www.idosr.org Kamanzi
©IDOSR PUBLICATIONS
ISSN: 2579-079X
International Digital Organization for Scientific Research IDOSR JST/26/1130000
IDOSR JOURNAL OF SCIENCE AND TECHNOLOGY 12(1):103-108, 2026.
https://doi.org/10.59298/IDOSR/JST/26/113.103108

Hepatotoxicity in Chronic Metabolic Disease: How Diabetes, Immune Activation, and Oxidative Stress Converge to Drive Liver Injury

Kamanzi Ntakirutimana G.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Chronic metabolic diseases-particularly type 2 diabetes mellitus (T2DM) and the metabolic syndrome-are major drivers of contemporary liver morbidity, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis. Hepatotoxicity in this context is not a single-pathway event but the outcome of sustained metabolic overload, maladaptive immune activation, and persistent oxidative stress that together create hepatocellular injury, organelle dysfunction, and maladaptive remodeling. This review synthesizes current mechanistic understanding of how hyperglycemia and insulin resistance perturb hepatocyte metabolism, how innate and adaptive immune responses amplify tissue damage, and how oxidative stress both mediates and perpetuates injury through mitochondrial dysfunction, lipid peroxidation, and disruption of antioxidant pathways (e.g., Nrf2). We discuss the role of cytochrome P450 (CYP) enzymes and xenobiotic handling in modifying susceptibility to drug-induced liver injury (DILI) in patients with metabolic disease, summarize emerging biomarkers and mechanistic readouts, and highlight therapeutic strategies targeting the metabolic–immune–oxidative axis. Recognizing the interconnectedness of these processes is essential to improving diagnosis, stratifying risk for hepatotoxic reactions, and developing targeted interventions for liver protection in people with chronic metabolic disease.

Keywords: hepatotoxicity, diabetes, oxidative stress, immune activation, cytochrome P450

INTRODUCTION

The global rise of obesity and type 2 diabetes mellitus has produced a parallel and increasingly concerning surge in metabolic liver disease[1]. Nonalcoholic fatty liver disease, once viewed primarily as a benign accumulation of hepatic fat, is now recognized as part of a broader spectrum of metabolic dysfunction. While simple steatosis may remain stable for some individuals, a substantial proportion progress to more severe inflammatory and fibrotic stages[2]. These advanced forms, collectively represented by nonalcoholic steatohepatitis, reflect a complex interplay of metabolic stress, immune activation, and oxidative injury rather than lipid excess alone. This evolving understanding highlights the liver's central position at the crossroads of nutrient metabolism, endocrine signaling, and innate immunity[3]. Several interconnected mechanisms drive hepatotoxicity in individuals with metabolic disease. Persistent hyperglycemia exposes hepatocytes to glucotoxic stress, altering mitochondrial activity and promoting the formation of reactive oxygen species. Elevated circulating lipids increase hepatic uptake of fatty acids, some of which become incorporated into harmful lipid intermediates that trigger cellular dysfunction[4]. At the same time, adipose tissue inflammation and altered gut–liver interactions stimulate immune pathways that further intensify hepatic injury. The liver's antioxidant defenses, although robust under physiological conditions, are often overwhelmed in this setting, allowing oxidative stress to accumulate and perpetuate damage[5].

These disturbances do not act in isolation but reinforce one another, generating a self-sustaining cycle of hepatocellular stress, inflammatory signaling, and impaired repair capacity[6]. As a result, individuals with metabolic disease are more susceptible not only to progressive liver injury but also to environmental and pharmacologic insults that may otherwise be well tolerated. Understanding how these metabolic, immunologic, and redox pathways converge is essential for improving early detection, refining risk stratification, and designing targeted therapeutic strategies[7]. As obesity and diabetes continue to rise globally, a comprehensive grasp of these mechanisms is critical for preventing future liver-related morbidity and improving long-term outcomes.

Lipid overload, insulin resistance, and lipotoxicity

A major contributor to hepatotoxicity in metabolic disease is the excessive flux of fatty acids to the liver[8]. In states of insulin resistance, adipose tissue becomes hyperactive in breaking down stored fats, resulting in elevated levels of free fatty acids in the bloodstream. The liver, attempting to manage this overload, increases uptake and conversion of these fatty acids into triglycerides[9]. While this initially serves as a protective buffer, the capacity for safe storage is limited. Once this threshold is exceeded, harmful lipid intermediates begin to accumulate. Molecules such as diacylglycerols, ceramides, and free cholesterol disrupt cellular signaling pathways, interfere with insulin action, and induce mitochondrial stress[10]. These toxic lipids can initiate cell death programs and stimulate inflammatory responses, marking the transition from simple fat accumulation to true liver injury[11]. This metabolic stress also heightens oxidative damage and enhances the expression of inflammatory mediators, reinforcing a cycle that gradually worsens liver function[12].

Organellar stress: ER and mitochondria

Chronic nutrient excess places considerable pressure on intracellular organelles. The endoplasmic reticulum becomes overloaded with demands for protein and lipid synthesis, triggering stress responses designed to restore balance[13]. When this stress becomes excessive, the protective response shifts toward pathways that promote inflammation and programmed cell death. Mitochondria, central to energy production and fatty acid oxidation, likewise become impaired as they struggle to process the surplus of nutrients[14]. Reduced efficiency in energy generation and increased production of reactive oxygen species weaken the cell's defenses. These disturbances make hepatocytes more susceptible to injury from infections, drugs, and additional metabolic stressors, reinforcing the path toward progressive liver damage[15]

Oxidative stress: mediator and perpetuator of hepatotoxicity

Sources and consequences of ROS in the diseased liver

Oxidative stress is one of the most significant and persistent drivers of liver injury in chronic metabolic disease[16]. In the metabolically overloaded liver, reactive oxygen species are generated from multiple intracellular sites. Mitochondria, which are responsible for energy production and fatty acid oxidation, become overwhelmed by excessive nutrient flux. As their capacity to oxidize fatty acids declines, they begin to leak electrons that react with oxygen, forming reactive oxygen species[17]. The endoplasmic reticulum also contributes to oxidative stress when it becomes overburdened with protein folding demands. During this process, oxidoreductase enzymes generate reactive oxygen species as by-products, which accumulate when the system is dysregulated[18]. Peroxisomes, which normally assist in lipid metabolism, become dysfunctional in the presence of chronic metabolic stress and release additional reactive oxygen species. Enzymatic reactions mediated by cytochrome P450, particularly under conditions of increased drug load or toxin exposure, further add to oxidative pressure[19]. Collectively, these sources contribute to a sustained environment of oxidative imbalance. The consequences of these reactive species are wide-ranging. One major outcome is lipid peroxidation, through which reactive oxygen species attack cellular membranes and generate harmful aldehydes such as malondialdehyde and 4-hydroxynonenal[20]. These aldehydes can form adducts with proteins, enzymes, and DNA, impairing normal cellular function and initiating inflammatory signaling cascades. Persistent oxidative stress disrupts metabolic pathways, triggers cell death mechanisms, and directly injures hepatocytes[21]. In addition, oxidative stress modifies immune cell behavior, promoting a shift toward a chronic inflammatory state that perpetuates tissue injury. Over time, this cycle of oxidative damage and inflammation contributes substantially to the progression of metabolic liver disease[22].

Antioxidant defenses and Nrf2 signaling

To counteract these damaging processes, the liver depends on an intricate network of antioxidant defenses. Nrf2, a transcription factor that orchestrates the expression of numerous protective genes, plays a central role in maintaining redox balance[23]. Under normal conditions, Nrf2 remains inactive, but in the presence of oxidative stress it becomes activated and translocates to the nucleus. There, it stimulates production of glutathione-generating enzymes, heme oxygenase-1, and other detoxifying proteins that help neutralize reactive oxygen species[24]. However, in metabolic disease, this antioxidant defense system often becomes inadequate. Chronic hyperglycemia, lipid overload, and inflammatory signaling can dampen Nrf2 activation or overwhelm its protective capacity. As a result, hepatocytes become increasingly vulnerable to oxidative damage, allowing reactive oxygen species to exert greater harm[25]. This weakened antioxidant response also reduces the liver's resilience against medications or environmental toxins, increasing the risk of drug-induced liver injury[26].

Drug metabolism, CYP450, and altered susceptibility to DILI

The interaction between metabolic disease and drug metabolism further complicates the hepatotoxic landscape. Individuals with diabetes or fatty liver disease frequently use multiple medications, and their livers undergo structural and functional changes that influence how drugs are processed[27]. Cytochrome P450 enzymes, which are responsible for metabolizing many drugs and xenobiotics, can exhibit altered activity in fatty or inflamed liver tissue. Some isoforms may be upregulated, increasing the formation of reactive metabolites, while others may be

suppressed, reducing detoxification capacity. These shifts can amplify the production of reactive oxygen species during drug metabolism, compounding oxidative stress in an already compromised liver[28]. As a result, individuals with metabolic disorders may have a heightened susceptibility to drug-induced liver injury, even at standard therapeutic doses. Reduced antioxidant capacity further increases this vulnerability, making careful monitoring and dose adjustment essential[29]. Clinicians must consider these metabolic and biochemical alterations when prescribing medications, particularly those known to carry hepatotoxic risks. The convergence of oxidative stress, impaired detoxification, and metabolic dysfunction underscores the importance of individualized therapeutic strategies in this high-risk population[30].

Therapeutic strategies and research directions

Metabolic control and lifestyle

Improving underlying metabolic health remains the foundation of hepatoprotective therapy in chronic metabolic disease[31]. Even modest weight loss is associated with significant reductions in hepatic fat accumulation, decreased inflammation, and improved insulin sensitivity, all of which weaken the drivers of oxidative and immune-mediated injury. Dietary interventions that lower caloric intake, reduce refined carbohydrates, and promote balanced nutrient composition are central to this effort[32]. Regular physical activity enhances mitochondrial efficiency, stimulates fatty acid oxidation, and improves systemic glucose handling. Achieving better glycemic control reduces chronic glucotoxicity and minimizes oxidative burden on hepatocytes[33]. Together, these lifestyle-centered approaches form a first-line strategy capable of slowing or reversing early liver injury in many individuals.

Targeting oxidative stress and mitochondrial health

Given the central role of oxidative stress in liver injury, therapeutic strategies aimed at enhancing antioxidant defenses or stabilizing mitochondria are a major focus of ongoing research. Pharmacologic antioxidants, such as N-acetylcysteine, may replenish glutathione stores in selected clinical scenarios, while experimental compounds designed to activate Nrf2 signaling seek to strengthen endogenous antioxidant pathways[34]. Parallel efforts are exploring agents that promote mitochondrial quality control through enhanced mitophagy or that support efficient beta-oxidation. While preclinical findings are encouraging, well-controlled clinical trials are needed to determine their long-term benefits and safety profiles[35].

Modulating immune responses

Chronic inflammation is a major driver of hepatocellular damage, making immune-targeted therapies an important area of investigation[36]. Agents that block chemokine receptors involved in the recruitment of inflammatory cells, or biologics that inhibit cytokines such as interleukin-1 beta, may help reduce persistent liver inflammation. Future strategies emphasize precision approaches that adjust immune activity without broadly suppressing host defenses[37]. Modifying macrophage polarization or regulating pathogenic T cell responses may provide more targeted and sustainable benefits.

Personalized medicine and drug safety

As understanding of metabolic liver disease deepens, personalized approaches to predicting hepatotoxic risk are becoming feasible. Genomic, metabolomic, and microbiome-derived data may help identify individuals who metabolize drugs differently or possess heightened vulnerability to oxidative or inflammatory injury[38]. Polymorphisms in drug-metabolizing enzymes, particularly within the cytochrome P450 family, can influence how medications are processed and the likelihood of harmful metabolite formation[39]. Incorporating such information into clinical decision-making offers the potential for safer prescribing, reduced incidence of drug-induced liver injury, and more effective individualized therapy.

CONCLUSION

Hepatotoxicity in chronic metabolic disease is a multifactorial process in which diabetes-related metabolic stress, maladaptive immune activation, and oxidative damage intersect to drive liver injury. The bidirectional interactions among these axes create feed-forward loops that transform metabolic overload into chronic inflammation, cell death and fibrosis. Clinically, this means patients with T2DM or metabolic syndrome require careful assessment for liver injury, judicious prescribing, and therapeutic strategies that address metabolism, inflammation and redox balance simultaneously. Future research should prioritize mechanistic biomarkers that capture the triad's activity, and clinical trials testing combination therapies that restore metabolic homeostasis while attenuating immune and oxidative drivers of hepatotoxicity.

REFERENCES

1. Hameed I, Masoodi SR, Mir SA, Nabi M, Ghazanfar K, Ganai BA. Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition. World J Diabetes. 2015 May 15;6(4):598-612. doi: 10.4239/wjd.v6.i4.598. PMID: 25987957; PMCID: PMC4434080.
2. Danpanichkul P, Suparan K, Diaz LA, Fallon MB, Chen VL, Namsathimaphorn K, Rakwong K, Inkongngam T, Kaeosri C, Kalligeros M, Wattanachayakul P, Ng CH, Takahashi H, Huang DQ, Muthiah MD, Arab JP, Kim D, White TM, Noureddin M, Bugianesi E, Jepsen P, Wong VWS, Lazarus JV,

Wijarnpreecha K. The Rising Global Burden of MASLD and Other Metabolic Diseases (2000-2021). United European Gastroenterol J. 2025 Sep;13(7):1141-1154. doi: 10.1002/ueg2.70072. Epub 2025 Jul 3. PMID: 40605557; PMCID: PMC12463718.

3. Aja O. A., Egba S. I., Uhuo Emmanuel Nnaemeka, Alaebo Prince Ogocukwu, Mba Obinna Joseph, and Oriaku Chinwe Edith. Hepatoprotective potentials of aqueous chloroform and methanol leaf extracts Whitfieldia lateritia 2, 4-dinitrophenylhydrazine induced anaemia in rats. Bio-research and Biotechnology, 2022; 20(2) 1434-1445
4. 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.
5. Ibiam U. A.,Uti, D. E., Ejeogo, C.C., Orji, O. U. Aja, P. M., Ezeani, N. N., Alum, E. U., Chukwu, C., Aloke, C., Itodo, M. O., Agada, S. A., Umoru, G. U., Obeten, U. N., Nwobodo, V. O. G., Nwadum, S. K., Udoudoh, M. P. Xylopiaaethiopica Attenuates Oxidative Stress and Hepatorenal Damage in Testosterone Propionate-Induced Benign Prostatic Hyperplasia in Rats. Journal of Health and Allied Sciences. 2024, 01: 1-148. https://doi.org/10.1055/s-0043-1777836.
6. Wan Z, Hallajzadeh J. The Beneficial Effects of Resveratrol on Hepatocellular Carcinoma and Nonalcoholic Fatty Liver Disease: Modulation of Apoptosis, Autophagy, Inflammation, and Oxidative Stress. Food Sci Nutr. 2025 Jul 24;13(7):e70555. doi: 10.1002/fsn3.70555. PMID: 40708783; PMCID: PMC12288622.
7. Jian Y, Li Y, Zhou Y, Mu W. Pollutants in Microenvironmental Cellular Interactions During Liver Inflammation Cancer Transition and the Application of Multi-Omics Analysis. Toxics. 2025; 13(3):163. https://doi.org/10.3390/toxics13030163
8. Badmus OO, Hillhouse SA, Anderson CD, Hinds TD, Stec DE. Molecular mechanisms of metabolic associated fatty liver disease (MAFLD): functional analysis of lipid metabolism pathways. Clin Sci (Lond). 2022 Sep 30;136(18):1347-1366. doi: 10.1042/CS20220572. PMID: 36148775; PMCID: PMC9508552.
9. Alves-Bezerra M, Cohen DE. Triglyceride Metabolism in the Liver. Compr Physiol. 2017 Dec 12;8(1):1-8. doi: 10.1002/cphy.c170012. PMID: 29357123; PMCID: PMC6376873.
10. Aja, P. M., Igwenyi, I. O., Ugwu, O. P. C., Orji, O. U., Alum, E. U. Evaluation of Anti-diabetic Effect and Liver Function Indices of Ethanol Extracts of *Moringa oleifera* and *Cajanus cajan* Leaves in Alloxan Induced Diabetic Albino Rats. Global Veterinaria 2015; 14(3): 439-447. DOI: 10.5829/idosi.gv.2015.14.03.93129.
11. Cheng Z, Chu H, Seki E, Lin R, Yang L. Hepatocyte programmed cell death: the trigger for inflammation and fibrosis in metabolic dysfunction-associated steatohepatitis. Front Cell Dev Biol. 2024 Jul 12;12:1431921. doi: 10.3389/fcell.2024.1431921. PMID: 39071804; PMCID: PMC11272544.
12. Nwadum, S.K., Ibiam, U.A., Uti, D.E., Umoru, G.U., Udoudoh, M.P., Aja, P.M., Alum, E.U.,Mordi, C.J., Ekpono, E.U., Obeten, U.N., Omang, W.A., Agada, S.A. *Cocos nucifera* Water Ameliorated Hepatic Complications and Attenuated Oxidative Stress in Cadmium-Induced Hepatotoxicity. Asian J. Biol. Sci, 2023; 16(4), 522-536. https://doi.org/10.17311/ajbs.2023.522.536.
13. Oakes SA, Papa FR. The role of endoplasmic reticulum stress in human pathology. Annu Rev Pathol. 2015;10:173-94. doi: 10.1146/annurev-pathol-012513-104649. Epub 2014 Oct 27. PMID: 25387057; PMCID: PMC5568783.
14. Guo Z, Chi R, Peng Y, Sun K, Liu H, Guo F, Guo J. The Role and Interactive Mechanism of Endoplasmic Reticulum Stress and Ferroptosis in Musculoskeletal Disorders. Biomolecules. 2024; 14(11):1369. https://doi.org/10.3390/biom14111369
15. Ukpabi-Ugo Jacinta Chigozie., Monanu, Michael Okechukwu., Patrick-Iwuanyanwu, Kingsley and Egbachukwu Simeon Ikechukwu. Potential hepatoprotective effect of different solvent fractions of *Ocimum gratissimum* (O G) in a paracetamol-induced hepatotoxicity in Wistar albino rats. *ScopeMed* 2016; 5(1): 10-16
16. Ogugua Victor Nwadiogbu., Uroko Robert Ikechukwu., Egba, Simeon Ikechukwu and Agu Obiora (2017) 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
17. Uhuo E N, Egba S I, Nwuke P C, Obike C A and Kelechi G K. Antioxidative properties of Adansonia digitata L. (baobab) leaf extractexert protective effect on doxorubicin induced cardiac toxicity in Wistar rats. Clinical Nutrition Open Science 2022; 45:3-16
18. Ugwu, CE., Sure, SM., Dike, CC., Okpoga, NA and Egba, SI. Phytochemical and *in vitro* antioxidant activities of methanol leave extract of *Alternanthera basiliana*. Journal of Pharmacy Research, 2018; 12(6): 835-839

19. Ali H, Hanna MM, Alziny N, Mahmoud S, Borham A, Mustafa A, Abdelnaser A. The impact of the exposome on cytochrome P450-mediated drug metabolism. Front Pharmacol. 2025 Oct 13;16:1639646. doi: 10.3389/fphar.2025.1639646. PMID: 41158125; PMCID: PMC12554611.
20. Durairaj P, Liu ZL. Brain Cytochrome P450: Navigating Neurological Health and Metabolic Regulation. Journal of Xenobiotics. 2025; 15(2):44. https://doi.org/10.3390/jox15020044
21. Alum, E.U., Uti, D.E. & Offor, C.E. Redox Signaling Disruption and Antioxidants in Toxicology: From Precision Therapy to Potential Hazards. *Cell Biochem Biophys* (2025). https://doi.org/10.1007/s12013-025-01846-8
22. Uroko, Robert I.., Adamude, Fatima A.., Egba, Simeon I., Ani, Chijioke C and 1 Ekpenyong, James E. Hepatoprotective Effects of Methanol Extract of *Acanthus montanus* (*acanthaceae*) Leaves on Acetaminophen Induced Liver Injury in Rats. *Pharmacologyonline*, 2020; 1: 248-260
23. He F, Ru X, Wen T. NRF2, a Transcription Factor for Stress Response and Beyond. Int J Mol Sci. 2020 Jul 6;21(13):4777. doi: 10.3390/ijms21134777. PMID: 32640524; PMCID: PMC7369905.
24. McCord JM, Gao B, Hybertson BM. The Complex Genetic and Epigenetic Regulation of the Nrf2 Pathways: A Review. Antioxidants. 2023; 12(2):366. https://doi.org/10.3390/antiox12020366
25. Cichoż-Lach H, Michalak A. Oxidative stress as a crucial factor in liver diseases. World J Gastroenterol. 2014 Jul 7;20(25):8082-91. doi: 10.3748/wjg.v20.i25.8082. PMID: 25009380; PMCID: PMC4081679.
26. Aja, P. M, Chukwu, C. A., Ugwu, O. P. C., Ale, B. A., Agu, P. C., Deusdedi, T., et al. Cucumeropsismannii seed oil protects against bisphenol A-induced hepatotoxicity by mitigating inflammation and oxidative stress in rats. *RPS Pharmacy and Pharmacology Reports*, 2023; rqad033, https://doi.org/10.1093/rpsppr/rqad033
27. Siddiqui MT, Amin H, Garg R, Chadalavada P, Al-Yaman W, Lopez R, Singh A. Medications in type-2 diabetics and their association with liver fibrosis. World J Gastroenterol. 2020 Jun 21;26(23):3249-3259. doi: 10.3748/wjg.v26.i23.3249. PMID: 32684739; PMCID: PMC7336333.
28. López-Pascual E, Rienda I, Perez-Rojas J, Rapisarda A, Garcia-Llorens G, Jover R, Castell JV. Drug-Induced Fatty Liver Disease (DIFLD): A Comprehensive Analysis of Clinical, Biochemical, and Histopathological Data for Mechanisms Identification and Consistency with Current Adverse Outcome Pathways. International Journal of Molecular Sciences. 2024; 25(10):5203. https://doi.org/10.3390/ijms25105203
29. Mohamed J, Nazratun Nafizah AH, Zariyantey AH, Budin SB. Mechanisms of Diabetes-Induced Liver Damage: The role of oxidative stress and inflammation. Sultan Qaboos Univ Med J. 2016 May;16(2):e132-41. doi: 10.18295/squmj.2016.16.02.002. Epub 2016 May 15. PMID: 27226903; PMCID: PMC4868511.
30. Manzoor MF, Arif Z, Kabir A, Mehmood I, Munir D, Razzaq A, Ali A, Goksen G, Coşier V, Ahmad N, Ali M, Rusu A. Oxidative stress and metabolic diseases: Relevance and therapeutic strategies. Front Nutr. 2022 Oct 17;9:994309. doi: 10.3389/fnut.2022.994309. PMID: 36324618; PMCID: PMC9621294.
31. Patel J, Roy H, Chintamaneni PK, Patel R, Bohara R. Advanced Strategies in Enhancing the Hepatoprotective Efficacy of Natural Products: Integrating Nanotechnology, Genomics, and Mechanistic Insights. ACS Biomater Sci Eng. 2025 May 12;11(5):2528-2549. doi: 10.1021/acsbiomaterials.5c00004. Epub 2025 Apr 11. PMID: 40211874; PMCID: PMC12076289.
32. Izah, S.C., Betiang, P.A., Ugwu, O.P.C., Ainebyoona, C., Uti, D.E., Echegu, D.A., Alum, B.N. The Ketogenic Diet in Obesity Management: Friend or Foe?. *Cell Biochem Biophys* (2025). https://doi.org/10.1007/s12013-025-01878-0
33. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.A. (2025). Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obesity Medicine, 2025; 100622. https://doi.org/10.1016/j.obmed.2025.100622
34. Sahasrabudhe SA, Terluk MR, Kartha RV. N-acetylcysteine Pharmacology and Applications in Rare Diseases-Repurposing an Old Antioxidant. Antioxidants (Basel). 2023 Jun 21;12(7):1316. doi: 10.3390/antiox12071316. PMID: 37507857; PMCID: PMC10376274.
35. Giustarini D, Milzani A, Dalle-Donne I, Rossi R. How to Increase Cellular Glutathione. Antioxidants. 2023; 12(5):1094. https://doi.org/10.3390/antiox12051094
36. Ramaite FT, Nkadimeng SM. Targeting inflammatory pathways in hepatocellular carcinoma: recent developments. Discov Oncol. 2025 Jun 22;16(1):1174. doi: 10.1007/s12672-025-03035-8. PMID: 40544399; PMCID: PMC12183140.
37. Galasso L, Cerrito L, Maccauro V, Termite F, Mignini I, Esposto G, Borriello R, Ainora ME, Gasbarrini A, Zocco MA. Inflammatory Response in the Pathogenesis and Treatment of Hepatocellular Carcinoma: A Double-Edged Weapon. International Journal of Molecular Sciences. 2024; 25(13):7191.

https://doi.org/10.3390/ijms25137191
38. Wilson ID, Nicholson JK. Gut microbiome interactions with drug metabolism, efficacy, and toxicity. Transl Res. 2017 Jan;179:204-222. doi: 10.1016/j.trsl.2016.08.002. Epub 2016 Aug 13. PMID: 27591027; PMCID: PMC5718288.
39. Mafe AN, Büsselberg D. The Effect of Microbiome-Derived Metabolites in Inflammation-Related Cancer Prevention and Treatment. Biomolecules. 2025; 15(5):688. https://doi.org/10.3390/biom15050688

CITE AS: Kamanzi Ntakirutimana G. (2026). Hepatotoxicity in Chronic Metabolic Disease: How Diabetes, Immune Activation, and Oxidative Stress Converge to Drive Liver Injury.
IDOSR JOURNAL OF SCIENCE AND TECHNOLOGY 12(1):103-108. https://doi.org/10.59298/IDOSR/JST/26/113.103108