for effective treatments against this formidable pathogen.

Sequence-structure analysis of OXA Variants of ESKAPE Pathogens

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ESKAPE pathogens are the leading cause of nosocomial infections. The Global Priority List of WHO has categorized ESKAPE as priority 1 and 2 pathogens. Even though several mechanisms contribute to antimicrobial resistance, OXA β-lactamase has emerged as a new threat in combating nosocomial infections. In the present study we have investigated the presence of OXA and their variants, copy number, distribution on chromosomes/plasmids, subfamilies, phylogenetic relationships, amino acid identities and structural variabilities in ESKAPE pathogens. Our results revealed that a total of 929 OXA were present in 2258 completely assembled genomes, which could be further subdivided into 16 sub-families. Among all the ESKAPE pathogens, OXA were highly prevalent in *A. baumannii*, followed by *P. aeruginosa* and *K. pneumoniae* but completely absent in *E. faecium* and *S. aureus* while, only a few copies were found in Enterobacter spp. Most of the OXA variants belonged to the OXA-51-like subfamily (200 proteins), followed by OXA-50-like subfamily (189 proteins), OXA-23- like subfamily (156 proteins) and OXA-1-like subfamily (154 proteins). OXA-51-like, OXA-213-like, OXA-134-like, OXA-58-like, OXA-24-like and OXA-20-like subfamilies were present exclusively in *A. baumannii*. Phylogenetic tree of the subfamilies revealed that OXA-1-like and OXA-33-like, OXA-51-like and OXA-213-like and, OXA-5-like and OXA-10-like belonged to the same branches with amino acid identities as 100%, 97.10% and 80.90% respectively. This indicates that the members of these subfamily-pairs might have evolved from the same ancestor or have recently diverged. Thus, a judicious use of carbapenems is warranted to curtail the rise of new OXA enzymes and preserve them. This is the first detailed report about the OXA of ESKAPE pathogens.

Identification of potential drug candidates against the pathogenicity of SARS-CoV-2

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The emergence of mutations in the receptor-binding domain (RBD) spike protein makes it a challenge to fight against COVID-19. Recently reported omicron variants played an important role in virus stabilization and evolution and led to drug resistance. Due to its rapid growth, intricate pathogenic mechanism, multifaceted structure, and sudden circulation around the world, no available therapies show a positive response against this infectious virus, thus designing novel drugs is urgently required. In this study, we aimed to evaluate the interactions between the Delta, Omicron, IHU variants and the spike receptor-binding domain (SRBD) of the human angiotensin-converting enzyme 2 (hACE2) as well as to assess the binding affinity of 200 antiviral peptides and 140,000 zinc compounds against RBD domain of omicron variants. Our findings revealed that the RBM (receptor-binding domain) of the Omicron variant exhibited enhanced binding efficiency to the ACE2 receptor compared to other variants. Through molecular docking and simulation, we assessed the binding and stability of SARS-CoV-2 variants with ACE2 as well as the interaction of these variants with natural peptides and zinc compounds. In this docking and simulation study, we found that Indolicidin, Griffithsin, and ZINC98355133 possess the highest affinity to the RBD domain of the spike showing binding energies between -9.3 to -11.7. Taken together, these results propose the efficiency of the ZINC98355133, Indolicidin, and Griffithsin to be considered as competitive inhibitors against omicron and other variants of spike protein. This work will provide a potential drug candidate for further in vitro and in vivo studies against COVID-19.

Keywords: Antiviral peptides; zinc compounds; COVID-19; Omicron; variants; Indolicidin; Griffithsin.

Host Cell Derived Peptide Design and Development to Inhibit Herpes Simplex Virus Entry and Replication

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Background: Herpes simplex virus type -1 (HSV-1) and type -2 (HSV-2) is known to infect 3.7 billion and 491 million global population, respectively. Resistance to existing anti-HSV drugs urges the need for alternative approaches. Interaction of host cell and viral glycoproteins (gC and gD) is critical for HSV attachment and entry. HSV gD V domain binds to its cognate receptors (nectin-1, HVEM, and 3-OS HS) and makes conformational changes in the gD structure that activate the fusion machinery (gB and gH/gL complex). In this study, we have developed a peptide decoy targeting the gD/nectin-1 interaction to inhibit HSV entry.

Methods: Positively charged herpesvirus protein binds to negatively charged heparan sulfate expressed on the host cell. A 10-mer anionic peptide (LQYPDDSDDE, 416-425 amino residues) was identified from the cytoplasmic domain of nectin-1. PEP FOLD-3 server, ClusPro 2.0 docking server, and MD simulation (Desmond) *in Silico* tools were used to study the stability of the protein-peptide complex. The peptide was custom synthesized, and its antiviral activity was tested in vitro against both HSV-1 and HSV-2 using a CPE inhibition assay using animal cell culture model.

Results: A docking study revealed that a 10-mer peptide interacts with HSV-1 gD and HSV-2 gD at the nectin-1/HSV gD binding interface. The peptide residues ASP6 and GLN10 form hydrogen bonds with critical HSV-1 gD ARG222 residues. The peptide residues GLN2, LEU1, ASP6 interact with HSV-2 gD residues GLN132, HIS39, and TYR38, respectively. In the MD simulation study, the peptide/protein complex showed stable interaction throughout a 50 ns time trajectory (RMSD < 3A0). The peptide was found to be nontoxic at all tested concentrations (209 µM, 104.5 µM, 52.25 µM, 26.12 µM, and 13.05 µM) on Vero cells. The peptide showed 49.37 % and 48.99 % protection against HSV-1 and HSV-2 infection at 209 µM concentration, respectively.

Conclusion: The identified peptide possesses moderate anti-HSV activity and may interrupt the HSV gD/nectin-1 interaction. Further improvement of the peptide using the peptidomimetic approach may improve its antiviral potency and stability.

Keywords: Herpes simplex virus, antiviral peptide, CPE inhibition assay

Genome sequencing from 50 autism trios identified novel candidate genes with mixed inheritance pattern in the Qatari population

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The advent of next-generation sequencing (NGS) has revolutionized human genetics in rare genetic disorders, improving the diagnostic yield and reducing the turnaround time. Despite challenges related to deep reads and managing large dataset, genome sequencing has successfully identified genetic variants associated with ASD due to its extensive coverage. To address the underrepresentation of genetic studies on autism in the Middle East, we conducted genome sequencing on 50 trios of independent simplex autism families from Qatar with unknown etiology including 14 consanguineous and 36 non-consanguineous families, consisting of 41 males and 9 females. Our analysis revealed various types of variants, including de novo, homozygous, X-linked, and compound heterozygous variants, totalling 42-missense, 2-frameshift, 2-nonsense, 1-splicing, 1-in-frame 3 nucleotide deletion,1-start loss, and 1 >200 CGG repeats of FMR-1 variants. These variants were found in 30-known and 20-novel candidate genes, providing an aetiologic diagnosis. The pathogenicity of these variants was substantiated by CADD scores, their frequency in gnomAD, reported sporadic variants, and physical direct interaction with products of known ASD genes. Of the participants, comprising 41-males and 9-females, 40-individuals had syndromic ASD and 10-had non-syndromic ASD. The cohort comprised individuals from various backgrounds, including 33-Qatari (66%), 5-Syrian (10%), 2-Egyptian (4%), 2-Yemeni (4%), 2-Sudanese (4%), 1-Saudi Arabian (2%), 1-Algerian (2%), 1-Jordanian (2%), 1-Indian (2%), 1-Tunisian (2%), and 1-Palestinian (2%).The most common phenotypes observed among the probands included autism, intellectual disability, epilepsy, developmental disorders, and language/speech delay. Our preliminary findings illustrate the mixed inheritance patterns in autism families in Qatar, characterized by a high rate of consanguinity (52%). Additionally, our results highlight the association of ASD with fundamental cellular processes such as ion transport pathway, ubiquitin pathway, neuron migration, and transcription activity, which are crucial for normal cognitive development and function.

Structure-based development of potent Natural Products to inhibit G9R-E4R interface from monkeypox and validation using free energy calculations

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The current monkeypox virus outbreak is probably linked with the novel substitutions in the G9R protein of the replication complex. This, G9R, interact with E4R of the RC and act as processing factor. The G9R-E4R interface act as a potential druggable site for the inhibition of mpox replication. Therefore, in the current study we used computational molecular search of potential natural products and molecular simulation-based validation to inhibit the G9R interface. Our results revealed that among the 5230 compounds only four compounds reported excellent docking scores. All-atoms simulation of the top hits 1-4 exhibit demonstrated consistent dynamics, indicating their stability, and have the potential to interact efficiently with the interface residues which was then validated by the radius of gyration (Rg). Residue's flexibility were reported to have minimal fluctuation which show that these compounds upon the binding stabilize the internal flexibility while the hydrogen bonding analysis revealed average number of hydrogen bonds formed between the top-ranked drug-G9R complexes (top hit 1-4), as 110, 120, 115 and 110, respectively. Finally, the total binding free energy demonstrated the best hits among the all. The BF energy results revealed -47.86 kcal/mol for the C1 complex, for the C2 complex -45.51 kcal/mol, for the C3 the BF energy was -41.63 kcal/mol while for the C4 complex the BF energy was calculated to be -43.81 kcal/mol. This show that these compounds i.e., C1-C4 exhibit stronger pharmacological potential than the control drug and therefore urgent experimental testing should be carried out for the clinical usage purpose.

Prediction of Intranasal Ketamine Pharmacokinetics in Pediatric Population using Physiologically Based Pharmacokinetic (PBPK) Model

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Background/Objectives: Intravenous ketamine (IVK) is commonly utilized for emergency pediatric procedural sedation but is resource-consuming and associated with significant child distress. Conversely, intranasal ketamine (INK) is noninvasive and provides rapid absorption and onset of action, which could improve patient outcomes. The objective of the present study is to model the pharmacokinetics of INK in pediatric patients using GastroPlus ® to aid in the design of a clinical trial.

Methods: A physiologically-based pharmacokinetic (PBPK) model of INK in pediatric patients was constructed and the Pulmonary Compartmental and Absorption and Transit (PCAT™) module was used to model nasal deposition. The model was calibrated against existing literature data of INK 3 mg/kg through optimization of nasal systemic absorption rate constant and inclusion of lysosomal trapping in the model. The population simulator was used to simulate INK in 200 pediatric patients weighing 10-65 kg at three dose levels (4, 6, and 9 mg/kg).

Results: The PBPK INK model was able to predict C_{max}, T_{max}, and $AUC_{0\text{-}inf}$ values that closely matched observed values of INK 3 mg/kg (R^2=0.923). The C_{max}, t_{max} and $AUC_{0\text{-}inf}$ were 622.5ng/mL, 0.43h, and 1693. 7ng.h/mL, respectively for the 4 mg/kg dose; 899.3ng/mL, 0.43h, and 2395ng.h/mL, respectively for the 6 mg/kg dose; and 1377.5ng/mL, 0.43h, and 3722. 5ng.h/mL, respectively for the 9 mg/kg dose.

Conclusion: A PBPK model was successfully developed and used to predict the pharmacokinetics of INK in the pediatric population at three different doses. This data represents a valuable strategic tool to aid in the careful planning of pediatric clinical trials.

QCAR$_x$E: Qatar-based cardiovascular risk assessment using the English/Arabic version of the EPI·R$_x$ISK™ mobile application

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Cardiovascular disease (CVD) is the leading cause of death worldwide (1). Early risk assessment and management (RAM) is effective in decreasing CVD-related burden (2). Mobile technology facilitates access to CVD-RAM for healthcare providers and patients, with limited availability and use of it in the Middle East region. This study was done to develop and implement an English/Arabic version of a mobile/web application for CVDRAM in community pharmacies and primary healthcare (PHC) centers in Qatar.

Methods: In phase 1, translation of EPI·RxISK™ CV risk calculator (ERC) into Arabic was conducted and the English/Arabic version was pilot tested by potential end users. Semi-structured interviews were conducted based on the Mobile Application Rating Scale. In Phase 2, a prospective observational study (QCARxE) is underway to explore the feasibility of using the ERC in patients accessing PHC services for CVDRAM.

Results: In phase 1, 10 pharmacists and 5 patients were interviewed. The data indicates that ERC was positively perceived as having quality engagement, functionality, aesthetics, information, and subjective quality attributes. To date, a total of 36 patients have enrolled, the initial mean CVD risk score was 28.3%, and the most prevalent risk factor was obesity (mean BMI = 30.2 kg/m2).

Conclusion: The themes derived from the interviews indicate that the ERC was overall positively perceived. Preliminary data derived from the QCARxE study indicated a significant proportion of patients accessing PHC services are at high CVD risk. It becomes evident that the incorporation of computational tools such as the ERC in pharmacy curriculum contributes to the advancement of pharmacy education.

Implications: Implementing the use of the ERC in community pharmacies and PHCCs in Qatar enables patients to easily access CVDRAM services and incorporate risk factor interventions, which consequently aids in decreasing CVD-related burden.

Key words: cardiovascular disease, cardiovascular risk

Structure-based discovery of SARS-CoV-2 Inhibitors by targeting its Papain-like Protease through In-silico and In-vitro attempts.

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COVID-19 was emerged as a highly infectious respiratory disease in late 2019, which is caused by a novel coronavirus, SARS-CoV-2. Subsequently this disease spread instantly around the globe and tremendously influenced the life of millions of people. SARS-CoV-2 has a single-stranded viral RNA genome which encodes several structural and nonstructural proteins, one of them is a papain-like protease (PLpro), which is essential for viral replication and immune evasion, thus considered as a promising therapeutic target of SARS-CoV-2. In the present work, several novel chemical scaffolds were identified through multiple computational techniques which inhibits the PLpro enzyme in the in-silico analysis with high binding energies (in range of >-7 to >-8 kcal/mol) and strong interactions. Those molecules were studied in molecular dynamic simulation which indicates that after binding with the selected molecules, the PLpro enzyme acquires closed conformation, thereby changing its normal function. In the in-vitro assay these molecules showed efficacy in disrupting the PLpro protease and deubiquitinase activities. Among the evaluated compounds, COMP1 and COMP2 showed the most potent inhibitory potential with protease activity of 2.24 ± 0.17 µM and 2.71 ± 0.33µM, and deubiquitinase activity of 1.43 ± 0.14 µM and 3.11±0.75 µM, respectively. Furthermore, these molecules showed no cytotoxic effect on human BJ cell line at a dosage of 30 µM. Thus, the identified compounds can serve as possible drug-like candidates for the treatment of SARS-CoV-2.

Keywords: SARS-CoV-2, Papain-like protease, Molecular Dynamic Simulations, Protease assay, Deubiquitinase assay.

SLFN11 modulation by CRISPR/dCas9 in pediatric cancer cells affects toxicity of DNA damaging agents.

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Background: Schlafen family member 11 (SLFN11) induces an irreversible cell cycle block as a DNA damage response. Its expression has been recently identified as a predictive biomarker to DNA damaging agents (DDA). SLFN11 has been found to increase tumor chemosensitivity upon increased expression in breast cancer cell lines. Which lead us to investigate a target dataset of pediatric cancer cell lines to perform preliminary analysis. Our findings indicated that heterogeneous SLFN11 expression levels and no consistent pattern was observed. Therefore, we were interested in studying if the mechanism of action of SLFN11 is consistent or not. Oncogenic downregulation is often driven by methylation of the SLFN11 promotor region. We investigated the role of 5-aza-2'-deoxycytidine (decitabine), as a general DNA demethylating agent to increase SLFN11 expression. Alternatively, to specifically increase SLFN11 expression we implemented SLFN11 dCas9 (dead CRISPR associated protein 9) systems.

Results: We confirmed a correlation between methylation of SLFN11 promoter and its expression. The decitabine drug had toxic effects on the cells, the methylation of the promoter was not significant in lower doses. The use of CRISPR-dCas9 SAM system could increase SLFN11 expression significantly (up to 7-fold), stably and specifically in two pediatric (Wilms and Medulloblastoma) cancer cell lines. We used the cell lines with increased SLFN11 expression to confirm the increased sensitivity of those cells to treatment with DDAs such as Cisplatin and Talazoparib in relation with SLFN11 expression.

Conclusion: As far as we know, this is the first documentation of a non-fatal increase in SLFN11 expression within pediatric cancer cell lines. Our findings demonstrate that upregulating SLFN11 expression increases the sensitivity of pediatric cancer cells to DDA. dCas9 systems may represent a novel approach to increase SLFN11 and achieve higher sensitivity to chemotherapeutic agents, improving outcome or decreasing required DDA concentrations.

Identification of new pharmacophore against SARS-CoV-2 spike protein by multi-fold computational and biochemical techniques.

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Corona disease or COVID-19 appeared as a highly contagious disease after its outbreak in December 2019 by the virus, named SARS-CoV-2. This disease spreads rapidly by respiratory droplets exchange during coughing and sneezing or direct contact with infected persons, or objects. Among different genomic products, spike protein of virus plays a crucial role in the initiation of the infection by binding to the human lung cells, therefore, SARS-CoV-2's spike protein is a promising therapeutic target. Using a combination of a structure-based virtual screening and biochemical assay, this study seeks possible therapeutic candidates that specifically target the viral spike protein. A database of ~850 compounds was screened against SARS-CoV-2 spike protein to find natural inhibitors. Using virtual screening and inhibitory experiments, we identified acetyl 11-keto-boswellic acid (AKBA) as a promising molecule for spike protein, which encouraged us to scan the rest of AKBA derivatives in our in-house database via 2D-similarity searching. Later 19 compounds with >85% similarity with AKBA were selected and docked with receptor binding domain (RBD) of spike protein. Those hits declared significant interactions at the RBD interface, possess excellent drug-likeness and gastrointestinal absorption without toxicity. Our in-silico observations were eventually validated by in vitro bioassay, interestingly, eleven compounds (A2-A3, A7, C3, C-6B, C-6C, C-6D, C-6E, C6-G, C-6J and C-6K) displayed significant inhibitory ability with good percent inhibition (range: >72 to 90). These findings demonstrate that these molecules particularly inhibit the function of spike protein, therefore have the potential to be evaluated as drug candidates against SARS-CoV-2.

Computational approaches in protein_ligand, lcRNA protein interactions and developing multi-epitope vaccine designing studies

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We are working on various computational approaches in protein_ligand, lcRNA protein interactions, developing multi-epitope vaccine designing studies and have published them and I would like to share the research work of our group summarizing the challenges that we have addressed and also scope our future works for collaboration. lNorovirus (NoV) belongs to the Calciviridae family that causes diarrhoea, vomiting, and stomach pain in people who have acute gastroenteritis (AGE). Identifying multi-epitope dependent vaccines for single stranded positive sense viruses and finding new epitopes for inducing immune responses against the T/B-cells which play an important role for the cell-mediated and humoral immunity. The current study focuses on identifying new epitopes lead to multi-epitope-based vaccine developed as potentially good vaccine against NoV. lDeciphering RNA–protein interactions could allow us to understand important cellular processes and design novel treatment therapies for various diseases. As non-coding RNAs do not have coding potential our knowledge about their functions is still limited. We have attempted a docking model to infer binding sites between lncRNA NONHSAT02007 and protein KIF13A for a rare disease phenotype that we are studying in our lab. lCurcumin, a natural bioactive molecule has been shown to have therapeutic potential for various diseases, and its effect on COVID-19 is also currently being explored. In this study, we show the binding potential of curcumin targeted to a variety of SARS-CoV-2 proteins. Protein-ligand complexes were validated using molecular dynamics simulations and mechanistic studies at 100 ns. Both the docking and simulation studies indicate that curcumin has the potential as an antiviral against COVID-19.

In silico Exploration of Cirsilineol for possible treatment of prostate cancer through Network Pharmacology and Molecular docking

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Prostate cancer is the most diagnosed male cancer and the sixth most prevalent cause of cancer mortality in males worldwide. The need for novel treatment options for prostate cancer, a serious health issue on a worldwide scale, remains critical. The object of the present study is to determine the *Teucrium polium* phytochemicals and lead compound for the treatment of Prostate cancer. Total 25 active compounds of *T. polium* were found by virtual screening and target gene analysis, however only Cirsilineol was utilized for this study due to its excellent ADMET properties, it conclusively contributed to the development of prostate cancer by affecting the EGFR, ESR1, and PTGS2 genes. The complex relationships between chemical compounds and target genes were discovered through the creation of a compound-target gene network. To further confirm the importance of these major targets, molecular docking, and protein-protein interaction (PPI) network analyses were also carried out. This led us to the conclusion that Cirsilineol has an anti-prostate cancer preventative effect. We discovered several molecular mechanisms and signaling pathways in Cirsilineol that participate. Docking results showed the strong binding of lead compound with target protein with significant energy scores. Based on network pharmacology and docking results, Cirsilineol has remarkable prostate cancer prevention potential. Our findings establish the framework for more study in this area further in vivo investigation are required for exploration of Cirsilineol anti-prostate cancer potential.

In silico Mechanism insights into the role of the _Mentha spicata_ efficacy for the Treatment of Digestive Problems

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Mentha spicata (spearmint) has been traditionally used for its potential therapeutic effects on digestive problems. However, the underlying pharmacological mechanisms and the multi-target interactions of its bioactive compounds remain largely unexplored. This study aimed to investigate the pharmacological mechanism of *Mentha spicata* in the treatment of digestive diseases or problems using network pharmacology. We utilized various databases and tools, including molecular docking, pathway enrichment analysis, and network visualization, to construct a holistic understanding of the multi-target interactions. We examined the active component target pathway network and revealed that PPARG, RXRB, PTGS2, PPARA and NR3C1 genes are key common targets of active compounds and disease. We concluded through network pharmacology methods that multiple biological processes and signaling pathways involved in *Mentha spicata* exerted a preventing effect in the treatment of digestive problems. According to network analysis, *Mentha spicata* includes multi-targeting chemicals that act on several disease-related pathways; henceforth, they might be evaluated as innovative treatment alternatives for digestive problem. The identified target proteins and pathways can serve as valuable information for future experimental studies and template for pharmaceutical industry.

Comprehensive *in-silico* analysis of chaperones identifies CRYAB and P4HA2 as potential therapeutic targets and their small molecule inhibitors for the treatment of Cholangiocarcinoma.

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Cholangiocarcinoma (CCA) is a subtype of liver cancer with increasing incidence, poor prognosis, and limited treatment modalities. It is, therefore, imperative to identify novel therapeutic targets for better management of the disease. Chaperones are known to be significant regulators of carcinogenesis; however, their role in CCA remains unclear. This study aims to screen chaperones involved in CCA pathogenesis and identify drugs targeting key chaperones to improve the therapeutic response to the disease. To achieve this first, we mined the literature to create an atlas of human chaperone proteins. Next, their expression in CCA was determined by publicly available datasets of patients at mRNA and protein levels. Further validated their protein level in patient tissues. In addition, our analysis involving protein-protein interaction and pathway analysis of eight key dysregulated chaperones revealed that they control crucial cancer-related pathways. Furthermore, topology analysis of the CCA network identified Crystallin alpha B protein (CRYAB) and Prolyl-4-hydroxylase subunit 2 (P4HA2) as novel therapeutic targets for the disease. Finally, drug repurposing of 286 clinically approved anti-cancer drugs against these two chaperones performed by molecular docking and molecular dynamics simulations showed that tucatinib and regorafenib had a modulatory effect on them and could be potential inhibitors of CRYAB and P4HA2, respectively. Overall, our study for the first time, provides insights into the pan-chaperone expression in CCA and explains the pathways that might drive CCA pathogenesis. Further, our identification of potential therapeutic targets and their inhibitors could provide new and complementary approaches to CCA treatment.

In-silico Docking Studies of Coumarin Derivatives as Caspase 8 and PDE4 Antagonist

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Coumarin, a well-known organic compound for its wide range of activities, incorporating a benzene and pyrone ring together, belongs to benzopyrone family. Piroxicam is the drug that is used in the treatment of inflammation as well as cancer, but it possesses certain side effects like constipation, blurred vision etc. Coumarin shows anti-inflammatory and anticancer activity based on different substitution on it. The purpose of this study is to screen the best target among Caspase-8 and PDE4. Arguslab 4.0.1 docking analysis was performed to find out the best ligand which shows highest score for anti-inflammatory and anti-cancer activity and compared with the standard drug piroxicam. The phytoconstituents like isofraxidin and scopoletin having coumarin pharmacophore were also used for docking analysis. Among the twenty-eight analogues of coumarin, twenty four showed good score for caspase 8 and all compounds possess good score for PDE4 compared to piroxicam. The best target among caspase 8 and PDE4 for anti- inflammatory and anti-cancer activity was found to be PDE4 and ethyl substitution at the 7th position of coumarin derivatives showed good affinity against PDE4.

Conformational Analysis and Solubility Enhancement Strategies for Curcumin and Its Derivatives: Insights from Molecular Dynamics Simulations and Prodrug Design

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Understanding the three-dimensional conformations of molecules, such as curcumin, is crucial for comprehending their pharmacokinetic and pharmacodynamic properties. These conformations play a pivotal role in biological activities as they dictate components related to recognition and selectivity. In this study, we utilized molecular dynamics simulations to predict the in-solution conformers of curcumin and its derivatives. We also conducted solubility predictions using ADMET Predictor™ and performed docking studies with Autodock Vina, followed by detailed solvation and water analysis using WATGEN. Our findings indicate that pegylated curcumin conjugates, particularly mPEG1000, hold promise for enhancing curcumin's solubility in water. Conversely, curcumin diethyl disuccinate failed to adopt a favorable conformation near the hydrophobic plane, prompting the development of curcumin dimethyl glutamate with improved attributes. However, the collapsed conformation of curcumin dimethyl glutamate enhances miscibility with the aqueous environment but also traps water molecules in the DNA minor groove, impacting its affinity. In conclusion, a comprehensive understanding of the spatial arrangements of molecules in solution can significantly aid in the discovery and development of novel drug candidates by providing insights into pharmacokinetics and pharmacodynamics.

Physiologically Based Pharmacokinetic Models of Two Prodrugs of Curcumin: Curcumin Diethyl Disuccinate and Curcumin Diglutaric Acid

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Curcumin has interesting medicinal properties, but poor bioavailability. Delivery may be improved using prodrugs such as curcumin diethyl disuccinate (CurDD) and curcumin diglutaric acid (CurDG). Here, we describe a predictive model for the pharmacokinetics of two curcumin prodrugs in rats. The absorptive phase and elimination phase was simulated using GastroPlus® and fitted to experimental pharmacokinetic curves from rats. We first show that experimental data for curcumin (Cmax 0.17±0.06 ng/ml, tmax 0.75±0.14 h, AUC0-t 0.50±0.20 ng-h/ml), are well reproduced by GastroPlus® (0.163 ng/ml, 0.88 h, 0.52 ng-h/ml) using experimental values for solubility, LogP, and fitting the elimination phase to metabolizing enzyme kinetics and the elimination t1/2. We then applied this approach to the prodrug CurDD. Data from the absorptive phase for the prodrug and fitting the elimination phase to curcumin, resulted in a plasma profile for the release of curcumin from CurDD (Cmax 0.108 ng/ml, tmax 0.746 h, AUC0-t 0.299 ng-h/ml), in good agreement with the experimental results (0.11±0.04 ng/ml, 0.75±0.14 h, 0.23±0.09 ng-h/ml). The same approach for CurDG gave a Cmax of 26.58 ng/ml with an AUC0-t of 65.62 ng-h/ml for released curcumin from CurDG, which was higher than CurDD. This trend is consistent with the greater antinociceptive effect of CurDG reported elsewhere.

Computational Assessment of Pharmacokinetics for Three Desert Plants with Promising Antibiotic Potential

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The growing worldwide danger of antibiotic resistance has spurred researchers to look for new antimicrobial medicines in natural sources. Desert habitats, which are often overlooked for their biodiversity, are home to plant species that have adapted to harsh circumstances. Some desert plants have shown interesting antibacterial properties. Understanding the pharmacokinetics (absorption, distribution, metabolism, and excretion) of their bioactive components is critical for harnessing their therapeutic capabilities. The three desert plants studied in this study are *Zygophyllum fontomesii*, *Scrophularia deserti*, and *Suaeda aegyptiaca*. We evaluate absorption, distribution, and elimination patterns using computational modeling, revealing insight on their potential as antibacterial agents and combining traditional herbal medicines with current pharmaceutical research.

Engineered antimicrobial peptides inhibit cell viability, promote apoptosis and induce cell cycle arrest in SW620 human colon adenocarcinoma cells.

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Background: Colorectal cancer (CRC) is the third most common cancer worldwide, and several therapeutic strategies have been proposed for CRC. Antimicrobial peptides have recently emerged as promising alternatives for cancer therapeutics. In this study, we aimed to investigate the effects of two In-silico engineered antimicrobial peptides (EAMPs) on SW620 colon cancer cells and determine their anti-cancer activity.

Methods: CellTiter-Glo Luminescence Assay was used to measure cell proliferation. Clonogenic assay was used to measure cell survival. Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) was used for detecting DNA fragmentation. Flow cytometry was performed to detect cell apoptosis, cell cycle distribution, and mitochondrial membrane Western blotting was used for measuring protein expression/activation in apoptotic and pro-carcinogenic cellular signaling pathways.

Results: Our *in vitro* data showed that EAMPs preferentially and, in a dose-dependent way, inhibited colon cancer cell proliferation but were not toxic to normal colon mucosa epithelial cells. EAMPs induced cellular DNA damage, cell cycle arrest at the S/G2 phase, cell apoptosis, and mitochondrial membrane depolarization. In addition, EAMPs inhibited the activation of NF-kB, STAT3, Akt, EGFR, β-catenin, and c-Myc signaling pathways and upregulated the expression of p21 and p27.

Conclusion: Our *in vitro* results revealed the anti-cancer activity of novel EAMPs in CRC cells. These findings pave the way for future *in vivo* studies of EAMPS to confirm their role as potential anti-tumor agents against CRC.

Keywords: Antimicrobial peptides, Apoptosis, Cell proliferation, Cell cycle, Colorectal cancer, Inflammation.

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