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Comprehensive Review Article: Diabetes, Herbal Medicine, and Histopathology: Intersections in Renal and Hepatic Safety

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ABSTRACT

Diabetes mellitus (DM) is a global health concern, and its prevalence continues to rise due to increasing lifestyle changes and aging populations. Chronic hyperglycemia in diabetic patients leads to various complications, including renal and hepatic damage. While conventional pharmacological treatments for diabetes manage blood glucose levels, there has been growing interest in the use of herbal medicine as complementary or alternative therapy. Herbal medicines, containing bioactive compounds with anti-diabetic, anti-inflammatory, and antioxidant properties, are often considered for the management of diabetes and its complications. However, despite their benefits, the safety of herbal medicines, particularly concerning renal and hepatic toxicity, remains a significant concern. This review aims to explore the intersections between diabetes, herbal medicine, and histopathology, with a particular focus on renal and hepatic safety. We analyze the potential effects of herbal medicine on diabetic kidney and liver dysfunction, examining the histopathological changes and underlying mechanisms involved in such interactions. The review also evaluates clinical findings, potential therapeutic benefits, and safety profiles of popular herbal medicines used in the management of diabetes.

Keywords: Diabetes mellitus, Herbal Medicine, Renal Safety, Hepatic Safety, Histopathology, Toxicity, Bioactive Compounds

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder marked by chronic hyperglycemia due to defects in insulin secretion, action, or both [1]. With an estimated 537 million people affected globally, the burden of diabetes is rising, and it is associated with a range of complications, particularly nephropathy and hepatopathy, which contribute significantly to patient morbidity and mortality [2]. The use of herbal medicine has gained popularity as an alternative or complementary therapy due to its perceived natural origin and fewer side effects compared to conventional treatments [3]. Various herbal preparations, such as Cinnamomum verum (cinnamon), Allium sativum (garlic), Gymnema sylvestre, and Berberis vulgaris, have demonstrated anti-diabetic properties and are widely studied for their potential to manage blood glucose levels and related complications [4]. Despite these benefits, concerns about the safety of herbal medicine, particularly regarding its impact on renal and hepatic function, have emerged [5]. The kidneys and liver are particularly vulnerable to damage in diabetic patients, making it essential to evaluate the safety of these herbs in managing diabetes [6]. Histopathological examination is a vital tool for identifying organ-specific damage and understanding the underlying mechanisms of toxicity. Changes in renal and hepatic tissues, such as glomerular damage, fibrosis, hepatocyte necrosis, and steatosis, can be indicators of toxicity induced by certain herbal compounds [7]. This review explores the intersections between diabetes, herbal medicine, and histopathology, focusing on the safety of the kidneys and liver when herbal remedies are used for diabetes management. It highlights the importance of understanding both the therapeutic potential and the risks associated with herbal treatments, particularly in vulnerable organ systems like the kidneys and liver, to ensure safe and effective clinical outcomes.

Diabetes and Organ-Specific Complications: Renal and Hepatic Damage

1. Diabetic Nephropathy

Diabetic nephropathy (DN) is a progressive kidney disorder that results from prolonged hyperglycemia

associated with diabetes mellitus [8]. It is one of the most common and serious complications of diabetes, leading to end-stage renal disease (ESRD) and often requiring renal replacement therapy, including dialysis or kidney transplantation [8]. The pathogenesis of DN is multifactorial, with several mechanisms contributing to kidney damage over time. These include glomerular hyperfiltration, glomerular hypertension, and the accumulation of advanced glycation end products (AGEs) [9]. Additionally, chronic hyperglycemia promotes the overproduction of reactive oxygen species (ROS), which induce oxidative stress, further exacerbating renal injury [10]. At the histopathological level, DN is characterized by several key changes within the kidney. The glomeruli, which are responsible for filtering blood, show thickening of the basement membrane, a hallmark of early-stage diabetic nephropathy [8]. In more advanced stages, there is mesangial expansion, where the mesangium (the tissue supporting the glomeruli) becomes enlarged due to the accumulation of extracellular matrix proteins, further impairing kidney function [11]. As the disease progresses, glomerulosclerosis (scarring of the glomeruli) and tubulointerstitial fibrosis (scarring of the tubules and surrounding tissues) occur, leading to irreversible kidney damage [12]. The kidney's ability to filter waste products and regulate fluid balance deteriorates as these histopathological changes worsen [13]. The accumulation of toxic waste in the body results in complications such as hypertension, electrolyte imbalances, and fluid retention [14]. Importantly, renal dysfunction often manifests late in the disease, which is why early diagnosis and intervention are crucial [15]. The role of proteinuria (the presence of excess protein in the urine) is particularly important in diagnosing DN, as it is often one of the earliest signs of kidney injury in diabetic patients [16]. The primary therapeutic strategies for managing diabetic nephropathy aim to control blood glucose levels and blood pressure [17]. However, new research is exploring potential adjunct therapies, including herbal remedies, to alleviate renal damage and slow the progression of DN. Some herbs, such as Curcuma longa (turmeric) and Camellia sinensis (green tea), have demonstrated antioxidant and anti-inflammatory properties that may help reduce the inflammation and fibrosis that characterize diabetic kidney damage [18].

2. Diabetic Hepatopathy

The liver plays a central role in maintaining glucose homeostasis through processes like gluconeogenesis, glycogen synthesis, and insulin clearance [19]. In diabetes mellitus, particularly in patients with type 2 diabetes, the liver is often subjected to dysfunction due to insulin resistance and chronic hyperglycemia [20]. This results in the development of diabetic hepatopathy, which encompasses a spectrum of liver conditions ranging from simple fatty liver (non-alcoholic fatty liver disease, or NAFLD) to more severe forms of liver damage such as cirrhosis [21]. NAFLD is commonly found in diabetic individuals and is characterized by the accumulation of fat in liver cells, particularly hepatocytes, without significant inflammation or fibrosis [22]. However, if left untreated, NAFLD can progress to non-alcoholic steatohepatitis (NASH), a more severe form of the disease, which involves inflammation and damage to liver cells, potentially progressing to liver fibrosis and cirrhosis [23]. The histopathological hallmark of NASH includes hepatocyte ballooning, which is the swelling of liver cells, along with steatosis (fat accumulation), lobular inflammation, and varying degrees of fibrosis [24].

The development of diabetic hepatopathy is closely linked to insulin resistance, a common feature in type 2 diabetes [19]. Insulin resistance in the liver leads to increased lipogenesis (fat production) and decreased fatty acid oxidation, contributing to fat buildup [25]. In addition, oxidative stress plays a significant role in liver injury, as elevated blood glucose levels promote the production of ROS, leading to inflammation and hepatocellular damage [26]. Inflammation in the liver further activates fibrotic pathways, which result in the accumulation of collagen and other extracellular matrix proteins, leading to the development of fibrosis [27].

Histopathologically, the liver in diabetic patients often shows signs of lipid infiltration, inflammatory cell infiltration, and, in advanced stages, fibrosis and cirrhosis [28]. These changes impair the liver's ability to detoxify the body, produce proteins, and regulate glucose, further complicating the management of diabetes [1]. The combination of liver dysfunction and diabetes contributes to an increased risk of cardiovascular disease, liver failure, and other systemic complications [28].

Like diabetic nephropathy, the management of diabetic hepatopathy involves strict control of blood glucose levels, as well as addressing underlying conditions such as obesity and dyslipidemia [29]. There is also growing interest in the use of herbal medicines to manage diabetic liver damage. Herbs like Silybum marianum (milk thistle) and Curcuma longa (turmeric) have demonstrated hepatoprotective effects in both experimental models and human studies, potentially mitigating the inflammatory and fibrotic processes associated with diabetic hepatopathy [30].

Herbal Medicine in Diabetes Management

Herbal medicine has been utilized for centuries as a therapeutic approach to manage various health conditions, including diabetes [31]. The use of plant-based remedies in diabetes treatment is largely driven by their perceived safety, natural origin, and growing body of evidence supporting their efficacy in managing blood glucose levels, improving insulin sensitivity, and reducing the complications associated with diabetes [32]. Many plants possess bioactive compounds, such as alkaloids, flavonoids, terpenoids, and phenolic compounds, which have shown antioxidant, anti-inflammatory, and hypoglycemic properties [33]. These compounds help counteract the oxidative stress and inflammation that play critical roles in the pathogenesis of diabetic complications, including nephropathy and hepatopathy [33]. Several herbal agents have been extensively studied for their potential benefits in managing diabetes and its complications:

Cinnamon (Cinnamomum verum): This widely used herb contains compounds such as cinnamaldehyde, which mimic insulin action and help improve glucose metabolism [34]. Cinnamon has been shown to enhance insulin sensitivity, reduce fasting blood glucose levels, and lower HbA1c levels in diabetic patients [35].

Garlic (Allium sativum): Garlic contains sulfur compounds like allicin, which have been found to possess anti-inflammatory, antioxidant, and antihyperglycemic properties [36]. These effects help reduce oxidative stress and inflammation in diabetic organs, including the kidneys and liver, thus potentially preventing or slowing the progression of diabetic nephropathy and hepatopathy [37].

Gymnema sylvestre: This herb has long been used in traditional medicine for its ability to enhance insulin secretion and promote the regeneration of pancreatic beta cells [38]. It also reduces the absorption of glucose from the intestines, helping to lower blood sugar levels. Gymnema has shown promise in improving renal and hepatic function in diabetic models by reducing oxidative stress and inflammation [38,39].

Berberis vulgaris: Known for its bioactive compound berberine, this herb has been shown to exert anti-hyperglycemic, anti-inflammatory, and anti-oxidant effects [40]. Berberine has been reported to improve insulin sensitivity, reduce blood glucose levels, and protect against diabetic complications, including kidney and liver damage [41].

While herbal medicine offers promising benefits in managing diabetes and related complications, it is essential to consider the potential for herb-drug interactions and organ toxicity. Herbal remedies, when used appropriately and in combination with conventional therapies, may enhance the therapeutic outcomes for diabetic patients [42]. However, more research, particularly clinical trials and long-term studies, is necessary to fully understand the safety and efficacy of these herbs in the management of diabetic nephropathy and hepatopathy.

Herbal Medicine and Histopathology: Renal and Hepatic Safety Concerns

1. Renal Toxicity

While herbal medicines offer numerous benefits in managing diabetes, some herbs have been associated with renal toxicity [43]. The kidneys are particularly vulnerable to damage because they play a central role in the metabolism, absorption, and excretion of many compounds, including herbal constituents [44]. Certain herbs may induce nephrotoxicity through several mechanisms, which can lead to irreversible kidney damage [43]. One of the primary mechanisms by which herbal medicines can induce renal damage is through oxidative stress [45]. Many herbal compounds, such as flavonoids and polyphenols, have antioxidant properties that provide therapeutic effects [46]. However, when taken in excess or for prolonged periods, some herbs may trigger excessive production of reactive oxygen species (ROS), overwhelming the body's antioxidant defenses and leading to oxidative injury to kidney tissues [47]. This can result in damage to renal cells and tissues, exacerbating kidney dysfunction [43]. Renal fibrosis is another mechanism of toxicity linked to some herbal medicines [48]. Herbs such as Cinnamomum and Camellia sinensis have been shown to induce mesangial expansion and glomerulosclerosis, two hallmarks of kidney damage that result from excessive extracellular matrix production [49]. Additionally, some herbs have been reported to cause interstitial fibrosis, further impairing kidney function [50]. Certain herbal bioactive compounds, such as those found in Aristolochia species, are known to produce nephrotoxic metabolites, contributing to renal damage [51]. These metabolites can directly damage renal cells, leading to severe nephropathy and renal failure. Histopathological evidence of herbal-induced kidney damage typically includes glomerular lesions, tubular atrophy, interstitial inflammation, and fibrosis [50].

2. Hepatic Toxicity

Herbal medicines can also lead to hepatic toxicity, especially when used over extended periods or in high doses. The liver, being the primary organ for metabolizing drugs and toxins, is particularly susceptible to damage from certain herbal compounds

[52]. Cytotoxicity is a primary mechanism of herbal-induced hepatotoxicity [53]. Many herbal compounds, including those found in Kava kava and Piper methysticum, are capable of directly damaging hepatocytes (liver cells), leading to cell death [54,55]. This can result in acute liver injury, which, if not addressed, may progress to chronic liver diseases. Cholestasis, a condition where bile flow is impaired, is another mechanism through which some herbal medicines cause liver damage [56]. Herbs that interfere with bile secretion can cause bile acid accumulation in the liver, leading to inflammation and hepatocellular damage [57]. This condition can progress to fibrosis and, eventually, cirrhosis if the herbal remedy is used long-term. Furthermore, chronic use of certain herbs has been linked to liver fibrosis and cirrhosis. Kava kava, for example, has been associated with hepatotoxicity, resulting in liver fibrosis in some patients [58]. Histopathological changes induced by herbal hepatotoxicity typically include hepatocyte necrosis, fatty infiltration, inflammatory cell infiltration, and collagen deposition, all of which are indicative of liver damage [59]. Given the potential for both renal and hepatic toxicity, it is essential to carefully monitor the use of herbal medicines in diabetic patients, particularly those with pre-existing renal or hepatic conditions. Histopathological analysis remains a critical tool in assessing the degree of damage caused by these herbs, helping clinicians make informed decisions about their use [60].

Safety Profile and Clinical Considerations

Although herbal medicines offer promising therapeutic benefits for managing diabetes, their safety profiles, particularly regarding long-term use, remain insufficiently understood. The effectiveness and safety of herbal remedies depend on multiple factors, including the quality of the herbal preparation, appropriate dosing, and the duration of treatment [61]. Inconsistent quality and potency of herbal medicines pose a significant challenge, as the concentration of active compounds may vary between batches or products, potentially leading to inconsistent therapeutic outcomes or adverse effects [62].

Given the potential for renal and hepatic toxicity, especially in patients with pre-existing organ conditions, it is essential to consider the possible risks when using herbal remedies in diabetic management. Herbs that have nephrotoxic or hepatotoxic potential should be used cautiously, and careful monitoring of renal and liver function is recommended during treatment. This includes regular blood tests to assess kidney function (such as serum creatinine and blood urea nitrogen levels) and liver enzymes (such as ALT, AST, and bilirubin levels), as well as ultrasonography or histopathological examination when necessary [45]. Furthermore, patients on concurrent pharmacological treatments for diabetes must be monitored for herb-drug interactions, as some herbal compounds may alter the metabolism of conventional medications, potentially leading to adverse effects or reduced efficacy [63]. For instance, herbs that affect cytochrome P450 enzymes or other metabolic pathways could increase or decrease the plasma levels of antidiabetic drugs, resulting in either toxicity or therapeutic failure [64]. Healthcare providers should be proactive in identifying potential interactions and adjusting dosages accordingly. Ultimately, the safety of herbal medicines in diabetes management necessitates further investigation through well-designed clinical trials. These studies should focus on the long-term effects, optimal dosage, and the mechanisms underlying potential toxicities, particularly with respect to renal and hepatic safety.

CONCLUSION

The use of herbal medicines in diabetes management offers significant promise, particularly for improving blood glucose control and reducing complications associated with the disease. However, the safety of these therapies, especially concerning their potential for renal and hepatic toxicity, remains a critical concern. Understanding the histopathological changes induced by herbal medicines in diabetic patients is essential for ensuring their safe and effective use. Both experimental and clinical research play crucial roles in addressing these concerns, as they can provide insights into the mechanisms by which herbal compounds affect organ systems and contribute to the development of complications such as nephropathy and hepatopathy. While current evidence supports the beneficial effects of many herbal remedies, more rigorous clinical trials and long-term studies are needed to establish their safety profiles. These studies should focus on evaluating the potential risks of herbal medicine on renal and hepatic function, particularly in vulnerable populations such as those with pre-existing kidney or liver disease. Additionally, further histopathological investigations will enhance our understanding of the cellular and tissue-level changes associated with herbal-induced In conclusion, herbal medicines should be used with caution in diabetic patients, especially those with existing organ dysfunction. Regular monitoring, including histopathological assessments, is crucial to ensuring that these natural remedies are both safe and effective in managing diabetes and its complications. By bridging the gap between clinical practice and

scientific research, we can optimize the therapeutic potential of herbal remedies while minimizing risks.

REFERENCES

1. 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
2. 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.
3. 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.
4. Hossain MdJ, Al-Mamun Md, Islam MdR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. *Health Science Reports*. 2024;7(3). doi:10.1002/hsr2.2004
5. Wachtel-Galor S, Benzie IFF. Herbal Medicine. *Herbal Medicine - NCBI Bookshelf*. 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92773/
6. 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
7. 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
8. 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
9. Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. *Hepatology*. 2016;65(1):363–73. doi:10.1002/hep.28813
10. 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
11. Agarwal R. Pathogenesis of diabetic nephropathy. *ADA Clinical Compendia*. 2021;2021(1):2–7. doi:10.2337/db20211-2
12. Uroko Robert Ikechukwu., Agbafor Amarachi, Uchenna Oluomachi Nancy, Achi Ngozi Kalu, Egba Simeon Ikechukwu**,** Nweje-Anyalowu Paul Chukwuemaka and Ngwu Ogochukwu Rita. Evaluation of Antioxidant Activity of Aqueous Extracts of Palm Friuts *(Elaeis guineensis)* Asian Journal of Biochemistry, 2017; 12: 49-57
13. Thomas HY, Versypt ANF. Pathophysiology of mesangial expansion in diabetic nephropathy: mesangial structure, glomerular biomechanics, and biochemical signaling and regulation. *Journal of Biological Engineering*. 2022;16(1). doi:10.1186/s13036-022-00299-4
14. 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
15. Murray IV, Paolini MA. Histology, kidney and glomerulus. *StatPearls - NCBI Bookshelf*. 2023. Availablefrom: https://www.ncbi.nlm.nih.gov/books/NBK554544/
16. Zemaitis MR, Foris LA, Katta S, Bashir K. Uremia. *StatPearls - NCBI Bookshelf*. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441859/

17. 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
18. Rout P, Jialal I. Diabetic nephropathy. *StatPearls - NCBI Bookshelf*. 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534200/
19. Abdel-Rahman EM, Saadulla L, Reeves WB, Awad AS. Therapeutic Modalities in Diabetic Nephropathy: Standard and emerging approaches. *Journal of General Internal Medicine*. 2011;27(4):458–68. doi:10.1007/s11606-011-1912-5
20. Alum, E. U., Umoru, G. U., Uti, D. E., Aja, P. M., Ugwu, O. P., Orji, O. U., Nwali, B. U., Ezeani, N., Edwin, N., Orinya, F. O. 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.
21. Sharabi K, Tavares CDJ, Rines AK, Puigserver P. Molecular pathophysiology of hepatic glucose production. *Molecular Aspects of Medicine*. 2015;46:21–33. doi:10.1016/j.mam.2015.09.003
22. Uroko RI., Uchenna ON., Achi NK., Agbafor A., Egba SI and Ojiakor CA (2019) Effects of aqueous extracts of palm fruits (*Elaeis guineensis*) on lipid profile and kidney function indices of male Wistar albino rats. *Jordan Journal of Biological Scienes*, 2019; 12(1): 5-16.
23. Bhatt HB, Smith RJ. Fatty liver disease in diabetes mellitus. *PubMed*. 2015;4(2):101–8. Available from: https://pubmed.ncbi.nlm.nih.gov/26005676
24. Akshintala D, Chugh R, Amer F, Cusi K. Nonalcoholic fatty liver disease: the overlooked complication of type 2 diabetes. *Endotext - NCBI Bookshelf*. 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544043/
25. Peng C, Stewart AG, Woodman OL, Ritchie RH, Qin CX. Non-Alcoholic steatohepatitis: A review of its mechanism, models and medical treatments. *Frontiers in Pharmacology*. 2020;11. doi:10.3389/fphar.2020.603926
26. 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
27. Smith GI, Shankaran M, Yoshino M, Schweitzer GG, Chondronikola M, Beals JW, et al. Insulin resistance drives hepatic de novo lipogenesis in nonalcoholic fatty liver disease. *Journal of Clinical Investigation*. 2019;130(3):1453–60. doi:10.1172/jci134165
28. 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
29. Tanwar S, Rhodes F, Srivastava A, Trembling PM, Rosenberg WM. Inflammation and fibrosis in chronic liver diseases including non-alcoholic fatty liver disease and hepatitis C. *World Journal of Gastroenterology*. 2020;26(2):109–33. doi:10.3748/wjg.v26.i2.109
30. Garcia-Compean D, Jaquez-Quintana JO, Gonzalez-Gonzalez JA, Maldonado-Garza H. Liver cirrhosis and diabetes: Risk factors, pathophysiology, clinical implications and management. *World Journal of Gastroenterology*. 2009;15(3):280. doi:10.3748/wjg.15.280
31. Orji, U. O., Ibiam, U. A., Awoke, J. N., Atoki, A. V., Eze, E. D., Obasi, O. D., … Aja, P. M. (2025). Ethanolic extract of *Cnidoscolus aconitifolius* leaves alleviates insulin resistance by modulating oxidative stress and inflammation in albino rats exposed to heavy metal mixture. *Natural Product Research*, 1–14. https://doi.org/10.1080/14786419.2025.2478654
32. Uti, D.E., Atangwho, I.J., Alum, E.U., Egba, S.I., Ugwu, O.P.C., Ikechukwu, G.C. Natural Antidiabetic Agents: Current Evidence and Development Pathways from Medicinal Plants to Clinical use. Natural Product Communications. 2025;20(3). doi:10.1177/1934578X251323393
33. Mitaki, N.B., Fasogbon, I.V., Ojiakor, O.V., Makena, W., Ikuomola, E. O., Dangana, R.S., et al. (2025). A systematic review of plant-based therapy for the management of diabetes mellitus in the East Africa community. Phytomedicine Plus, 5(1): 100717. https://doi.org/10.1016/j.phyplu.2024.100717
34. Yedjou CG, Grigsby J, Mbemi A, Nelson D, Mildort B, Latinwo L, et al.

The management of diabetes mellitus using medicinal plants and vitamins. *International Journal of Molecular Sciences*. 2023;24(10):9085. doi:10.3390/ijms24109085
35. Gonfa YH, Tessema FB, Bachheti A, Rai N, Tadesse MG, Singab AN, et al. Anti-inflammatory activity of phytochemicals from medicinal plants and their nanoparticles: A review. *Current Research in Biotechnology*. 2023;6:100152. doi:10.1016/j.crbiot.2023.100152
36. Qin B, Panickar KS, Anderson RA. Cinnamon: Potential role in the prevention of insulin resistance, metabolic syndrome, and type 2 diabetes. *Journal of Diabetes Science and Technology*. 2010;4(3):685–93. doi:10.1177/193229681000400324
37. Qin B, Panickar KS, Anderson RA. Cinnamon: Potential role in the prevention of insulin resistance, metabolic syndrome, and type 2 diabetes. *Journal of Diabetes Science and Technology*. 2010;4(3):685–93. doi:10.1177/193229681000400324
38. Shang A, Cao SY, Xu XY, Gan RY, Tang GY, Corke H, et al. Bioactive Compounds and Biological Functions of Garlic (Allium sativum L.). *Foods*. 2019;8(7):246. doi:10.3390/foods8070246
39. Lee DY, Li H, Lim HJ, Lee HJ, Jeon R, Ryu JH. Anti-Inflammatory Activity of Sulfur-Containing Compounds from Garlic. *Journal of Medicinal Food*. 2012;15(11):992–9. doi:10.1089/jmf.2012.2275
40. Tiwari P, Mishra BN, Sangwan NS. Phytochemical and Pharmacological Properties of Gymnema sylvestre: An Important Medicinal Plant. *BioMed Research International*. 2014;2014:1–18. doi:10.1155/2014/830285
41. Venkatakrishnan K, Chiu HF, Wang CK. Popular functional foods and herbs for the management of type-2-diabetes mellitus: A comprehensive review with special reference to clinical trials and its proposed mechanism. *Journal of Functional Foods*. 2019;57:425–38. doi:10.1016/j.jff.2019.04.039
42. Dinesh P, Rasool M. Herbal formulations and their bioactive components as dietary supplements for treating rheumatoid arthritis. In: *Elsevier eBooks*. 2019. p. 385–99. doi:10.1016/b978-0-12-813820-5.00022-2
43. Utami AR, Maksum IP, Deawati Y. Berberine and its study as an antidiabetic compound. *Biology*. 2023;12(7):973. doi:10.3390/biology12070973
44. Sriraman S, Sreejith D, Andrew E, Okello I, Willcox M. Use of herbal medicines for the management of type 2 diabetes: A systematic review of qualitative studies. *Complementary Therapies in Clinical Practice*. 2023;53:101808. doi:10.1016/j.ctcp.2023.101808
45. Asif M. A brief study of toxic effects of some medicinal herbs on kidney. *Advanced Biomedical Research*. 2012;1(1):44. doi:10.4103/2277-9175.100144
46. Dalal R, Bruss ZS, Sehdev JS. Physiology, renal blood flow and filtration. *StatPearls - NCBI Bookshelf*. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482248/
47. Xu X, Zhu R, Ying J, Zhao M, Wu X, Cao G, et al. Nephrotoxicity of herbal medicine and its prevention. *Frontiers in Pharmacology*. 2020;11. doi:10.3389/fphar.2020.569551
48. Ogugua, Victor N., Njoku, Obioma U., Egba, Simeon I., Uroko, Robert I and Ignatius Glory. In vitro study of nutritional and antioxidant properties of methanol extract of *Nauclea latifolia* root bark. Biomedical Research, 2018; 29(21): 3766-3773
49. Ochulor Okechukwu C., Njoku Obioma U., Uroko Robert I and Egba Simeon I. Nutritional composition of *Jatropha tanjorensis* leaves and effects of its aqueous extract on carbon tetrachloride induced oxidative stress in male Wistar albino rats. Biomedical Research 2018; 29(19): 3569-3576
50. Huang R, Fu P, Ma L. Kidney fibrosis: from mechanisms to therapeutic medicines. *Signal Transduction and Targeted Therapy*. 2023;8(1). doi:10.1038/s41392-023-01379-7
51. Egba, SI., Ogbodo, JO., Ogbodo PO and Obike CA (2017) Toxicological Evaluation of Two Named Herbal Remedies Sold Across Orumba South Local Government of Anambra State, South-Eastern Nigeria. Asian Journal of Research in Biochemistry, 1(1):1-6
52. Asif M. A brief study of toxic effects of some medicinal herbs on kidney. *Advanced Biomedical Research*. 2012;1(1):44. doi:10.4103/2277-9175.100144
53. Abolhassanzadeh Z, Ansari S, Lorigooini Z, Anjomshoa M, Bijad E, Ramezannezhad P, et al. The nephrotoxicity of Aristolochia rotunda L. in rats: Mitochondrion as a target for renal toxicity of Aristolochic acids-containing plants. *Heliyon*. 2023;9(11):e21848. doi:10.1016/j.heliyon.2023.e21848

54. Gu X, Manautou JE. Molecular mechanisms underlying chemical liver injury. *Expert Reviews in Molecular Medicine*. 2012;14. doi:10.1017/s1462399411002110
55. Rashid NA, Halim SASA, Teoh SL, Budin SB, Hussan F, Ridzuan NRA, et al. The role of natural antioxidants in cisplatin-induced hepatotoxicity. *Biomedicine & Pharmacotherapy*. 2021;144:112328. doi:10.1016/j.biopha.2021.112328
56. National Institute of Diabetes and Digestive and Kidney Diseases. Kava kava. *LiverTox - NCBI Bookshelf*. 2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548637/
57. Zhou P, Gross S, Liu JH, Yu BY, Feng LL, Nolta J, et al. Flavokawain B, the hepatotoxic constituent from kava root, induces GSH-sensitive oxidative stress through modulation of IKK/NF-κB and MAPK signaling pathways. *The FASEB Journal*. 2010;24(12):4722–32. doi:10.1096/fj.10-163311
58. Kullak-Ublick GA. Drug-Induced cholestatic liver Disease. *Madame Curie Bioscience Database - NCBI Bookshelf*. 2013. Available from: https://www.ncbi.nlm.nih.gov/books/NBK6102/
59. Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. *Hepatology*. 2016;65(1):363–73. doi:10.1002/hep.28813
60. Teschke R, Sarris J, Schweitzer I. Kava hepatotoxicity in traditional and modern use: the presumed Pacific kava paradox hypothesis revisited. *British Journal of Clinical Pharmacology*. 2011;73(2):170–4.doi:10.1111/j.1365-2125.2011.04070.x
61. Kleiner DE. Drug-induced liver injury. *Gastroenterology Clinics of North America*. 2017;46(2):273–96. doi:10.1016/j.gtc.2017.01.004
62. Gurina TS, Simms L. Histology, staining. *StatPearls - NCBI Bookshelf*. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557663/
63. Wachtel-Galor S, Benzie IFF. Herbal Medicine. *Herbal Medicine - NCBI Bookshelf*. 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92773/#_ncbi_dlg_citbx_NBK92773
64. Wang H, Chen Y, Wang L, Liu Q, Yang S, Wang C. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. *Frontiers in Pharmacology*. 2023;14. doi:10.3389/fphar.2023.1265178
65. Gupta RC, Chang D, Nammi S, Bensoussan A, Bilinski K, Roufogalis BD. Interactions between antidiabetic drugs and herbs: an overview of mechanisms of action and clinical implications. *Diabetology & Metabolic Syndrome*. 2017;9(1). doi:10.1186/s13098-017-0254-9
66. Jack BU, Malherbe CJ, Mamushi M, Muller CJF, Joubert E, Louw J, et al. Adipose tissue as a possible therapeutic target for polyphenols: A case for Cyclopia extracts as anti-obesity nutraceuticals. *Biomedicine & Pharmacotherapy*. 2019;120:109439. doi:10.1016/j.biopha.2019.109439

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