Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0075
Abstract Submission No.：APCN20250041

A Novel Approach For Diabetic Nephropathy Therapeutics Via HuGLP-1 Formulation

AAKANCHHA JAIN[1]

[1] Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research-Ahmedabad, Opp. Airforce station, Palaj, Gandhinagar, Gujarat, India

Abstract

Background:

Literature reports that RAGE expression is elevated in diabetic nephropathy, promoting aberrant glycolysis and activation of the EMT program, resulting in severe glomerular pathology and exacerbated albuminuria. In contrast, evidence suggests that GLP-1 peptide inhibition of RAGE, corrected the hyperglycemia induced elevated toxic metabolites in kidney cells, reversed metabolic imbalances, and protected against renal disease in podocytes. As a result, inhibition of RAGE may restore the altered disease phenotype by reducing EMT, providing a novel target for preventing fibrotic kidney disease.

Methods:

We at Department of Pharmaceutics, NIPER-Ahmedabad has developed a novel HuGLP-1 peptide liposomal formulation by hand shaken method. The formulation was characterized for binding affinity with RAGE receptor, immunocytochemical analysis in Hrptec cell line.

Results:

The results indicate that HuGLP-1 peptide and RAGE receptors have shown binding affinity with the binding energy -1031 Kj/mol. The formulation showed low toxicity at higher concentration (100 μM) in untreated Hrptec cell line. Also, immunocytochemical analysis showed significant decrease in nuclear translocation of RAGE in the HuGLP-1 peptide formulation treated group as compared to the control group.

Conclusion:

The HuGLP-1 peptide formulation treated group has shown decreased progression of diabetic nephropathy as compared to disease group as assessed by histopathological analysis.

Keywords：Diabetic nephropathy, RAGE, Human GLP-1, hyperglycemia

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0076
Abstract Submission No.：APCN20250042

Computational Study of Human Glp-1 In Diabetic Nephropathy and In Vitro/In Vivo Assessment of Its Formulation

AAKANCHHA JAIN[1]

[1] Department of Pharmaceutics, National Institute of Pharmaceutical Education and Research-Ahmedabad, Opp. Airforce station, Palaj, Gandhinagar, Gujarat, India

Abstract

Objectives: Diabetic nephropathy (DN) is a life-threatening consequence of diabetes mellitus (DM) affecting 40% of individuals with diabetes worldwide. It is strongly associated with a significant increase in end-stage renal disease (ESRD). Hyperglycemia leads to metabolic disturbances in diacylglycerol (DAG) and methylglyoxal (MG), which result in elevated levels of reactive oxygen species (ROS) and mitochondrial dysfunction, thus contributing to the progression of DN.

Methods: This research focuses on various in-silico techniques for human GLP-1 (HuGLP-1), which may act as a nephroprotective agent in diabetic nephropathy by suppressing the Receptor for Advanced Glycation Endproducts (RAGE). In-silico techniques such as molecular docking, molecular dynamics, and other computational approaches were employed to analyze the interaction of HuGLP-1 with RAGE. To validate the findings from in-silico investigations, in-vitro and in-vivo studies were conducted to explore novel therapeutic applications of HuGLP-1-loaded liposomes.

Results: HuGLP-1-loaded liposomes were formulated and evaluated. The in-silico results indicated three different docking scores of -134, -103.1, and -306.416 kcal/mol for the HuGLP-1-RAGE complex obtained from the CABS-DOCK, ClusPro, and Schrodinger (Maestro) rigid docking platforms. The ClusPro complex, which exhibited the highest binding energy, underwent GROMACS simulations, which confirmed its stability through various metrics. Furthermore, HuGLP-1 liposomes were formulated, and in-vitro studies on DN-induced Human Renal Proximal Tubule Epithelial Cells (hRPTEC) demonstrated that HuGLP-1 liposomes showed potent RAGE inhibitory activity and provided significant renal protection. In-vivo studies also indicated that HuGLP-1 liposomes may serve as a novel therapeutic strategy for DN.

Conclusions: In summary, the in-silico results indicated RAGE inhibition, while the in-vitro and in-vivo outcomes suggested that HuGLP-1 liposomes may have therapeutic potential in DN and could represent a promising formulation for RAGE inhibition.

Keywords：GLP-1, Advanced Glycation Endproducts, Liposomes, Diabetes Mellitus

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0077
Abstract Submission No.：APCN20250105

Resistin and Diabetic Nephropathy in Type 2 Diabetes Mellitus

Rizki Fajar Utami[1]; Ratna Dewi Puspita[2]

[1] Department of Biochemistry, Medical Faculty, Universitas Negeri Yogyakarta, Yogyakarta, Indonesia

[2] Department of Physiology, Medical Faculty, Universitas Gadjah Mada, Yogyakarta, Indonesia

Abstract

Background: Diabetic nephropathy (DN) is a major microvascular complication of type 2 diabetes mellitus (T2DM) and a leading cause of end-stage renal disease. Resistin, an adipokine, is suspected to play a role in the pathogenesis of DN in T2DM. This study aimed to conduct a review of the existing evidence on the association between resistin and DN in T2DM.

Methods: A literature search was conducted in the PubMed databases for relevant articles published up to March 2025. The inclusion criteria were observational studies evaluating the association between resistin levels and DN in patients with T2DM. The quality of the studies was assessed using appropriate assessment tools.

Results: This review included 5 studies. The results showed a significant positive association between resistin levels and the risk of DN in T2DM. Increased resistin levels were associated with a decrease in the glomerular filtration rate (GFR) and an increase in albuminuria. Other study shows resistin levels were observed as risk factors for diabetic nephropathy in T2DM patients with normal BMI, but not in the overweight and obesity groups.The reviewed studies showed that resistin may contribute to the pathogenesis of DN through the induction of inflammation, oxidative stress, and renal fibrosis.

Conclusion: The existing evidence suggests that resistin plays a role in the pathogenesis and progression of DN in T2DM. Resistin levels may serve as a potential biomarker for the diagnosis and monitoring of DN in patients with T2DM.

Keywords：Diabetic nephropathy; Resistin; Diabetes Mellitus

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0078
Abstract Submission No.：APCN20250124

Spermine Oxidase Drives Mitochondrial Bioenergetic Collapse to Promote Diabetic Tubulointerstitial Fibrosis

Dan Luo[1]; Xue-qi Liu[1]; Mi Liu[1]; Shu-ting Li[1]; Qi-mei Luo[1]; Xian-rui Dou[1]
[1] Department of Nephrology, The Eighth Affiliated Hospital, Southern Medical University (The First People's Hospital of Shunde, Foshan), Foshan City, Guangdong

Abstract

Introduction

Emerging evidence positions diabetic kidney disease (DKD) as a tubulocentric disorder, where mitochondrial dysfunction in renal tubular epithelial cells (RTECs) initiates a cascade of metabolic derangements and fibrotic transition. Despite the clinical significance of tubular atrophy in DKD progression, early molecular triggers remain elusive. Transcriptomic analysis of human DKD biopsies revealed tubular spermine oxidase (SMOX) upregulation inversely correlating with eGFR. Here, we will further dissect the role and mechanism of SMOX in RTEC injury during early DKD progression.

Methods

Multi-model validation included: (1) DKD patient biopsies, (2) streptozotocin-induced Smox-/- mice, (3) high glucose/AGEs-stimulated RTEC, and (4) human kidney organoids. Mechanistic studies integrated MS-proteomics, Co-IP, and RNA-seq. Mitochondrial function was analyzed using Seahorse analyzer. Mitochondrial morphology was measured by super-resolution microscopy.

Results

We revealed significant SMOX upregulation in RTEC from DKD patients, STZ-induced mice, and kidney organoids, independent of spermine level alterations. Genetic SMOX ablation substantially ameliorated renal tubulointerstitial fibrosis in DKD models. Compared to wild-type DKD mice, Smox-/- STZ mice exhibited comparable blood glucose but 31% lower serum BUN levels ($p<0.01$). Consistent with functional improvement, Smox-/- mice showed preserved tubular architecture on PAS staining and substantially diminished interstitial collagen deposition (Sirius red staining), indicating protection against DKD progression. Mechanistically, RNA sequencing implicated mitochondrial metabolic dysfunction in SMOX-mediated injury. TEM revealed that mitochondria morphology, including decreased area and cristae density, and increased roundness, was improved in the kidney of Smox-/- STZ mice. Mitochondrial translocation of SMOX was confirmed via immunofluorescence colocalization and mitochondrial isolation assays. Subsequent MS-based proteomics and Co-IP techniques identified that SMOX could interact with ATP5F1A (independent of its canonical polyamine catabolic function). This binding impaired ATP synthase activity, inducing bioenergetic failure and ROS overproduction in RTECs.

Conclusion

Our findings reveal a novel non-enzymatic role for SMOX in DKD progression through mitochondrial ATP5F1A targeting. By disrupting complex V function, SMOX induces RTEC bioenergetic failure and fibrosis, nominating the SMOX-ATP5F1A interface as a therapeutic target.

Keywords：Diabetic Tubulointerstitial Fibrosis；Spermine Oxidase；mitochondrial dysfunction

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0079
Abstract Submission No.：APCN20250131

Astragaloside IV restores autophagy and inhibits apoptosis for podocyte protection in diabetic kidney disease by inhibiting the Notch1 signaling via SIRT6-mediated deacetylation

Qiyu Yue[1,2]; Chen Yong[2,4]; Wei-wei Tao[3]; En-chao Zhou[1,2,4]

[1] The First School of Clinical Medicine, Nanjing University of Chinese Medicine, Nanjing City, China

[2] Affiliated Hospital of Nanjing University of Chinese Medicine, Jiangsu Province Hospital of Chinese Medicine, Nanjing City, China

[3] School of Integrative Medicine, Nanjing University of Chinese Medicine, Nanjing City, China

[4] Jiangsu University Key Laboratory of Tonifying Kidney and Anti-senescence, Nanjing City, China

Abstract

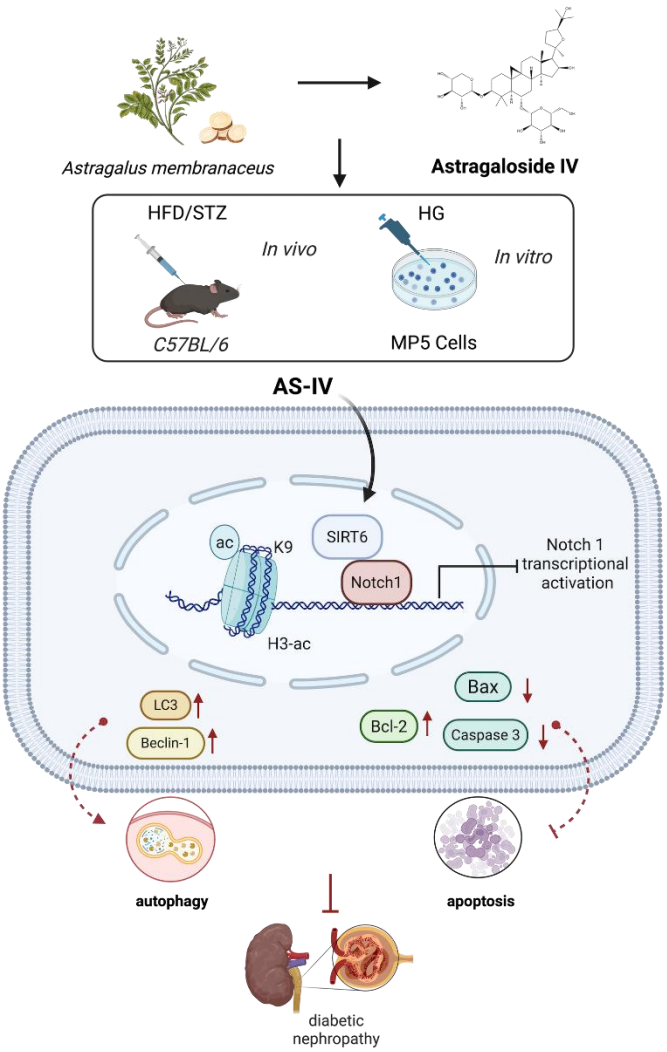
Purpose: Astragaloside IV (AS-IV), a major bioactive component purified from Astragalus membranaceus (Fisch.) Bunge, has demonstrated efficacy in reducing hyperglycemia, ameliorating proteinuria, and attenuating renal tubular damage in preclinical diabetic nephropathy (DN) models. This study tests whether AS-IV protects against DN by activating SIRT6-dependent epigenetic pathway.

Methods: DN was induced in mice using a combination of a high-fat diet (HFD) and intraperitoneal injection of streptozotocin (STZ). MPC5 cell line was selected in cell experiment. The kidney function parameters were evaluated, and the histomorphology of glomerular tissues was examined. Molecular docking was used to confirm that AS-IV was able to directly bind to SIRT6, and then furtherly explored the downstream regulation mechanism related to podocyte autophagy and apoptosis by immunofluorescence staining, Quantitative Real-Time PCR, and western blotting assays. Chromatin Immunoprecipitation was used to detect whether histone H3K9ac was indeed able to bind to the notch1 promoter region. SIRT6 knockdown was used to confirm its role in AS-IV's podocyte protection.

Results: This study discovered that AS-IV might alleviate renal biochemical and pathological damage and podocyte injury in mice modeled by STZ. Molecular docking reveals that AS-IV directly binds to SIRT6, which was previously believed to be its target. SIRT6 deacetylates histone H3K9 to prevent Notch1 transcription. Subsequent research showed that the protective benefits of AS-IV against damage in HG-stimulated podocytes were diminished when SIRT6 was depleted.

Conclusion: AS-IV protects podocytes in DN mice both in vitro and in vivo by activating the SIRT6/Notch1 pathway, which mediates autophagy regulation and reduces apoptosis.

Keywords：Astragaloside IV (AS-IV) | Diabetic nephropathy (DN) | SIRT6 | Autophagy | Notch1| H3K9ac


Astragalus membranaceus
Astragaloside IV
HFD/STZ
In vivo
C57BL/6
HG
In vitro
MP5 Cells
AS-IV
ac
K9
SIRT6
Notch1
Notch 1
transcriptional
activation
H3-ac
LC3
Beclin-1
Bax
Bcl-2
Caspase 3
autophagy
apoptosis
diabetic
nephropathy

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0081
Abstract Submission No.：APCN20250164

Azomethine-Clubbed Thiazole Scaffolds as Dual GLP-1R Agonists and SGLT2 Inhibitors: A Pharmacoinformatic Strategy for Diabetic Nephropathy and Cardiovascular Protection

Rizki Rachmad Saputra[1]; Muhammad Priyadi[2]; Eka Novitasari[3]; Dwi Hermayantiningsih[1]
[1] Department of Chemistry, Universitas Palangka Raya, Palangka Raya, Indonesia
[2] Department of Pharmacy, Universitas Palangka Raya, Palangka Raya, Indonesia
[3] Department of Applied Chemistry, Ritsumeikan University, Shiga, Japan

Abstract
Introduction: Diabetic nephropathy (DN), a leading cause of chronic kidney disease (CKD), significantly heightens cardiovascular risk through its integration within the cardio-renal-metabolic continuum. Current treatments, including GLP-1 receptor agonists and SGLT2 inhibitors, offer metabolic and organ-specific benefits but are limited by suboptimal dual efficacy and poor solubility. Given the interconnected pathophysiology of DN and cardiovascular disease (CVD), there is a critical need for multifunctional small molecules that target both metabolic and renal pathways. This study evaluates azomethine-clubbed thiazole derivatives as dual GLP-1 receptor agonists and SGLT2 inhibitors, while exploring β-cyclodextrin (β-CD) inclusion to improve their bioavailability and formulation potential.

Methods: Seven azomethine-clubbed thiazole derivatives were computationally screened through molecular docking against GLP-1R (PDB ID: 5VEX) and SGLT2 (PDB ID: 8HDH) using AutoDock Vina. ADMET properties were predicted via the pkCSM server to assess pharmacokinetics and safety. Inclusion complex modeling with β-CD was conducted to estimate solubility enhancement potential.

Results: Among the candidates, compounds 3a and 3h demonstrated compelling dual-target profiles. Compound 3a showed strong binding to SGLT2 (-10.3 kcal/mol) and moderate affinity for GLP-1R (-6.6 kcal/mol), indicating a reno-metabolic effect. Compound 3h offered balanced binding with added central nervous system (CNS) accessibility (log BB: 0.256), supporting broader therapeutic potential. Physicochemical profiles revealed optimal lipophilicity (Log P: 2.81–3.38) and favorable water solubility (log S: -3.418 to -2.37), supporting membrane permeability and systemic distribution. ADMET profiling confirmed high intestinal absorption (>90%), acceptable clearance (0.104–0.285 log ml/min/kg), and no Lipinski rule violations. Both compounds showed low predicted toxicity (oral rat LD50: 2.22–2.64 mol/kg). Additionally, β-CD modeling confirmed stable inclusion complexes for both 3a and 3h, supporting improved aqueous solubility and potential for formulation into advanced delivery systems.

Conclusion: Azomethine-clubbed thiazole derivatives, particularly 3a and 3h, exhibit strong promise as dual modulators of GLP-1R and SGLT2, combining glycemic control with renoprotective and cardiometabolic benefits. Favorable ADMET profiles and β-cyclodextrin inclusion suggest practical applicability in formulation science. These findings justify further preclinical validation of 3a and 3h as next-generation agents for integrated management of diabetic nephropathy and CVD.

Keywords：Diabetic nephropathy, Cardiovascular disease, Azomethine-Clubbed thiazole

GENERAL PROFILES			
Molecules/Pubchem ID	**3a**	**3g**	**3h**
MW	325.38	275.33	312.39
Binding Affinity			
SGLT2 (kcal/mol)	-10.3	-8.5	-9.3
GLP-1 (kcal/mol)	-6.6	-6.4	-5.9
LIPOPHILICITY			
Consensus Log P	3.38	2.81	3.01
WATER SOLUBILITY			
Log solubility (log mol/L)	-2.89	-3.418	-2.37
PHARMACOKINETICS			
BBB Permeability (log BB)	-0.407	-0.423	0.256
CYP1A2 inhibitor	yes	yes	yes
Intestinal Absorption (Human) (% Absorbed)	90.26	90.57	92.8
Total Clearance (log ml/min/kg)	0.285	0.104	0.19
DRUGLIKENESS			
Lipinski #violations	0	0	0
Bioavailability Score	0.55	0.55	0.55
MEDICINAL CHEMISTRY			
Leadlikeness #violations	1	1	1
Synthetic Accessibility	3.25	2.99	3.24
TOXICITY			
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.22	2.34	2.64

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0082
Abstract Submission No.：APCN20250240

Saffron: A Potential Natural Therapy Targeting Fibrosis-Related Pathways In Kidney Disease

Iman Nabilah Abd Rahim[1]; Yasmin Mohd Zainal Abidin Shukri[1]; Nur Aqasyah Amran[1]; Opik Taupiqurrohman[2]

[1] Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Malaysia

[2] Biotechnology Doctoral Program Graduate School, Universitas Padjadjaran, Jawa Barat, Indonesia

Abstract

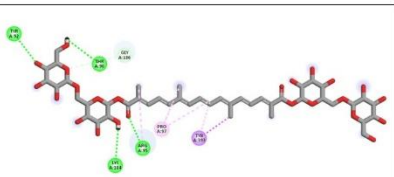
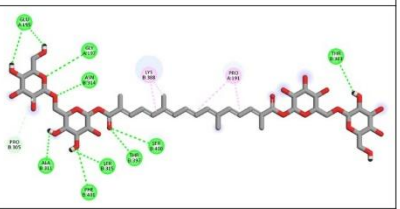
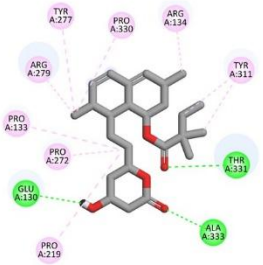
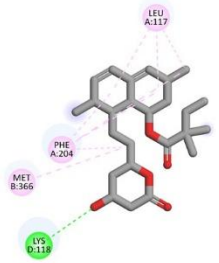
Introduction: Matrix metalloproteinase-9 (MMP-9) and its endogenous inhibitor, tissue inhibitor of metalloproteinase-1 (TIMP-1), play pivotal roles in extracellular matrix remodeling within the kidney. Dysregulation of the MMP-9/TIMP-1 axis contributes to renal fibrosis and inflammation, particularly in diabetic kidney disease and hypertensive nephropathy. While statins have demonstrated protective effects in slowing cardio-renal progression, their clinical utility may be limited by adverse effects or intolerance. Saffron, the stigma of the flower Crocus sativus L., contains bioactive compounds such as crocin, crocetin, and safranal, all of which exhibit cardiovascular and anti-inflammatory properties. However, the potential molecular mechanisms by which saffron compounds interact with MMP-9 and TIMP-1 in the context of renal protection remain unclear. This study investigates the molecular interactions of saffron-derived compounds with MMP-9 and TIMP-1 compared to simvastatin, aiming to evaluate saffron's potential as a renoprotective agent.

Methods: Crystal structures of human MMP-9 and TIMP-1 were retrieved from the Protein Data Bank and prepared using UCSF ChimeraX. Ligand structures (crocin, crocetin, safranal, simvastatin) were downloaded from PubChem and energy-minimized in Avogadro. Molecular docking was conducted using AutoDock Vina via the CB-Dock2 platform. Binding affinities were compared, and key ligand–receptor interactions were analyzed with BIOVIA Discovery Studio, focusing on hydrogen bonding, hydrophobic contacts, van der Waals forces, and π–π stacking. Docking reliability was assessed using RMSD values and validated by redocking native ligands to ensure pose accuracy.

Results: Crocin exhibited the strongest binding affinity to both TIMP-1 (−9.0 kcal/mol) and MMP-9 (−8.7 kcal/mol). In the TIMP-1 complex, crocin formed four hydrogen bonds with ASN314, GLY197, TYR52, and ARG95, and interacted with ARG233 via van der Waals and hydrophobic forces. In the MMP-9 complex, crocin established hydrogen bonds with ARG424, ARG426, and GLY197, alongside non-covalent interactions with GLU402 and TYR423. Crocetin showed moderate affinities (−6.6 and −7.0 kcal/mol), mainly via hydrophobic contacts and no hydrogen bonding. Safranal exhibited weaker affinities (−5.4 and −6.1 kcal/mol). Simvastatin had the lowest binding (−5.3 and −6.0 kcal/mol), forming only hydrophobic and π–π interactions.

Conclusion: This study demonstrates that crocin exhibits superior binding profiles with both MMP-9 and TIMP-1 compared to simvastatin. These interactions suggest that crocin may inhibit matrix remodeling and inflammatory signaling pathways central to renal fibrosis. Overall, the findings highlight the potential of saffron-derived compounds, particularly crocin, as natural renoprotective agents for patients with cardio-renal metabolic syndrome, especially those intolerant to statins. Further studies are warranted to validate their efficacy and translational potential.

Keywords：Saffron, Statin Intolerance, Kidney Disease, Molecular Docking, Matrix Metalloproteinase

Protein/Ligand	MMP9	TIMP1
Crocin		
Simvastatin		

Interactions

- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Sigma
- Alkyl
- Pi-Alkyl

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0083
Abstract Submission No.：APCN20250326

Pegmolesatide Ameliorates Indoxyl sulfate-induced Cardiomyocyte Hypertrophy through Modulating the EPOR-CD131-dependent JAK2/STAT3 Signaling Pathway

Xinyu Zhang[1]; Li Zhu[1]; Sufang Li[1]; Tingru Lin[1]; Liangying Gan[1]; Li Zuo[1]
[1] Peking University People's Hospital, Beijing, China

Abstract
Background: Cardiovascular events remain the leading cause of mortality in chronic kidney disease (CKD). Pegmolesatide(P), a novel long-acting EPO receptor modulator, shows cardiovascular benefits in clinical studies. This study aims to demonstrates Pegmolesatide suppressed the formation of EPOR-CD131 heterodimer and explore its cardioprotective mechanisms against indoxyl sulfate (IS)-induced cardiomyocyte hypertrophy.
Methods: H9c2 cardiomyocytes were grouped into phenotypic experiments (vehicle, IS, IS+P, P) and RNA sequencing was performed to identify dysregulated signaling pathways. Mechanistic exploration groups supplemented with CD131 agonist ARA290, STAT3 activator Colivelin, or STAT3 inhibitor Stattic for rescue experiments. Analyses included realtime-qPCR/Western blot for cardiac hypertrophy markers and EPOR-CD131/JAK2/STAT3 axis components, phalloidin staining for cell size and co-immunoprecipitation (Co-IP) for EPOR-CD131 heterodimerization.
Results: Pegmolesatide significantly attenuated IS-induced cardiomyocyte hypertrophy, as evidenced by suppressed expression of cardiac hypertrophy markers (ANP, BNP, and β-MHC), reduced cell surface area, and improved cytoskeletal organization($P < 0.05$). Mechanistically, Pegmolesatide upregulated EPOR expression while suppressing CD131 expression and the activation of the JAK2/STAT3 signaling. Co-IP analysis demonstrated that Pegmolesatide suppressed the formation of EPOR-CD131 heterodimer. Functional rescue experiments demonstrated that the cardioprotective effects of Pegmolesatide were reversed by CD131 agonist ARA290 or STAT3 activator Colivelin. Notably, combined treatment with ARA290 and STAT3 inhibitor Stattic partially restored its anti-hypertrophic activity.
Conclusion: Pegmolesatide exerts protective effects against IS-induced cardiomyocyte hypertrophy by inhibiting the EPOR-CD131/JAK2/STAT3 signaling axis. It may be a promising strategy for CKD-related cardiovascular complications.

Keywords：Pegmolesatide; Indoxyl sulfate; Cardiomyocyte hypertrophy; EPOR-CD131 heterodimer; JAK2/STAT3 signaling pathway

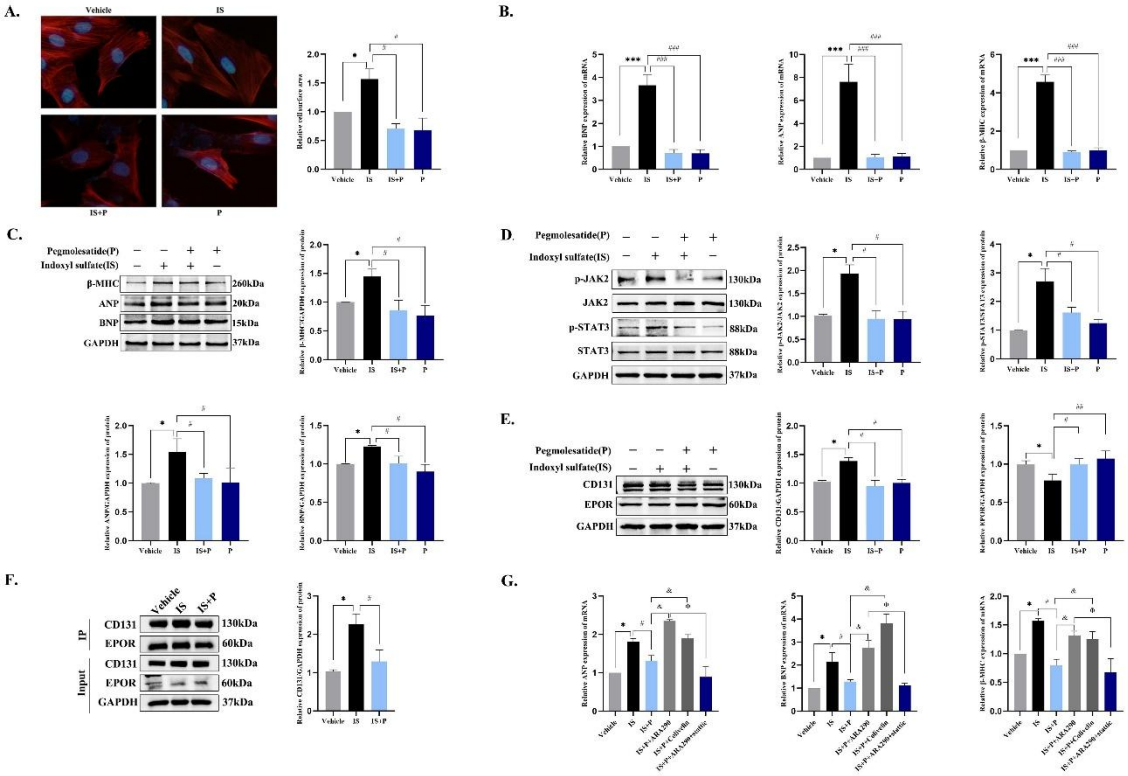


Figure 1: The effect of Pegmolesatide on the EPOR-CD131-JAK2/STA13 axis in H9c2 cardiomyocytes (A)Phalloidin staining was used to detect the cell surface area. (B)RT-qPCR analysis of mRNA levels of cardiac hypertrophy-associated genes (BNP, ANP, β-MHC). (C) Western blot was used to determine the expression levels of the cardiac hypertrophy markers (BNP, ANP, β-MHC). (D)JAK2/STAT3 pathway activation under differential treatments. (E) Western blot was used to determine the expression levels of EPOR and CD131. (F)EPOR-CD131 heterodimer interaction assessed by co-immunoprecipitation (Co-IP). (G)Pharmacological rescue: Cardiac hypertrophy-associated genes (BNP, ANP, β-MHC) quantified via RT-qPCR. (*/#< 0.05 and **/##< 0.01 vs. Vehicle; $/$$< 0.05 and $$/$$$< 0.01 vs. IS; &/&&< 0.05 vs. IS+P; Φ/ΦΦ< 0.05 vs. IS+P+ARA290. P, Pegmolesatide; IS, Indoxyl sulfate; ARA290, CD131 agonist; Colivelin, STAT3 activator; Stattic, STAT3 inhibitor)

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0084
Abstract Submission No.：APCN20250473

Harnessing Indonesian Biodiversity: In Silico Discovery of Novel GPR40 Agonists Targeting Cardio-Renal Crosstalk

Dykall[2]; Satwikanti Maeswari[1]

[1] Department of Rehabilitation Medicine, Universitas Islam Indonesia, Indonesia

[2] Department of Orthopaedics and Traumatology, Universitas Sebelas Maret, Indonesia

Abstract

Introduction: Cardio-renal metabolic syndrome represents a complex pathophysiological network involving interconnected cardiovascular, renal, and metabolic dysfunctions. GPR40, a G-protein-coupled receptor for free fatty acids, has emerged as a promising therapeutic target due to its role in glucose-dependent insulin secretion and anti-inflammatory properties. GPR40 activation improves type 2 diabetes mellitus, metabolic syndrome, and associated complications including nonalcoholic fatty liver disease and cardiovascular diseases. The clinical potential was demonstrated by TAK-875, which achieved robust HbA1c reduction (-1.12%). Indonesia's rich biodiversity, documented in databases containing approximately 1,000 compounds from medicinal plants, provides an untapped resource for discovering novel GPR40 modulators with improved safety profiles.

Methods: A computational screening of 519 Indonesian phytochemicals from HerbalDB, filtered via Lipinski's rule of five, targeted the GPR40 crystal structure (PDB:4PHU). Macromolecule preparation in AutoDock Tools 1.5.6 involved water removal, polar hydrogen addition, and Kollman charge assignment. Molecular docking simulations utilized PyRx 0.8 with AutoDock Vina (exhaustiveness=8), generating 10 binding conformations per ligand. Protein-ligand interactions were analyzed in PyMOL 2.5.2, focusing on residues Tyr91, Arg183, and Ala83. Compounds were evaluated against TAK-875 (-10.1 kcal/mol) using: (1) binding energy ≤-10.1 kcal/mol, (2) RMSD ≤2 Å, and (3) interaction with ≥2 key residues.

Results: Three Indonesian phytochemicals demonstrated superior GPR40 binding: 1) Piperyline (PubChem CID 636537; binding affinity: -10.3 kcal/mol) from Piper nigrum (Indonesian black pepper); 2) (1S,5S)-3-methyl-8-methylidene-5-propan-2-yl-2,4a,5,6,7,8a-hexahydro-1H-naphthalen-1-ol (CID 91746535; -10.3 kcal/mol) isolated from Dipterocarpus retusus; and 3) α-Copaene (CID 19725; -10.2 kcal/mol) sourced from clove oil (Syzygium aromaticum), native to Indonesia. All compounds exhibited binding affinities exceeding TAK-875 (-10.1 kcal/mol) and stable RMSD values (0.0 Å), indicating robust molecular compatibility. Their structural diversity and Indonesian botanical origins suggest potential to modulate GPR40-mediated metabolic pathways, potentially reducing glomerular hyperfiltration and tubulointerstitial fibrosis in CKD.

Conclusion: These Indonesian phytochemicals demonstrated enhanced GPR40 binding affinities compared to synthetic TAK-875, with optimal structural compatibility. Given that GPR40 activation protects against renal injury by inhibiting oxidative stress and inflammatory pathways, and that tubulointerstitial fibrosis contributes to progressive nephron loss, these natural compounds may interrupt pathological cascades in cardio-renal metabolic syndrome. Future investigations should validate computational predictions through in vitro GPR40 activation assays and animal models.

Keywords：GPR40 agonist - Molecular docking - Indonesian medicinal plants - Chronic kidney disease - Metabolic syndrome - Cardio-renal crosstalk

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0086
Abstract Submission No.：APCN20250520

Antihypertensive and renal protective effect of Resveratrol -Chitosan nanobeads against Hypertensive Nephropathy Rats via Modulation of Nrf-2/HO-1 and PI3K/Akt/mTOR Signaling Pathways

Deeksha Chauhan[1]; Vikas Kumar[2]
[1] Department of Applied Physics, Rajkamal institute of management, haridwar, India
[2] Department of Pharmacy, SHUATS, India

Abstract
Background: Hypertensive nephropathy (HN) is a kidney condition caused by essential hypertension, frequently resulting in both functional and structural renal impairment. As per the reports, hypertension has become the most common chronic disease globally. In this study, we fabricate the resveratrol-chitosan loaded nanobeads (RT-NBs) and scrutinized against HN in rats and explore underlying mechanism.
Methods: An enhanced ionic gelation method was used to fabricate the RT-NBs and entrapment efficiency, drug loading capacity, particle size and invitro release study was estimated. For the induction of HN in the rats, high sugar and high fat diet was given to the rats for 8 weeks, from the 5th week, the rats were received the oral administration of RT-NBs was orally given to the rats. The blood pressure parameters were estimated via using the tail cuff method. Renal parameters, oxidative stress, inflammatory cytokines, lipid, inflammatory parameters were estimated. The mRNA expressions were determined in the renal tissue.
Results: RT-NBs showed the entrapment efficiency (55.67±1.95%) and drug loading capacity (23.41±0.57%). RT-NBs demonstrated the reduction in the diastolic, mean arterial pressures and systolic pressure. RT-NBs showed the alteration in the level of renal parameters such as creatinine, total protein, bilirubin, albumin; antioxidant parameters include MDA, SOD, CAT, GPx, GSH; inflammatory cytokines viz., TNF-α, IL-1β, IL-6, IL-10; lipid parameters such as TC, TG, LDL, HDL, VLDL; inflammatory parameters include COX-2, NF-κB, iNOS, PGE2, respectively. RT-NBs showed the alteration in the mRNA expression of HO-1, Nrf2, PI3k mTOR and Akt.
Conclusion: The current finding showed the antihypertensive and renal protective effect of Resveratrol -Chitosan nanobeads against Hypertensive Nephropathy Rats via Modulation of Nrf-2/HO-1 and PI3K/Akt/mTOR Signaling Pathways.

Keywords：Acute kidney injury, Inflammation, Ursolic acid, metformin, HO-1/Nrf2 Signaling pathway

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0087
Abstract Submission No.：E_APCN20251299

Development of a Kidney Proximal Tubule-on-a-Chip Model of Obesity-Induced Metabolic Disease for Advanced Biopharmaceutical Evaluation

Seoyoung Choi[1], Seung Yeon Lee[2], Jaebeen Im[2], Sejoong Kim[1,2]*
[1]Department of Medicine, Seoul National University College of Medicine, Seoul, Korea.
[2]Department of Nephrology, Seoul National University Bundang Hospital, Seongnam, Korea

Abstract
Obesity promotes the accumulation of free fatty acids, which induces lipotoxicity in renal proximal tubules and, in combination with hyperglycemia, progresses to glucolipotoxicity. These sequential processes are central to the development of metabolic kidney disease, yet conventional animal models and two-dimensional cultures fail to recapitulate the stepwise pathophysiology. In this study, we established a kidney-on-a-chip by co-culturing human renal proximal tubule epithelial cells and endothelial cells to mimic the proximal tubule–vascular interface. Lipotoxic conditions were induced by treatment with free fatty acids, and subsequent high-glucose exposure reproduced the glucolipotoxic stage. The model exhibited increased lipid accumulation, elevated pro-inflammatory cytokine expression, and disruption of tight junction proteins leading to impaired barrier function. This kidney proximal tubule-on-a-chip provides a physiologically relevant platform for modeling obesity-induced metabolic kidney disease and offers potential utility for preclinical evaluation of advanced biopharmaceutical candidates..

Acknowledgement : This invention was derived from a research project supported by the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (Project Number: RS-2025-02223065).

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Keywords: Kidney-on-a-chip; Lipotoxicity; Glucolipotoxicity; Metabolic kidney disease; Advanced biopharmaceuticals

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0088
Abstract Submission No.：APCN20250577

Comparative Effects of HFD and CDAHFD on Metabolic Dysfunction-Associated Fatty Liver Disease-Related Disruption of Liver and Kidney Immunometabolism and Gut Microbial Landscapes

YU-CHIN HUANG[1]; Po-Chun Huang[2]; Jia-Rou Hsu[3]; Chih-Lin Wang[3]; Li-Ling Wu[3,4,5]

[1] Nephrology Department, New Taipei City Hospital, New Taipei City 241204, Taiwan

[2] School of Medicine, National Tsing Hua University, Hsinchu, Taiwan R.O.C

[3] Department and Institute of Physiology, National Yang Ming Chiao Tung University, Taipei, Taiwan

[4] Health Innovation Center, National Yang Ming Chiao Tung University, Taipei, Taiwan

[5] Microbiota Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan

Abstract

Background: Metabolic-associated steatotic liver disease (MASLD) has emerged as a significant global health burden and is frequently accompanied by systemic complications, including chronic kidney disease (CKD). Emerging evidence implicates disruptions in gut microbiota and immune regulation as critical mediators of MASLD-related multi-organ injury. This study aimed to systematically compare the systemic effects of two dietary MASLD models—16 weeks of high-fat diet (HFD) versus 8 weeks of choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD)—on liver and kidney injury, immune activation, and gut microbiota composition.

Methods: C57BL/6 mice were randomized to receive either HFD (60% kcal from fat) for 16 weeks or CDAHFD for 8 weeks. At the end of the feeding period, systemic metabolic evaluations were performed, including serum measurements of alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, triglycerides, and cholesterol. Liver and kidney tissues were assessed histologically using hematoxylin and eosin (H&E), Picrosirius Red, and periodic acid–shiff (PAS) staining. Renal immune profiling was conducted via flow cytometry of single-cell suspensions to quantify monocytes, dendritic cells, and T lymphocytes. Gut microbiota composition was analyzed through 16S rRNA gene sequencing, and differentially abundant taxa were identified using STAMP analysis with Welch's t-test.

Results: CDAHFD induced more severe hepatic steatosis, inflammation, and fibrosis compared to HFD, along with greater renal tubular injury and immune cell infiltration ($CD11b^+Ly6C^+$ monocytes, $CD8^+$ T cells). Unlike HFD-induced glomerular hypertrophy, CDAHFD caused glomerular shrinkage. STAMP analysis of 16S rRNA sequencing data revealed distinct microbiota signatures between the two groups. Kineothrix alysoides, an inflammation-associated, mucin-degrading anaerobe, was markedly enriched in CDAHFD-fed mice. This taxon is implicated in gut barrier disruption and may facilitate the translocation of pro-inflammatory microbial products into the systemic circulation, thereby exacerbating renal inflammation and promoting CKD progression. In contrast, Faecalibaculum rodentium and Dubosiella newyorkensis, both known producers of short-chain fatty acids (SCFAs), were enriched in HFD-fed mice. These beneficial taxa may enhance intestinal barrier integrity, mitigate hepatic inflammation, and exert renoprotective effects through SCFA-mediated immune modulation and metabolic support.

Conclusion: Eight weeks of CDAHFD feeding induces faster and more severe disruption of liver and kidney immunometabolism and microbial composition than prolonged HFD. Specifically, the depletion of SCFA-producing commensals and enrichment of pro-inflammatory taxa may play key

roles in mediating gut-liver–kidney axis disruption. These findings highlight diet-specific pathophysiological trajectories and establish CDAHFD as an efficient MASLD-CKD model for investigating immune–microbiota–organ interactions.

Keywords：Metabolic-associated steatotic liver disease (MASLD),chronic kidney disease (CKD),high-fat diet (HFD),choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD)

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0089
Abstract Submission No.：APCN20250581

FNDC5/Irisin Mitigates Mitochondrial Dysfunction in Renal Cells Under Diabetic Stress

CHIEN-WEI HUANG[1,2,8]; Chia-Jung Li[3,4]; Hsin-Hung Chen[5]; Jin-Shuen Chen[6,7]

[1] Division of Nephrology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

[2] School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

[3] Department of Obstetrics and Gynaecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

[4] Institute of Biopharmaceutical Sciences, National Sun Yat-sen University, Kaohsiung, Taiwan

[5] Department of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

[6] Department of Administration, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

[7] Institute of Precision Medicine, National Sun Yat-Sen University, Kaohsiung, Taiwan

[8] Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

Abstract

Introduction: Diabetic nephropathy (DN) is a major complication of type 2 diabetes mellitus, driven in part by mitochondrial dysfunction in glomerular podocytes and tubular cells. Irisin, a myokine cleaved from FNDC5, has emerged as a regulator of energy metabolism and mitochondrial biogenesis, yet its role in renal cell homeostasis under diabetic conditions remains unclear. This study investigates the potential role of FNDC5/irisin in maintaining mitochondrial integrity in renal cells during hyperglycemic stress.

Methods: Publicly available human single-nucleus RNA-sequencing data (GSE131882) were analyzed to assess FNDC5 expression in DN. Mouse podocytes and human HK-2 cells were cultured under high-glucose (HG) conditions. FNDC5 expression was assessed via RT-PCR and immunohistochemistry. Mitochondrial morphology and dynamics were examined using MitoTracker staining and Western blot analysis of key fission/fusion regulators. FNDC5 are expected to be overexpressed in selected experiments to assess its effect on mitochondrial phenotype.

Results: FNDC5 expression was broadly reduced in diabetic kidneys and further suppressed by HG treatment in both podocytes and HK-2 cells. HG stress induced mitochondrial fragmentation, increased DRP1 phosphorylation, and decreased MFN1 and OPA1 levels. Experiments are planned to determine whether FNDC5 overexpression can alleviate mitochondrial disruption under diabetic conditions. Furthermore, in silico analysis identified CREB1 as a putative upstream transcriptional regulator of FNDC5. A ChIP-PCR assay is planned to evaluate CREB1 binding to the FNDC5 promoter under hyperglycemic stress.

Conclusion: FNDC5/irisin is downregulated in diabetic kidneys and may play a key role in modulating mitochondrial dynamics in renal cells. Ongoing studies will further clarify the therapeutic potential of targeting FNDC5 in DN.

Keywords：FNDC5, irisin, diabetic nephropathy, podocyte, HK-2 cells, mitochondria,

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0090
Abstract Submission No.：APCN20250593

Molecular mechanisms of Reno protective Potential of Hesperidin in diabetic nephropathy

Dharmendra Kumar Khatri[1]
[1] Department of Pharmacology, Nims University Jaipur, Rajasthan, India

Abstract
Introduction:
Recent research has placed a strong emphasis on the role that mitochondria play, not only in renal function but also in renal damage. There is a strong correlation between poor mitochondrial quality control mechanisms and the advancement of diabetic renal damage. These processes include mitochondrial fusion, fission, and mitophagy. The present study was done to evaluate the renoprotective role of hesperidin against diabetic nephropathy (DN) by utilizing streptozotocin (STZ) induced DN in rat model.

Methods & Materials:
The study comprised of 60 Sprague-Dawley rats (6 group having 10 animals in each group) . Diabetes was induced by single intraperitoneal STZ injection (dissolved in ice cold citrate buffer pH-4.5, at dose of 55 mg/kg). After the confirmation of diabetes, animals were administered with hesperidin at three doses (low dose-20, mid dose-50, and 100 mg/kg b.w. p.o.) for 21 days. After 21 days animals were sacrificed and assessed for various biochemical analysis of serum (Creatinine and BUN) and urine (Albumin, Urea and Creatinine) for renal functional parameters and histopathological evaluation (prohibitin (PHB) and NIX) for renal ultrastructure. In addition, renal cortex and mitophagy protein (SIRT1,PGC-1α, and TFAM) were using western blot to decipher the molecular mechanisms of hesperidin.

Results:
Hesperidin ameliorated albuminuria and enhanced the renal function as indicated significant improvement in urinary creatinine and urea levels in a dose dependent manner. Hesperidin administration positively modulates mitophagy.

Conclusion:
The overall findings suggest that the hesperidin provides renoprotective action against STZ induced kidney damage and could serve as potential molecule for further clinical investigation.

Keywords：Diabetic Nephropathy; renal function; Mitophagy

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0091
Abstract Submission No.：APCN20250648

Magneto-Primed Soybean (Glycine max) Extract Enriched with Isoflavonoids Restores Insulin and Kidney Function through DPP-IV and SGLT-2 Inhibitions in a Diabetic Kidney Disease Model

Anand Krishna Singh[1]; Purnima Tripathi[1]
[1] Department of Life Science/Biotechnology, Shri Vaishnav Institute of Science, Shri Viashnav Vidyapeeth Vishwavidyalaya, Indore, Madhya Pradesh India

Abstract
Introduction: Diabetic kidney disease (DKD), a serious complication of diabetes, affects nearly 40% of diabetic patients and often progresses to chronic kidney disease (CKD) or end-stage renal disease (ESRD), necessitating dialysis or kidney transplantation. Dipeptidyl peptidase IV (DPP-IV) and Sodium-glucose co-transporter-2 (SGLT-2) inhibitors have demonstrated promising effects in mitigating diabetic complications by reducing oxidative stress, improving cardiovascular function, and enhancing GLP-1 receptor (GLP-1R) signalling. This study investigates the therapeutic efficacy of an isoflavonoid-rich fraction derived from magneto-primed soybean extract, a natural source of DPP-IV and SGLT-2 inhibitors, in restoring insulin sensitivity and kidney function in a DKD rat model
Methods: A diabetic kidney disease (DKD) model was established in rats by administering streptozotocin (40 mg/kg) in combination with a high-fat diet. Comprehensive assessments including biochemical, toxicological, and histopathological analyses were performed, with a focus on the inhibition of SGLT-2 and DPP-IV. Key biomarkers evaluated included HbA1c, serum insulin, GLP-1, and phosphorylated eIF2α, alongside oxidative stress markers such as AMPK, PPARα, SOD, CAT, and GSH. Renal function was assessed through serum creatinine, blood urea nitrogen (BUN), cystatin C, and the albumin-to-creatinine ratio. Additionally, serum lipid profiles and inflammatory mediators (TNF-α, IL-6, and adiponectin) were analysed. Histological examination of kidney tissues was conducted to corroborate biochemical findings
Result: Diabetes induction was confirmed by elevated HOMA-IR (2.8%) and reduced HOMA sensitivity (43.9%). In vivo analysis demonstrated significant inhibition of SGLT-2 ($63.5 \pm 2.7\%$) and DPP-IV ($69.3 \pm 3.8\%$) following treatment. These effects were associated with activation of AMPK and PPARα pathways, suppression of p-eIF2α expression, and significant ($P < 0.05$) improvements in renal function, insulin sensitivity, HbA1c, triglyceride and cholesterol levels, and oxidative stress markers when compared to the DKD control group. The extract also enhanced antioxidant defense, reduced lipid peroxidation, improved renal histoarchitecture, and lowered proinflammatory cytokines, indicating its broad therapeutic efficacy
Conclusion: The isoflavonoid-rich fraction of magneto-primed soybean extract demonstrates significant therapeutic potential in the management of diabetic kidney disease (DKD) by enhancing renal function, reducing inflammatory responses, and improving insulin sensitivity, supporting its candidacy for further clinical evaluation.

Keywords：Diabetic kidney disease , Magneto-Primed Soybean, end-stage renal disease, Dipeptidyl peptidase IV Inhibitor, Sodium-glucose co-transporter-2 Inhibitor.

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0092
Abstract Submission No.：APCN20250660

Early protective effects of N-acetylcysteine on mitochondrial and redox regulation in a 5/6Nx-induced cardio-renal syndrome type IV.

Omar Emiliano Aparicio Trejo[1]; Karen Peralta-Buendia[1]; Belén Cuevas-López[1]; Fernando E. García-Arroyo[1]; Miriam Díaz-Rojas[2]; Alejandro Silva-Palacios[3]; Edilia Tapia[1]; José Pedraza-Chaverri[4]; Laura Gabriela Sánchez-Lozada[1]

[1] Department of Cardio-Renal Physiology, National Institute of Cardiology Ignacio Chávez, Mexico 14080, Mexico.

[2] Division of Medicinal Chemistry and Phytochemistry, College of Pharmacy, The Ohio State University, 43210 Columbus Ohio, USA

[3] Laboratorio Department of Cardiovascular Biomedicine, National Institute of Cardiology Ignacio Chávez, Mexico City 14080, Mexico

[4] Laboratorio F-315, Departamento de Biología, Facultad de Química, Universidad Nacional Autónoma de Mé-xico, Mexico City 04510, Mexico

Abstract
The chronic kidney disease (CKD) is associated with an increased prevalence of cardiovascular dysfunction, like cardiorenal syndrome type IV (CRS-IV). Mitochondria are key regulators of cellular signaling and metabolism. Mitochondria proteins and regulatory factors of bioenergetic and biogenesis are sensitive to changes in redox status. The early imbalance in these mitochondrial processes in kidney and heart has been linked to CRS-IV development. Thus, therapeutic alternatives have been proposed to normalize this redox imbalance, particularly those involving the regulation of the mechanisms of the AMPK-Sirt1/3-PGC-1 α biogenesis pathway. On the other hand, N-acetylcysteine (NAC) is an antimucolytic capable of restoring redox balance. It has shown promise in preventing mitochondrial dysfunction in kidney and heart diseases. However, the understanding of the role of NAC in mitochondrial modulation and interaction with the AMPK-Sirt1/3-PGC-1 α pathway in the context of CRS-IV is still limited.
Experimental design: The model consisted of 4 groups of male Wistar rats (n=6), weighing 230-250 g. Sham. They underwent sham surgery and administered only 300 mM NaHCO3 intragastrical. Nx. Corresponds to the rats that underwent nephrectomy surgery 5/6 and. NAC+Nx. They received pretreatment (2h) with 300 mg/kg/day NAC intragastrical, then they will undergo the Nx5/6 surgical intervention. NAC. Administered only with NAC. The animals evolved for a period of 10 days after surgery.
Our result showed that NAC pre-administration decrease the Nx induced increase in renal and cardiac damage markers, as well as the inflammatory and uric acid cardio-renal mediators in plasma. NAC+NX group also improves fractional shortening (FS) and the ejection fraction (EF). Regarding stroke volume (SV) and end-systolic volume (ESV), NAC pretreatment improved both parameters to values like those in Sham. Similarly, pretreatment with NAC prevented alterations in all respiratory parameters in mitochondria isolated from kidney and heart, implying an OXPHOS capacity restore in both organs. In kidney tissue, these protective effects can be attributed to CI and CIII protection. Meanwhile, in the heart, CI activity is preserved. Interestingly, NAC effects were also related to the Sirt1/3- PGC-1α pathway overactivation and mitochondrial ROS regulation, proposing that mitochondrial biogenesis induction and redox regulation in early stages after renal damage is strategy to prevent the bioenergetic alteration in kidney and heart, that lead to inflammation and CRS-4 development
Keywords：Cardio-renal syndrome type 4; nephrectomy; N-acetylcysteine and mitochondria bioenergetics; mitochondrial redox regulation

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0093
Abstract Submission No.：APCN20250707

Identification of Repurposed Drug Candidates for Diabetic Nephropathy Using Network Pharmacology and Machine Learning

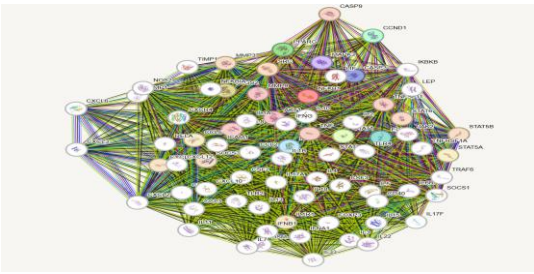
Putrya Hawa[1]

[1] Department of Clinical Pharmacology, Faculty of Military Medicine, Indonesia Defense University, Indonesia

Abstract

Diabetic nephropathy (DN) is a leading cause of end-stage renal disease globally. Despite therapeutic advances, many patients continue to experience renal decline, highlighting the need for new treatment strategies. This study combines network pharmacology and machine learning to systematically identify repurposed drug candidates for DN. Multiple transcriptomic datasets from the Gene Expression Omnibus (GEO) were curated and analyzed. Differential expression and co-expression analyses were conducted, followed by construction of protein-protein interaction (PPI) networks to pinpoint key molecular targets. Machine learning models prioritized these targets based on network topology and gene expression features. Molecular docking simulations evaluated the binding affinities of four candidate drugs—pentoxifylline, bardoxolone methyl, finerenone, and niclosamide—against prioritized targets. Five hub genes (AKT1, TNF, EGFR, MMP9, and NFKB1) were identified as central players in DN pathogenesis. Both Random Forest and Support Vector Machine classifiers achieved robust predictive performance (ROC-AUC > 0.90). Docking studies revealed stable, high-affinity interactions between candidate drugs and targets. Supported by clinical evidence, these findings highlight promising repurposed drugs for DN therapy

Keywords：diabetic nephropathy, drug repurposing, machine learning, network pharmacology



Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0094
Abstract Submission No.：APCN20250709

Multitarget Disruption of the β₂GPI/TNF-α/JAK2 Axis by Azomethine-clubbed Thiazoles Derivatives: A Pharmacoinformatic Strategy to Attenuate Immune-Mediated Inflammation in Diabetic and Hypertensive Kidney Disease

Rizki Rachmad Saputra[1]; Muhammad Priyadi[2]

[1] Department of Chemistry, Universitas Palangka Raya, Palangka Raya, Indonesia

[2] Department of Pharmacy, Universitas Palangka Raya, Palangka Raya, Indonesia

Abstract

Introduction: Chronic kidney diseases associated with metabolic syndrome, such as diabetic kidney disease (DKD) and hypertensive nephropathy, involve persistent immune activation, oxidative stress, and cytokine-driven vascular injury. β₂-glycoprotein I (β₂GPI) promote immune complex formation in response to oxidized LDL, contributing to endothelial dysfunction and glomerular damage. TNF-α, a pro-inflammatory cytokine, amplifies renal inflammation and activates the JAK2/STAT pathway, leading to mesangial proliferation and progressive fibrosis. This study aims to identify azomethine-clubbed thiazoles derivatives as multitarget inhibitors of the β₂GPI/TNF-α/JAK2 axis, leveraging pharmacoinformatic tools to propose a novel therapeutic strategy for metabolic kidney inflammation.

Methods: Seven azomethine-clubbed thiazoles were evaluated via molecular docking against β₂GPI (PDB: 1C1Z), TNF-α (PDB: 2AZ5), and JAK2 JH1 (PDB: 6VN8). ADMET profiling using SwissADME and pkCSM predicted drug-likeness, pharmacokinetics, and toxicity. β-Cyclodextrin inclusion complex modeling was performed to assess formulation feasibility and solubility enhancement.

Results: Three azomethine-clubbed thiazoles (3a, 3d, and 3h) exhibited strong multitarget inhibition, with binding affinities ranging from –5.1 to –9.1 kcal/mol. Notably, compound 3a demonstrated the highest affinity for JAK2 JH1 (–9.1 kcal/mol), suggesting effective inhibition of cytokine-mediated inflammation, while binding to β₂GPI (–6.1 to –5.7 kcal/mol) and TNF-α (–8.0 to –7.0 kcal/mol) indicates potential to suppress cytokine cascades and vascular inflammation in renal tissues. ADMET profiling revealed high intestinal absorption (90.26–92.8%), no Lipinski violations, and low blood-brain barrier permeability (–0.423 to 0.256 log BB), supporting oral bioavailability and systemic safety. β-Cyclodextrin complexation predicted enhanced solubility, mitigating a key limitation in drug formulation. These findings position azomethine-conjugated thiazoles as promising dual-action immunomodulators.

Conclusions: Azomethine-clubbed thiazoles derivatives demonstrate multitarget inhibition of β₂GPI, TNF-α, and JAK2, key players in immune-metabolic inflammation underlying diabetic and hypertensive kidney disease. This pharmacoinformatic approach offers a novel scaffold for immunomodulatory therapy targeting the intersection of oxidative stress, cytokine signaling, and endothelial dysfunction.

Keywords：Diabetic kidney disease, Immunoinflammation, Azomethine-clubbed thiazoles Derivatives

GENERAL PROFILES			
Molecules/Pubchem ID	**3a**	**3d**	**3h**
MW	325.38	275.33	312.39
Binding Affinity			
β2GPI (kcal/mol)	-6.1	-5.7	-5.1
TNF-α (kcal/mol)	-8.0	-7.0	-7.1
JAK2 JH1 (kcal/mol)	-9.1	-7.6	-8.0
LIPOPHILICITY			
Log P (octanol-water solubility test)	3.96	2.8	3.12
Consensus Log P	3.38	2.36	3.01
PHARMACOKINETICS			
BBB Permeability (log BB)	-0.407	-0.423	0.256
CYP1A2 inhibitor	yes	yes	yes
Intestinal Absorption (Human) (% Absorbed)	90.26	90.57	92.8
Total Clearance (log ml/min/kg)	0.285	0.284	0.19
DRUGLIKENESS			
Lipinski #violations	0	0	0
Bioavailability Score	0.55	0.55	0.55
MEDICINAL CHEMISTRY			
Leadlikeness #violations	1	0	1
Synthetic Accessibility	3.25	3.04	3.24
TOXICITY			
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.22	2.34	2.64

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0095
Abstract Submission No.：APCN20250723

Levels of Matrix Metalloproteinase-9 at Various Degrees of Albumin-Creatinine Ratio in Patients with Type 2 Diabetes Mellitus with Nephropathy

NAMIRA AMANDA. G.[1]; Elfiani E[2]; Suhaimi N[3]; Ali Z[3]; Effendi I[3]; Slamet S[3]; Abdillah N[2]; Rery TF[2]; Elvia O[1]; Julita E[2]

[1] General Practitioners of Raden mattaher Hospital Jambi, Indonesia

[2] Resident of Internal Medicine Subspecialty Program in Nephrology and Hypertension, Faculty of Medicine, Sriwijaya University/Dr. Mohammad Hoesin Hospital, Palembang, Indonesia

[3] Staff of the Nephrology and Hypertension Division, Department of Internal Medicine, Faculty of Medicine, Sriwijaya University/Dr. Mohammad Hoesin Hospital, Palembang, Indonesia

Abstract

Introduction : Diabetic Nephropathy is a microvascular complication in patients with Diabetes Mellitus. The risk of kidney failure in nephropathy, according to KDIGO, is classified based on the level of albuminuria. The classification of kidney failure risk based on ACR is divided into three categories: A1 is normal (ACR <30 mg/g), A2 is microalbuminuria (ACR ≥ 30-299 mg/g), and A3 is macroalbuminuria with an ACR value ≥ 300 mg/g. Matrix Metalloproteinase-9 (MMP-9) is a cytokine in the blood that increases in response to cell damage, such as the destruction of podocyte slit diaphragms in the kidneys. The aim of this study is to determine whether the levels of matrix metalloproteinase-9 also increase at various degrees of ACR values based on the criteria established by KDIGO.

Methods: This research was an observational analytic study using a cross sectional approach. Sampling using nonprobability sampling techniques in consecutive sampling with respondents of type 2 diabetes mellitus patients with nephropathy totaling 30 people.

Results: The average ACR level in the A1 category was 14.86 ± 7.41 mg/g and 59.85 ± 43.09 mg/g in the A2 category and in the A3 category was 2074.74 ± 1721.62 mg/g. In A1, the average levels of MMP-9 are 634.87 ± 178.13 ng/ml and respectively the average levels of MMP-9 A2 and A3 are 730.30 ± 151.59 ng/ml and 2876.33 ± 1826.87 ng/ml with a value of p = 0,000.

Discussion : The recommended urine test for detecting albuminuria is the Albumin Creatinine Ratio (ACR) test. Metalloproteinase-9 (MMP-9) activity causes damage to the podocyte diaphragm gap which will trigger the development from microalbumnuria to macroalbuminuria.

Conclusion: There is a significant difference in matrix metalloproteinase-9 levels between group A1 & A3, as well as between group A2 & A3.

Keywords：Diabetic Nephropathy, Albumin Creatinine Ratio, Matrix Metalloproteinase-9

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0096
Abstract Submission No.：APCN20250733

5-lipoxygenase inhibition ameliorates diabetic kidney disease by attenuating proximal tubular cell ferroptosis

Min Heui Ha[1]; Hyun-Ju An[1]; Min-Ji Sung[1]; Ha-Jin Yi[1]; Hye Yun Jeong[1]; Jihyun Baek[1]; So-Young Lee[1]; Yu Ho Lee[1]

[1] Division of Nephrology, Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea

Abstract

The enzyme 5-lipoxygenase plays a pivotal role in the conversion of arachidonic acid into 5-hydroperoxyeicosatetraenoic acid (5-HPETE), which is a key source of lipid peroxides and leukotrienes. This study aims to elucidate the pathophysiological implications of 5-lipoxygenase in diabetic kidney disease (DKD), focusing on its impacts on lipid peroxidation and tubular cell ferroptosis. HKC-8 cells, a human-derived renal proximal tubular cell line, was used to perform in vitro experiments. Diabetes was induced in male wild-type C57BL/6J mice and proximal tubular epithelial cell-specific 5-lipoxygenase knockout mice by streptozotocin injection. Zileuton was administered to inhibit 5-lipoxygenase activity. Analysis of 5-lipoxygenase expression in human diabetic kidney disease was performed using the Nephroseq open database. Hyperglycemic stimuli upregulated the expression of 5-lipoxygenase both in HKC-8 cells. The overexpression of 5-lipoxygenase aggravated hyperglycemia-induced increases in the expression of profibrotic cytokines and reactive oxygen species (ROS) production, while its suppression mitigated these detrimental effects. High glucose also led to downregulations of glutathione peroxidase 4 (GPX4) and upregulations of Acyl-CoA synthetase long chain family member 4 (ACSL4), ferritin heavy chain 1 (FTH-1), and malondialdehyde (MDA), indicating the activation of pro-ferroptotic pathways. The overexpression of 5-lipoxygenase exaggerated hyperglycemia-induced ferroptotic cell death, which is attenuated by the inhibition of 5-lipoxygenase or ferrostatin-1 treatment . Additionally, streptozotocin-induced diabetic mice exhibited worse kidney function and interstitial fibrosis in association with decreased GPX4 and increased ACSL4 and FTH-1 levels compared to normoglycemic mice. Zileuton administration and proximal tubular cell-specific deletion of 5-lipoxygenase significantly ameliorated hyperglycemia-induced kidney dysfunction and ferroptosis activation. These findings demonstrate the central role of 5-lipoxygenase in intracellular lipid peroxidation and subsequent tubular cell ferroptosis under sustained hyperglycemic conditions. Inhibition of 5-lipoxygenase not only mitigates ferroptotic tubular cell death but also alleviates hyperglycemia-induced renal dysfunction. This suggests that 5-lipoxygenase could serve as a potential therapeutic target for the treatment of DKD.

Keywords：Diabetic kidney disease, Ferroptosis, lipid peroxidation, 5-lipoxygenase, fibrosis

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0097
Abstract Submission No.：APCN20250742

High glucose–induced oxidative stress impairs podocyte cytoskeletal integrity and mechanical adaptation

LU YUHSIEN[1]; Bo-Yan Chen[1]; Hsiao-Hui Lee[1]
[1] Department of Life Sciences and Institute of Genome Sciences, National Yang Ming Chiao Tung University, Taiwan

Abstract
Diabetic kidney disease (DKD) is the leading cause of end-stage renal failure (ESRD) in Taiwan and worldwide. It is characterized by a progressive decline in renal function accompanied by albuminuria, with podocyte injury playing a central role. Podocytes, specialized glomerular epithelial cells, are crucial for maintaining the structure and function of the glomerular filtration barrier (GFB). Numerous studies have highlighted hyperglycemia and filtration mechanical stress as two key risk factors contributing to podocyte injury in the pathogenesis of DKD. However, our understanding of the interplay between these two factors in podocytes remains limited. In this study, we utilized conditionally immortalized mouse podocytes, induced to differentiate in vitro, to investigate the mechanisms underlying high glucose-induced podocyte injury. We demonstrated that high glucose treatment significantly reduced the formation of focal adhesions (FAs) and stress fibers in podocytes. Additionally, we observed an increase in cellular reactive oxygen species (ROS) and mitochondrial oxidation levels induced by high glucose. Co-treatment with antioxidants effectively reduced oxidative stress and cytoskeletal damage caused by high glucose exposure. Furthermore, we found that the mechanical responses of podocyte monolayers to filtration stimulation, including the strengthening of cell adhesion and cytoskeletal structures, were compromised, resulting in monolayer leakage. Taken together, our findings suggest that high glucose-induced elevated oxidative stress may reduce the biophysical resilience of podocytes by impairing cytoskeletal rearrangements required for adaptation to filtration-induced mechanical stress.

Keywords：podocyte injury, high glucose, oxidative stress, cytoskeleton, Filtration

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0098
Abstract Submission No.：APCN20250771

Artificial Intelligence aided discovery of Novel Pyrazole Derivative (PD421) inhibits hyperglycaemia-induced kidney fibrosis via the miRNA-34a-5p/SIRT1 signalling pathway

Dr. Amitabh Tripathi[1]; Hans Raj Bhat[2]; Udaya Pratap Singh[1]

[1] Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, India

[2] Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, India

Abstract

Introduction:
Renal fibrosis is the excessive accumulation of extracellular matrix in the kidneys, leading to scarring and loss of function. It results from chronic kidney injury caused by hypertension, diabetes, infections, or autoimmune diseases. The available current treatment options are insufficient to curb the menace of the disease. Thus, in the present work, we have adopted artificial intelligence techniques to develop a novel molecule that can be used to inhibits hyperglycaemia-induced kidney fibrosis.

Methods:
We utilized de novo design algorithms based on deep learning to virtually screen over 2 million molecules, evaluating them based on physicochemical properties, docking scores, and interaction energy. The most promising compound, a pyrazole derivative (PD421), was selected. Biomarker levels, including serum and urine creatinine and urine protein expression, were analyzed in diabetic kidney disease (DKD) mice. Additionally, the expression of miRNA-34a-5p, SIRT1, and fibrosis-related molecules (TGF-β, CTGF, and α-SMA) was assessed in renal tissue using qPCR and Western blot analysis. The toxicity and pharmacokinetics of PD421 were also evaluated.

Results:
We developed an AI-based model to predict molecular bioactivity, identifying PD421 as a potential therapeutic for diabetic kidney disease. PD421 significantly reduced urine protein expression and creatinine levels in both serum and urine, indicating improved kidney function. Further analysis showed that miRNA-34a-5p was upregulated in DKD mice and primarily localized in the nucleus. PD421 treatment effectively downregulated miRNA-34a-5p by modulating SIRT1, TGF-β, CTGF, and α-SMA expression, suggesting its potential to mitigate renal fibrosis and disease progression.

Conclusion:
Our study identified PD421, through an AI-based model, which improves kidney function by reducing key biomarkers and modulating SIRT1 expression. Its ability to downregulate miRNA-34a-5p suggests potential therapeutic value in mitigating renal fibrosis and disease progression.

Keywords：Renal fibrosis, miRNA, pyrazole, deep learning

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0099
Abstract Submission No.：APCN20250782

Effects of Suppressed Indoxyl Sulfate Production on Cardiorenal Crosstalk in Sulfotransferase 1a1-Deficient Mice

Aina Sugiura[1]; Kaito Makise[1]; Yuki Narita[2]; Yutaka Kakizoe[3]; Yuichiro Izumi[3]; Takashige Kuwabara[3]; Takashi Minami[1]; Yuichiro Arima[4]; Kenichi Tsujita[5]; Hirofumi Jono[6]; Hideyuki Saito[6]

[1] Department of Clinical Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan

[2] Department of Pharmacy, Sojo University, Kumamoto Japan

[3] Department of Nephrology, Kumamoto University, Kumamoto, Japan

[4] Laboratory of Developmental Cardiology, Kumamoto University, Kumamoto, Japan

[5] Department of Cardiovascular Medicine, Kumamoto University, Kumamoto, Japan

[6] Department of Pharmacy, Kumamoto University Hospital, Kumamoto, Japan

Abstract

Introduction: Chronic kidney disease (CKD) is a major risk factor for cardiovascular disease (CVD), with CVD mortality increasing as renal function declines. However, the mechanism underlying CVD in CKD patients remains unclear. Indoxyl sulfate (IS), a sulfate-conjugated uremic toxin is generated exclusively in the liver by the enzymes CYP2A6/2E1 and Sulfotransferase (SULT)1A1. Systemic accumulation of IS has been reported as a risk factor for cardio-renal disease development in CKD patients. In this study, we focused on IS and investigated cardiac pathological alterations in a model of kidney and heart damage using Sult1a1-deficient (Sult1a1-/-) mice, to determine whether restricted IS production could prevent these alterations.

Methods: C57BL/6J (WT) and Sult1a1-/- mice were used to create an ANS model by angiotensin II administration, nephrectomy, and saline drinking. Mice were sacrificed 4 weeks after treatment, and blood and tissue samples were collected. Blood pressure was measured before sacrifice. Serum IS levels were quantified by LC-MS/MS. Heart tissues were analyzed for heart failure markers and oxidative stress genes by RT-qPCR and subjected to RNA sequencing.

Results: WT-ANS mice increased serum and kidney IS concentrations, while Sult1a1-/--ANS mice maintained significantly lower IS levels (WT vs Sult1a1-/-: 12.50±4.14 vs 3.21±2.24μM in serum). WT-ANS mice showed increased blood pressure compared to Sult1a1-/--ANS mice (systolic: 174.76±30.17 vs 134.03±16.84mmHg; diastolic: 141.20±13.14 vs 105.33±17.91mmHg). WT-ANS mice developed cardiomyocyte hypertrophy and pulmonary edema, while Sult1a1-/--ANS mice showed attenuated changes. Both mice showed elevated heart failure marker BNP, but Sult1a1-/--ANS mice maintained lower expression of other markers (ANP, Atp2a2, Rcan1) than WT-ANS mice. NOX4 mRNA expression, an IS-inducible oxidative stress marker, increased in WT-ANS mice but remained suppressed in Sult1a1-/--ANS mice. We performed RNA sequencing of cardiac tissue. This analysis revealed significant upregulation of fibrosis-related genes (Clip, Comp, Ltbp2) in WT-ANS mice, a change that was largely absent in Sult1a1-/--ANS mice. Through RNA sequencing analysis, we identified FoxM1 as a potential upstream regulator that strongly correlates with these fibrosis markers. Since FoxM1 regulates Ace expression, we examined their relationship and found that both FoxM1 and Ace were highly expressed in WT-ANS mice but suppressed in Sult1a1-/--ANS mice. Furthermore, both FoxM1 and Ace expression showed strong positive correlations with Nox4. This suggests the existence of a potential Nox4-FoxM1-Ace axis in IS-induced cardiac damage.

Conclusion: Sult1a1 deficiency prevented heart failure through reduced IS accumulation. This

prevention was associated with suppressed NOX4 expression and reduced FoxM1-Ace expression. Therefore, suppressing IS accumulation may prevent cardiac pathology in renal failure.

Keywords：cardiorenal, indoxyl sulfate

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0100
Abstract Submission No.：APCN20250790

Renoprotective Efficacy of 2β-Hydroxybetulinic Acid 3β-Oleiate from Euryale ferox in Experimental Diabetic Nephropathy.

Danish Ahmed[1]; Mohd. Ibrahim Khan[1]
[1] Department of Pharmaceutical Sciences, Faculty of Health Sciences, Sam Higginbottom University of Agriculture, Technology and Sciences (SHUATS), Prayagraj, Uttar Pradesh, INDIA

Abstract
Introduction: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease worldwide, characterized by progressive renal dysfunction, glomerular hypertrophy, and extracellular matrix accumulation. The search for safe and effective nephroprotective agents remains a critical priority. Euryale ferox Salisb., traditionally used in Asian medicine, has demonstrated antidiabetic and antioxidant activities. This study investigates the efficacy of 2β-hydroxybetulinic acid 3β-oleiate (HBAO), a triterpenoid derivative isolated from Euryale ferox, in mitigating diabetic nephropathy in experimental models.

Methods: 2β-hydroxybetulinic acid 3β-oleiate (HBAO) was isolated and characterized using spectroscopic techniques. Streptozotocin-induced diabetic rats were administered HBAO at graded doses for 8 weeks. Biochemical parameters, including blood glucose, serum creatinine, blood urea nitrogen, and urinary albumin excretion, were evaluated. Renal oxidative stress markers (MDA, SOD, catalase) and pro-inflammatory cytokines (TNF-α, IL-6) were assessed. Histopathological analysis of kidney tissue was performed to evaluate structural changes.

Results: 2β-hydroxybetulinic acid 3β-oleiate (HBAO) treatment significantly reduced hyperglycemia and improved renal function parameters compared to untreated diabetic controls ($p<0.05$). Oxidative stress was markedly attenuated, evidenced by reduced malondialdehyde levels and restoration of antioxidant enzymes. Furthermore, HBAO downregulated pro-inflammatory cytokine expression and ameliorated glomerular and tubular structural damage, as confirmed by histopathology.

Conclusion: The findings suggest that 2β-hydroxybetulinic acid 3β-oleiate (HBAO) isolated from Euryale ferox Salisb. confers significant renoprotective effects in diabetic nephropathy, likely mediated through its antioxidative and anti-inflammatory actions. HBAO could be a promising phytotherapeutic candidate for managing diabetic kidney disease.

Keywords：2β-hydroxybetulinic acid 3β-oleiate , Euryale Ferox Salisb, Diabetic Nephropathy

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0102
Abstract Submission No.：APCN20250975

Phytosynthesized Silver Nanoparticles from Albizia lebbeck Bark Attenuate Type 2 Diabetes and Diabetic Nephropathy in a Streptozotocin Induced Rat Model

MOHD. IBRAHIM KHAN[1]; DANISH AHMED[1]; SAIF M.S. ANSARI[2]; HIMANSHU PATEL[1]

[1] Department of Pharmaceutical Science, FHS, Sam Higginbottom University of Agriculture Technology and Sciences (SHUATS), Prayagraj, India

[2] Faculty of Health Sciences, Sam Higginbottom University of Agriculture Technology and Sciences (SHUATS), Prayagraj, India

Abstract

Introduction

Diabetes, a chronic metabolic disorder with rising global prevalence, leads to persistent hyperglycemia and oxidative stress, damaging key organs, especially the kidneys. Diabetic nephropathy, a major cause of chronic kidney disease (CKD), results in progressive renal dysfunction and contributes significantly to diabetes related mortality. Silver nanoparticles (AgNPs) exhibit renoprotective potential due to their antioxidant, anti-inflammatory, and cytoprotective properties, which help reduce oxidative stress, regulate insulin-glucose balance, and preserve kidney structure. Albizia lebbeck, a traditional medicinal plant with antioxidant, anti-inflammatory, and mast cell-stabilizing effects, offers a green route for AgNPs synthesis. This study explores the efficacy of Albizia lebbeck mediated AgNPs in treating type 2 diabetes mellitus (T2DM) and preventing CKD in a streptozotocin (STZ) induced diabetic rat model.

Methods

We investigated the therapeutic effects of both plain and silver nanoparticles (AgNPs) synthesized from Albizia lebbeck bark extract in a rat model of type 2 diabetes mellitus (T2DM). The study included seven groups of six rats each, comprising normal, diabetic, and standard control groups, along with four treatment groups that received low and high doses of the plain extract and its AgNP form for 3 weeks. Primary outcomes assessed included glycemic regulation and markers of kidney and heart function.

Results

Both the plain extract and AgNPs derived from Albizia lebbeck effectively reduced albuminuria and helped slow CKD progression in T2DM subjects. However, the group treated with the nanoparticle formulation demonstrated greater improvements, including a more pronounced reduction in blood glucose levels, albuminuria, and body weight compared to those receiving the plain extract. Furthermore, the incidence of cardiovascular events particularly myocardial infarction was hypothesized to be lower in the AgNPs treated group than in the control group.

Conclusion

A silver nanoformulation of Albizia lebbeck exhibited enhanced cardio-renal protection compared to the plain extract, with greater reductions in albuminuria and improved kidney function. By targeting glucose metabolism and glomerular hyperfiltration, this nanoformulation offers a promising therapeutic approach for managing T2DM-CKD, highlighting the need for further long-term studies to validate its efficacy.

Keywords： Albizia lebbeck; Diabetes; CKD; Nanoformulations

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0103
Abstract Submission No.：APCN20250989

Network pharmacology and biblometric studies of Chlorogenic acid and it fabricated gold nanoparticles ameliorate STZ- and high fat diet induced diabetic nephropathy via targeting EGFR/AKT/GSK3β Signaling

DeepikaSingh[1]
[1] Department of Pharmaceutical Sciences, SIHAS

Abstract
Introduction: The most common problem associated with diabetes is diabetic nephropathy, which is the leading cause of end-stage renal diseases. Chlorogenic acid has various therapeutic properties, such as antibacterial, antiviral, diabetes, antioxidant, and inhibiting fibrosis. The goal of this study is to create gold nanoparticles that contain chlorogenic acid and to examine how they work using network pharmacology and preclinical studies.
Method: Gold nanoparticles of Clorogenic acid were prepared using green synthesis method and characterized by different instrumentation. Affinity between hub protein and CA were measured by molecular docking process, Analysis of overlapping genes of diabetes nephropathy and chlorogenic acid were established by network pharmacology and hub pathway was analysed by the help of KEGG and Gene ontology. STZ and HFD were given to rats for the induction of diabetes nephropathy and CA and AuNPs-CA (3, 6 and 9 mg/kg b.w.) were administered to diabetic rats. Tissue and blood sample were used to measure biochemical and molecular profile and western blot analysis for detection of protein related expression.
Result: SEM studies showed particle size ranged from 60 to 153 nm and zeta potential of good value. Network pharmacology showed the multitarget and multi pathway features of CA for diabetes nephropathy therapy. In the overlapping genes for CA and diabetes nephropathy EGFR was found to be as hub gene. Preclinical studies show that AuNPs-CA improves level of glucose tolerance, creatinine, urine microprotein and albumin level catalase, total antioxidant capacity glomerular filtration rate, kidney weight, MDA, urine level of potassium, sodium albumin and glucose, fractional excretions of potassium and sodium and proinflammatory cytokines and mediators. CA and AuNPs-CA could obstruct EGFR/PTRF protein expression levels and modulates AKT/GSK-3β signaling pathway.
Conclusion: In short, AuNPs-CA can be used as potential therapeutic agent in the treatment of the diabetes nephropathy.

Keywords：Gold Nanoparticles, Diabetes nephropathy, chlorogenic acid, AKT/GSK-3β signaling pathway.

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0104
Abstract Submission No.：APCN20251026

Urinary Post-Translationally Modified Fetuin-A (uPTM-FetA) Change Following SGLT2 Inhibitors Treatment in Diabetic Patients

Han-En Wang[1]; Chih-Chien Sung[1]
[1] Division of Nephrology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Tawan, Attending Physician

Abstract
Background: Urinary post-translational modified Fetuin-A (uPTM-FetA) has recently been reported as a biomarker for kidney damage in diabetic patients, patients with chronic kidney disease, and kidney transplant recipients. Sodium-glucose cotransporter 2 (SGLT2) inhibitors provide the reno-protection effect to reduce albuminuria, but the change of uPTM-FetA after SGLT2 inhibitors in diabetic patients remains unknow. We aim to evaluate the longitudinal effect of SGLT2 inhibitors on changes of uPTM-FetA in diabetic patients.
Methods: We collected urine from eighty-eight diabetic patients before SGLT2 inhibitors and prospectively collected urine at 3 months (n=54), 6 months (n=54), and 12 months (n=56) after SGLT2 inhibitors. uPTM-FetA and albumin-to-creatinine ratio (UACR) were measured at each time point.
Results: We analyzed the association between the reduction change in UACR and uPTM-FetA from the baseline before SGLT2 inhibitors, and there were moderate correlations between the changes in uPTM-FetA and UACR with correlation coefficients of $r = 0.26$ ($p = 0.066$), $r = 0.33$ ($p = 0.014$), and $r = 0.32$ ($p = 0.018$) at 3, 6, and 12 months, respectively, especially statistically significant associations at 6 and 12 months, suggest long-term use of SGLT2 inhibitors reducing uPTM-FetA and albuminuria. We further stratified diabetics patients into the reduction group (>20% decrease) and the non-reduction group (<20% decrease) based on uPTM-FetA reduction from baseline: We identified that a higher proportion of patients in the uPTM-FetA reduction group achieved >20% UACR reduction compared to the non-reduction group, with rates of 53%, 66%, and 60% at time point of 3, 6, and 12 months, respectively.
Conclusion: Our findings suggest that uPTM-FetA may serve as a potential biomarker for monitoring therapeutic response about reduction of albuminuria in diabetic patients after SGLT2 inhibitors treatment.

Keywords：Biomarker, Urine PTM-Fetuin-A, Sodium-glucose cotransporter-2 (SGLT2) inhibitors, Diabetic nephropathy

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0105
Abstract Submission No.：APCN20251030

Selective Inhibition of Ketohexokinase-C Suppresses Renal Fructose Metabolism and Ameliorates Diabetic Kidney Disease.

Takuji Ishimoto[1]; Kentaro Imai[1]; Junichiro Hagita[1]; Genri Tagami[1]; Makoto Yamaguchi[1]; Hiroshi Kinashi[1]; Yasuhiko Ito[1]

[1] Department of Nephrology and Rheumatology, Aichi Medical University, Japan

Abstract

Introduction:

Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease worldwide. In diabetes, endogenous fructose is produced from glucose via the polyol pathway and metabolized by ketohexokinase (KHK), which has two isoforms: KHK-A and KHK-C. We previously demonstrated that excessive fructose metabolism exacerbates metabolic syndrome and DKD, and that global deletion of both isoforms protects against these conditions. Interestingly, deletion of KHK-A alone worsens renal injury, suggesting that KHK-A may exert a protective effect in the presence of KHK-C. However, the specific contribution of KHK-C to DKD progression remains unclear.

Methods:

To clarify the distinct roles of KHK isoforms, we generated a KHK-C knockout (KO) mouse line using CRISPR-Cas9 technology. Four groups—wild-type (WT), KHK-A KO, KHK-A/C double KO, and KHK-C KO mice—were compared. Diabetes was induced by five consecutive daily intraperitoneal injections of streptozotocin. Renal function, albuminuria, tubular injury markers (NGAL), renal histology, and inflammatory markers were assessed. Comprehensive metabolome analysis focusing on fructose metabolism and related pathways was conducted.

Results:

KHK-C KO mice showed higher serum fructose levels than WT and KHK-A KO mice but lower than KHK-A/C KO mice, indicating partial retention of fructose metabolism via KHK-A. Blood fructose-1-phosphate levels were reduced in KHK-C KO mice. KHK-A KO mice exhibited marked albuminuria and elevated urinary NGAL, while these were suppressed in KHK-C KO mice, indicating attenuation of tubular injury. Renal expression of CCL2 and F4/80 was also lower in KHK-C KO mice than in WT and KHK-A KO mice. KHK-A/C KO mice showed similar protective effects, suggesting that KHK-C plays a dominant detrimental role.

Conclusion:

Our results indicate that KHK-C–mediated fructose metabolism contributes directly to DKD progression, while KHK-A may have a protective role. Selective inhibition of KHK-C effectively suppresses harmful fructose metabolism and reduces tubular injury and inflammation in diabetic kidneys. Therefore, targeting KHK-C may represent a promising new therapeutic strategy for DKD.

Keywords：DKD, fructose, hetohexokinase

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0106
Abstract Submission No.：APCN20251049

Acrolein Promotes Renal Injury and Fibrotic Progression in a Mouse Model of Diabetic Kidney Disease

JUI-TING CHANG[1,2,3,4]; YU-MING KUO[5]; HSIANG-TSUI WANG[5,6,7]

[1] School of Medicine, Fu Jen Catholic University, NewTaipei City, Taiwan

[2] Division of Nephrology, Department of Internal Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei City, Taiwan

[3] Department of Nutrition, Shin Kong Wu Ho-Su Memorial Hospital, Taipei City, Taiwan

[4] Center of Quality Management, Shin Kong Wu Ho-Su Memorial Hospital, Taipei City, Taiwan

[5] Institute of Pharmacology, College of Medicine, National Yang Ming Chiao Tung University, Taipei City, Taiwan.

[6] Institute of Food Safety and Health Risk Assessment, National Yang Ming Chiao Tung University, Taipei City, Taiwan.

[7] Toxicology, Kaohsiung Medical University, Kaohsiung City, Taiwan.

Abstract

Background: Acrolein, a reactive aldehyde produced from lipid peroxidation and environmental sources, has been implicated in chronic inflammation and oxidative stress. However, its pathogenic role in diabetic kidney disease (DKD) remains insufficiently characterized.

Methods: To investigate the in vivo effects of acrolein on DKD progression, we established a murine model using male C57BL/6J mice fed a high-fat diet (HFD) and injected with streptozotocin (STZ) to induce diabetes. Experimental groups included: (1) HFD/STZ (HF), (2) HF with oral acrolein (2.5 mg/kg/day), (3) normal diet with acrolein alone, and (4) control group receiving normal diet and vehicle. Treatments were administered over 16 weeks. Metabolic profiles, renal function parameters, histopathology, immunohistochemistry, and Western blot analyses were conducted.

Results: Mice in the HF and HF+acrolein groups developed significant hyperglycemia and glucose intolerance. Acrolein alone did not alter glucose levels but induced insulin resistance and impaired insulin tolerance. Both the HF and HF+acrolein groups demonstrated elevated urine albumin-to-creatinine ratios (UACRs) and blood urea nitrogen (BUN), with the HF+acrolein group showing further deterioration in renal function. Notably, acrolein monotherapy also significantly increased UACR and BUN, suggesting nephrotoxicity independent of hyperglycemia. Histological analysis revealed glomerular atrophy, tubular disarray, and interstitial inflammation in acrolein-treated kidneys. Periodic acid–Schiff staining showed mesangial matrix expansion, while immunohistochemistry detected strong acrolein-protein conjugate signals in renal tissues. Western blot confirmed upregulation of acrolein and collagen I in the HF+acrolein and acrolein-alone groups.

Conclusion: This study demonstrates that acrolein exacerbates renal injury and fibrosis in DKD and can independently induce nephrotoxic effects even in the absence of diabetes. These findings highlight acrolein as a potential pathogenic mediator and therapeutic target in DKD, offering novel insights into environmental-metabolic interactions in renal fibrosis.

Keywords：Acrolein, Diabetic Kidney Disease, Renal Fibrosis, Urine Albumin-to-Creatinine Ratio, Insulin Resistance

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0107
Abstract Submission No.：APCN20250825

Infection Risk Associated with Transcatheter Aortic Valve Replacement (TAVR) and Transcatheter Mitral Valve Repair (TMVR) in Elderly with Cardiometabolic Disorder

Ester Marnita Purba[1,2]; Yesika Simbolon[1,4]; Wahyuni Kurniawati[1,3]; Rosinta Purba[1]; Hepri Ardianson[1]; Lintong Simbolon[1]

[1] The Pranala Institute

[2] Raff Tindal NT

[3] Incision Care

[4] Atmajaya University

Abstract

Background: Transcatheter aortic valve replacement (TAVR) and transcatheter mitral valve repair (TMVR) are transformative procedures for managing valvular heart disease in elderly patients, offering minimally invasive alternatives to traditional surgery. Despite their clinical success, post-procedural infections remain a critical complication, particularly in patients with underlying cardiometabolic disorders. This systematic review aims to synthesize existing evidence on infection risks associated with TAVR and TMVR in elderly patients, providing insights into predictors, risk factors, and prevention strategies.

Methods: The sample of elderly patients (≥65 years) with cardiometabolic disorders (diabetes, hypertension, obesity). A systematic review was conducted following PRISMA guidelines from PubMed, Scopus, and Cochrane Library. Infection risk was the primary outcome, defined as infections within 30 days to one-year post-procedure. Variables analyzed included procedure type (TAVR, TMVR), diabetes, chronic kidney disease (CKD), smoking, physical activity, and age. Meta-analysis using random-effects models determined odds ratios (ORs) and confidence intervals (CIs).

Results: Infection rates were notably higher among patients with diabetes (14.2%) compared to non-diabetic individuals (7.4%), highlighting the impact of compromised immune function and poor wound healing in diabetic populations. Smokers, who made up 25% of the sample, had an infection rate of 12.1%, exceeding the overall average and underscoring the detrimental effects of smoking on immune defenses. The highest infection rate was observed in patients with chronic kidney disease (CKD) at 16.3%, reflecting the heightened vulnerability due to systemic inflammation and immune dysfunction commonly associated with CKD. The overall pooled infection rate was 9.8% (TAVR: 10.5%; TMVR: 8.6%). Diabetes significantly increased infection risk (OR = 1.78, 95% CI: 1.45-2.19, $p < 0.001$), as did CKD (OR = 2.12, 95% CI: 1.67-2.69, $p < 0.001$). Smoking was also associated with higher infection risk (OR = 1.42, 95% CI: 1.10-1.84, $p = 0.005$), while physical activity was protective (OR = 0.81, 95% CI: 0.68-0.96, $p = 0.014$). TAVR patients exhibited higher infection rates than TMVR patients (OR = 1.25, 95% CI: 1.10-1.41, $p < 0.001$).

Conclusions: This systematic review highlights a significant infection risk associated with TAVR and TMVR, particularly among elderly patients with cardiometabolic disorders. Diabetes, chronic kidney disease, and advanced age are key predictors of post-procedural infections. Tailored pre- and post-procedural strategies are essential to mitigate infection risks, especially for high-risk patients.

Keywords：Infection Risk, TAVR, TMVR, Elderly, Cardiometabolic Disorders.

Group	Infection Rate (%)	Key Insights
TAVR	10.5%	Higher risk compared to TMVR
TMVR	8.6%	Lower overall infection rates
Diabetes	14.2%	Most significant predictor
CKD	16.3%	Highest infection rate among all groups
Smokers	12.1%	Smoking exacerbates infection risk
Physically Active	Lower than 9.8%	Protective factor against infection

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0108
Abstract Submission No.：APCN20251060

Renal Denervation and SGK1 Blockade Attenuate Renocardiac Syndrome in 5/6 Nephrectomy Rats

Hsin-Hung Chen[1]; Po-Ming Chen[2]; Yu-He Li[3]

[1] Department of Medical Education and Research, Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan

[2] Research Assistant Center, Show Chwan Memorial Hospital, Changhua City, Taiwan

[3] Department of Laboratory Medicine, Zuoying Armed Forces General Hospital, Kaohsiung City, Taiwan

Abstract

Introduction: Renocardiac syndrome (RCS), a manifestation of the bidirectional relationship between cardiac and renal dysfunction, poses significant challenges in clinical management due to its complex pathophysiology. This study investigated the molecular and physiological mechanisms underlying RCS, focusing on the role of serum and glucocorticoid-regulated kinase 1 (SGK1) and the therapeutic potential of renal denervation (RD) in mitigating RCS-associated complications. Using a 5/6 nephrectomy (Nx) rat model to induce RCS, we examined the effects of RD and SGK1 inhibition on hypertension, cardiac remodeling, metabolic disturbances, and neurohormonal activity.

Methods: The Nx rats exhibited increased systolic blood pressure (SBP), sympathetic nerve activity, and renal and cardiac structural changes, including glomerular sclerosis, left ventricular hypertrophy, and vascular remodeling. RD was applied to modulate sympathetic overactivity, while GSK650394, an SGK1 inhibitor, was used to assess the role of SGK1 in RCS. Histological analysis, Western blotting, and biochemical assays were conducted to evaluate changes in structural remodeling, inflammatory markers, metabolic parameters, and signaling pathways in the NTS and peripheral tissues.

Results: RD effectively reduced SBP, suppressed sympathetic hyperactivity, and downregulated SGK1 expression in the NTS at both mRNA and protein levels. Inflammatory cytokines, such as TNF-α, IL-6, and NF-κB, were significantly reduced by RD, highlighting its anti-inflammatory effects. Additionally, RD improved metabolic parameters, including fasting glucose and triglyceride levels, and decreased urine glucose, suggesting improved glucose metabolism. SGK1 inhibition via GSK650394 mitigated cardiac hypertrophy, reduced the phosphorylation of SGK1 at critical sites (e.g., pSGK1S78), and modulated downstream targets, including PDK1 and FOXO1A. However, SBP was not significantly altered by SGK1 inhibition, indicating that SGK1 primarily affects structural and metabolic pathways rather than hemodynamic regulation.

Conclusions: The combined findings highlight the intertwined roles of SGK1 and sympathetic overactivity in RCS. RD demonstrated therapeutic benefits by alleviating hypertension, inflammation, and metabolic dysfunction, while SGK1 inhibition reduced structural remodeling and metabolic disturbances. These findings suggest a complementary therapeutic approach targeting both sympathetic nerve activity and SGK1-associated molecular pathways, providing novel insights into the management of RCS and its associated complications.

Keywords：Renocardiac syndrome, Renal denervation, SGK1

Table 1. Metabolic characteristics and biochemical data from sham-operated (control), 5/6 nephrectomized (Nx), and Nx combined renal denervated (RD) in WKY rats.

Parameter	Sham	Nx	Nx+ RD
Fasting glucose (mg/dL)	101.00 ± 2.02	174.41 ± 7.47[a]	136.31 ± 4.13 [b]
dHDL (mg/dL)	101.67 ± 2.42	111.00 ± 3.3[a]	111.60 ± 1.81[a]
Triglyceride (mg/dL)	60.00 ± 1.91	93.63 ± 14.55[a]	57.10 ± 4.53 [b]
Cholesterol (mg/dL)	149.17 ± 5.48	143.38 ± 4.28	142.30 ± 4.13
Urine glucose (mg/dL)	20.17 ± 3.18	48.38 ± 20.47	17.9 ± 3.81

High-density lipoprotein (HDL) cholesterol. The values are presented as the means ± SEM, [a] $P < 0.05$ vs Ctrl, [b] $P < 0.05$ vs the Nx group.

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0110
Abstract Submission No.：APCN20251067

Efficacy and Safety of Subcutaneous Insulin versus Intraperitoneal Insulin Administration in The Treatment Of Patient with Diabetic Nephropathy on Peritoneal Dialysis An Evidence-Based Case Report

Derizal[1]; Roland Helmizar[2]

[1] IP Trisakti, South Jakarta City, Jakarta, Indonesia

[2] Internal Medicine, Baiturrahmah University, Padang City, Indonesia

Abstract

Objectives: Due to its high prevalence, diabetic nephropathy remains one of the most concerning complications of diabetes mellitus (DM). The acceptable glycemic control for the condition is insulin. Insulin therapy during peritoneal dialysis can be given through subcutaneous (SC) or intraperitoneal (IP). The use of intraperitoneal (IP) insulin in diabetic patients on peritoneal dialysis (PD) can restore glucose control to near normal values. The safety and efficacy of this method are unclear - thus questioning which administration of insulin type is more suitable for these patients.

Methods: Several databases (PubMed, Cochrane Library) were used to look for randomized clinical trials (RCTs), systematic review or meta-analysis studies with keywords of “subcutaneous insulin”, “intraperitoneal insulin”, “chronic kidney disease”, or “diabetic nephropathy” and “peritoneal dialysis”. Studies were appraised using Oxford 2004 therapy and meta-analysis appraisal checklists from Clinical Evidence-Based Medicine.

Results: Two eligible articles were found, one meta-analysis of non-RCT and one prospective cohort fulfilled the inclusion criteria and duplication screening. The meta-analysis of non-RCT showed that IP insulin provides adequate glycemic control, which appears superior to that seen following treatment with conventional SC insulin. The plasma lipids are adversely affected by IP insulin, possibly contributing to increased cardiovascular risk. Meanwhile, the cohort showed the advantages of intraperitoneal insulin administration including a more physiologic effect of insulin in patients with diabetic nephropathy during dialysis treatment. Major fluctuations of blood glucose, hyperinsulinemia, and the formation of insulin antibodies can be minimized.

Conclusions: Intraperitoneal insulin administration in the treatment of patients with diabetic nephropathy on peritoneal dialysis is still controversial and unclear. Data are limited and further studies are needed to assess the long-term safety of this approach.

Keywords：Subcutaneous Insulin, Intraperitoneal Insulin, Chronic Kidney Disease , Peritoneal Dialysis, Diabetic Nephropathy

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0111
Abstract Submission No.：APCN20251069

Comprehensive Analysis of Metabolic and Environmental Risk Factors Influencing the Prevalence of Diabetic Kidney Disease in Type 1 Diabetes Mellitus Patients in Indonesia: Insights from Multiple Regression Modeling

Derizal[1]; Roland Helmizar[2]; Siska Azizah[3]

[1] IP Trisakti, South Jakarta City, Jakarta, Indonesia

[2] Internal Medicine, Baiturrahmah University, Padang City, Indonesia

[3] Medicine, Baiturrahmah University, Padang City, Indonesia

Abstract

Objectives: Diabetic kidney disease (DKD) is a leading cause of chronic kidney disease (CKD) in type 1 diabetes mellitus (T1DM) patients, influenced by both metabolic and environmental factors. While poor glycemic control, hypertension, and dyslipidemia are key metabolic risks, environmental factors such as pollution, diet, and healthcare access may further accelerate kidney damage. This study uses multiple regression analysis to evaluate the impact of these factors on DKD prevalence in Indonesia, aiming to inform targeted prevention and management strategies.

Methods: This study employs an ordinary least squares (OLS) regression with multiple linear analysis. Data were sourced from the Global Burden of Disease database (1980–2021). The dependent variable is chronic kidney disease (CKD) attributed to type 1 diabetes mellitus (T1DM), while the independent variables include high fasting plasma glucose as a metabolic risk indicator and temperature extremes (high and low) as environmental risk indicators.

Results: The analysis revealed that 69.18% of the variation in chronic kidney disease (CKD) due to type 1 diabetes mellitus (T1DM) in Indonesia is explained by high fasting plasma glucose and temperature extremes (both high and low), while the remaining 31.82% is attributed to other unexamined factors. High fasting plasma glucose was found to be a significant positive predictor of CKD prevalence (CI = 95%, $p < 0.001$), indicating that higher glucose levels correlate with an increased prevalence of CKD due to T1DM. Similarly, environmental factors, including extreme temperatures, also showed a significant positive association with CKD prevalence (CI = 95%, $p < 0.001$).

Conclusions: High fasting plasma glucose and temperature extremes significantly influence CKD prevalence in T1DM patients in Indonesia. Targeted interventions for glycemic control and environmental adaptation are essential to reduce CKD risk.

Keywords：Metabolic Risks, Environmental Risks, Prevalence of Chronic Kidney Disease , Indonesia, OLS

```
. reg ckd_dueto_dmtypelok high_fasting_plasma_glucose high_temperature low_temperature
```

Source	SS	df	MS		
Model	8.7785e-06	3	2.9262e-06	Number of obs	= 32
Residual	3.9118e-06	28	1.3971e-07	F(3, 28)	= 20.95
				Prob > F	= 0.0000
Total	.00001269	31	4.0937e-07	R-squared	= 0.6918
				Adj R-squared	= 0.6587
				Root MSE	= .00037

ckd_dueto_dmtypelok	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
high_fasting_plasma_glucose	121.7052	29.79258	4.09	0.000	60.67782	182.7325
high_temperature	121.7136	29.69652	4.10	0.000	60.883	182.5441
low_temperature	-121.6705	29.76316	-4.09	0.000	-182.6376	-60.70343
_cons	.0012902	.0006585	1.96	0.060	-.0000585	.002639

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0112
Abstract Submission No.：APCN20251071

Hypertension and Oral Health Problems Jointly Associated with Higher Prevalence of Kidney Failure: An Ecological Study in Java, Indonesia

Dagun Raisah Laksmi Pratiwi[1]; Bagas Suryo Bintoro[1,2]

[1] Center of Health Behavior and Promotion, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada

[2] Department of Health Behavior, Environment, and Social Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada

Abstract

Background: Chronic kidney disease (CKD) continues to rise in Indonesia, placing an increasing burden on the healthcare system. Hypertension is widely recognized as a major driver of CKD, but recent evidence suggests that poor oral health may also contribute through shared inflammatory pathways. Despite these insights, the interaction between oral and systemic health in the context of kidney disease remains underexplored, particularly at the population level.

Objective: This study aimed to explore whether poor oral health and hypertension might act together, rather than independently, in contributing to kidney failure prevalence in Java, Indonesia.

Methods: Ecological analysis was conducted using district-level data from 119 districts and cities across Java, from Indonesia's 2018 Basic Health Survey (Riset Kesehatan Dasar/Riskesdas). Hypertension and oral health prevalence were categorized based on the national average ($<$ or $\geq$ mean). Multiple linear regression models assessed the individual and joint effects of these variables on kidney failure prevalence.

Results: Districts with above-average hypertension prevalence had significantly higher kidney failure rates ($\beta = 0.060$; 95% CI: 0.027 to 0.092; $p < 0.001$). Likewise, higher prevalence of oral health problems was independently associated with increased kidney failure ($\beta = 0.043$; 95% CI: 0.014 to 0.073; $p = 0.004$). Notably, in the interaction model, districts with both high hypertension and poor oral health showed the strongest association with kidney failure ($\beta = 0.097$; 95% CI: 0.056 to 0.139; $p < 0.001$), suggesting a synergistic effect.

Conclusion: This study reinforces the growing recognition that oral health is deeply connected to systemic health. The findings highlight a possible synergy between hypertension and poor oral conditions in amplifying kidney failure risk. These insights underline the importance of integrated, cross-disciplinary approaches in public health, where dentists and physicians work together to prevent chronic diseases and protect kidney health at the community level.

Keywords：Kidney failure, hypertension, oral health, ecological study, Java

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0113
Abstract Submission No.：APCN20251095

Elucidating Asprosin's Role as an Intracellular Metabolism Regulator in Diabetic Kidney Disease

JIHEE LIM[1,2]; Yaeni Kim[1]; Tae Woo Kim[1,2]; Eun Nim Kim[1]; Cheol Whee Park[1,2]

[1] Division of Nephrology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

[2] Institute for Aging and Metabolic Diseases, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

Abstract

Background: Asprosin is an adipokine with a multifaceted function that encompasses inducing insulin resistance, promoting inflammation, and stimulating appetite. We seek to establish its pivotal role as a mediator in regulating cellular energy metabolism, particularly in the context of diabetic kidney disease.

Materials and Methods: Type 2 diabetic db/db mice were categorized into two groups: one received Asprosin neutralizing antibodies (250 μg/mouse/21 days), targeting the 28-amino acid peptide located proximal to Asprosin's C-terminus (KKKELNQLEDRYDKDYLSGELGDNLKMK), while the other received an AMP-activated protein kinase (AMPK) activator (Metformin) associated with the regulation of Asprosin receptors (OLFR734/G proteins-cAMP-PKA). Additionally, we cultured renal constituent cells (mesangial cells, glomerular endothelial cells) in high glucose and palmitic acid conditions and treated them with an AMPK inhibitor (Compound C) after silencing Asprosin expression using siRNA. We assessed the levels of Asprosin, AMPK, and their respective downstream signaling pathways.

Results: Asprosin was found to be overexpressed in the serum and kidney tissues of db/db mice, as well as in renal constituent cells cultured under high glucose and palmitic acid conditions. Interfering with Asprosin led to reduced body and liver weight in mice, improved glucose tolerance, and mitigated renal injury in vivo. Asprosin knockdown ameliorated lipid accumulation and inflammatory infiltration, both in vitro and in vivo. Moreover, Asprosin absence activated the AMPK/Sirts/mTOR signaling pathway, while the AMPK inhibitor Compound C reversed the effects of Asprosin on lipid accumulation and inflammatory response, confirming Asprosin's direct role in intracellular lipid metabolism.

Conclusion: The mechanism of intracellular energy metabolism regulation mediated by Asprosin presents promising potential for targeted organ therapy in the development and prevention of diabetic kidney disease. Inhibiting Asprosin suppressed lipid accumulation and inflammation in diabetic kidney disease through the activation of AMPK-associated signaling pathway.

Keywords：Asprosin, Diabetic Kidney Disease, AMPK

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0114
Abstract Submission No.：APCN20251113

Confirmation method for Identification of Diuretics in human urine: A common antihypertensive in clinical use and kidney diseases.

awanish Kumar Upadhyay[1]; Akhilesh Bhardwaj[1]; Kamna Sharma[1]; Puranlal Sahu[1]
[1] National Dope Testing Laboratory, New Delhi, India

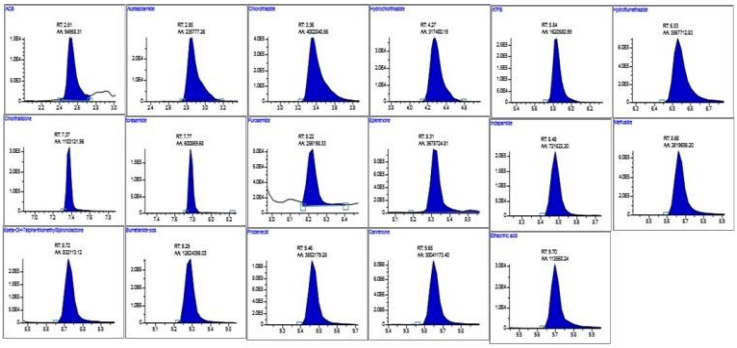
Abstract
Objectives: Diuretics are often used in conditions defined by an excess of extracellular fluid, such as chronic renal disease, nephrotic syndrome, cirrhosis, and heart failure. Patients with these disorders are treated with a variety of diuretic classes, including thiazide-type diuretics, loop diuretics, and K+-sparing diuretics, either alone or in combination. A confirmation method for the identification of several diuretic classes, such as thiazide-type diuretics, loop diuretics, and K+-sparing diuretics, in clinical investigations and other kidney research utilizing a sophisticated LC-MS/MS technique in human urine.

Methods: An analytical method involving liquid-liquid extraction and detection by Liquid Chromatography Mass spectrometric analysis (LC-MS/MS) in MRM mode (multiple reaction monitoring) using polarity switching. The diuretics detection method was developed and validated as per ISO17025 & WADA ISL guidelines for LOI (Limit of Identification), specificity, robustness, selectivity, carryover, and matrix effect.

Results: A confirmatory method has been developed combining polarity switching and scheduled multiple reaction scanning to discover more than 40 diuretics in a single 13-minute run. The validation results were within acceptable limits. The new approach can detect diuretics at nanogram and picogram levels (LOI <1 ng/ml for a select few). The approach has been successfully used in the confirmation analysis of diuretics.

Conclusions: The method could be beneficial for confirming various diuretic classes in a single run in nephrology, medicine, clinical applications, and anti-doping control. This method has enhanced the identification of diuretics at extremely low concentrations in human urine. The method's applicability was also confirmed by examining a real sample for confirmatory analysis.

Keywords：Diuretics, Antihypertensives, Nephrology, LC-MS/MS



Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0116
Abstract Submission No.：APCN20251152

Empagliflozin inhibits the protease activity, migration, and cancer stemness in renal pelvis urothelial carcinoma BFTC-909 cells

Horng-Rong Chang[1,2]; Chin-Yin Lin[3]; Yi-Hsun Lee[3]; Pei-Ni Chen[3]

[1] Division of Nephrology, Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan

[2] School of Medicine, Chung Shan Medical University, Taichung, Taiwan

[3] Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan

Abstract

Empagliflozin (EMPA) is an inhibitor of the sodium glucose co-transporter-2 (SGLT-2) for the treatment of type 2 diabetes, and causes sugar in the blood to be excreted by the kidneys and eliminated in the urine. EMPA is now a widely used diabetes drug, but so far, the effects and detailed mechanisms of Empagliflozin on carcinogenesis, cell metastasis, epithelial-to-mesenchymal transition, cell growth, cytokine secretion, cancer stemness and drug resistance of human renal pelvis transitional cell carcinoma were still unclear. In this study, we investigate the long-term effect of EMPA on renal pelvis urothelial carcinoma BFTC-909 cells. Long-term treatment of EMPA (> 40 days) decreased the invasion, migration, and activities of matrix metalloproteinase-2 (MMP-2) and urokinase-type plasminogen activator (u-PA) protease in BFTC 909 cells. Empagliflozin also decreased cell viability and self-renewal capacity in BFTC 909 cells. The conditioned medium from EMPA-treated cells, levels of IL-1ra, IL-8, G-CSF, and VEGF were significantly reduced. In summary, the results confirmed that EMPA inhibited the protease activity, and inhibited the invasion and cancer stemness in BFTC 909 cells.

Keywords：Empagliflozin, SGLT-2 inhibitor, urothelial carcinoma

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0117
Abstract Submission No.：APCN20251180

Confirmation method for Identification of Desmopressin in human urine: A synthetic analog of the antidiuretic hormone vasopressin

awanish Kumar Upadhyay[1]; Akhilesh Bhardwaj[1]; Kamna Sharma[1]; Puranlal Sahu[1]
[1] National Dope Testing Laboratory, New Delhi, India

Abstract
Objectives: Desmopressin (DDAVP) has been shown to improve platelet function and decrease bleeding due to uremia. As a result, desmopressin has been routinely used to prevent bleeding after kidney biopsy. This medication replaces the missing antidiuretic hormone (ADH) and lowers the amount of urine the body makes. Desmopressin is available as a pill, as a nasal spray and as a shot. A sensitive confirmation method was developed and validated for the identification of desmopressin. The identification of desmopressin at picogram level in human urine was achieved utilizing a sophisticated LC-MS/MS technique in human urine.

Methods: 1 ml of the urine add 20 µl of internal standard mix solution and 1 ml of 1.88M sodium acetate buffer (pH-5.2). Precondition the Oasis WCX cartridges. Load the sample and wash the cartridge with 1 ml Milli-Q water and then with 1 ml of methanol. Elute the retained analyte by loading 1 ml of elution mix (methanol: formic acid: Milli-Q water. Dry the eluent under refrigerated vacuum concentrator reconstitute in 70 µl of reconstitution solution and Inject on LC-MS/MS. The analytical method was validated as per ISO17025 & WADA International Standard for Laboratories guidelines for validation parameter like, Limit of Identification (LOI), Specificity, Robustness, and Carryover.

Results: A confirmatory method has been developed combining polarity switching and Scheduled multiple reaction scanning for identification of desmopressin. The validation results were within acceptable limits. The Limit of identification for desmopressin is 400 pg/ml. The approach has been successfully used in the confirmation analysis of desmopressin.

Conclusions: The method could be beneficial for confirming desmopressin in nephrology, medicine, clinical applications, and anti-doping control. This method has enhanced the identification of desmopressin at extremely low concentrations in human urine. The method's applicability was also confirmed by examining a real sample for confirmatory analysis.

Keywords：Vasopressin, Antidiuretic, Nephrology, LC-MS/MS

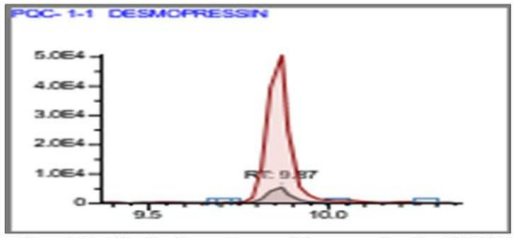


Figure-1 Identification Chromatogram of Desmopressin using LC-MS/MS

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0118
Abstract Submission No.：E_APCN20251258

Podocyte Heterogeneity in Diabetic Kidney Disease: Deciphering the Metabolic Subtype and Its Crosstalk with Parietal Epithelial Cells

Jiaying Li, Li Zhang, Xinling Liang*
Division of Nephrology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, 510080, China

Background: Podocyte injury critically contributes to diabetic kidney disease (DKD) progression, yet the cellular heterogeneity of podocytes and their distinct contributions to disease progression remains poorly characterized.
Methods: Single-cell RNA sequencing (scRNA-seq) was performed on kidneys from db/db (n=4) and db/m (n=4) mice to identify podocyte subtypes. We analyzed their functional characteristics, key transcription factors, interactions with parietal epithelial cells (PECs), and clinical relevance.
Results: Podocyte heterogeneity was mapped through single-cell RNA sequencing analysis. We identified three distinct subtypes: Cryab^{hi} metabolic subtype (Metab-subtype), Slc6a6^{hi} transitional phenotype (Trans-subtype), Magi2^{hi} adhesion subtype (Differentiated-subtype). Notably, we discover that both the Trans-subtype and Differentiated-subtype originated from the Metab-subtype. Transcription factor analysis suggested that Wt1 may play a key role in subpopulation conversion. Conjoint trajectory analysis of podocytes and PECs revealed impaired differentiation of PECs into Cryab^{hi} podocytes in DKD. The CDKN1A^{hi} subsets of PECs present during the DKD were classified, and CDKN1A^{hi} PECs were suggested as a primary podocyte subset associated with regeneration. We further uncovered intercellular crosstalk between Cryab^{hi} podocytes and PECs, predominantly mediated by the JAG-NOTCH2 and APP-SORL1/VEGFA_NRP2 ligand-receptor pairs. Clinically, the Cryab^{hi} subtype exhibited a negative correlation with proteinuria and serum creatinine but a positive correlation with eGFR, suggesting that its decline contributes to unfavorable prognosis of DKD.
Conclusion: These findings provide novel insights into podocyte heterogeneity and regeneration in DKD, highlighting potential therapeutic targets.
Key words: diabetic kidney disease; scRNA-seq; podocyte heterogeneity; Cryab; Cdkn1a; JAG1-NOTCH2

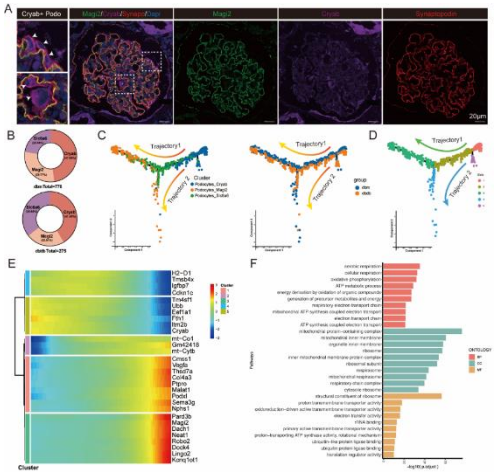


Figure 1. Identification and characterization of Cryab+ podocyte subpopulations in DKD using trajectory analysis.

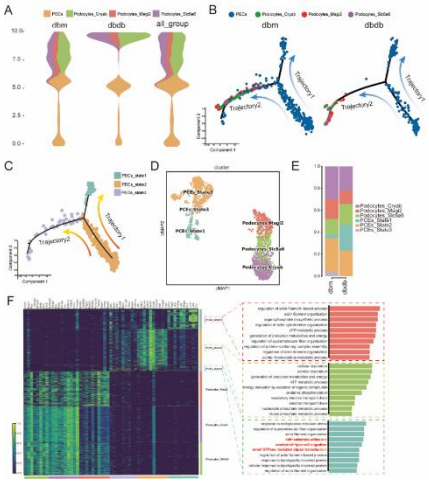


Figure 2. Cellular trajectory profiling reveal dynamic states of PECs and podocyte subpopulations in diabetic and control conditions.

Poster Presentation：Cardio-Renal Metabolic Syndrome, Diabetic Kidney Disease, and Hypertensive Kidney Disease
Poster No.：B0119
Abstract Submission No.：E_APCN20251275

Nogo-B deficiency contributes to kidney dysfunction and fibrosis in hypertensive nephropathy through inhibiting IL-17 signaling pathway

Haosen Xu, Xiaoyan Bai
Guangdong Provincial People's Hospital

Background
Glomerular endothelial cells (ECs) dysfunction is a common feature of hypertensive nephropathy (HTN). Nogo-B, an endoplasmic reticulum protein, is known to play a critical role in vascular function and blood pressure homeostasis. However, its specific role in glomerular ECs and the underlying mechanisms during HTN remain unclear.

Method
The localization and expression of Nogo-B were confirmed in kidneys of HTN patients and Angiotensin II (Ang II)-induced mice. The relationships between Nogo-B and blood pressure and fibrosis were investigated by generating Ang II and two-kidney, one-clip (2K1C) models, basically on Nogo-A/B knockout and Nogo-B overexpression mice. In vitro, ECs were treated with Ang II and Nogo-B was silenced by small interfering RNA. Potential mechanisms are screened by RNA sequencing and validated by further study. Recombinant protein was used to rescue downstream signal.

Result
Absence of Nogo-B enhanced renal ECs dysfunction and accelerated the progression of HTN. We found that Nogo-B expression was obviously increased in renal ECs under hypertensive conditions in vivo and in vitro. Mice lacking Nogo-B exhibited aggravated albuminuria, glomerular damage and renal fibrosis in hypertensive mouse models induced by angiotensin II or 2K1C procedure. Conversely, Nogo-B overexpression attenuated 2K1C-induced kidney dysfunction and fibrosis. Meanwhile, Nogo-B silencing worsened angiotensin II-induced fibrotic markers expression in ECs in vitro. Mechanistically, Nogo-B knockdown inhibited IL-17 signaling (IL-17A, IL-17RA, Act1, TRAF6, TAK1 and JUND), and subsequent IL-17 activation reversed the Nogo-B deficiency-induced upregulation of fibrotic markers.

Conclusion
Collectively, our findings indicate that systemic Nogo-B deletion worsens kidney dysfunction and fibrosis in HTN. Thus, targeting kidney Nogo-B may serve as a promising therapeutic strategy for HTN.