THE ATHENS INSTITUTE FOR EDUCATION AND RESEARCH

Abstract Book

12th Annual International Conference on Pharmacy and Pharmaceutical Sciences 5-8 May 2025, Athens, Greece

Edited by
Parisa Gazerani & Olga Gkounta

2025

Abstracts

12th Annual International Conference on Pharmacy and Pharmaceutical Sciences,

5-8 May 2025, Athens, Greece

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Parisa Gazerani & Olga Gkounta

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Preface

This book includes the abstracts of all the papers presented at the *12th Annual International Conference on Pharmacy and Pharmaceutical Sciences* (5-8 May 2025), organized by the Athens Institute for Education and Research.

A full conference program can be found before the relevant abstracts. In accordance with Athens Institute's Publication Policy, the papers presented during this conference will be considered for inclusion in one of Athens Institute's many publications only after a blind peer review process.

The purpose of this abstract book is to provide members of Athens Institute and other academics around the world with a resource through which they can discover colleagues and additional research relevant to their own work. This purpose is in congruence with the overall mission of the association. Athens Institute was established in 1995 as an independent academic organization with the mission to become a forum where academics and researchers from all over the world can meet to exchange ideas on their research and consider the future developments of their fields of study.

To facilitate the communication, a new references section includes all the abstract books published as part of this conference (Table 1). I invite the readers to access these abstract books –these are available for free– and compare how the themes of the conference have evolved over the years. According to Athens Institute's mission, the presenters in these conferences are coming from many different countries, presenting various topics.

Table 1. *Publication of Books of Abtracts of Proceedings, 2014-2025*

Year	Papers	Countries	References
2025	29	18	Gazerani and Gkounta (2025)
2024	32	19	Zahariadis and Gkounta (2024)
2023	31	16	Boutsioli and Gkounta (2023)
2022	21	11	Boutsioli and Gkounta (2022)
2021	19	9	Papanikos (2021)
2020	22	12	Papanikos (2020)
2019	27	16	Papanikos (2019)
2018	33	16	Papanikos (2018)
2017	39	17	Papanikos (2017)
2016	35	18	Papanikos (2016)
2015	37	19	Papanikos (2015)
2014	33	15	Papanikos (2014)

It is our hope that through Athens Institute's conferences and publications, Athens will become a place where academics and researchers from all over the world can regularly meet to discuss the developments of their disciplines and present their work. Since 1995, Athens Institute has organized more than 400 international conferences and has published over 200 books. Academically, the institute is organized into 6 divisions and 37 units. Each unit organizes at least one annual conference and undertakes various small and large research projects.

For each of these events, the involvement of multiple parties is crucial. I would like to thank all the participants, the members of the organizing and academic committees, and most importantly the administration staff of Athens Institute for putting this conference and its subsequent publications together. Specific individuals are listed on the following page.

Gregory T. Papanikos
President

Editors' Note

These abstracts provide a vital means to the dissemination of scholarly inquiry in the field of Pharmacy and Pharmaceutical Sciences. The breadth and depth of research approaches and topics represented in this book underscores the diversity of the conference.

Athens Institute's mission is to bring together academics from all corners of the world in order to engage with each other, brainstorm, exchange ideas, be inspired by one another, and once they are back in their institutions and countries to implement what they have acquired. The 12th Annual International Conference on Pharmacy and Pharmaceutical Sciences accomplished this goal by bringing together academics and scholars from 18 different countries (Australia, Benin, Bulgaria, China, Denmark, Finland, Italy, Jordan, New Zealand, Norway, Poland, Serbia, South Africa, Saudi Arabia, Switzerland, Turkey, Ukraine, USA), which brought in the conference the perspectives of many different country approaches and realities in the field.

Publishing this book can help that spirit of engaged scholarship continue into the future. With our joint efforts, the next editions of this conference will be even better. We hope that this abstract book as a whole will be both of interest and of value to the reading audience.

George Zahariadis & Olga Gkounta
Editors

12th Annual International Conference on Pharmacy and Pharmaceutical Sciences, 5-8 May 2025, Athens, Greece

Organizing & Scientific Committee

All Athens Institute's conferences are organized by the Academic Council. This conference has been organized with the assistance of the following academic members of Athens Institute, who contributed by reviewing the submitted abstracts and papers.

1. Dr. Gregory T. Papanikos, President, Athens Institute.
2. Dr. George Zahariadis, Director, Health & Medical Sciences Division, Athens Institute & Associate Professor, Faculty of Medicine, Memorial University of Newfoundland, Canada.
3. Dr. Parisa Gazerani, Head, Pharmaceutical Unit, Athens Institute & Professor, Department of Life Sciences and Health, Oslo Metropolitan University, Norway.
4. Dr. Paul Contoyannis, Head, Health Economics & Management Unit, Athens Institute & Associate Professor, McMaster University, Canada.
5. Dr. Carol Anne Chamley, Head, Nursing Unit & Associate Professor, School of Health and Social Care, London South Bank University UK.
6. Dr. Andriana Margariti, Head, Medicine Unit, Athens Institute & Professor, Queen's University Belfast, UK.

FINAL CONFERENCE PROGRAM

12th Annual International Conference on Pharmacy and Pharmaceutical Sciences, 5-8 May 2025, Athens, Greece

PROGRAM

Monday 5 May 2025
08.30-09.15
Registration
09:15-10:00
Opening and Welcoming Remarks:

- Gregory T. Papanikos, President, Athens Institute.

Session 1b
Moderator: Mitra Esfandiarei, Professor, Midwestern University, USA.

1. Parisa Gazerani, Professor, Oslo Metropolitan University, Norway.
   Title: State of Artificial Intelligence in Clinical Pharmacy: Current Tools, Benefits, and Barriers to Implementation.
2. Jeremy Johnson, Professor, University of Illinois Chicago, USA.
   Title: Xanthones from Garcinia Mangostana Target Drug-Resistant Androgen Receptor Mutants for Degradation in Prostate Cancer.
3. Beat Ernst, Professor Emeritus, Research Fellow, University of Basel, Switzerland.
   Title: Orally available of E-selectin Antagonists.
4. Saad Alkahtani, Professor, Najran University, Saudi Arabia.
   Title: Innovative Analytical Approaches for Quantifying Lipid-Lowering Drugs in Clinical and Pharmaceutical Samples.

Session 2b
Moderator: Parisa Gazerani, Professor, Oslo Metropolitan University, Norway.

1. Semako Omedine Koukoui, Professor, ENSBBA/UNSTIM, Benin.
   Title: Evaluation of the Cytotoxicity, Antioxidant, Anti-Inflammatory and Anti-Diabetic Activities of Extracts of Mangifera Indica L. and Parkia Biglobosa (Jacq.) R. Benth on Human Cells THP-1.
2. Inas Almazari, Associate Professor, Zarqa University, Jordan.
   Title: Curcumin Modulation of Liver Immune Cell Infiltration and Inflammatory Biomarkers in Diabetic Rat Models.
3. Marko Antonijevic, Research Associate, University of Kragujevac, Serbia.
   Title: Nature's Pharmacy: Grape Skin Polyphenols Target Diabetic Wounds.

13:00-14:30 Session 3 – Microsymposium on "Uncoding Cardiac and Vascular Pathologies in Premature Aging and Metabolic Disorders"
Moderator: Yasmine Kanaan, Associate Professor, Howard University, USA.

1. Mitra Esfandiarei, Professor, Midwestern University, USA.
   Title: Unraveling the Sex-Dependent Relationship between Central, Peripheral and Cerebral Arteries Function in a Mouse Model of Marfan Syndrome: Benefits of Exercise Training on Vascular Function and Blood Flow.
2. Roshanak Rahimian, Professor, University of the Pacific, Stockton, USA.
   Title: Sex Differences in Diabetic Vascular Dysfunction: A Deep Dive into Diabetes-Induced Vascular Aging in Males vs Females and the Impact of Exercise.
3. Nafisa Jadavji, Assistant Professor, Southern Illinois University, USA.
   Title: Sex-Specific Consequences of Maternal Choline and Folic Acid Deficiency: Differential Impact on Stroke Recovery in Offspring.

14:30-15:30 Lunch

15:30-17:00 Session 4 – Microsymposium on Ethics and Human Rights
Moderator: Paul Anisef, Professor Emeritus, York University, Canada.

1. Marzia Coltri, Extraordinary Professor, UNISA, South Africa & GUS Fellow, Lecturer, Arden University, UK.
   Title: Menopause and Perimenopause: Ethics, Rights, Well-being.
2. Ujjwal Kango, Assistant Professor, Indian Institute of Management Sirmaur, India.
   Title: The Ethics of Gig Work: An Ethnographic Study of Food Delivery Platforms in India.

17:00-19:00 Session 5 – A Symposium on What's Next for US Universities?
Moderator: Gregory T. Papanikos, President, The Athens Institute.

Invited Speakers:

1. Mitra Esfandiarei, Professor, Biomedical Sciences Program, College of Graduate Studies, Midwestern University. Title: *The Future of Medical Research in the U.S. and Canada?*
2. Jun Qu, Professor and Director, Center of Excellence in Bioinformatics and Life Sciences, State University of New York at Buffalo, USA. Title: *Striking a Balance of Funding Seeking and Conducting Research.*
3. Steven M. Oberhelman, Professor (Holder of the George Sumey, Jr., Endowed Professorship), Texas A & M University, USA. Title: *Is There a Future for Classics in an Age of Woke Culture?*
4. Robert Earle, David W. Wilson Ethics Fellow & Assistant Professor of Instruction, University of Northern Iowa, USA. Title: *Academic Freedom and the Right to Learn: Reflections from a US Educator.*
5. Joyce Victor, Associate Professor, Wilkes University, USA. Title: *Experiential and Distance Learning.*

Short Interventions

1. John Spiridakis, Chair of the Department of Education Specialties and Professor, St. John University, USA.
2. Sonia Salari, Professor, University of Utah, USA.
3. Jan Reid, President, Coast Economic Consulting, USA.

Discussion

20:30-22:30
Athenian Early Evening Symposium (Sequence of Events: Ongoing Academic Discussions, Dinner, Wine and Water, Music, Dance)

Tuesday 6 May 2025

09:30-11:00 Session 6
Moderator: Jun Qu, Professor and Director, State University of New York at Buffalo, USA.

1. Steven Oberhelman, Professor, Texas A&M University, USA.
   Title: Medical Schools for Practical (Empirical) Doctors in Eighteenth- and Nineteenth-Century Greece: The Schools of Ioannina and Mystras.
2. Marcin Sniadecki, Assistant Professor, Medical University of Gdańsk, Poland.
   Title: How Renaissance Paintings Can be used to Teach Students to Interpret Patient Symptoms: The Example of Breast Cancer.
3. Fiona Singh, Lecturer, University of Zululand, South Africa.
   Ntombizodwa Linda, Senior Lecturer, University of Zululand, South Africa.
   Title: A Conceptual Framework for Blended Learning in Nursing Education at Historically Disadvantaged Institutions in South Africa.

4. Ingrid Brenner, Associate Professor, Trent University, Canada.
   Ayla Saiz Campomar, Student, Trent University, Canada.
   Leslie Kerr, Associate Professor, Trent University, Canada.
   Title: Effects of Training for Dragon Boat Racing on Fitness and Quality of Life in Breast Cancer Survivors.

11:00-12:30 Session 7

Session 7b
Moderator: Angelos Halaris, Professor & Chair Emeritus, Loyola University Medical Center, USA.

1. Jun Qu, Professor and Director, State University of New York at Buffalo, USA.
   Title: Whole-Tissue Mapping of >10,000 Proteins and >30,000 Phosphosites by Micro-Scaffold Assisted Spatial Proteomics (MASP).
2. Iwona Inkielewicz-Stepniak, Head, Department of Pharmaceutical Pathophisiology, Medical University of Gdańsk, Poland.
   Title: Functionalized Silver Nanomaterials with Therapeutic Applications.
3. Hussam Murad, Professor, King Abdulaziz University, Saudi Arabia.
   Title: Evaluating the Association between Family-Related Factors and Levels of Substance use Severity as Determined by the Arabic DAST-10 Score.
4. Wenfang Chen, Professor, Qingdao University, China.
   Yu Gu, Professor, Qingdao University, China.
   Junxia Xie, Professor, Qingdao University, China.
   Title: Ginsenoside Rg1 Ameliorates LPS-Induced Neuroinflammation via G Protein-Coupled Estrogen Receptor in Experimental Parkinson's Disease.

12:30-14:00 Session 8

Session 8b
Moderator: Hussam Murad, Professor, King Abdulaziz University, Saudi Arabia.

1. Leilei Chen, Associate Professor, Qingdao University, China.
   Junxia Xie, Professor, Qingdao University, China.
   Xizhen Ma, Professor, Qingdao University, China.
   Ning Song, Professor, Qingdao University, China.
   Title: Linoleic Acid, a PPAR-γ Activator, Plays a Neuroprotective Role in Mouse Model of Parkinson's Disease.
2. Huan Liu, Assistant Professor, Xi'an Jioatong University, China.
   Xiong Guo, Professor, Xi'an Jioatong University, China.
   Title: The Establishment of hiPSC-derived Disease Models of Kashin-Beck Disease and the Mechanism of HT-2 Toxin-induced Damage via PI3K/AKT/NF-κB Signalling Pathway.
3. Aysu Yurdasiper, Assistant Professor, Ege University, Türkiye.
   Title: Permeation of Dry Powders Including Peramivir as an Antiviral Agent Across Human Respiratory Epithelium: An in Vitro Study with Calu-3 Cells.
4. Andrii Pantus, Professor, Ivano-Frankivsk National Medical University, Ukraine.
   Nataliia Kovalchuk, Associate Professor, Ivano-Frankivsk National Medical University, Ukraine.
   Title: Effectiveness of the Developed Biopolymeric Microfiber Matrix as a Local Drug Delivery System and a Scaffold for the Reconstruction of Bone Tissue Defects.

14:00-15:00 Lunch

15:00-16:30 Session 9 – Microsymposium on Ethics and Human Rights
Moderator: Marzia Coltri, Extraordinary Professor, UNISA, South Africa & GUS Fellow, Lecturer, Arden University, UK.

1. Dipane Hlalele, Professor & Chair, Humanities and Social Sciences Research Ethics Committee, University of KwaZulu-Natal, South Africa.

Title: Geographies of Ethics: A Critical Analysis of Rural Tourism, Community Development, Religion and Education.

2. Robert Earle, Assistant Professor, University of Northern Iowa, USA.
   Title: Against Ignorance: The Normative Ethics Consensus Requiring Our Seeking to Know the Interests of Others.
3. Matthias Huehn, Mary S. Carey Chair in Ethics & CST, Saint Vincent College, USA.
   Title: The Common Good as the Opposite of the Collective Good: Theoretical and Practical Insights from Aristotelian and Thomistic Virtue Ethics.
4. Stavros Prineas, Head of Anaesthetics, Blue Mountains Hospital, Australia.
   Title: I Guess Therefore I Am.
5. Maria Mut Bosque, Senior Lecturer, International University of Catalonia, Spain.
   Title: The Erosion of Informed Consent: Transparency Failures and Vaccine Victims during the COVID-19 Pandemic.

16:45-20:00 Session 10
Old and New-An Educational Urban Walk

The urban walk ticket is not included as part of your registration fee. It includes transportation costs and the cost to enter the Parthenon and the other monuments on the Acropolis Hill. The urban walk tour includes the broader area of Athens. Among other sites, it includes: Zappion, Syntagma Square, Temple of Olympian Zeus, Ancient Roman Agora and on Acropolis Hill: the Propylaea, the Temple of Athena Nike, the Erechtheion, and the Parthenon. The program of the tour may be adjusted, if there is a need beyond our control. This is a private event organized by ATINER exclusively for the conference participants.

20:30-22:00
An Ancient Athenian Symposium: Continuous Dialogues, Timeless Flavors (featuring authentic ancient Athenian dishes, local wine, and sweet delicacies from ancient Athens)

Wednesday 7 May 2025
An Educational Visit to Selected Islands
or Mycenae Visit

Thursday 8 May 2025
Visiting the Oracle of Delphi
Friday 9 May 2025
Visiting the Ancient Corinth and Cape Sounion

Saad Alkahtani
Professor, Najran University, Saudi Arabia

Innovative Analytical Approaches for Quantifying Lipid-Lowering Drugs in Clinical and Pharmaceutical Samples

The accurate quantification of lipid-lowering drugs in pharmaceutical and biological matrices is essential for drug efficacy and safety evaluation. This study develops and validates advanced analytical methodologies for the determination of several key lipid-lowering agents: atorvastatin, simvastatin, rosuvastatin, ezetimibe, fenofibrate, and gemfibrozil. Utilizing a combination of electrochemical and fluorescence-based techniques, each drug was analyzed using a tailored approach to enhance specificity and sensitivity. For atorvastatin and rosuvastatin, voltammetric methods were employed using chemically modified electrodes and molecularly imprinted polymers, respectively. Simvastatin and ezetimibe were analyzed using fluorescence-based assays involving carbon dots and metal nanoclusters, optimized for interaction specificity. Fenofibrate and gemfibrozil quantifications were conducted through multiplexed and ratiometric fluorescence assays, respectively, leveraging the unique emission properties of carbon dots and nanoclusters. Each method was rigorously validated for linearity, sensitivity, selectivity, and interference, and applied to real-world samples from pharmaceutical formulations and biological fluids like plasma and serum. The results dem

Research Objectives

1. Develop Custom Analytical Methods: Establish tailored analytical techniques for quantifying key lipid-lowering drugs, focusing on the development of chemically modified electrodes and synthesis of nanomaterials for fluorescence assays.
2. Enhance Method Sensitivity and Selectivity: Optimize the analytical methods to improve sensitivity and selectivity, adjusting technical variables such as material composition and functionalization.
3. Validate Analytical Techniques: Conduct thorough validation of each method for accuracy, precision, sensitivity, and robustness against interferences.
4. Application to Real Samples: Apply the validated methods to analyze lipid-lowering drugs in pharmaceutical and biological samples, demonstrating their practical utility.
5. Performance Comparison: Compare the developed methods with existing techniques to highlight their efficiency, cost-effectiveness, and

ease of use in clinical and pharmaceutical settings.

6. Promote Interdisciplinary Collaboration: Foster collaboration across disciplines to ensure the developed methods are scientifically sound and clinically applicable, enhancing their integration into routine analysis.

Inas Almazari
Associate Professor, Zarqa University, Jordan

Curcumin Modulation of Liver Immune Cell Infiltration and Inflammatory Biomarkers in Diabetic Rat Models

Introduction: Diabetes mellitus (DM) is linked to inflammation, contributing to liver damage through pro-inflammatory cytokines like TNF-α and IL-6 and macrophages. Curcumin, a natural anti-inflammatory compound, has shown potential to reduce inflammation, lower blood sugar, and prevent liver damage by inhibiting the recruitment of harmful monocytes and modulating key signaling pathways.

The Study objectives: The study aims to determine if curcumin is linked to lowering blood sugar and managing type 1 diabetes in various diabetic rats and to examine the impact of curcumin on the expression of proinflammatory cytokines immune cell profiles infiltrating liver tissue of diabetic rats, such as IL-6, TNF-α, and macrophages.

Methodology: Animal diabetic models were induced in rats,30 albino rats were divided into three groups, and they were randomly selected intocontrol, diabetic, and curcumin(N=10 each). Type 1 diabetes (T1D) was induced in the diabetic and curcumin groups using a single intraperitoneal injection of alloxan monohydrate. The curcumin group received curcumin post-diabetes induction. After one month, liver tissues were collected for histological and immunohistochemical analysis to assess inflammation markers (TNF-α, IL-6, and macrophages).

Results: A significantassociation was observed between IL-6 expression and curcumin ($p=0.000$). The macrophagelevel was slightly decreased in the curcumin group, but it was insignificant ($p=0.415$). Tumor Necrosis-Alpha (TNF-α) slightly decreased in the curcumin treatment but was insignificant ($p=0.779$). Biochemical analysis revealed significantly higher glucose, triglyceride, and cholesterol levels in the diabetic group than controls ($p<0.001$). Curcumin treatment reduced glucose levels noticeably ($p<0.001$) but affected triglycerides and cholesterol levels insignificantly. Histological analysis showed that curcumin reduced inflammatory liver changes induced by diabetes. Immunohistochemical findings revealed significantly increased TNF-α, IL-6, and macrophage expressions in diabetic rats ($p<0.005$).

Conclusion: The study showed that diabetes causes liver damage with increased inflammation. Curcumin helped reduce glucose levels, liver inflammation, and IL-6 expression. However, curcumin did not significantly mitigateTNF-α or macrophage expression, highlighting its limited impact on all inflammatory pathways. Further research is needed to enhance curcumin's therapeutic potential in managing diabetes-induced liver damage.

Marko Antonijevic
Research Associate, University of Kragujevac, Serbia

Nature's Pharmacy: Grape Skin Polyphenols Target Diabetic Wounds

Diabetic wounds constitute a significant challenge among chronic wound types, characterized by compromised wound healing processes stemming from ongoing inflammation, oxidative stress, microbial infection, and diminished angiogenesis. Polyphenolic compounds derived from grape skin extracts have garnered significant attention due to their strong antioxidant, anti-inflammatory, and antimicrobial properties. This positions them as a promising natural strategy for improving the healing process of chronic diabetic wounds.

This research sought to explore the molecular mechanisms underlying grape skin-derived polyphenolic extracts, which were obtained through ultrasound-assisted extraction utilizing environmentally friendly solvents such as water, ethanol, and ethyl acetate. Additionally, the study examined their potential therapeutic applications in the management of diabetic wounds. The analysis employed high-performance liquid chromatography (HPLC) to effectively identify and quantify bioactive phenolic compounds, including gallic acid, chlorogenic acid, quercetin, naringenin, ferulic acid, and apigenin. Molecular docking analyses were utilized to investigate the potential interactions between these significant compounds and essential molecular targets associated with diabetic wound pathology. These targets include nuclear factor-kappa B (NF-κB), vascular endothelial growth factor receptor-2 (VEGFR-2), transforming growth factor-beta (TGF-β1), and matrix metalloproteinase-9 (MMP-9). The molecular docking results reveal significant binding affinities of polyphenolic compounds toward key protein targets involved in diabetic wound healing. Apigenin exhibited the strongest interaction with NF-κB (-8.74 kcal/mol; 0.39 μM), highlighting its pronounced potential in modulating inflammatory pathways. Chlorogenic acid displayed notable affinity toward VEGFR-2 (-7.69 kcal/mol; 2.31 μM), suggesting its promising role in promoting angiogenesis. Additionally, quercetin showed the strongest binding to TGF-β1 (-7.41 kcal/mol; 3.70 μM), indicating its capability to enhance tissue regeneration and collagen synthesis. Apigenin (-7.35 kcal/mol; 4.10 μM) and naringenin (-7.26 kcal/mol; 4.77 μM) also demonstrated significant inhibitory potential against MMP-9, suggesting beneficial effects on extracellular matrix remodeling. It is worth noting that lipoxygenase (LOX) is an important target as well; however, due to the fact that compounds such as gallic acid and quercetin are already established LOX inhibitors and considering that LOX inhibition

typically involves interactions with Fe ions, this enzyme has been extensively studied in our previous research. Furthermore, the antioxidative and antimicrobial properties of grape skin extracts have been thoroughly documented both in existing literature and our current study, suggesting that these properties may act synergistically with the interactions investigated here, further enhancing the therapeutic potential of these polyphenolic compounds for diabetic wound healing.

Moreover, investigated extracts are currently being incorporated into hydrogels in order to prolong their effect and improve the overall activity. The findings so far suggest that grape skin polyphenolic extracts demonstrate considerable biological activity, which may beneficially influence diabetic wound healing by modulating inflammation, oxidative stress, microbial control, and promoting enhanced tissue regeneration. This study underscores the therapeutic potential of grape skin extracts, highlighting their appropriateness for integration into advanced topical formulations designed to enhance clinical outcomes for patients with diabetic chronic wounds. Current ongoing investigations include incorporations into hydrogels and testing on Wistar albino rats.

Maria Mut Bosque
Senior Lecturer, International University of Catalonia, Spain

The Erosion of Informed Consent: Transparency Failures and Vaccine Victims during the COVID-19 Pandemic

The COVID-19 pandemic posed significant challenges to the fundamental right to free and informed consent, as guaranteed under Article 3 of the Charter of Fundamental Rights of the European Union (CFREU). This right entails a consent process that is voluntary, informed, and based on clear, accurate, and transparent communication between medical professionals and patients. However, during the pandemic, several measures and circumstances undermined adherence to these essential principles.

Coercive policies, such as the implementation of COVID certificates at the EU level and mandatory vaccination for specific professional groups in member states, conflicted with the concept of free consent. Consent could not be fully informed due to the simultaneous rollout of vaccinations and ongoing clinical trials. Furthermore, the dissemination of contradictory and opaque information hindered transparency. The healthcare system's collapse exacerbated the problem, preventing meaningful dialogue between patients and medical professionals. This lack of dialogue and the novelty of mRNA technology left medical professionals and the public largely uninformed about the vaccines' long-term side effects and efficacy, raising serious concerns about the obligation to provide truthful information. Among the most concerning consequences was the emergence of numerous vaccine victims who suffered adverse effects due to the lack of transparency about the unknown long-term side effects of the novel mRNA vaccines. These individuals represent a tragic outcome of policies that prioritized rapid implementation over patient safety and informed consent.

A significant failure lies in the lack of EU coordination to ensure compliance with Article 3 CFREU. While the European Commission negotiated advanced purchase agreements for vaccines on behalf of member states, it did not adequately enforce measures to ensure that all EU citizens could provide free and informed consent. The Commission’s lack of transparency further compounded these issues. Investigations by the European Ombudsman, the European Court of Auditors, and members of the European Parliament revealed systemic opacity in vaccine procurement and communication processes. For instance, the General Court of the European Union ruled in 2024 that the Commission had violated public access rights by withholding vaccine-related documents. Similarly, ongoing cases, such as one involving text messages between the Commission

President and Pfizer's CEO, highlight the broader failures of transparency and accountability.

The implications of these shortcomings are profound, as they threaten democratic principles and fundamental rights, even in the context of public health emergencies. The pandemic underscored the critical importance of upholding the doctrine of informed consent as a cornerstone of human rights. Moving forward, we strongly recommend that, in the event of future health crises, EU institutions and member states must prioritize transparency, open communication, and public trust. A pre-established, coordinated action strategy must be implemented to protect the right to free and informed consent, ensuring that measures taken during emergencies do not undermine democratic principles or human rights.

In conclusion, the COVID-19 pandemic revealed significant violations of the right to informed consent within the EU, driven by a lack of transparency, coordination, and respect for ethical medical practices. To prevent a repeat of such failures, robust frameworks that prioritize transparency, accountability, and the protection of individual rights are imperative for future health emergencies.

Ingrid Brenner
Associate Professor, Trent University, Canada
Ayla Saiz Campomar
Student, Trent University, Canada
&
Leslie Kerr
Associate Professor, Trent University, Canada

Effects of Training for Dragon Boat Racing on Fitness and Quality of Life in Breast Cancer Survivors

Dragon Boat Paddling has been proven to be an ideal sporting activity to decrease the treatment related side-effects and to improve both physical and emotional health of breast cancer survivors, eventually improving their quality of life. The purpose of this study was to assess the benefits associated with participation in a Dragon Boat Paddling training program by comparing physically active patients to a sedentary comparison group. It was hypothesized that women who participated in the training program experienced a reduction in symptoms associated with breast cancer treatment as well as enhanced quality of life. Participants were recruited from a local chapter of the Breast Cancer Survivor's Group. A Qualtrics survey containing 57 questions was distributed electronically to all interested participants. Questions on basic demographics, health, breast cancer diagnosis and treatment, as well as questions from the International Physical Activity Questionnaire (IPAQ) and the Quality-of-Life Breast Cancer (QOL-BC) Questionnaire were included in the survey. The results showed statistically significant differences between the two groups in the overall quality of life, depression, ability to concentrate, degree of hope felt and social support (which were five of the variables measured by the QOL-BC questionnaire). These results suggest that Dragon Boat Paddling training programs could be an ideal physical activity to improve breast cancer survivors' quality of life and general health.

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Linoleic Acid, a PPAR-γ Activator, Plays a Neuroprotective Role in Mouse Model of Parkinson's Disease

Parkinson's disease (PD), the second most common neurodegenerative disorder, is characterized by the accumulation of pathological protein aggregates (namely Lewy bodies) in dopaminergic neurons in the substantia nigra region of the brain. Substantial evidence points to the early onset of inflammation in the periphery during the development of PD, lending credence to the "body-first" hypothesis. Therefore, targeting the inflammation in the early stage may be an effective strategy for PD prevention or treatment. In this study, C-X-C motif chemokine ligand-1 (CXCL1) was identified as an essential molecule to induce dysregulation of gut microbiota and PD-related pathology in the rotenone-induced PD mice model. The motor disorders and pathological changes in the substantia nigra region were successfully reproduced in mice which were intravenously injected with CXCL1 for two weeks (5 days per week) at a dose of 20 ng/kg/day. Notably, PPAR pathway was identified as a key pathway involved in the neuronal damage induced by rotenone or CXCL1. Furthermore, neuroprotective role of linoleic acid, which is a PPAR-γ activator, were observed in the above PD mice models. All these findings not only indicate the involvement of the PPAR signaling pathway in the inflammation-mediated neuronal damage, but also highlight the potential beneficial effect of linoleic acid in PD. Additionally, the CXCL1-injected mouse model reduces the cycle-time of chronic PD mouse model to two weeks, offers a promising tool for studying the inflammatory processes in PD, providing insights into potential therapeutic target.

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Ginsenoside Rg1 Ameliorates LPS-Induced Neuroinflammation via G Protein-Coupled Estrogen Receptor in Experimental Parkinson's Disease

Objective: Ginsenoside Rg1 is the main active ingredient of traditional Chinese medicine Panax ginseng. Our previous study has clearly demonstrated the estrogen-like property of ginsenoside Rg1. In the present study, we aimed to investigate whether G protein-coupled estrogen receptor (GPER) is related to the anti-inflammatory effects of ginsenoside Rg1 in vivo and vitro after inflammatory challenge.

Methods: LPS-induced astrocytes activation and GPER knockout (GPER-/-) mouse model of Parkinson's disease was established to reveal the anti-inflammatory effects and potential molecular targets of ginsenoside Rg1.

Results: Our results showed ginsenoside Rg1 could ameliorate the behavioral deficits of Parkinson's disease (PD) mice, inhibit the activation of microglia and astrocytes, reduce the loss of TH-positive neurons, down-regulate levels of TNF-α, IL-1β, iNOS, COX-2 and NLRP3 in the substantia nigra of PD mice. GPER mutation abrogated the neuroprotective effects of Rg1. Further in vitro study indicated that ginsenoside Rg1 inhibited LPS-induced up-regulation of TNF-α and IL-1β in a dose-dependent manner in astrocytes. Similar to GPER-specific agonist G1, the anti-inflammatory effect of ginsenoside Rg1 could be significantly antagonized by GPER antagonist G15. GPER silencing mitigated the inhibitory effect of ginsenoside Rg1 on the gene and protein expressions of TNF-α, IL-1β, iNOS and COX-2.

Conclusions: Taken together, our results reveal a key role of GPER in the anti-inflammatory effect of ginsenoside Rg1 in PD and support GPER as a potential target against neuroinflammation

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Menopause and Perimenopause: Ethics, Rights, Well-being

Human rights and healthcare converge distinctly when examining how life changes like perimenopause and menopause impact emotional health, interpersonal relationships and human connections. This paper examines both medical and cultural factors of these natural transitions, emphasising their effects on physical-mental changes, social belonging and personal identity. Psychophysical symptoms, anxiety, cognitive challenges and mood alterations, as observed in counselling and health settings, can affect relationship quality and lead to stigma, isolation and misunderstanding. Medical and philosophical perspectives underline the importance of early recognition of physical and emotional symptoms. This approach, alongside appropriate healthcare and counselling is essential for supporting women during significant life changes. A key interpretation of these physical and emotional symptoms is also found in the Aristotelian concept of the "matter-form/soul-body" relationship. Creating supportive environments through education, workplace policies, empathetic communication, and governance involvement enhances well-being, human rights and strengthens relationships. Through case study analysis, this paper advocates for holistic support approaches integrating medical care with therapeutic interventions like Person Centred Approach, CBT, mindfulness and pluralistic approaches to improve understanding and connection during these significant life phases.

Robert Earle

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Against Ignorance: The Normative Ethics Consensus Requiring Our Seeking to Know the Interests of Others

It is common to think one has special obligations to those one knows best. Between sending my own child to college and donating to a stranger's college fund, most would elect the former. This dilemma, however, takes for granted established relationships. Assuming that one does have special obligation to those with whom one is in some special way related, this would yet pose a further question which is the subject of this paper: should one take up the task of coming to know the interests of strangers? That is, in terms of the distinction introduced above, if one knew that familiarity enhances responsibility, should one set about coming to know about what "other" people need and by doing so further burden oneself?

Here it is maintained that deontology, virtue ethics, and utilitarianism all prescribe an obligation to come to better know the interests of distant strangers (with "distance" and "strangers" taken to have broad and vague denotations). All else being equal, not endeavoring to gain such knowledge would constitute a moral failure.

The upshots of this thesis include the following. First, the original assumption (that one has special obligations to those with whom one is close) is met with a subtle challenge. One might, as a result, say: yes, you have special obligations to send your child to college, but you should have done more to better know, and thus oblige yourself toward, the interests of other youths as well.

Second, investigation into the values of distinct others is not supererogatory, not merely a laudable hobby, but rather an essential activity for any moral agent.

Third, if all these theories agree in this regard, it suggests a broader convergence on other issues as well. Indeed, this analysis lends credence to a universalized (or cosmopolitan) account of morality in two ways. It suggests the major theories may share a univocal underlying account or spirit regarding morality, and it suggests all major accounts of morality recommend that people move toward coming together in harmony and mutual understanding.

This work was developed with a mind toward its applicability not only toward engaging in an important philosophical issue but also for

use as an introduction to ethics. It is hoped that the student of introductory ethics may make use of this work in building an understanding of the distinctions within normative theories in a manner that emphasizes complementarity rather than sharp contrast.

Focus is on the canonical figures associated with deontology (Kant), utilitarianism (Bentham and Mill), and virtue ethics (Ancient Greek and Chinese) with only brief notes regarding the ethics of care and social contract theories. Famous applications of normative theory in cases of famine (Singer 1972, Onora O'Neill 1980, Amartya Sen 1998) and Elizabeth Anderson's recent analysis of ideologies associated with the "work ethic" (*Hijacked*, 2023) are discussed as an extended application of the underlying thesis.

Beat Ernst
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Orally available of E-selectin Antagonists

E-selectin, a C-type lectin, plays a dominant role in atherosclerosis, ischemia-reperfusion injury, inflammatory diseases, and metastatic spreading of some cancers. It is expressed on endothelial cells of blood vessels adjacent to inflammatory stimuli. The main motive recognized by E-selectin is the tetrasaccharide sialyl Lewis^x (sLe^x) present on glycoproteins expressed on leukocytes. When interacting with E-selectin, the inflammatory adhesion cascade and the extravasation of the leukocytes to the side of inflammation is initiated. This process is highly regulated under physiological conditions, but alterations of the inflammatory adhesion cascade can lead to chronic inflammatory diseases.

Previous developments of E-selectin antagonists starting from the natural ligand sLe^x led to potent antagonists, which, however are lacking oral availability. When intravenously applied, two selectin antagonists from GlycoMimetics Inc and our lab (Rivipansel for the treatment of in the sickle cell disease and Uproleselan for resistance multiple myeloma) showed positive therapeutic effects. Since these diseases are severe and acute conditions requiring intensive care, an intravenous application is tolerated.

However, for a broader therapeutic application of selectin antagonists, oral bioavailability is a prerequisite. The lack of oral availability is, among others, a consequence of the large polar surface area (PSA) of Rivipansel and Uproleselan. Specifically, their carboxylic acid function, a pharmacophore crucial for the formation of a salt bridge with E-selectin, impedes oral availability.

In the present study, this problem was tackled by replacing the carboxylic acid function by bioisosteres. Numerous bioisosteric E-selectin antagonists with affinities in the low micromolar range were synthesized and their pharmacokinetic (PK) properties were evaluated. Among them, lipophilic amides yielded the most promising results. Their oral availability was determined with two *in vitro* permeability assays; first, with PAMPA (passive, transcellular permeation) and second, with Caco-2 cells (both passive and active transport). To further verify the active uptake and/or passive absorption potential of the successful *in vitro* compounds, oral bioavailability was tested in a mouse model, leading to the identification of the first orally available E-selectin antagonist. Finally, with further structural modifications to improve affinity, an E-selectin antagonist with nanomolar affinity and drug-like PK properties, especially oral availability, was identified.

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Unraveling the Sex-Dependent Relationship between Central, Peripheral and Cerebral Arteries Function in a Mouse Model of Marfan Syndrome: Benefits of Exercise Training on Vascular Function and Blood Flow

Marfan syndrome (MFS) is a connective tissue disorder caused by mutations in the fibrillin-1 gene, affecting multiple systems including the musculoskeletal, cardiovascular, and pulmonary systems. Vascular complications, particularly aortic root aneurysm, dissection, and rupture, are hallmark features of MFS. In recent decades, advances in diagnostics and treatments have significantly improved life expectancy for individuals with MFS; however, other vascular complications have become more concerning. Aging, a dominant risk factor for a dominant risk factor for atherosclerosis, often affects the carotid arteries, and carotid artery tortuosity is strongly associated with connective tissue disorders such as MFS. Additionally, hospitalized MFS patients show an increased prevalence of intracranial aneurysms and ischemic stroke compared to healthy controls. Despite these insights, cerebrovascular and carotid artery structure and function in MFS remain poorly understood.

The cardiovascular benefits of moderate exercise are well-documented, with evidence also suggesting that aerobic exercise improves cognitive function and reduces neuropsychiatric and neurodegenerative symptoms. The present study investigates the effects of mild aerobic exercise on the progression of aortic aneurysm in male and female MFS mice. Using high-resolution in vivo ultrasound imaging, the study assesses the functional properties of multiple key arteries, including the aorta, posterior cerebral, carotid, coronary, pulmonary, and renal arteries, and explore the relationship between aortic root diameters, arterial wall stiffness, and phenotypic changes across these arteries, aiming to identify key predictors that could provide insights into vascular health and the influence of exercise on arterial function and structure.

At 6 weeks of age, male and female control (Fbn1+/+) and MFS (Fbn1C1041G/+) were divided into three experimental groups: Control (Ctrl), MFS, and MFS + exercise. The exercise group underwent the exercise regimen of 8m/min, 30min/day, 5days/week. At 7 months of age, in vivo ultrasound imaging was performed to measure aortic root diameter, aortic and carotid artery pulse wave velocity (PWV), carotid wall thickness and distensibility, as well as peak systolic velocity (PSV) in the posterior cerebral arteries, coronary, pulmonary, and renal arteries.

Based on our findings, MFS mice exhibited significant increases in aortic root diameter, aortic and carotid PWV (wall stiffness), carotid wall thickness, coupled with reduced carotid distensibility, in both sexes compared to controls. Reduced PSV was observed in the pulmonary and posterior cerebral arteries of MFS mice, while coronary and renal arteries showed no changes. Mild exercise attenuated aortic and carotid pathology, reversing aortic root diameter growth, PWV, and carotid wall thickness, while improving carotid distensibility and restoring posterior cerebral artery blood flow, particularly in female MFS mice. In males, aortic PWV strongly correlated with posterior cerebral and pulmonary artery flow, while sinus of Valsalva diameter predicted carotid artery PWV and wall thickness in both sexes. Notably, the relationship between carotid distensibility and vascular metrics varied by sex.

These findings underscore the vascular impacts of MFS, the therapeutic potential of mild exercise, and notable sex-specific differences in disease progression and arterial function.

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State of Artificial Intelligence in Clinical Pharmacy: Current Tools, Benefits, and Barriers to Implementation

Background: Clinical pharmacy services (CPS) have improved patient care and healthcare systems by enhancing medication safety, optimizing therapy, and ensuring better outcomes. With healthcare systems facing increased demand due to an aging population and workforce shortages, CPS is critical for addressing these challenges. Integrating artificial intelligence (AI) into CPS is a promising approach to further enhance efficiency, accuracy, and scalability. AI can assist pharmacists in decision-making, reduce workload, and optimize time, allowing for greater focus on patient-centered care. Given rapid advancements in AI, an updated overview is warranted to assess its current integration and future opportunities.

Objective: To provide a comprehensive overview of AI tools used in clinical pharmacy, evaluate their contributions, and identify challenges and areas for improvement.

Method: A scoping review was conducted using Arksey and O'Malley's framework. Literature published in English since 2013 was retrieved from PubMed, Web of Science, and Scopus. Studies on AI applications in CPS were included and analyzed for their applications, benefits, and challenges.

Results: Several AI tools were identified, including medication error detection systems, clinical decision support systems (CDSS), chatbots, and medication management platforms. AI-based error detection systems help prevent prescribing and dispensing errors, enhancing safety. CDSS tools assist with high-risk prescriptions, drug interaction checks, and therapy optimization. Chatbots are useful for logistical queries and show potential for improving patient engagement, though they require further development for clinical decision-making. Comprehensive medication management platforms, such as CMM-Wrap, integrate clinical data to identify at-risk patients.

Challenges identified include data privacy concerns, the need for high-quality datasets, and reluctance to adopt AI tools among healthcare professionals. Variability in AI literacy and the lack of standardized training for pharmacists were also noted as barriers. Pharmacists' perceptions of AI as a threat to professional autonomy highlight the need for education on AI's role as an assistive tool.

Conclusion: AI tools such as error detection systems, CDSS, chatbots, and management platforms show promise in supporting clinical pharmacy

services. While these tools improve medication safety and workflows, challenges remain, including enhancing AI's decision-making capabilities, addressing privacy concerns, and better integrating AI into practice. Targeted training is needed to enhance AI literacy among pharmacists, ensuring they can effectively use these technologies. Addressing these challenges will be crucial for maximizing the benefits of AI in CPS and ensuring that it complements and enhances the role of pharmacists in patient care.

Dipane Hlalele
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Geographies of Ethics: A Critical Analysis of Rural Tourism, Community Development, Religion and Education

Researchers conducting research with vulnerable populations in rural African settings are confronted with distinctive ethical and cultural challenges due to the community context of their research, their methods of investigation, and the implications of their findings. An ethical approach to rural tourism, community development, religion as well education research should invariably acknowledge the effects of geography and location on the design, funding, implementation and reporting of research. The current study explores the geographies of ethics in rural tourism research conduct with and about rural people and communities. The problematic (problem statement) crystallises itself on the premise that dynamism imbues the ethics of research since no two rural spaces are identical and researchers may not necessarily be expected to be monolithic in their approach. Assuming that ethical judgements by their very nature ponder a variety of realities (relative or actual) and are therefore diverse, diversity foregrounds plurality, fluidity, and a multiplicity of geographies. For the purpose of this paper, the concept geography is understood as a space in a psycho-, socio-political and recursively constructed sense. Geographies include exceptionism, situationism, subjectivism and absolutism mapped across relativism and idealism as dimensions. Drawing from the Swedish metaphor of 'potato ethics', Fors (2023) recognizing the rural context as a vulnerable space, maintains that the holistic responsibility of those involved in rural communities should draw on work from the domains of care ethics, relational ethics, pragmatic psychology, feminist ethics of embodiment, social location theory, and reflections on geographical narcissism. So, the question of geographies of ethics in rural religiosity research becomes pertinent. The intention here is to ponder the ethical conduct of researchers with rural religious people and communities. Community Development with rural people thrives on building and enhancing local knowledge stocks of the environment and culture to influence the vitality and quality of life. Banks et. al. (2023) use the concept of 'ethics work' to highlight the cognitive and emotional efforts community development workers expend to identify and handle matters of responsibilities, rights, harms, and benefits. Rural tourism dates to the romanticism movement that began in the late eighteenth century (Ayazlar & Ayazlar, 2015). The first creative

tours in rural areas were rurally based on the holiday concept, but modern rural tourism began after the World War II era (Lane, 2009). Drawing from diverse international literature (+-500 peer reviewed articles and book chapters) published in the last ten years on rural tourism, community development, religion and education, and using PRISMA as an analytical tool, this scoping review finds that some publications make no reference, even in the tacit sense, to ethical issues. We conclude with an observation that varying ethical geographies may create conflicting, competing, or crosscutting ethical obligations and ramifications, reflecting both the relative vulnerabilities of rural communities, power implicit in these scholarly relationships, and the diverse ethical frameworks.

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The Common Good as the Opposite of the Collective Good: Theoretical and Practical Insights from Aristotelian and Thomistic Virtue Ethics

How exactly individual flourishing and societal flourishing are connected is a central question in the social sciences in general and in business ethics in particular. This article argues that the main theories of flourishing and its relation to the common good have developed along a trajectory going from Aristotle via Aquinas to the current, prevailing understanding of the relation between individual and communal flourishing. The current concept of a collective good has no specific individual author but has its origins in the second political wave of the Enlightenment. These three concepts of the mutual good/advantage (Aristotle), the common good (Aquinas), and the collective good can be seen as existing on a continuum. Aristotle argues for politically embedded individuals who possess the potential and authority to achieve their own flourishing (eudaimonia). Aristotle's understanding of politically embedded eudaimonia is subsequently modified by Thomas Aquinas in light of his concept of persons who seek to flourish by sanctifying their souls and through friendship with God. The evolution of these ideas of the good or end culminates in modern approaches to flourishing that bestow authority upon political representatives to act for the sake of the collective good. Although the three concepts have developed along a historical continuum, the collective good is, in many important respects, the exact opposite of the common good and is threatening to replace not only the person endowed with dignity but also to invert the meaning of good. Re-embracing the pre-Enlightenment common good has major ethical and managerial implications.

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Functionalized Silver Nanomaterials with Therapeutic Applications

Despite advances in the management of advanced pancreatic cancer, outcomes remain dismal. With current systemic therapy options, 2-year overall survival is less than 10% in patients with metastatic disease, with substantial toxicity from systemic chemotherapy

We synthesized the new analogs of opioid growth factor (OGF) to explore their potential as a novel therapy. We evaluated their effectiveness on 3D patient-derived organoids, blood platelets and pancreatic cancer cell lines.

Assessment of cytotoxicity was carried out on human pancreatic cancer cells (MIA PaCa-2, PANC-1 and AsPC-1) and on non-tumor-transformed cells using an MTT test. Cell-Titer Glo 3D reagent was used to test cytotoxic activity against patient-derived pancreatic cancer organoids (3D model). The neoplastic nature of the organoids was confirmed histologically and immunohistochemically. Antiproliferative activity was assessed on using an BrdU assay. Detection of inhibition cell cycle was performed by flow cytometry and western blotting. Detection of reactive oxygen species, cell apoptosis/necrosis in cells were performed by flow cytometry. The induction senescence of cells was investigated using flow cytometry and optical microscopy. The influence of tested compound on pancreatic cancer cells and platelets interaction was study by light aggregometer, flow cytometer and immunofluorescence microscopy.

In summary, we demonstrate that the novel compounds showed selective cytotoxicity to pancreatic cancer cells in vitro and ex vivo. Importantly, the synthesized compounds inhibit the process of platelet aggregation induced by cancer cells, suggesting a reduction in the risk of metastasis. We envision that this type of compounds could pave the way for the development of potent anticancer agents.

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Sex-Specific Consequences of Maternal Choline and Folic Acid Deficiency: Differential Impact on Stroke Recovery in Offspring

Cardiovascular disease (CVD) is the leading cause of death among men and women. Women have more risk factors and worse outcomes than men with CVD. One of the many reasons these problems exist is that preclinical studies are targeted towards males. Over 90% of preclinical studies use strictly male mice, whereas all clinical studies use equal numbers of male and female participants. This makes clinical pharmaceutical findings favor better outcomes in males. Our work has tried to expand the preclinical CVD data by using both female and male animals. We study preclinical ischemic stroke which is among the leading causes of death globally and its prevalence as a major health concern is predicted to increase as the global population ages and the demographics of populations change. Nutrition is a modifiable risk factor for ischemic stroke. Maternal one-carbon metabolism, including dietary intake of folic acid and choline, play an important role in early life programming. There is a well-established connection between the fetal environment and the health status of offspring. However, there is a gap in knowledge on how maternal nutrition will affect the health status of the offspring with CVD, like ischemic stroke. Our work has investigated the role of maternal dietary deficiencies in folic acid or choline on stroke outcome in offspring. We have shown that both 3-month-old female and male offspring from mothers deficient in choline or folic acid have worse stroke outcome after ischemic stroke. In 11-month-old mice there was no impact of maternal diet on motor function, but we observed sex differences on stroke outcome. Male middle-aged adult mice had worse motor function compared to female offspring. In brain tissue, there was no impact of maternal diet on ischemic damage volume in 3-month-old animals. Interestingly, maternal diet impacted ischemic damage in 11-month-old male and female offspring. Neurodegeneration and -inflammation were reduced in offspring at 3 and 11-month-old female and male offspring from mothers with deficient diets. We report significantly reduced levels of matrix metalloproteinase-2 in brain and blood of male offspring. The findings of our study suggest that a maternal diet deficient in either choline or folic acid impacts stroke outcome in young animals compared to middle-aged animals. Our data highlight how sex impacts outcomes after stroke. Furthermore, these results point to the important role

of the maternal diet in early life programming, while emphasizing its effects on both fetal development and long-term cerebrovascular health.

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Xanthones from Garcinia Mangostana Target Drug-Resistant Androgen Receptor Mutants for Degradation in Prostate Cancer

The mangosteen (Garcinia mangsotana) is a rich source of naturally occurring polyphenols known as xanthones. Our group has isolated selected xanthones from the purple mangosteen fruit (Garcinia mangostana) for mechanistic and structure activity relationship (SAR) studies. α-Mangostin, the most common and abundant xanthone, was chosen for further mechanistic studies. We identified a simultaneous decrease in AR (androgen receptor) protein expression and an increase in BiP protein expression in prostate cancer cells treated with α-mangostin. This study revealed a novel mechanism for AR and AR-V7 degradation, and the BiP-AR-V7 complex may be a unique druggable target for overcoming drug resistance prostate cancer. Through immunoprecipitation and in-cell western assays, we validated that AR and BiP interact in LNCaP cells treated with α-mangostin, and that AR is ubiquitinated and degraded by the proteasome. Interestingly, α-mangostin also promotes degradation of AR protein with clinically relevant mutations and AR splice variants, both of which are currently not targetable by any FDA approved drugs. The mechanism of AR degradation was observed using an in vivo xenograft confirming this approach is feasible in an animal model being administered α-mangostin by oral gavage. We hypothesize that α-mangostin promotes degradation of wild type and mutant AR through the protein interaction between AR and BiP. This represents a novel strategy to targeting AR and has the potential to provide a new therapeutic approach to drug resistant prostate cancer cases. Our preliminary results using surface plasmon resonance (SPR) revealed that α-mangostin directly binds to BiP. In this study, we investigated whether other xanthones from mangosteen fruit could bind BiP. To isolate the allosteric BiP binder from mangosteen extract, four distinct mangosteen fractions were separated by high-performance liquid chromatography (HPLC). Next, we developed an assay to identify allosteric binders of small molecules to BiP using surface plasmon resonance (SPR). This assay confirmed direct binding of α-mangostin to BiP. This assay was then optimized for high throughput screening in a 384 well format using the TargetMol library. Using this HTS SPR assay we screened >5,000 compounds using the TargetMol library to validate a method allowing us to sort and rank small molecules that directly bind BiP.

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The Ethics of Gig Work: An Ethnographic Study of Food Delivery Platforms in India

The rise of on-demand platforms underscores the need to investigate the ethical challenges posed by algorithmic management in managing gig workers associated with these platforms. Digital platforms utilise algorithms to direct, evaluate and discipline a distributed workforce leading to intensified monitoring and lack of worker voice, raising critical issues around transparency, accountability, and the erosion of worker autonomy. Based on ethnographic fieldwork conducted between 2021-2023 on two food delivery platforms in two Indian cities, this study explores how these challenges manifest in practice. The author worked as a food delivery worker on one of these platforms. This study analyses the processes by which algorithms direct, evaluate and discipline food delivery workers. The findings present that algorithmic control is reinforced through end-users and human managers, reinscribing human agency in algorithmic management on labour platforms. Overall, this paper makes two arguments. First, it emphasizes that rather than automation, heteromation, that pushes several tasks to complementors (restaurants, customers) and human managers, is a better way to characterise algorithmic control. Consequently, we categorize the role of human managers and complementors within digital platforms into: computational labour and direct control. Second, we argue that increased access to worker data empowers human managers to exert more direct control, facilitating enhanced oversight, wage discrimination, and the manipulation of workers, thereby deepening power imbalances on digital labour platforms. This research contributes to ethical discourse making a case for misclassification of workers as independent contractors, and calls for policy interventions to protect workers' rights in digital labour platforms. Specifically, it emphasizes the need to improve algorithmic transparency, as algorithmic decisions on these platforms often remain opaque, leaving workers unsure of whether decisions are made by algorithms or manipulated by human managers under the guise of an algorithmic boss.

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Evaluation of the Cytotoxicity, Antioxidant, Anti-Inflammatory and Anti-Diabetic Activities of Extracts of Mangifera Indica L. and Parkia Biglobosa (Jacq.) R. Benth on Human Cells THP-1

Type 2 diabetes is a non-communicable disease that is widespread in poor countries and in Benin. Majority of the population use herbal medicines to treat type 2 diabetes because of their availability and affordable prices. The leaves of the ordinary mango tree Mangifera indica L. and the leaves of Parkia biglobosa (Jacq.) R. Br. ex G. Don) are usually used for the treatment of type 2 diabetes in Benin. The main objective of this project is to evaluate on human cells THP-1 the cytotoxicity, antioxidant, anti-inflammatory and antidiabetic activities of hydro-ethanolic extracts of the leaves of Mangifera indica and Parkia biglobosa. Cytotoxicity was measured in the presence of different doses of extracts by the lactate dehydrogenase test. Antioxidant activity was measured on THP-1 cells after induction of free radical (ROS) production by hydrogen peroxide. In vitro anti-inflammatory activity was determined by the production of proinflammatory cytokines TNFα, IL1β, and the anti-inflammatory cytokine IL10 by the ELISA technique activation of THP-1 cells with LPS/IFN g and treatment with plant extracts. Antihyperglycemic activity was evaluated by measuring insulin-induced cell glucose uptake under insulin resistance conditions in the presence or absence of plant extracts. Our results showed that the extracts of both plants are very little toxic up to 250ug/mL which is a very high concentration. Both plants have a remarkable antioxidant activity. They decrease the production of TNFα at 50ug/mL and 100ug/mL and not Ilβ production at these concentrations. We also observed an increase in glucose uptake by cells treated with Mangifera indica. These results allow us to confirm that these plants are not toxic and would be able to inhibit oxidative stress and inflammation. In addition Mangifera indica could inhibit insulin resistance. These plants could therefore be used to treat type 2 diabetes and its complications.

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The Establishment of hiPSC-derived Disease Models of Kashin-Beck Disease and the Mechanism of HT-2 Toxin-induced Damage via PI3K/AKT/NF-κB Signalling Pathway

Introduction: Kashin–Beck disease (KBD) is an endemic, chronic, and degenerative osteoarthritis with unclear etiology and pathogenesis, which was called 'a medical mystery in middle China' by *Science*. Up to 2022, there were more than 171,212 patients with KBD and 98.26 million high-risk populations in 379 counties in China. In contrast to OA, clinical symptoms, such as the deformed joints in the fingers and feet, begin to appear already at the age of 5 years or even earlier. However, the lack of spontaneous and induced animal and cellular disease models has hampered groundbreaking research on the etiopathogenesis, early diagnosis and prevention of KBD. Our goal was to establish the first disease-specific human induced pluripotent stem cell (hiPSC) cellular disease model of KBD, and then use it to determine the mechanism of cartilage ECM degradation induced by HT-2 toxin, an environmental risk factors of KBD.

Methods: HiPSCs were reprogrammed from dermal fibroblasts of two KBD and one healthy control donor via integration-free vectors. Subsequently, hiPSCs were differentiated into chondrocytes through three-week culture. Gene expression profiles in KBD, normal primary chondrocytes, and hiPSC-derived chondrocytes (hiPSC-Ch) were defined by RNA sequencing. A Venn diagram was constructed to show the number of shared differentially expressed genes (DEGs) between KBD and normal. Gene oncology and KEGG annotations were performed, and six DEGs were further validated in other individuals by RT-qPCR. Normal-hiPSC-Ch were treated with HT-2 toxin and/or pathway inhibitor for 4 days. Type II collagen, aggrecan, MMP13 and ADAMTS5 were detected by RT-qPCR and Western blotting. Pathway markers were detected by Western blotting.

Results: KBD cellular disease models were successfully established by generation of hiPSC lines. Seventeen consistent and significant DEGs present in all compared groups (KBD and normal) were identified. RT-qPCR validation gave consistent results with the sequencing data. ECM-

related pathways such as ECM-receptor interactions, Relaxin and PI3K/AKT were identified to be altered in KBD. After HT-2 toxin treatments, the gene and protein expression levels of type II collagen and aggrecan were significantly decreased (P<0.05), the gene and protein expression levels of MMP13 and ADAMTS5 were significantly increased (P<0.05), and the protein expression of p-PI3K, p-AKT, p-IκBα and p-p65 were significantly upregulated (P<0.05). After treatment with pathway inhibitor, the phosphorylation levels of PI3K, AKT, IκBα and NF-κB p65 induced by HT-2 toxin were significantly reduced (P<0.05), and the down-regulation of type II collagen and aggrecan, as well as the up-regulation of MMP13 and ADAMTS5, induced by HT-2 toxin were significantly inhibited.

Conclusion: Differentiated chondrocytes derived from KBD-origin hiPSCs provide the first cellular disease model for etiological studies of KBD. HT-2 toxin can induce cartilage ECM degradation by activation of PI3K/AKT/NF-κB signaling pathway. This study not only expand the disease resources of KBD chondrocytes, but also effectively advance the research progress of pathogenic mechanism of environmental high-risk factors of KBD, which has important scientific significance and application value.

Hussam Murad
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Evaluating the Association between Family-Related Factors and Levels of Substance use Severity as Determined by the Arabic DAST-10 Score

Recently in a research project funded by the Scientific Endowment (WAQF) at King Abdulaziz University, Jeddah, Saudi Arabia (grant number: 83–1441) in 2022, the author and colleagues developed and validated an Arabic version of the Drug Abuse Screening Test-10 (DAST-10) as a reliable and valid screening tool for drug use-related problems in Arabic speakers. The study involved 360 young adult Arabic-speaking drug users (18-35 years old) who were recruited from Alamal Complex for Mental Health, Jeddah, Saudi Arabia. The Arabic DAST-10 version shows scores of 1–2, 3–5, 6–8, and 9–10 indicating low, intermediate, substantial, and severe levels of the problems respectively. The distribution percentages of the drug users were 11.4%, 32.2%, 41.7%, and 14.7% in the four categories respectively. The current study was designed to detect the association between the family-related factors and the magnitude of the drug use-related problems as determined by the Arabic DAST-10 score. This secondary analysis study involved analysis of the responses to the family-related questions previously obtained from the participants in the above-mentioned research. These questions related to the family structure, causes of family incompleteness, emotional and financial support by the family, and parental supervision.

The results showed that the family incompleteness due to divorce significantly correlated with the severity of substance use, while that due to death of a parent did not. This may be attributed to the support and care of orphans commonly provided by their relatives. Moreover, both low emotional support by the family and poor parental supervision significantly correlated with the severity of substance use. In contrast, the drug use severity did not differ significantly in the users with easily met financial needs compared to those without. This may be explained by the fact that some abused drugs e.g., the synthetic cathinone drugs (widely known as bath salts) are cheap but very dangerous causing severe consequences. The relatively small number of females (25% of the participants) is considered a limitation of the current study, and it is due to under-reporting of drug use by females in Arabic populations.

In conclusion, the family incompleteness due to divorce, low emotional support by the family, and poor parental control significantly correlated with the severity of substance use, while the family incompleteness due to

death of a parent, and the financial support by the family did not. This study will help recognise the important effects of the family-related factors in evaluating the substance use severity as determined by the Arabic DAST-10 score, assisting the substance use prevention efforts.

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Medical Schools for Practical (Empirical) Doctors in Eighteenth- and Nineteenth-Century Greece: The Schools of Ioannina and Mystras

On 24 December 1958, an obituary appeared in the newspaper Εφημερίδα Ταχυδρόμος της Λακωνίας. It was noted that a Giórgos Vachaviolōs, nicknamed the 'Old General,' had passed away. Vachaviolōs was said to be a beloved practical doctor who specialized in bone-setting and herbal concoctions for the local populace. Why do I mention him? Because of his hometown: Mystras, a village close to the famous Byzantine castle town of Mystra. As I will discuss in my paper, Mystras can provide important information on the history of Greek medicine of the last two centuries of the Tourkokratia (the rule of Greece by the Ottoman Turks) and the first century after Greek independence, for it was there that a school for practical doctors was established.

In the eighteenth- and nineteenth centuries, Greeks eager to be a doctor left Greece and studied medicine in Western European cities like Padua, Paris, and Vienna. Many returned as diplomate physicians to establish their practice in the cities. The vast majority of people, and nearly everyone on the islands and in the inlands, however, were treated by empirical or practical doctors (praktikoí yiatroí), who relied on herbs and plants, animal and mineral substances, folk remedies, and religious and magical treatments to heal their patients. These practical doctors existed until the 1970s when diplomate physicians and the National Health Service (Εθνικό Σύστημα Υγείας) took over the healthcare of all Greeks. It is commonly known that most practical doctors received their training from their fathers and grandfathers. The practical doctor was typically a position handed down for generations in the same family. What is very little known, however, is that there were also medical schools for producing practical doctors.

In my paper I will discuss two such schools: one at Mystras, which graduated our praktikós Vachaviōlos mentioned above; and one at Ioannina, founded in 1840 by Adam Gorgidas, a famous praktikós and botanist from the University of Budapest. These schools produced many of the healers who restored health and wellbeing for most of the people of northwest Greece and the southern Peloponnesus. As such, these schools for praktikoí yiatroí deserve recognition in the history of medicine.

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Effectiveness of the Developed Biopolymeric Microfiber Matrix as a Local Drug Delivery System and a Scaffold for the Reconstruction of Bone Tissue Defects

The aim of the research was to study the framework ability of the fibrous non-woven PCL matrices we've created during the restoration of bone tissue.

Materials and methods of the research. Samples of microfibrous non-woven matrices made by our technology out of polycaprolactone PCL were used in the work. Antibiotic retention in samples of matrix materials was evaluated during the 1st, 3rd, 5th, 7th, 14th, 18th and 21st days of the experiment. The experimental study was performed on laboratory animals (rabbits). 30 animals of the main group were implanted with a polymer matrix in the area of bone defect, 30 animals of the control group were formed bone defect. There were performed some spectroscopic, histological and immunohistochemical analyses of the effectiveness of microfibrous non-woven PCL polycaprolactone matrices developed by us, in the work.

The results. The results of microbiological studies indicated the pronounced hydrophilic properties of the matrices we've created; it was confirmed by a decrease in the activity of the antibiotic only at 16.4 % after 7 days ($p<0.05$). The results of experimental studies confirmed that percentage of osteoid in the main group, compared with the control indicators, showed a pronounced framework effect of the implanted microfiber polymer matrix. This matrix effect was confirmed by the compact and circular arrangement of the collagenous fibers around groups of polymer microfibers at the early stages of the experiment with the percentage of osteoid (34.38% ($p<0.05$)) and the subsequent creation of a formed and organized bone structure in three mutually perpendicular directions. That is, a group of polymer fibers created a kind of substrate for building bone tissue on it. The active synthesis of bone tissue at the early stages of the experiment was also indicated by the growth of the osteoinductive proteins of osteocalcin and osteopontin.

Conclusions. The matrix material developed by us, is not only a means of delivering some other substances and materials into the damaged area, but also serves as a kind of framework for the restoration of bone tissue.

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I Guess Therefore I Am

Generation of situation awareness (SA) is a key function of human consciousness, and a fundamental attribute of clinical human factors/ ergonomics (HF/E) from which all others are derived. SA is the ability to form perceptions about elements in time and space (Perception - Level I SA), mental models that make sense of those perceptions (Comprehension - Level II SA), and projections about future states based on those models (Level III SA). Individual SA predicates individual clinical decision making, as well as risk perception and planning/prioritisation skills; shared (or team) SA requires communication, teamworking and leadership skills. Ergonomic sociotechnical designs of external environments (layout, displays, checklists, forcing functions etc.) work through by supporting individual and team SA, making it easier to see and do 'the right thing' and harder to do 'the wrong thing'. Taken together these comprise many of the basic elements of a clinical HF/E training curriculum.

Emerging research in neuroscience and artificial intelligence reveals that the true nature of human consciousness is not what we intuitively think it to be. Our bodies inhabit a dynamic physical universe, but 'reality' as we experience it turns out to be more than a mere live recording from which we extrapolate meaning: it is a filtered and embellished model constructed by our brains - a kind of 'practical hallucination' with much pre-determined meaning already baked into it , our 'best guess' of what should be happening and what is about to happen, designed through millions of years of natural selection to enhance our ability to function (and survive). As George Box famously said: all models are wrong, but some are useful. A better (i.e. more useful) model of consciousness and how it evolves and develops over time would help us better understand the factors that shape SA, which would in turn better inform other aspects of HF/E and human performance in clinical environments. This session presents some of the research relevant to this topic.

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Whole-Tissue Mapping of >10,000 Proteins and >30,000 Phosphosites by Micro-Scaffold Assisted Spatial Proteomics (MASP)

Spatially resolved, quantitative proteome-wide characterization of proteins and post-translational modifications (PTMs) across entire tissue sections provides critical insights into the spatial organization of regulatory processes and networks. Such information is essential for understanding disease mechanisms and evaluating drug effects. However, achieving deep and robust proteomic mapping at the whole-tissue level—including phosphoproteomes—has remained highly challenging, with most existing methods offering limited depth or coverage.

To address this unmet need, we developed Micro-Scaffold Assisted Spatial Proteomics (MASP), which enables comprehensive and quantitative mapping of >10,000 proteins and >30,000 phosphosites across intact tissue slices. MASP integrates three core innovations:

1. Micro-compartmentalization using a 3D-printed micro-scaffold uniformly pressed against the tissue to preserve spatial information and achieve precise, distortion-free sectioning.
2. Micro-SEPOD extraction and digestion, combined with highly sensitive and reproducible LC–MS analysis for each micro-compartment.
3. UHR-IonStar quantification and a dedicated informatics platform (MAsP) that reconstructs high-fidelity distribution maps with mean quantitative error of only ~12.9%.

We demonstrate two applications. First, MASP revealed the intra-brain distributions of intracerebroventricularly (ICV) dosed IgG1 and IgG2 monoclonal antibodies, uncovering high penetration in the lower cortical regions and highly correlated distributions (r=0.93). By mapping >6,000 cerebral proteins concurrently, we identified numerous proteins positively or negatively correlated with antibody distribution, providing fresh insights into brain delivery and spatial drug effects.
Second, we applied MASP to the 3xTg Alzheimer's disease (AD) mouse model, simultaneously mapping >30,000 phosphosites and ~9,000 proteins. We captured >90% of proteins involved in AD pathways and >95% of known AD-related phosphorylation sites. Notably, MASP identified >80 phosphosites on tau alone, revealing striking spatial differences between diseased and control animals. Beyond established AD markers, many proteins involved in

metabolism, inflammation, immune response, and cognitive functions showed distinct spatial patterns across disease stages. Ongoing informatics analysis will further elucidate novel spatially-organized signaling pathways linked to AD onset and progression, underscoring MASP's utility for discovering new therapeutic targets.

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Sex Differences in Diabetic Vascular Dysfunction: A Deep Dive into Diabetes-Induced Vascular Aging in Males vs Females and the Impact of Exercise

Over the past decade, type 2 diabetes (T2D) has reached epidemic levels worldwide, becoming one of the most challenging health problems in the 21st century. Cardiovascular diseases (CVD) are one of the primary causes of morbidity and mortality in patients with diabetes. Premenopausal women have a lower incidence of CVD when compared with age matched men. However, premenopausal women with diabetes not only lose the sex-based cardiovascular protection but also experience a higher relative risk of CVD compared to diabetic men. Hyperglycemia and diabetes exert differential effects on male vs female vascular function. Yet, the mechanisms underlying the interaction of biological sex and diabetes on vasculature remain to be investigated. This presentation focuses on the effects of both types of diabetes on the rat macrovascular (aorta) and microvascular (mesenteric artery) function with respect to biological sex. Further, the impact of moderate intensity exercise (MIE) on mesenteric arterial function in T2D will be presented. Endothelium-dependent vasorelaxation (EDV) was measured as a reproducible parameter for assessing endothelial function. Interestingly, both types of diabetes impaired EDV to a greater extent in female than in male rat vasculature. In smaller arteries, the predisposition of female to vascular injury in diabetes was due to a shift away from endothelium-derived hyperpolarization (EDH), initially considered as the major vasodilatory factor, toward a greater reliance on nitric oxide (NO). However, in larger artery, a decrease in NO level resulting from decreased endothelial NO synthase (eNOS) expression or elevated superoxide in part contributed to the susceptibility of female vasculature to injury in diabetes. One intriguing observation of this study was that MIE (50 min/day, 5days/week for 8 weeks, running at 55% of VO2max) improved EDV in T2D male vasculature, partially by restoring the EDH-type (NO and prostanoid-independent) relaxation in arteries of this model (Funding: NIH, HL128988 and University of the Pacific).

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A Conceptual Framework for Blended Learning in Nursing Education at Historically Disadvantaged Institutions in South Africa

Introduction: The Fifth Industrial Revolution (5IR) warrants the inclusion of technology into nursing education to address the changing needs in healthcare and academic environments. The COVID-19 pandemic acted as a catalyst for the incorporation of online learning with face-to-face learning in nursing education at higher education institutions in South Africa.

Problem statement: The pressure to continue with learning and teaching during challenging times saw the rapid integration of technology into nursing education. However, the blended learning approach was relatively new in nursing education at historically disadvantaged institutions in South Africa.

Aim of the study: The aim of the study was to develop a conceptual framework for the generation of a practice theory for blended learning in nursing education at historically disadvantaged institutions in South Africa.

Methodology: A convergent mixed methods research design was used to obtain empirical data for the development of the conceptual framework. Data was collected from student nurses and nurse educators at three rural historically disadvantaged universities in South Africa to determine their readiness for blended learning. Quantitative data was collected via online questionnaires from the students and educators. Qualitative data was collected via focus groups with the student nurses and one-on-one interviews with the nurse educators. The findings from the statistical and thematic data analysis were merged via narrative format. The meta-inferences from the integrated data analysis were used in the development of the conceptual framework for blended learning.

Findings: The integrated data analysis indicated the requirements, strengths and challenges to the implementation of blended learning. Both the student nurses and nurse educators displayed positive attitudes to blended learning and emphasized its benefits and importance in a technological world. However, communication, collaboration and commitment were key to the success of the innovative approach. Furthermore, there was no denying that electricity and connectivity issues

in the rural environments posed the biggest challenge to the online component of blended learning.

Conclusion: The developed conceptual framework provides the foundation for the generation of the practice theory. It presents a comprehensive overview of the essential components to ensure successful implementation of blended learning in nursing education in South Africa. Furthermore, the conceptual framework specifies the roles and responsibilities of the student nurse and nurse educator including the resources and support required for blended learning specific to historically disadvantaged contexts.

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How Renaissance Paintings Can be used to Teach Students to Interpret Patient Symptoms: The Example of Breast Cancer

Progress in breast cancer diagnosis is continuous and undeniable. Nevertheless, from time to time, new indicators of breast cancer are discovered in the depiction of breasts of models in Italian Renaissance paintings, confirming the alleged diagnosis of breast cancer and supposedly attesting to the historical epidemiology of the disease. However, as medical diagnosis is commonly considered to be both science and art, one in which a disease is identified through the art of recognizing and interpreting its signs and symptoms, we propose a comparison between the two. By comparing medical diagnosis (and, by association, interpretation in the natural sciences) with the interpretation of works of art, we aim highlight the interpretive functions of diagnostic testing.

As diagnosticians, we face similar situations to art experts; as we both interpret signs, and the objects of our analysis, diagnostic images, and art works (especially oil paintings) share a power to convey verisimilitude. We are also aware that our interpretations are neither absolute nor final. They are dependent on criteria that are never exhaustive, meaning that there are many different methods that can be used to interpret visual representations. Furthermore, we are required to justify interpretation itself as the chosen method for understanding, interpreting and deciphering signs.

By demonstrating our process of analyzing paintings, we aim to make our students understand how diagnosing is merely observing a given sign objectively. Diagnosing is the interpretation of all information coming from the patient – including that processed in the form of a medical image.

Analyzing disputes between researchers as a clash of methodologies in the way's interpretation transforms signs into meanings, is a critical and educational methodological reflection. In this regard, it is worth remembering that the paramount objective of diagnosis is not the disease, but the patient.

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Permeation of Dry Powders Including Peramivir as an Antiviral Agent Across Human Respiratory Epithelium: An in Vitro Study with Calu-3 Cells

Respiratory viral infections are diseases that are quite common in the world and often have viral agents in their etiology. They can affect people of all age groups, causing hospitalizations and death, especially in high-risk groups. Since respiratory viral infections primarily affect the respiratory tract, delivering antivirals directly to the infection site is the most logical approach, ensuring effective drug concentration with a low dose, minimal side effects, and passing first-pass metabolism. Inhaled dry powder formulations of antiviral agents represent a novel approach to managing respiratory viral infections. Dry powder inhaler (DPI) formulations were prepared by spray-drying process using chitosan (F1) and hyaluronic acid (F2) as polymers. Peramivir trihydrate content in DPIs was analyzed by HPLC. The method was validated according to the guideline Q2 (R1) of ICH. The human bronchial epithelial cell line Calu-3 is a very promising in vitro model of the airway epithelial barrier. Peramivir has high solubility and low permeability properties (BCS, Class III). Therefore, the aim of this study was to evaluate the influence of chitosan and hyaluronic acid as polymers on the peramivir transport across the Calu 3 cell system. Permeability studies were performed from apical to basolateral (A→B) and basolateral to apical (B→A) directions. Powder peramivir, F1 and F2 formulations were incubated with cells for 120 min at 37°C. Samples were collected at different time intervals (30, 60, 90 and 120 min). The apparent permeability coefficient (Papp) was calculated in either the apical to basolateral (absorption) or the basolateral to apical (efflux) direction and pure peramivir and formulations' efflux ratio were calculated. Transepithelial/endothelial electrical resistance (TEER) was measured to confirm the integrity and permeability of the monolayer, before and after the permeation study. Cell toxicity was determined using MTT assay. Pure peramivir was poorly permeable with a Papp (A→B) value of 1.80 ± 0.64 10-5 cm/s. Papp value in (B→A) study was found out to be 1.07± 0.12 10-5 cm/s ($p < 0.05$), thus ruling out the role of efflux pathways in poor pulmonary bioavailability of peramivir. On the other hand, around 3-fold increase of peramivir permeability was observed when DPI formulation prepared with hyaluronic acid (5.29± 1.02 10-5 cm/s), compared to the pure peramivir. This increase in vitro transepithelial permeation of peramivir

without compromising cellular viability might be induced by interactions upon contact between hyaluronic acid and the Calu 3 cells, leading to the opening of the tight junctions. Pure peramivir, F1 and F2 formulations exhibited a higher permeability value in the (A→B) direction when compared to (B→A) direction, indicating that peramivir is not likely a substrate for active transport. At the beginning of the permeation study, the highest TEER value was 498.6± 14.5 Ωcm2, while after 120 minutes the lowest TEER value was 336± 22.1 Ωcm2 . According to MTT assay, pure peramivir, F1 and F2 formulations did not affect the viability of the cells in culture. Based on the studies of in vitro cell culture, F2 is a promising formulation as an alternative for pulmonary drug delivery of peramivir.

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