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Mitochondrial Dysfunction in Type 2 Diabetes: Implications for Immunity and Organ Toxicity

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ABSTRACT

Mitochondrial dysfunction has emerged as a central mechanism linking metabolic derangements, immune dysregulation, and multi-organ toxicity in Type 2 Diabetes Mellitus (T2DM). Beyond its classical features of insulin resistance and hyperglycaemia, T2DM is characterized by impaired mitochondrial oxidative phosphorylation, altered mitochondrial dynamics, defective mitophagy, and excessive reactive oxygen species (ROS) production. These disturbances compromise cellular energy homeostasis and propagate oxidative stress, triggering inflammatory pathways and the release of mitochondrial damage-associated molecular patterns (DAMPs), which impair immune cell function. Dysfunctional mitochondria in metabolic tissues like skeletal muscle, liver, pancreas, and adipose tissue contribute directly to insulin resistance and β-cell failure, while in immune cells, they reduce regenerative capacity, promote apoptosis, and impair pathogen responses. Organ-specific consequences include hepatic steatosis, diabetic nephropathy, cardiomyopathy, skeletal muscle dysfunction, and cognitive decline. Additionally, extracellular vesicle-mediated transfer of dysfunctional mitochondria may amplify systemic inflammation and multi-organ stress. Therapeutic strategies targeting mitochondrial health, including mitochondria-specific antioxidants, modulators of mitochondrial dynamics, and enhancers of mitophagy and biogenesis, hold promise for mitigating both metabolic and immune dysfunction. Understanding mitochondrial impairment as a unifying mechanism in T2DM provides a framework for integrative interventions aimed at improving energy metabolism, immune competence, and organ resilience, potentially reducing disease progression and complications.

Keywords: Mitochondrial dysfunction, Type 2 diabetes mellitus, Immune dysregulation, Oxidative stress, multi-organ toxicity

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a prevalent and complex metabolic disorder defined by chronic hyperglycemia, insulin resistance, and a progressive decline in pancreatic β-cell function [1-4]. Traditionally, the pathophysiology of T2DM has focused on impaired insulin signaling, reduced glucose uptake in peripheral tissues, and insufficient insulin secretion. However, recent research has highlighted that these classical metabolic disturbances represent only part of a broader pathological landscape, in which mitochondrial dysfunction plays a central and pivotal role [5-9]. Mitochondria, often described as the powerhouses of the cell, are essential for generating adenosine triphosphate (ATP) through oxidative phosphorylation, regulating reactive oxygen species (ROS), and coordinating metabolic signaling pathways that maintain cellular homeostasis [10-15]. In T2DM, mitochondrial dysfunction manifests through multiple interconnected mechanisms, including reduced oxidative phosphorylation, excessive ROS production, dysregulated mitochondrial dynamics, impaired mitophagy, and defective biogenesis [16-20]. These alterations compromise cellular energy metabolism, trigger oxidative stress, and perturb key signaling networks, ultimately promoting apoptosis, chronic inflammation, and tissue damage. Notably, mitochondrial impairment affects not only classical metabolic tissues such as skeletal muscle, liver, and pancreatic β-cells but also influences immune cell function, thereby linking metabolic dysregulation with immune

compromise [21-23]. The resulting interplay between mitochondrial stress, inflammation, and insulin resistance creates a vicious cycle that accelerates disease progression and contributes to the development of multi-organ complications, including cardiovascular, renal, hepatic, and neurocognitive disorders [24-30]. This review aims to provide a comprehensive examination of the role of mitochondrial dysfunction in T2DM, with particular emphasis on its contributions to metabolic derangements, immune dysregulation, and organ-specific toxicity [31-34]. We explore the underlying mechanisms that drive mitochondrial impairment, summarize evidence from organ-specific studies highlighting how mitochondrial defects translate into functional decline, and discuss potential therapeutic interventions aimed at restoring mitochondrial integrity. By framing T2DM through the lens of mitochondrial health, this review underscores the central importance of these organelles in disease pathogenesis and offers insights into integrative strategies that target mitochondrial function to improve clinical outcomes and mitigate the systemic complications of T2DM [35-38].

1. Mitochondrial Function and Its Derangement in T2DM

1.1 Normal Roles of Mitochondria in Cells

Mitochondria are vital for cellular energy metabolism and overall homeostasis [39-44]. They generate ATP through oxidative phosphorylation (OXPHOS) by metabolizing substrates such as glucose, pyruvate, and fatty acids [45-50]. In addition to energy production, mitochondria regulate the generation of ROS, which, at physiological levels, serve as signaling molecules for cellular adaptation and stress responses. Mitochondria also coordinate lipid metabolism, including fatty acid oxidation and the regulation of lipid intermediates, thereby integrating cellular energy demands with nutrient availability [51-58]. Their dynamic quality control, through processes such as fusion, fission, mitophagy, and biogenesis, ensures the maintenance of a healthy mitochondrial population, while their roles in calcium homeostasis and programmed cell death are essential for proper cellular function [59-62]. The integrity of these organelles is particularly critical in metabolically active tissues, including skeletal muscle, liver, pancreatic β-cells, kidney, and brain, where energy demand is high and cellular stress can have profound systemic consequences [63-67].

1.2 Mechanisms of Mitochondrial Dysfunction in T2DM

In T2DM, several interrelated mechanisms compromise mitochondrial function [68-73]. Impaired oxidative capacity, observed as reduced mitochondrial respiration and ADP-stimulated ATP synthesis in skeletal muscle, leads to insufficient energy production and accumulation of metabolic intermediates [74-79]. The dynamic balance between mitochondrial fusion and fission is disrupted, with altered expression of regulatory proteins such as MFN1, MFN2, OPA1, DRP1, FIS1, and MFF, resulting in fragmented and inefficient mitochondria [80-83]. Defective mitophagy and mitochondrial biogenesis further exacerbate dysfunction by allowing damaged mitochondria to accumulate, amplifying ROS production, and reducing cellular energy availability.

Excessive ROS and reactive nitrogen species (RNS), stemming from inefficient electron transport and electron "leak" within the respiratory chain, cause oxidative damage to mitochondrial DNA, lipids, and proteins [84-89]. Additionally, the structural organization of the electron transport chain into supercomplexes or "respirasomes" is often compromised, further reducing electron transfer efficiency and increasing ROS generation [90-94]. Metabolic overload, particularly elevated free fatty acids and lipid intermediates such as diacylglycerol and ceramides, exacerbates lipotoxic stress, interferes with insulin signaling pathways, and contributes to systemic metabolic dysregulation [95-97]. Collectively, these disturbances in energy production, oxidative balance, and mitochondrial quality control establish a milieu conducive to cellular dysfunction and stress across multiple tissues, laying the foundation for insulin resistance, β-cell failure, immune dysregulation, and organ-specific toxicity [98].

3. Immunological Consequences: Mitochondrial Dysfunction and Immune Dysregulation

Emerging research indicates that mitochondrial dysfunction in Type 2 Diabetes Mellitus (T2DM) has profound effects on immune function, contributing to increased susceptibility to infections, impaired immune responses, and chronic low-grade inflammation [20]. The interplay between mitochondrial impairment, oxidative stress, and immune dysregulation provides a mechanistic link between metabolic derangements and the heightened risk of infections and inflammatory complications observed in T2DM patients [21].

3.1 ROS, Mitochondrial Damage, and Inflammation

Dysfunctional mitochondria in T2DM produce excessive reactive oxygen species (ROS) and reactive nitrogen species (RNS), resulting in a state of oxidative stress that damages mitochondrial DNA (mtDNA), proteins, and lipid membranes [22]. This damage further compromises mitochondrial function, leading to reduced ATP generation and energetic deficits [23]. Impaired mitophagy, the process by which cells selectively remove damaged mitochondria, exacerbates this problem by allowing dysfunctional mitochondria to accumulate [24]. The presence of damaged mitochondria elevates cytosolic ROS levels and promotes the release of mitochondrial components such as oxidized mtDNA [25]. These mitochondrial constituents act as damage-associated molecular patterns (DAMPs), activating pattern recognition receptors (PRRs) on immune cells and triggering the

production of pro-inflammatory cytokines, including interleukin-1β (IL-1β), IL-18, and type I interferons [26]. Chronic exposure to these cytokines establishes a state of persistent, low-grade inflammation.

This inflammatory milieu feeds back into metabolic pathways, as cytokines such as tumor necrosis factor-alpha (TNF-α), IL-6, and IL-1β activate stress-responsive signaling cascades, including the c-Jun N-terminal kinase (JNK) and IκB kinase β (IKKβ)/nuclear factor-kappa B (NF-κB) pathways [27]. These pathways mediate serine phosphorylation of insulin receptor substrates (IRS), inhibiting downstream insulin signaling and worsening insulin resistance [28]. Consequently, mitochondrial dysfunction not only drives inflammation but also exacerbates the metabolic disturbances central to T2DM, creating a vicious cycle of oxidative stress, immune activation, and insulin resistance.

3.2 Impact on Immune Cell Function and Hematopoiesis

Mitochondrial dysfunction in T2DM extends beyond metabolic tissues to affect the immune system directly. Hematopoietic stem and progenitor cells (HSPCs) are particularly sensitive to metabolic stress [29]. Chronic hyperglycemia and insulin resistance impair mitochondrial oxidative phosphorylation, disrupt mitophagy, and elevate ROS levels in HSPCs, limiting their capacity for self-renewal and differentiation [30]. This impairment can result in reduced production of immune cells and compromised hematopoiesis, leaving patients more vulnerable to infections and reducing the efficacy of immune surveillance.

Furthermore, mature immune cells such as monocytes and lymphocytes also exhibit mitochondrial deficits in T2DM [31]. Mitochondrial biogenesis is decreased, mitochondrial membrane potential is reduced, oxidative enzyme activity is impaired, and cell survival is compromised. These defects diminish the functional capacity of immune cells, impairing pathogen recognition, antigen presentation, and effector responses [32]. Collectively, these abnormalities explain the increased susceptibility to infections, delayed wound healing, and impaired immune responses observed in individuals with poorly controlled T2DM.

3.3 Immune-Metabolic Crosstalk via Extracellular Vesicles

An additional mechanism by which mitochondrial dysfunction influences immune regulation is through extracellular vesicle (EV)-mediated intercellular communication [33]. Under conditions of metabolic stress, including hyperglycemia and lipotoxicity, stressed cells such as pancreatic β-cells and skeletal muscle fibers release EVs containing mitochondrial fragments or dysfunctional mitochondria. These vesicles can be transported to distant tissues or immune cells, spreading mitochondrial stress and amplifying oxidative damage systemically [34]. EV-mediated crosstalk can propagate inflammatory signaling, activate immune cells, and further impair metabolic function in remote organs. This mechanism demonstrates that mitochondrial dysfunction in T2DM is not confined to canonical metabolic tissues but contributes to systemic immune dysregulation, linking metabolic disturbances with heightened inflammatory responses and multi-organ vulnerability [35]. In summary, mitochondrial dysfunction in T2DM compromises immune competence through ROS-mediated inflammation, impaired hematopoiesis, and intercellular communication via extracellular vesicles [36]. These effects create a self-perpetuating cycle of oxidative stress, immune activation, and metabolic disturbance, highlighting mitochondria as a central node in the intersection of metabolism, immunity, and disease progression.

CONCLUSION

Mitochondrial dysfunction is increasingly recognized not just as a metabolic epiphenomenon in T2DM, but as a central, unifying mechanism linking insulin resistance, β- cell failure, immune dysregulation, and multi-organ toxicity. The compromised ability of mitochondria to produce energy efficiently, their increased generation of ROS, failure of quality control processes (dynamics, mitophagy, biogenesis), and deranged interorganelle communication combine to create a landscape of cellular stress, inflammation, and eventual tissue damage. Understanding T2DM through a "mitochondrial lens" reframes the disease - from being a disorder solely of glycaemia to a systemic disorder of cellular energetics and organ resilience. This has important implications: for research (multi-organ, systems-level studies), for clinical care (monitoring mitochondrial health, organ-specific surveillance), and for therapy (targeting mitochondrial health through pharmacological or lifestyle interventions). Given the global burden of T2DM and its complications, especially in low- and middle-income countries, prioritising mitochondrial health may offer a promising route towards reducing disease progression, preventing complications, and improving long-term outcomes.

REFERENCES

1. Uti DE, Atangwho IJ, Alum EU, Egba SI, Ugwu OPC, Ikechukwu GC. Natural Antidiabetic Agents: Current Evidence and Development Pathways from Medicinal Plants to Clinical use. Natural Product Communications. 2025;20(3). doi:10.1177/1934578x251323393
2. Ugwu, O.P.C., Kungu, E., Inyangat, R., Obeagu, E. I., Alum, E. U., Okon, M. B., Subbarayan, S. and Sankarapandiyan, V. Exploring Indigenous Medicinal Plants for Managing Diabetes Mellitus in Uganda: Ethnobotanical Insights, Pharmacotherapeutic Strategies, and National Development Alignment. INOSR Experimental Sciences.2023; 12(2):214-224. https://doi.org/10.59298/INOSRES/2023/2.17.1000.

3. Casanova A, Wevers A, Navarro-Ledesma S, Pruimboom L. Mitochondria: It is all about energy. Front Physiol. 2023 Apr 25;14:1114231. doi: 10.3389/fphys.2023.1114231. PMID: 37179826; PMCID: PMC10167337.
4. Li X, Chen W, Jia Z, Xiao Y, Shi A, Ma X. Mitochondrial Dysfunction as a Pathogenesis and Therapeutic Strategy for Metabolic-Dysfunction-Associated Steatotic Liver Disease. International Journal of Molecular Sciences. 2025; 26(9):4256. https://doi.org/10.3390/ijms26094256
5. Kim JA, Wei Y, Sowers JR. Role of mitochondrial dysfunction in insulin resistance. Circ Res. 2008 Feb 29;102(4):401-14. doi: 10.1161/CIRCRESAHA.107.165472. PMID: 18309108; PMCID: PMC2963150.
6. Darwish R, Alcibahy Y, Abu-Sharia G, Butler AE. β-Cell Mitochondrial Dysfunction: Underlying Mechanisms and Potential Therapeutic Strategies. Cells. 2025; 14(23):1861. https://doi.org/10.3390/cells14231861
7. Pinti MV, Fink GK, Hathaway QA, Durr AJ, Kunovac A, Hollander JM. Mitochondrial dysfunction in type 2 diabetes mellitus: an organ-based analysis. Am J Physiol Endocrinol Metab. 2019 Feb 1;316(2):E268-E285. doi: 10.1152/ajpendo.00314.2018. Epub 2019 Jan 2. PMID: 30601700; PMCID: PMC6397358.
8. Brand MD, Orr AL, Perevoshchikova IV, Quinlan CL. The role of mitochondrial function and cellular bioenergetics in ageing and disease. Br J Dermatol. 2013 Jul;169 Suppl 2(0 2):1-8. doi: 10.1111/bjd.12208. PMID: 23786614; PMCID: PMC4321783.
9. du Plessis SS, Agarwal A, Mohanty G, van der Linde M. Oxidative phosphorylation versus glycolysis: what fuel do spermatozoa use? Asian J Androl. 2015 Mar-Apr;17(2):230-5. doi: 10.4103/1008-682X.135123. PMID: 25475660; PMCID: PMC4650467.
10. Antunes BC, Mateus T, Morais VA. In the Brain, It Is Not All about Sugar. NeuroSci. 2024; 5(2):209-221. https://doi.org/10.3390/neurosci5020016
11. Ye L, Fu X, Li Q. Mitochondrial Quality Control in Health and Disease. MedComm (2020). 2025 Aug 15;6(8):e70319. doi: 10.1002/mco2.70319. PMID: 40821693; PMCID: PMC12356995.
12. Zhang Z, Zhang M, Jin H, Lv S, Li Y, Li Y. Mitochondrial Quality Control and Cell Death. International Journal of Molecular Sciences. 2025; 26(22):11084. https://doi.org/10.3390/ijms262211084
13. Pinti MV, Fink GK, Hathaway QA, Durr AJ, Kunovac A, Hollander JM. Mitochondrial dysfunction in type 2 diabetes mellitus: an organ-based analysis. Am J Physiol Endocrinol Metab. 2019 Feb 1;316(2):E268-E285. doi: 10.1152/ajpendo.00314.2018. Epub 2019 Jan 2. PMID: 30601700; PMCID: PMC6397358.
14. Chen TH, Koh KY, Lin KM, Chou CK. Mitochondrial Dysfunction as an Underlying Cause of Skeletal Muscle Disorders. Int J Mol Sci. 2022 Oct 26;23(21):12926. doi: 10.3390/ijms232112926. PMID: 36361713; PMCID: PMC9653750.
15. Masenga SK, Kabwe LS, Chakulya M, Kirabo A. Mechanisms of Oxidative Stress in Metabolic Syndrome. International Journal of Molecular Sciences. 2023; 24(9):7898. https://doi.org/10.3390/ijms24097898
16. Puddu P, Puddu GM, Cravero E, De Pascalis S, Muscari A. The emerging role of cardiovascular risk factor-induced mitochondrial dysfunction in atherogenesis. J Biomed Sci. 2009 Dec 9;16(1):112. doi: 10.1186/1423-0127-16-112. PMID: 20003216; PMCID: PMC2800844.
17. Rugolo M, Zanna C, Ghelli AM. Organization of the Respiratory Supercomplexes in Cells with Defective Complex III: Structural Features and Metabolic Consequences. Life (Basel). 2021 Apr 17;11(4):351. doi: 10.3390/life11040351. PMID: 33920624; PMCID: PMC8074069.
18. Ősz F, Nazir A, Takács-Vellai K, Farkas Z. Mutations of the Electron Transport Chain Affect Lifespan and ROS Levels in C. elegans. Antioxidants. 2025; 14(1):76. https://doi.org/10.3390/antiox14010076
19. Bhatti JS, Bhatti GK, Reddy PH. Mitochondrial dysfunction and oxidative stress in metabolic disorders - A step towards mitochondria based therapeutic strategies. Biochim Biophys Acta Mol Basis Dis. 2017 May;1863(5):1066-1077. doi: 10.1016/j.bbadis.2016.11.010. Epub 2016 Nov 9. PMID: 27836629; PMCID: PMC5423868.
20. Pinti MV, Fink GK, Hathaway QA, Durr AJ, Kunovac A, Hollander JM. Mitochondrial dysfunction in type 2 diabetes mellitus: an organ-based analysis. Am J Physiol Endocrinol Metab. 2019 Feb 1;316(2):E268-E285. doi: 10.1152/ajpendo.00314.2018. Epub 2019 Jan 2. PMID: 30601700; PMCID: PMC6397358.
21. Iheagwam FN, Joseph AJ, Adedoyin ED, Iheagwam OT, Ejoh SA. Mitochondrial Dysfunction in Diabetes: Shedding Light on a Widespread Oversight. Pathophysiology. 2025; 32(1):9. https://doi.org/10.3390/pathophysiology32010009
22. Zhang Z, Huang Q, Zhao D, Lian F, Li X, Qi W. The impact of oxidative stress-induced mitochondrial dysfunction on diabetic microvascular complications. Front Endocrinol (Lausanne). 2023 Feb 7;14:1112363. doi: 10.3389/fendo.2023.1112363. PMID: 36824356; PMCID: PMC9941188.

23. Veluthakal R, Esparza D, Hoolachan JM, Balakrishnan R, Ahn M, Oh E, Jayasena CS, Thurmond DC. Mitochondrial Dysfunction, Oxidative Stress, and Inter-Organ Miscommunications in T2D Progression. International Journal of Molecular Sciences. 2024; 25(3):1504. https://doi.org/10.3390/ijms25031504
24. Higgins GC, Coughlan MT. Mitochondrial dysfunction and mitophagy: the beginning and end to diabetic nephropathy? Br J Pharmacol. 2014 Apr;171(8):1917-42. doi: 10.1111/bph.12503. PMID: 24720258; PMCID: PMC3976613.
25. Li A, Gao M, Liu B, Qin Y, Chen L, Liu H, Wu H, Gong G. Mitochondrial autophagy: molecular mechanisms and implications for cardiovascular disease. Cell Death Dis. 2022 May 9;13(5):444. doi: 10.1038/s41419-022-04906-6. PMID: 35534453; PMCID: PMC9085840.
26. Deus CM, Tavares H, Beatriz M, Mota S, Lopes C. Mitochondrial Damage-Associated Molecular Patterns Content in Extracellular Vesicles Promotes Early Inflammation in Neurodegenerative Disorders. Cells. 2022; 11(15):2364. https://doi.org/10.3390/cells11152364
27. Saha S, Buttari B, Panieri E, Profumo E, Saso L. An Overview of Nrf2 Signaling Pathway and Its Role in Inflammation. Molecules. 2020 Nov 23;25(22):5474. doi: 10.3390/molecules25225474. PMID: 33238435; PMCID: PMC7700122.
28. Keane KN, Cruzat VF, Carlessi R, de Bittencourt PI Jr, Newsholme P. Molecular Events Linking Oxidative Stress and Inflammation to Insulin Resistance and β-Cell Dysfunction. Oxid Med Cell Longev. 2015;2015:181643. doi: 10.1155/2015/181643. Epub 2015 Jul 14. PMID: 26257839; PMCID: PMC4516838.
29. Jacobs K, Doerdelmann C, Krietsch J, González-Acosta D, Mathis N, Kushinsky S, Guarino E, Gómez-Escolar C, Martinez D, Schmid JA, Leary PJ, Freire R, Ramiro AR, Eischen CM, Mendez J, Lopes M. Stress-triggered hematopoietic stem cell proliferation relies on PrimPol-mediated repriming. Mol Cell. 2022 Nov 3;82(21):4176-4188.e8. doi: 10.1016/j.molcel.2022.09.009. Epub 2022 Sep 23. PMID: 36152632; PMCID: PMC10251193.
30. González P, Lozano P, Ros G, Solano F. Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. International Journal of Molecular Sciences. 2023; 24(11):9352. https://doi.org/10.3390/ijms24119352
31. Deck K, Mora C, Deng S, Rogers P, Rafferty T, Palade PT, Mu S, Liu Y. Immune Dysregulation Connecting Type 2 Diabetes and Cardiovascular Complications. Life. 2025; 15(8):1241. https://doi.org/10.3390/life15081241
32. Zhou T, Hu Z, Yang S, Sun L, Yu Z, Wang G. Role of Adaptive and Innate Immunity in Type 2 Diabetes Mellitus. J Diabetes Res. 2018 Nov 8;2018:7457269. doi: 10.1155/2018/7457269. PMID: 30533447; PMCID: PMC6250017.
33. Kong J, Sun R, Du C, Tang Y, Xie C, Li Q, Lin L, Wang H. Mitochondrial Extracellular Vesicles: A Novel Approach to Mitochondrial Quality Control. Biomolecules. 2025 Aug 8;15(8):1145. doi: 10.3390/biom15081145. PMID: 40867590; PMCID: PMC12384377.
34. Shahannaz DC, Sugiura T, Ferrell BE, Yoshida T. Targeting Mitochondrial Dynamics via EV Delivery in Regenerative Cardiology: Mechanistic and Therapeutic Perspectives. Cells. 2025; 14(21):1738. https://doi.org/10.3390/cells14211738
35. Shimu SJ, Mahir JUK, Shakib FAF, Ridoy AA, Samir RA, Jahan N, Hasan MF, Sazzad S, Akter S, Mohiuddin MS, et al. Metabolic Reprogramming Through Polyphenol Networks: A Systems Approach to Metabolic Inflammation and Insulin Resistance. Medical Sciences. 2025; 13(3):180. https://doi.org/10.3390/medsci13030180
36. Caturano A, Rocco M, Tagliaferri G, Piacevole A, Nilo D, Di Lorenzo G, Iadicicco I, Donnarumma M, Galiero R, Acierno C, et al. Oxidative Stress and Cardiovascular Complications in Type 2 Diabetes: From Pathophysiology to Lifestyle Modifications. Antioxidants. 2025; 14(1):72. https://doi.org/10.3390/antiox14010072
37. Okon MB, Ugwu OP, Ugwu CN, Ogenyi FC, Swase DT, Anyanwu CN, Eze VH, Ugwu JN, Akinola SA, Mujinya R, Anyanwu EG. From pandemics to preparedness: harnessing AI, CRISPR, and synthetic biology to counter biosecurity threats. Frontiers in Public Health. 2025 Nov 26;13:1711344.
38. Ugwu OP, Ogenyi FC, Ugwu CN, Basajja M, Okon MB. Mitochondrial stress bridge: Could muscle-derived extracellular vesicles be the missing link between sarcopenia, insulin resistance, and chemotherapy-induced cardiotoxicity?. Biomedicine & Pharmacotherapy. 2025 Dec 1;193:118814.
39. Annamalai A, Tek C. An overview of diabetes management in schizophrenia patients: office based strategies for primary care practitioners and endocrinologists. International journal of endocrinology. 2015;2015(1):969182.

40. Kremers SH, Wild SH, Elders PJ, Beulens JW, Campbell DJ, Pouwer F, Lindekilde N, de Wit M, Lloyd C, Rutters F. The role of mental disorders in precision medicine for diabetes: a narrative review. Diabetologia. 2022 Nov;65(11):1895-906.
41. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Sustainable development goals (SDGs) and resilient healthcare systems: Addressing medicine and public health challenges in conflict zones. Medicine. 2025 Feb 14;104(7):e41535.
42. Ongesa TN, Ugwu OP, Ugwu CN, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Okon MB, Ejemot-Nwadiaro RI. Optimizing emergency response systems in urban health crises: A project management approach to public health preparedness and response. Medicine. 2025 Jan 17;104(3):e41279.
43. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Medical preparedness for bioterrorism and chemical warfare: A public health integration review. Medicine. 2025 May 2;104(18):e42289.
44. Basiri R, Seidu B, Rudich M. Exploring the interrelationships between diabetes, nutrition, anxiety, and depression: implications for treatment and prevention strategies. Nutrients. 2023 Sep 30;15(19):4226.
45. Paul-Chima UO, Nneoma UC, Bulhan S. Metabolic immunobridge: Could adipose-derived extracellular vesicles be the missing link between obesity, autoimmunity, and drug-induced hepatotoxicity?. Medical Hypotheses. 2025 Sep 28:111776.
46. Yadav S, Hong YR, Westen S, Marlow NM, Haller MJ, Walker AF. Sociodemographic factors associated with major depressive episodes and suicidal ideation among emerging adults with diabetes in the US. Frontiers in endocrinology. 2023 Dec 7;14:1276336.
47. Ugwu OP, Alum EU, Ugwu JN, Eze VH, Ugwu CN, Ogenyi FC, Okon MB. Harnessing technology for infectious disease response in conflict zones: Challenges, innovations, and policy implications. Medicine. 2024 Jul 12;103(28):e38834.
48. Sweileh WM. Analysis of global research output on diabetes depression and suicide. Annals of general psychiatry. 2018 Oct 23;17(1):44.
49. Mason J, Meal A, Shaw I, Adams GG. Outcomes of mindfulness-based stress reduction and mindfulness-based cognitive therapy in adults with diabetes: a systematic review. Diabetes Treat. 2018;10:2574-7568.
50. Paul-Chima UO, Ugwu CN, Alum EU. Integrated approaches in nutraceutical delivery systems: optimizing ADME dynamics for enhanced therapeutic potency and clinical impact. RPS Pharmacy and Pharmacology Reports. 2024 Oct;3(4):rqae024.
51. Ugwu OP, Ogenyi FC, Ugwu CN, Ugwu MN. Gut microbiota-derived metabolites as early biomarkers for childhood obesity: A policy commentary from urban African populations. Obesity Medicine. 2025 Sep 1;57:100641.
52. Isaac Edyedu PMA, Ugwu OPC, Ugwu CN, Alum EU, et al. The role of pharmacological interventions in managing urological complications during pregnancy and childbirth: A review. Medicine. 2025;104(7):e41381.
53. Alum EU, Ugwu OPC, Obeagu EI, et al. Nutritional care in diabetes mellitus: A comprehensive guide. Int J Innov Appl Res. 2023;11(12):16-25.
54. Obeagu EI, Ahmed YA, Obeagu GU, Bunu UO, Ugwu OPC, Alum EU. Biomarkers of breast cancer: Overview. Int J Curr Res Biol Med. 2023;1:8-16.
55. Uti DE, Alum EU, Atangwho IJ, Ugwu OPC, et al. Lipid-based nano-carriers for the delivery of anti-obesity natural compounds: Advances in targeted delivery and precision therapeutics. J Nanobiotechnol. 2025;23:336.
56. Ugwu CN, Ugwu OPC, Alum EU, Eze VHU, Basajja M, Ugwu JN, Ogenyi FC, et al. Medical preparedness for bioterrorism and chemical warfare: A public health integration review. Medicine. 2025;104(18):e42289.
57. Obeagu EI, Scott GY, Amekpor F, Ugwu OPC, Alum EU. COVID-19 infection and diabetes: A current issue. Int J Innov Appl Res. 2023;11(1):25-30.
58. Offor CE, Ugwu OPC, Alum EU. Anti-diabetic effect of ethanol leaf extract of *Allium sativum* on albino rats. Int J Pharm Med Sci. 2014;4(1):1-3.
59. Asogwa FC, Okechukwu PCU, Esther UA, Chinedu OE, Nzubechukwu E. Hygienic and sanitary assessment of street food vendors in selected towns of Enugu North District, Nigeria. Am-Eurasian J Sci Res. 2015;10(1):22-26.
60. Alum EU, Uti DE, Agah VM, Orji OU, Nkeiru N, et al. Physico-chemical and bacteriological analysis of water used for drinking and domestic purposes in Amaozara Ozizza, Afikpo North, Nigeria. Niger J Biochem Mol Biol. 2023;38(1):1-8.

61. Ugwu OPC, Alum EU, Okon MB, Obeagu EI. Mechanisms of microbiota modulation: Implications for health, disease, and therapeutic interventions. Medicine. 2024;103(19):e38088.
62. Ezekwe CI, Uzomba CR, Ugwu OPC. Effect of methanol extract of *Talinum triangulare* on hematology and liver parameters in rats. Glob J Biotechnol Biochem. 2013;8(2):51-60.
63. Alum EU, Inya JE, Ugwu OPC, Obeagu EI, Aloke C, Aja PM, Okpata MG, et al. Ethanolic leaf extract of *Datura stramonium* attenuates methotrexate-induced biochemical alterations in Wistar rats. RPS Pharmacol Rep. 2023;2(1):1-6.
64. Ugwu OPC, Erisa K, Inyangat R, Obeagu EI, et al. Indigenous medicinal plants for managing diabetes in Uganda: Ethnobotanical and pharmacotherapeutic insights. INOSR Exp Sci. 2023;12(2):214-224.
65. Alum EU, Aja W, Ugwu OPC. Vitamin composition of ethanol leaf and seed extracts of *Datura stramonium*. Avicenna J Med Biochem. 2023;11(1):92-97.
66. Ezenwaji CO, Alum EU, Ugwu OPC. Digital health in pandemic preparedness and response: Securing global health? Glob Health Action. 2024;17(1):2419694.
67. Adonu CC, Ugwu OP, Bawa A, Ossai EC, Nwaka AC. Intrinsic blood coagulation studies in patients with diabetes and hypertension. Int J Pharm Med Bio Sci. 2013;2(2):36-45.
68. Offor CE, Ugwu PC, Okechukwu PM, Igwenyi IO. Proximate and phytochemical analyses of *Terminalia catappa* leaves. Eur J Appl Sci. 2015;7(1):9-11.
69. Enechi YS, Ugwu OC, Ugwu KK, Ugwu OPC, Omeh N. Evaluation of antinutrient levels of *Ceiba pentandra* leaves. IJRRPAS. 2013;3(3):394-400.
70. Alum EU, Uti DE, Ugwu OPC, Alum BN, Edeh FO, Ainebyoona C. Microbiota in cancer development and treatment. Discov Oncol. 2025;16(1):646.
71. Asogwa FC, Okoye COB, Ugwu OPC, Edwin N, Alum EU, Egwu CO. Phytochemistry and antimicrobial assay of *Jatropha curcas* extracts. Eur J Appl Sci. 2015;7(1):12-16.
72. Enechi OC, Oluka HI, Ugwu PCO. Acute toxicity and ameliorative properties of *Alstonia boonei* leaf extract on diabetic rats. Afr J Biotechnol. 2014;13(5).
73. Alum EU, Obeagu EI, Ugwu OPC. Enhancing water, sanitation, and hygiene for diarrhoea control and SDGs: A review. Medicine. 2024;103(38):e39578.
74. Odo CE, Nwodo OFC, Joshua PE, Ugwu OPC, Okonkwo CC. Anti-diarrhoeal effect of chloroform–methanol extract of *Persea americana* seeds in rats. J Pharm Res. 2013;6(3):331-335.
75. Ugwu OPC, Obeagu EI, Alum EU, Michael M, et al. Effect of ethanol leaf extract of *Chromolaena odorata* on hepatic markers in diabetic rats. IAA J Appl Sci. 2023;9(1):46-56.
76. Ibiam UA, Alum EU, Orji OU, Aja PM, Nwamaka EN, Ugwu OPC, et al. Anti-inflammatory effects of *Buchholzia coriacea* leaf extract in arthritic rats. Indo Am J Pharm Sci. 2018;5(7):6341-6357.
77. Obeagu EI, Obeagu GU, Odo EO, Alum EU. Nutritional approaches for enhancing immune competence in HIV-positive individuals. IDOSR J Appl Sci. 2024;9(1):40-50.
78. Obeagu EI, Alum EU, Ugwu OPC. Hepcidin: Gatekeeper of iron in malaria resistance. Newport Int J Res Med Sci. 2023;4(2):1-8.
79. Nyamboga TO, Ugwu OPC, Ugwu JN, et al. Biotechnological innovations in soil health management: a systematic review of integrating microbiome engineering, bioinformatics, and sustainable practices. Cogent Food Agric. 2025;11(1):2519811.
80. Madu ANB, Alum EU, Aloh HE, Ugwu OPC, Obeagu EI, Uti DE, Egba SI, Ukaidi CUA. The price of progress: Assessing the financial costs of HIV/AIDS management in East Africa. Medicine. 2025;104(18):e42300.
81. Alum EU, Ugwu OPC. Beyond pregnancy: Understanding long-term implications of gestational diabetes mellitus. INOSR Sci Res. 2024;11(1):63-71.
82. Ugwu OPC, Alum EU, Okon MB, Aja PM, Obeagu EI, Onyeneke EC. Anti-nutritional and GC-MS analysis of ethanol root extract and fractions of *Sphenocentrum jollyanum*. RPS Pharmacol Pharm Rep. 2023;2(2):rqad007.
83. Eze VHU, Eze CE, Mbabazi A, Ugwu CN, Ugwu PO, Ogenyi CF, Ugwu JN, et al. Qualities and characteristics of a good scientific research writing: Step-by-step approaches. IAA J Appl Sci. 2023;9(2):71-76.
84. Igwenyi IO, Nchi PO, Okechukwu UPC, Igwenyi IP, Obasi DC, Edwin N. Nutritional potential of *Azadirachta indica* seeds. Indo Am J Pharm Sci. 2017;4(2):477-482.
85. Enechi OC, Oluka IH, Ugwu OPC, Omeh YS. Effect of ethanol leaf extract of *Alstonia boonei* on lipid profile of alloxan-induced diabetic rats. Afr J Biotechnol. 2013;24.
86. Ugwu OPC. Anti-malaria effect of ethanol extract of *Moringa oleifera* leaves on malaria-induced mice. University of Nigeria Nsukka; 2011:39.

87. Alum EU, Ugwu OPC, Obeagu EI. Nutritional interventions for cervical cancer patients: Beyond conventional therapies. J Cancer Res Cell Ther. 2024;8(1):1-6.
88. Obeagu EI, Obeagu GU. Advancements in immune augmentation strategies for HIV patients. IAA J Biol Sci. 2024;11(1):1-11.
89. Okechukwu PU, Nzubechukwu E, Ogbanshi ME, Ezeani N, Nworie MO. Effect of ethanol leaf extract of *Jatropha curcas* on chloroform-induced hepatotoxicity in albino rats. Glob J Biotech Biochem. 2015;10:11-15.
90. Ilozue NM, Ikezu UP, Okechukwu PCU. Antimicrobial and phytochemical screening of *Persea americana* seed extracts. IOSR J Pharm Biol Sci. 2014;9(2):23-25.
91. Onyeze R, Udeh SM, Akachi B, Ugwu OP. Isolation and characterization of fungi associated with spoilage of corn (*Zea mays*). Int J Pharm Med Biol Sci. 2013;2(3):86-91.
92. Obeagu EI, Alum EU, Ugwu OPC. Hepcidin: The gatekeeper of iron in malaria resistance. Newport Int J Res Med Sci. 2023;4:1-8.
93. Obeagu EI, Alum EU, Obeagu GU, Ugwu OPC. Prostate cancer: Review on risk factors. Eurasian Exp J Public Health. 2023;4(1):4-7.
94. Offor CE, Okaka ANC, Ogbugo SO, Egwu CO, Okechukwu PC. Effects of ethanol leaf extract of *Pterocarpus santalinoides* on haemoglobin, packed cell volume and platelets. IOSR J Nurs Health Sci. 2015;4:108-112, 93.
95. Offor C, Aja PC, Ugwu O, Agbafor KN. Effects of ethanol leaf extract of *Gmelina arborea* on serum proteins in albino rats. Glob J Environ Res. 2015;9(1):1-4.
96. Alum EU, Uti DE, Obeagu EI, Ugwu OPC, Alum BN. Cancer's psychosocial aspects: Impact on patient outcomes. Elite J Med. 2024;2(6):32-42.
97. Alum EU, Ugwu OPC, Egba SI, Uti DE, Alum BN. Climate variability and malaria transmission: Unravelling the complex relationship. INOSR Sci Res. 2024;11(2):16-22.
98. Alum EU, Obeagu EI, Ugwu OPC, Egba SI, EjimUti DE, Ukaidi CUA, et al. Confronting dual challenges: Substance abuse and HIV/AIDS. Elite J HIV. 2024;2(5):1-8.

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