IAA Journal of Applied Sciences 13(2):43-50, 2025. www.iaajournals.org
©IAAJOURNALS ISSN: 2636-7246
https://doi.org/10.59298/IAAJAS/2025/435000 IAAJAS: 132.4350

Phytochemical Strategies to Counteract Nephrotoxicity and Hepatotoxicity in Diabetic Models

Nambi Namusisi H.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Diabetes mellitus is associated with long-term complications, including nephrotoxicity and hepatotoxicity, largely due to hyperglycemia-induced oxidative stress and inflammation. Persistent hyperglycemia generates excessive reactive oxygen species (ROS), disrupts mitochondrial function, and activates various pro-inflammatory signaling pathways, such as NF-κB and MAPKs. These processes contribute to cellular injury, fibrosis, and organ dysfunction, especially in the kidneys and liver. Diabetic nephropathy manifests as glomerular hypertrophy, mesangial expansion, and proteinuria, whereas diabetic hepatopathy is characterized by hepatic steatosis, inflammation, and elevated transaminase levels. Conventional pharmacotherapies often inadequately address these complications and may present undesirable side effects. As such, there is a growing interest in natural therapeutic alternatives. Phytochemicals, the bioactive compounds derived from plants, have emerged as promising therapeutic agents due to their antioxidant, anti-inflammatory, anti-apoptotic, and organ-protective properties. Compounds such as curcumin, resveratrol, quercetin, and berberine have demonstrated significant efficacy in mitigating diabetes-induced renal and hepatic damage in preclinical studies. These agents modulate multiple cellular pathways, enhance endogenous antioxidant defenses, and improve glycemic control. This article reviews recent advances in phytochemical-based strategies for counteracting nephrotoxicity and hepatotoxicity in diabetic models, highlighting their mechanisms of action, experimental evidence, and potential for clinical translation. A comprehensive understanding of these strategies can inform the development of integrative therapeutic approaches in diabetes management

Keywords: Phytochemicals, Diabetes Mellitus, Nephrotoxicity, Hepatotoxicity, Oxidative Stress, Inflammation, Curcumin, Resveratrol, Nanotherapy

INTRODUCTION

Diabetes mellitus (DM), particularly type 2 diabetes, is a global health burden that predisposes individuals to multiorgan complications, notably affecting the kidneys and liver [1]. The increasing prevalence of DM worldwide has heightened concerns regarding its systemic impact and the development of chronic complications. Among the most debilitating consequences are diabetic nephropathy and hepatopathy, which significantly contribute to morbidity and mortality [2] Diabetic nephropathy is characterized by glomerular basement membrane thickening, mesangial matrix expansion, and eventual progression to end-stage renal disease [2]. Similarly, diabetic hepatopathy encompasses a spectrum of liver pathologies, including non-alcoholic fatty liver disease (NAFLD), steatohepatitis, and hepatic fibrosis, driven by insulin resistance and metabolic dysregulation [3]. Both complications are underpinned by a complex interplay of hyperglycemia-induced oxidative stress, accumulation of advanced glycation end-products (AGEs), lipid peroxidation, mitochondrial dysfunction, and persistent low-grade inflammation [4]. Despite advancements in glycemic control and the availability of conventional antidiabetic medications, current therapies often fail to adequately

prevent or reverse end-organ damage [5]. This therapeutic gap has prompted the exploration of adjunctive or alternative strategies to combat diabetes-associated organ toxicity. Phytochemicals, naturally occurring compounds in fruits, vegetables, herbs, and spices, exhibit a broad spectrum of bioactivities [6]. Their antioxidant, anti-inflammatory, anti-apoptotic, and metabolic regulatory effects make them promising candidates for organ protection [7]. Investigating phytochemical interventions offers a complementary approach to traditional diabetic management, with the potential to attenuate or delay the onset of nephrotoxic and hepatotoxic outcomes.

2. Pathophysiology of Diabetic Nephrotoxicity and Hepatotoxicity

Diabetes mellitus, particularly when poorly controlled, leads to persistent hyperglycemia, which initiates a cascade of metabolic and cellular alterations culminating in organ dysfunction [8]. Among the most affected organs are the kidneys and liver, with nephrotoxicity and hepatotoxicity being major complications [2]. Central to the pathophysiology of these complications is the overproduction of reactive oxygen species (ROS), which overwhelms the endogenous antioxidant defense mechanisms and leads to oxidative stress [9]. This oxidative milieu damages cellular components, including lipids, proteins, and DNA, disrupting normal cell function and promoting cell death [10].

In the kidneys, chronic hyperglycemia induces glomerular hyperfiltration and hypertrophy, which contribute to mesangial expansion and basement membrane thickening [2]. These structural changes impair the filtration barrier, resulting in proteinuria and a progressive decline in renal function [11]. ROS further exacerbate this by activating key pro-inflammatory and fibrotic signaling pathways, notably nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPKs) [12]. These pathways enhance the expression of pro-inflammatory cytokines, chemokines, and fibrotic markers such as transforming growth factor-beta (TGF-β), promoting glomerulosclerosis and interstitial fibrosis [13].

In the liver, hyperglycemia triggers lipid accumulation in hepatocytes, leading to steatosis or non-alcoholic fatty liver disease (NAFLD) [14]. Concurrently, mitochondrial dysfunction and oxidative stress initiate hepatocyte apoptosis and necrosis [15]. Inflammatory signaling, mediated by NF-κB and MAPKs, also contributes to hepatic inflammation and fibrosis [16]. Chronic hepatic injury eventually impairs liver function and may predispose individuals to cirrhosis [17]. Additionally, advanced glycation end products (AGEs) formed under hyperglycemic conditions bind to their receptors (RAGE), amplifying oxidative stress and inflammation in both renal and hepatic tissues [19] Collectively, these molecular and cellular disruptions underscore the importance of targeting oxidative stress and inflammation in managing diabetic nephrotoxicity and hepatotoxicity. Phytochemicals with antioxidant and anti-inflammatory properties offer promising avenues for intervention.

3. Antioxidant and Anti-inflammatory Phytochemicals

A variety of plant-derived bioactive compounds have shown protective effects against diabetic organ damage through antioxidant and anti-inflammatory mechanisms:

Curcumin: This polyphenol exerts potent antioxidant effects by activating the nuclear factor erythroid 2–related factor 2 (Nrf2)/antioxidant response element (ARE) pathway, enhancing the expression of detoxifying and antioxidant enzymes [18]. It also suppresses pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), thereby mitigating renal and hepatic inflammation [20].

Resveratrol: Resveratrol enhances mitochondrial function and biogenesis, attenuates oxidative stress, and inhibits NF-κB activation [21]. It has been shown to preserve renal glomerular structure and hepatic histoarchitecture in diabetic models [22].

Quercetin: Quercetin reduces lipid peroxidation, boosts endogenous antioxidants like glutathione (GSH), and downregulates fibrotic and inflammatory markers, thereby preventing structural and functional deterioration of kidneys and liver [23].

Berberine: Berberine activates adenosine monophosphate-activated protein kinase (AMPK), improving lipid metabolism and insulin sensitivity [24]. It lowers serum levels of liver enzymes (ALT, AST) and kidney function markers (creatinine, urea), indicating protection against organ injury [25].

Silymarin: This flavonolignan complex stabilizes hepatocyte membranes, scavenges free radicals, and reduces cytokine production [26]. It has shown

efficacy in preserving liver function and preventing fibrosis in diabetic conditions.

These phytochemicals represent promising adjuncts in the management of diabetic complications, offering multi-targeted protection through their antioxidant and anti-inflammatory actions.

Mechanisms of Action

Phytochemicals exert their protective effects against diabetic nephrotoxicity and hepatotoxicity through a complex interplay of molecular mechanisms that counteract the oxidative, inflammatory, and metabolic disturbances associated with diabetes. One of the most prominent mechanisms is antioxidant activity, wherein phytochemicals neutralize reactive oxygen species (ROS) directly or enhance endogenous antioxidant defenses [27]. Compounds like curcumin, quercetin, and resveratrol upregulate the expression and activity of key antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [23,28,29]. These enzymes mitigate oxidative stress, which is a central driver of cellular injury in diabetic organs [30].

Another critical pathway involves anti-inflammatory effects: Chronic inflammation, sustained by high glucose levels and oxidative stress, activates signaling cascades like NF-κB and MAPKs, leading to increased expression of pro-inflammatory mediators [31]. Phytochemicals inhibit the expression of cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), thereby reducing inflammatory cell infiltration and tissue damage [32]. In addition, several phytochemicals modulate apoptotic signaling pathways. They inhibit pro-apoptotic proteins like Bax and caspases (particularly caspase-3 and caspase-9) while upregulating anti-apoptotic proteins such as Bcl-2. This balance helps preserve the viability and integrity of renal and hepatic cells under diabetic conditions, preventing excessive cell loss and organ dysfunction [33].

Phytochemicals also contribute to improved glycemic control, which indirectly reduces diabetes-related complications. By enhancing insulin sensitivity, promoting glucose uptake, and modulating enzymes involved in glucose metabolism, phytochemicals such as berberine and silymarin reduce hyperglycemia-induced oxidative and inflammatory stress [34]. These glycemic effects further synergize with antioxidant and anti-inflammatory properties to provide comprehensive protection.

Experimental Evidence from Diabetic Models

A substantial body of experimental evidence from preclinical studies supports the efficacy of phytochemicals in ameliorating diabetic nephrotoxicity and hepatotoxicity [35,36,38]. Diabetic models induced by agents like streptozotocin (STZ), alloxan, or high-fat diets exhibit consistent patterns of renal and hepatic injury, characterized by elevated serum levels of creatinine, urea, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) [37]. Treatment with phytochemicals significantly lowers these biomarkers, indicating functional restoration [39]. Histological analyses further reveal reductions in glomerular hypertrophy, mesangial expansion, and tubular necrosis in the kidneys, along with improvements in liver architecture, including reduced steatosis, hepatocyte ballooning, and fibrosis [40]. Biochemical assays show restoration of antioxidant enzyme levels and a decrease in lipid peroxidation markers such as malondialdehyde (MDA), confirming mitigation of oxidative stress [41].

Synergistic Effects and Polyherbal Formulations

Emerging research suggests that combining phytochemicals enhances therapeutic efficacy through synergistic effects [42]. These combinations can improve bioavailability, target multiple molecular pathways simultaneously, and reduce the required therapeutic dosages, minimizing toxicity. For example, the combination of curcumin and piperine enhances the bioavailability of curcumin, leading to greater systemic antioxidant and anti-inflammatory effects [43]. Polyherbal formulations composed of medicinal plants such as Gymnema sylvestre, Momordica charantia, and Phyllanthus niruri have shown promising results in animal models, with superior glycemic control and organ protection compared to single-compound therapies [44]. These formulations represent a holistic approach and are gaining attention in integrative diabetic management strategies.

Nanotechnology-Enhanced Phytotherapy

Recent advances in nanotechnology have significantly improved the therapeutic potential of phytochemicals in managing diabetic nephrotoxicity and hepatotoxicity [45]. One of the major limitations of many bioactive plant compounds, such as curcumin and resveratrol, is their poor aqueous solubility,

instability in the gastrointestinal tract, and rapid systemic clearance, which limit their bioavailability and therapeutic efficacy [46]. Nanotechnology-based delivery systems offer innovative solutions to these challenges.

Nanoparticle formulations—such as liposomes, solid lipid nanoparticles, polymeric nanoparticles, and nanoemulsions—enable enhanced delivery of phytochemicals by improving solubility, stability, and absorption [47]. These carriers can protect the phytochemical from degradation, facilitate sustained and controlled release, and improve targeting to specific organs such as the liver and kidneys. For example, nano-curcumin has demonstrated markedly improved bioavailability and tissue distribution compared to its conventional form [48]. Studies in diabetic animal models show that nano-curcumin more effectively reduces oxidative stress, inflammation, and histological damage in renal and hepatic tissues [49]. Similarly, resveratrol-loaded nanoparticles have shown enhanced mitochondrial protection, anti-inflammatory activity, and insulin-sensitizing effects, contributing to improved organ function and metabolic control [50] Moreover, nanocarriers can be engineered with surface modifications to enable targeted delivery, minimizing off-target effects and enhancing therapeutic efficacy [51]. Co-loading of multiple phytochemicals or combining phytochemicals with conventional drugs in nanoformulations is an emerging area of interest, potentially offering synergistic benefits in managing complex diabetic complications [52]. Thus, nanotechnology represents a transformative approach to overcoming pharmacokinetic limitations and maximizing the therapeutic benefits of phytotherapy in diabetic care.

Challenges and Future Directions

Despite the growing body of preclinical evidence supporting the efficacy of phytochemicals, several challenges hinder their clinical translation. One major issue is the lack of standardization of plant extracts, which can vary in composition due to differences in cultivation, harvesting, and extraction methods [53]. This variability affects reproducibility and reliability of results. Dose optimization and safety profiling are also critical concerns. While many phytochemicals show low toxicity in experimental models, high doses or prolonged use may pose risks, especially in combination with other medications [54]. Detailed toxicological studies and long-term safety data are necessary to guide appropriate dosing regimens. Furthermore, human clinical trials evaluating phytochemicals in diabetic nephrotoxicity and hepatotoxicity are still limited. Most existing evidence is derived from in vitro studies and animal models, which may not fully replicate human physiology and disease complexity [55]. Rigorous clinical investigations are essential to validate efficacy, determine therapeutic windows, and evaluate patient outcomes. Another important area of focus is herb-drug interactions. Many phytochemicals can modulate drug-metabolizing enzymes or transporters, potentially altering the pharmacokinetics of concurrently administered medications [54]. Understanding these interactions is crucial to ensuring the safe integration of phytotherapy into conventional treatment regimens.

CONCLUSION

Phytochemicals represent a promising adjunctive strategy for mitigating diabetic nephrotoxicity and hepatotoxicity, thanks to their multifaceted antioxidant, anti-inflammatory, anti-apoptotic, and metabolic regulatory properties. The integration of nanotechnology has further enhanced their therapeutic potential by improving delivery and bioavailability. However, to fully harness the benefits of phytotherapy, comprehensive research is needed to address challenges related to standardization, safety, and clinical validation. With continued interdisciplinary efforts, phytochemicals may become integral components of personalized, organ-protective strategies in diabetes management.

REFERENCES

1. Alum EU. Optimizing patient education for sustainable self-management in type 2 diabetes. *Discov Public Health* **22**, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5
2. Rout P, Jialal I. Diabetic nephropathy. StatPearls - NCBI Bookshelf. 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534200/
3. Goh GBB, Pagadala MR, Dasarathy J, Unalp-Arida A, Sargent R, Hawkins C, et al. Clinical spectrum of non-alcoholic fatty liver disease in diabetic and non-diabetic patients. BBA Clinical. 2014;3:141–5. doi:10.1016/j.bbacli.2014.09.001

4. Ugwu, O. P.C., Alum, E. U., Obeagu, E. I, Okon, M. B., Aja, P. M., Samson, A. O., Amusa, M. O. and Adepoju, A. O. Effect of Ethanol Leaf extract of *Chromolaenaodorata* on hepatic markers in streptozotocin-induced diabetic wistar albino rats. *IAA Journal of Applied Sciences*, 2023; 9(1):46-56. https://doi.org/10.5281/zenodo.7811625
5. Sena CM, Bento CF, Pereira P, Seiça R. Diabetes mellitus: new challenges and innovative therapies. The EPMA Journal. 2010;1(1):138–63. doi:10.1007/s13167-010-0010-9
6. Alum, E. U., Krishnamoorthy, R., Gatasheh, M. K., Subbarayan, S., Vijayalakshmi, P., Uti, D. E. Protective Role of Jimson Weed in Mitigating Dyslipidemia, Cardiovascular, and Renal Dysfunction in Diabetic Rat Models: In Vivo and in Silico Evidence. Natural Product Communications. 2024;19(12). doi:10.1177/1934578X241299279
7. Mitaki, N.B., Fasogbon, I.V., Ojiakor, O.V., Makena, W., Ikuomola, E. O., Dangana, R.S., et al A systematic review of plant-based therapy for the management of diabetes mellitus in the East Africa community. Phytomedicine Plus, 2025; 5(1): 100717. https://doi.org/10.1016/j.phyplu.2024.100717
8. Godfrey Ogochukwu Ezema, Ndukaku Yusuf Omeh, Egba Simeon Ikechukwu, Ejiofor C Agbo, Adachukwu Ada Ikeyiand Emmanuel Ifeanyi Obeagu. Evaluation of Biochemical Parameters of Patients with Type 2 Diabetes Mellitus Based on Age and Gender in Umuahia (2023) Asian Journal of Dental and Health Sciences 2023; 3(2):32-36
9. M.C. Udeh Sylvester, O.F.C. Nwodo, O.E. Yakubu, E.J. Parker, S. Egba, E. Anaduaka, V.S. Tatah, O.P. Ugwu, E.M. Ale, C.M. Ude and T.J. Iornenge. Effects of Methanol Extract of *Gongronema latifolium* Leaves on Glycaemic Responses to Carbohydrate Diets in Streptozotocin-induced Diabetic Rats. Journal of Biological Sciences, 2022; 22: 70-79.
10. Chimaroke Onyeabo, Paul Anyiam Ndubuisi, Anthony Cemaluk Egbuonu, Prince Chimezie Odika, Simeon Ikechukwu Egba, Obedience Okon Nnana, Polycarp Nnacheta Okafor. Natural products-characterized Moringa oleifera leaves methanolic extractand anti-diabetic properties mechanisms of its fractions in streptozotocin-induced diabetic rats The Nigerian Journal of Pharmacy, 2022; 56(1):18-29
11. Haider MZ, Aslam A. Proteinuria. StatPearls - NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564390/
12. Ahmed SMU, Luo L, Namani A, Wang XJ, Tang X. Nrf2 signaling pathway: Pivotal roles in inflammation. Biochimica Et Biophysica Acta (BBA) - Molecular Basis of Disease. 2016;1863(2):585–97. doi:10.1016/j.bbadis.2016.11.005
13. Frangogiannis NG. Transforming growth factor–β in tissue fibrosis. The Journal of Experimental Medicine. 2020;217(3). doi:10.1084/jem.20190103
14. Alum EU, Umoru GU, Uti DE, Aja PM, Ugwu OP, Orji OU, Nwali BU, Ezeani N, Edwin N, Orinya FO. Hepato-protective effect of Ethanol Leaf Extract of *Datura stramonium* in Alloxan-induced Diabetic Albino Rats. *Journal of Chemical Society of Nigeria*. 2022; 47 (3): 1165 – 1176. https://doi.org/10.46602/jcsn.v47i5.819.
15. Shi S, Wang L, Van Der Laan LJW, Pan Q, Verstegen MMA. Mitochondrial dysfunction and oxidative stress in liver transplantation and underlying Diseases: New insights and therapeutics. Transplantation. 2021;105(11):2362–73. doi:10.1097/tp.0000000000003691
16. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2017;9(6):7204–18. doi:10.18632/oncotarget.23208
17. Sharma B, John S. Hepatic cirrhosis. StatPearls - NCBI Bookshelf. 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482419/
18. Eze Chukwuka W., Egba Simeon, Nweze Emeka I., Ezeh Richard C. and Ugwudike Patrick. Ameliorative Effects of *Allium cepa* and *Allium sativum* on Diabetes Mellitus and Dyslipidemia in Alloxan-induced Diabetic *Rattus novergicus*. *Trends Applied Sci Res*, 2020; 15(2): 145-150
19. Twarda-Clapa A, Olczak A, Białkowska AM, Koziołkiewicz M. Advanced Glycation End-Products (AGEs): formation, chemistry, classification, receptors, and diseases related to

AGEs. Cells. 2022;11(8):1312. doi:10.3390/cells11081312
20. Peng Y, Ao M, Dong B, Jiang Y, Yu L, Chen Z, et al. Anti-Inflammatory effects of curcumin in the inflammatory diseases: Status, limitations and countermeasures. Drug Design Development and Therapy. 2021;15:4503–25. doi:10.2147/dddt.s327378
21. Zhou J, Yang Z, Shen R, Zhong W, Zheng H, Chen Z, et al. Resveratrol improves mitochondrial biogenesis function and activates PGC-1A pathway in a preclinical model of early brain injury following subarachnoid hemorrhage. Frontiers in Molecular Biosciences. 2021;8. doi:10.3389/fmolb.2021.620683
22. Grujić-Milanović J, Jaćević V, Miloradović Z, Milanović SD, Jovović D, Ivanov M, et al. Resveratrol improved kidney function and structure in malignantly hypertensive rats by restoration of antioxidant capacity and nitric oxide bioavailability. Biomedicine & Pharmacotherapy. 2022;154:113642. doi:10.1016/j.biopha.2022.113642
23. Ogugua Victor Nwadiogbu., Uroko Robert Ikechukwu., Egba, Simeon Ikechukwu and Agu Obiora. Hepatoprotective and Healthy Kidney Promoting Potentials of Methanol Extract of *Nauclea latifolia* in Alloxan Induced Diabetic Male Wistar Albino Rats. *Asian Journal of Biochemistry*, 2017; 12: 71-78
24. Ogugua Victor Nwadiogbu., Agu Obiora Uroko., Egba, Simeon Ikechukwu and Robert Ikechukwu. Modulation of Blood Glucose Concentration, Lipid Profile and Haematological Parameters in Alloxan Induced Diabetic Rats Using Methanol Extract of *Nauclea latifolia* Root Bark. *Asian Journal of Biological Sciences*, 2017; 10(1): 1-8
25. Uhuo E N, Egba S I, Nwuke P C and Odinamadu H Renoprotective effects of adansonia digitata leaf extracts on renal functions and histopatological changes vancomycin induced nephrotoxicity in Wistar rats. Comparative Clinical Pathology, 2022; 31(1):1-14
26. Surai P. Silymarin as a natural antioxidant: An overview of the current evidence and perspectives. Antioxidants. 2015;4(1):204–47. doi:10.3390/antiox4010204
27. Ogugua, V N., Egba, S I., Anaduaka, E. G and Ozioko B O. Phytochemical analysis, anti-hyperglycaemic and anti-oxidant effect of the aqueous extracts of *Chromolaena odorata* on alloxan induced diabetic Rats. *Pharmanest*, 2013; 4(5): 970-977
28. Ramírez-Mendoza AA, Ramírez-Herrera MA, Cortez-Álvarez CR, Nery-Flores SD, Tejeda-Martínez AR, De Jesús Romero-Prado MM, et al. Curcumin Modifies the Activity of Plasmatic Antioxidant Enzymes and the Hippocampal Oxidative Profile in Rats upon Acute and Chronic Exposure to Ozone. Molecules. 2022;27(14):4531. doi:10.3390/molecules27144531
29. Constantinescu T, Mihis AG. Resveratrol as a privileged molecule with antioxidant activity. Food Chemistry Advances. 2023;3:100539. doi:10.1016/j.focha.2023.100539
30. Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP, Salvatore T, et al. Oxidative Stress in Type 2 Diabetes: Impacts from Pathogenesis to Lifestyle Modifications. Current Issues in Molecular Biology. 2023;45(8):6651–66. doi:10.3390/cimb45080420.
31. Anaduaka, Emeka G., Ogugua, Victor N., Egba, Simeon I and Apeh Victor O. Investigation of some important nutritional and phytochemical properties, toxicological potentials of *Newbouldia leavis* ethanol leaf and stem extracts. *African Journal of Biotechnology*, 2013; 12(3): 5846-5854
32. Nisar A, Jagtap S, Vyavahare S, Deshpande M, Harsulkar A, Ranjekar P, et al. Phytochemicals in the treatment of inflammation-associated diseases: the journey from preclinical trials to clinical practice. Frontiers in Pharmacology. 2023;14. doi:10.3389/fphar.2023.1177050
33. Rahman MdA, Hannan MdA, Dash R, Rahman MdH, Islam R, Uddin MJ, et al. Phytochemicals as a complement to cancer chemotherapy: Pharmacological modulation of the Autophagy-Apoptosis pathway. Frontiers in Pharmacology. 2021;12. doi:10.3389/fphar.2021.639628
34. García-Muñoz AM, Victoria-Montesinos D, Ballester P, Cerdá B, Zafrilla P. A descriptive review of the antioxidant effects and mechanisms of action of berberine and silymarin. Molecules. 2024;29(19):4576. doi:10.3390/molecules29194576
35. Kong M, Xie K, Lv M, Li J, Yao J, Yan K, et al. Anti-inflammatory phytochemicals for the treatment of diabetes and its complications:

Lessons learned and future promise. Biomedicine & Pharmacotherapy. 2020;133:110975. doi:10.1016/j.biopha.2020.110975

36. Alam S, Sarker MdMR, Sultana TN, Chowdhury MdNR, Rashid MA, Chaity NI, et al. Antidiabetic phytochemicals from Medicinal plants: Prospective candidates for new drug discovery and development. Frontiers in Endocrinology. 2022;13. doi:10.3389/fendo.2022.800714
37. Rehman HU, Ullah K, Rasool A, Manzoor R, Yuan Y, Tareen AM, et al. Comparative impact of streptozotocin on altering normal glucose homeostasis in diabetic rats compared to normoglycemic rats. Scientific Reports. 2023;13(1). doi:10.1038/s41598-023-29445-8
38. Momin A, Shukla P, Nikambe R, Patil R, Aswar U. Anti-Inflammatory phytochemicals for the treatment of diabetic nephropathy. Current Functional Foods. 2023;2(1). doi:10.2174/2666862901666230601100713
39. Heidari-Soreshjani S, Asadi-Samani M, Yang Q, Saeedi-Boroujeni A. Phytotherapy of nephrotoxicity-induced by cancer drugs: an updated review. Journal of Nephropathology. 2017;6(3):254–63. doi:10.15171/jnp.2017.41
40. Takahashi Y. Histopathology of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. World Journal of Gastroenterology. 2014;20(42):15539. doi:10.3748/wjg.v20.i42.15539
41. Mas-Bargues C, Escrivá C, Dromant M, Borrás C, Viña J. Lipid peroxidation as measured by chromatographic determination of malondialdehyde. Human plasma reference values in health and disease. Archives of Biochemistry and Biophysics. 2021;709:108941. doi:10.1016/j.abb.2021.108941
42. Chihomvu P, Ganesan A, Gibbons S, Woollard K, Hayes MA. Phytochemicals in Drug Discovery—A confluence of tradition and innovation. International Journal of Molecular Sciences.2024;25(16):8792. doi:10.3390/ijms25168792
43. Panahi Y, Hosseini MS, Khalili N, Naimi E, Majeed M, Sahebkar A. Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis. Clinical Nutrition. 2015;34(6):1101–8. doi:10.1016/j.clnu.2014.12.019
44. Salehi B, Ata A, Kumar NVA, Sharopov F, Ramírez-Alarcón K, Ruiz-Ortega A, et al. Antidiabetic potential of medicinal plants and their active components. Biomolecules. 2019;9(10):551. doi:10.3390/biom9100551
45. Robert I. Uroko., Charles N. Chukwu., Simeon I. Egba., Fatima A. Adamude andJoy C. Ajuzie (2020) Combined ethanol extract of *Funtumia africana* and *Abutilon mauritianium* leaves improves the lipid profile and kidney function indices of benign prostatic hyperplasia in rats. *Acta Sci. Pol. Technol. Aliment.* 2020; 19(4): 395-4045
46. Sohn SI, Priya A, Balasubramaniam B, Muthuramalingam P, Sivasankar C, Selvaraj A, et al. Biomedical applications and bioavailability of Curcumin—An updated overview. Pharmaceutics. 2021;13(12):2102. doi:10.3390/pharmaceutics13122102
47. Awlqadr FH, Majeed KR, Altemimi AB, Hassan AM, Qadir SA, Saeed MN, et al. Nanotechnology-Based Herbal Medicine: Preparation, synthesis, and applications in food and medicine. Journal of Agriculture and Food Research. 2025;101661. doi:10.1016/j.jafr.2025.101661
48. Karthikeyan A, Senthil N, Min T. Nanocurcumin: a promising candidate for therapeutic applications. Frontiers in Pharmacology. 2020;11. doi:10.3389/fphar.2020.00487
49. Hamed AM, Elbahy DA, Ahmed AR, Thabet SA, Refaei RA, Ragab I, et al. Comparison of the Efficacy of Curcumin and its Nano Formulation on Dexamethasone-Induced Hepatic Steatosis, Dyslipidemia, and Hyperglycemia in Wistar rats. Heliyon. 2024;10(24):e41043. doi:10.1016/j.heliyon.2024.e41043
50. Chung IM, Subramanian U, Thirupathi P, Venkidasamy B, Samynathan R, Gangadhar BH, et al. Resveratrol Nanoparticles: A Promising Therapeutic Advancement over Native Resveratrol. Processes. 2020;8(4):458. doi:10.3390/pr8040458
51. Din FU, Aman W, Ullah I, Qureshi OS, Mustapha O, Shafique S, et al. Effective use of nanocarriers as drug delivery systems for the treatment of selected tumors. International

Journal of Nanomedicine. 2017;12:7291–309. doi:10.2147/ijn.s146315
52. Stoleru OA, Burlec AF, Mircea C, Felea MG, Macovei I, Hăncianu M, et al. Multiple nanotechnological approaches using natural compounds for diabetes management. Journal of Diabetes & Metabolic Disorders. 2024;23(1):267–87. doi:10.1007/s40200-023-01376-1
53. Bitwell C, Indra SS, Luke C, Kakoma MK. A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants. Scientific African. 2023;19:e01585. doi:10.1016/j.sciaf.2023.e01585
54. Gómez-Garduño J, León-Rodríguez R, Alemón-Medina R, Pérez-Guillé BE, Soriano-Rosales RE, González-Ortiz A, et al. Phytochemicals that interfere with drug metabolism and transport, modifying plasma concentration in humans and animals. Dose-Response. 2022;20(3). doi:10.1177/15593258221120485
55. Mukherjee P, Roy S, Ghosh D, Nandi SK. Role of animal models in biomedical research: a review. Laboratory Animal Research. 2022;38(1). doi:10.1186/s42826-022-00128-1

CITE AS: Nambi Namusisi H. (2025). Phytochemical Strategies to Counteract Nephrotoxicity and Hepatotoxicity in Diabetic Models. IAA Journal of Applied Sciences 13(2):43-50. https://doi.org/10.59298/IAAJAS/2025/435000