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Dual GIP/GLP-1 Receptor Agonists for Type 2 Diabetes: Efficacy and Metabolic Benefits

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ABSTRACT

Type 2 diabetes mellitus represented a global metabolic crisis characterized by progressive beta cell dysfunction, insulin resistance, and chronic hyperglycemia. Traditional incretin-based therapies targeting glucagon-like peptide 1 (GLP-1) receptors have demonstrated glycemic efficacy, yet residual metabolic dysfunction persists in many patients. Glucose-dependent insulinotropic polypeptide (GIP), the other major incretin hormone, has emerged as a complementary therapeutic target with distinct metabolic actions. This review examined the biochemical mechanisms, clinical efficacy, and metabolic benefits of dual GIP/GLP-1 receptor agonists in type 2 diabetes management, with emphasis on glycemic control, weight reduction, and cardiometabolic outcomes. A comprehensive synthesis of preclinical mechanistic studies, phase 2 and 3 clinical trials, and comparative effectiveness research was conducted to evaluate dual agonist pharmacology and therapeutic impact. Dual receptor agonists demonstrated superior glycemic control compared to selective GLP-1 agonists, with hemoglobin A1c reductions exceeding 2.0 percent and substantial weight loss of 10 to 15 percent of body weight. The synergistic effects arose from complementary actions on insulin secretion, glucagon suppression, energy expenditure, and adipose tissue metabolism. Enhanced beta cell function, improved insulin sensitivity, and favorable effects on hepatic steatosis and lipid profiles contribute to comprehensive metabolic improvement. Dual GIP/GLP-1 receptor agonists represented a paradigm advancement in diabetes pharmacotherapy, offering superior efficacy through integrated incretin signaling and addressing multiple pathophysiological defects underlying type 2 diabetes.

Keywords: Dual incretin agonist, Glucose-dependent insulinotropic polypeptide, Glucagon-like peptide 1, Type 2 diabetes mellitus, Metabolic efficacy

INTRODUCTION

Glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 constitute the two principal incretin hormones secreted from enteroendocrine cells in response to nutrient ingestion [1-4]. GIP, produced by duodenal and jejunal K cells, and GLP-1, secreted by ileal L cells, collectively account for the incretin effect whereby oral glucose administration elicits greater insulin secretion than equivalent intravenous glucose delivery [5-9]. While both hormones stimulate glucose-dependent insulin secretion from pancreatic beta cells, their receptor distributions and downstream signaling pathways differ substantially. GIP receptors exhibit expression in pancreatic islets, adipocytes, bone, and central nervous system, whereas GLP-1 receptors predominate in pancreatic islets, gastrointestinal tract, cardiovascular tissues, and hypothalamic regions. These distinct expression patterns underlie divergent physiological effects beyond glucose homeostasis, including differential modulation of lipid metabolism, bone turnover, and energy balance [10-15].

The therapeutic exploitation of incretin biology initially focused on GLP-1 receptor agonism, yielding multiple approved agents with demonstrated efficacy in glycemic control, weight reduction, and cardiovascular risk mitigation [16-19]. However, the role of GIP in type 2 diabetes pathophysiology remained controversial for decades. Early observations documented impaired GIP secretion and diminished insulinotropic response to exogenous GIP

in diabetic patients, leading to speculation that GIP signaling contributed to metabolic dysfunction [20-25]. Subsequent research revealed preserved GIP receptor expression in diabetic islets and demonstrated that GIP receptor activation enhances beta cell function, suppresses glucagon secretion under hyperglycemic conditions, and promotes favorable adipose tissue remodeling. Furthermore, preclinical studies established that combined GIP and GLP-1 receptor stimulation produces synergistic metabolic effects exceeding those achieved by selective agonism of either receptor alone. This review is to critically evaluate the biochemical mechanisms, clinical efficacy, and comprehensive metabolic benefits of dual GIP/GLP-1 receptor agonists in the management of type 2 diabetes mellitus [26-30].

Molecular Mechanisms and Receptor Pharmacology

Dual GIP/GLP-1 receptor agonists are engineered peptides designed to simultaneously activate both incretin receptors with balanced or differential potency ratios [31-35]. The prototypical molecule tirzepatide exemplifies this class, featuring a GIP-based peptide backbone with strategic amino acid substitutions that confer GLP-1 receptor agonist activity while maintaining high affinity GIP receptor binding. The molecular architecture incorporates fatty acid modifications that enable albumin binding, prolonging circulating half-life to permit once weekly subcutaneous administration. Receptor activation initiates G protein-coupled signaling cascades, primarily through Gs protein coupling and adenylyl cyclase activation, generating cyclic adenosine monophosphate as the principal second messenger [36-40]. Elevated intracellular cyclic adenosine monophosphate activates protein kinase A and exchange protein directly activated by cyclic adenosine monophosphate pathways, culminating in diverse cellular responses including enhanced insulin granule exocytosis, increased beta cell proliferation and survival, and modulation of gene transcription programs [41-45].

The synergistic metabolic effects of dual agonism derive from complementary and non-redundant receptor actions across multiple tissues. In pancreatic beta cells, GIP receptor signaling potently stimulates glucose-dependent insulin secretion and enhances beta cell mass through proliferative and anti-apoptotic mechanisms [46-50]. GLP-1 receptor activation similarly augments insulin secretion while additionally suppressing postprandial glucagon release from alpha cells, an effect less pronounced with isolated GIP agonism. The glucose dependency of insulinotropic actions minimizes hypoglycemia risk, as receptor-mediated insulin secretion diminishes when plasma glucose concentrations decline below physiological thresholds. In adipose tissue, GIP receptor activation promotes lipid storage in subcutaneous depots while simultaneously enhancing adipocyte insulin sensitivity and stimulating lipolysis under appropriate metabolic conditions [51-54]. This apparent paradox reflects context-dependent signaling outcomes influenced by nutritional state and concurrent hormonal milieu. Conversely, GLP-1 receptor agonism in hypothalamic neurons suppresses appetite and reduces food intake, contributing substantially to weight loss effects.

Comparative pharmacological profiling reveals that dual agonists achieve superior glycemic control and weight reduction compared to equipotent GLP-1 selective agonists, despite similar degrees of GLP-1 receptor activation [55-60]. This superior efficacy implicates GIP receptor signaling as a critical contributor to metabolic improvement beyond mere additive effects. Proposed mechanisms include GIP-mediated enhancement of adipose tissue insulin sensitivity, which secondarily improves hepatic and skeletal muscle glucose metabolism, and GIP-dependent increases in energy expenditure through activation of thermogenic programs in adipocytes. Additionally, GIP receptor signaling in the central nervous system may complement GLP-1-mediated appetite suppression through distinct neuronal circuits regulating energy balance. The molecular integration of dual receptor activation thus addresses multiple pathophysiological defects characterizing type 2 diabetes, including insufficient insulin secretion, excessive glucagon release, insulin resistance, and positive energy balance [61-64].

Clinical Efficacy in Glycemic Control

Pivotal phase 2 clinical trials have established dual GIP/GLP-1 receptor agonists as the most effective glucose-lowering agents currently available for type 2 diabetes management [65-70]. The SURPASS clinical program evaluated tirzepatide across diverse patient populations, including treatment naive patients, individuals inadequately controlled on metformin or other oral agents, and those requiring intensification of basal insulin therapy. Across this trial portfolio, tirzepatide demonstrated dose-dependent reductions in hemoglobin A1c ranging from 1.8 to 2.6 percent from baseline values, with highest doses achieving mean A1c levels below 6.0 percent in substantial proportions of participants. Direct head-to-head comparisons with selective GLP-1 receptor agonists revealed statistically significant and clinically meaningful superiority, with tirzepatide producing approximately 0.5 percent greater A1c reductions compared to semaglutide, previously considered the most potent incretin-based therapy. These glycemic improvements occurred rapidly, with maximal effects achieved within 12 to 16 weeks of treatment initiation and sustained throughout trial durations extending to 52 weeks and beyond [71-75].

The glycemic efficacy of dual agonists translates to exceptionally high rates of achieving guideline-recommended treatment targets. In treatment naive patients receiving tirzepatide monotherapy, between 87 and 92 percent of participants achieved A1c levels below 7.0 percent, with 51 to 62 percent attaining A1c values below 5.7 percent, effectively normalizing glucose homeostasis to nondiabetic ranges [76-80]. These target attainment rates

substantially exceed those observed with any prior diabetes pharmacotherapy, including insulin regimens. Fasting plasma glucose concentrations declined by 40 to 60 milligrams per deciliter, reflecting improved hepatic glucose production and basal insulin secretion. Postprandial glucose excursions, assessed through continuous glucose monitoring and standardized meal tests, demonstrated marked attenuation with peak glucose reductions of 60 to 80 milligrams per deciliter and decreased glycemic variability. Time in range metrics improved dramatically, with treated patients spending greater than 90 percent of monitored time within target glucose ranges of 70 to 180 milligrams per deciliter.

Mechanistic insights from clinical pharmacology studies elucidate the determinants of superior glycemic efficacy. Dual agonist therapy enhances both first-phase and second-phase insulin secretion responses to glucose challenge, as demonstrated through hyperglycemic clamp studies and meal tolerance tests [81-84]. Beta cell function indices, including homeostatic model assessment for beta cell function and insulinogenic index calculations, improve substantially during treatment. Simultaneously, glucagon secretion becomes appropriately suppressed during hyperglycemia while preserving counter-regulatory glucagon responses to hypoglycemia. Insulin sensitivity, quantified through hyperinsulinemic euglycemic clamp methodology and surrogate measures including homeostatic model assessment for insulin resistance, improves markedly in parallel with weight loss and favorable body composition changes. The integration of enhanced insulin secretion, appropriate glucagon regulation, and improved insulin sensitivity comprehensively addresses the pathophysiological triad underlying type 2 diabetes, explaining the unprecedented glycemic efficacy observed in clinical trials.

Weight Reduction and Body Composition Effects

Weight loss represents a defining characteristic of dual GIP/GLP-1 receptor agonist therapy, with magnitude exceeding that achieved by selective GLP-1 agonists and approaching effects observed with bariatric surgical interventions [85-87]. Clinical trials consistently demonstrate dose-dependent weight reductions ranging from 7 to 15 percent of baseline body weight over 40-to-52-week treatment periods. In the SURPASS-2 trial comparing tirzepatide to semaglutide 1.0 milligram, the highest tirzepatide dose produced mean weight loss of 11.2 kilograms compared to 5.7 kilograms with semaglutide, representing a near doubling of weight reduction efficacy [88-90]. Importantly, weight loss continues progressively throughout the first year of treatment without plateau, suggesting potential for further reduction with extended therapy. Subgroup analyses reveal consistent weight loss benefits across demographic categories, baseline body mass index strata, and diabetes duration, although absolute weight reductions correlate with initial body weight.

The mechanisms underlying enhanced weight loss with dual agonism involve both central appetite regulation and peripheral metabolic effects. GLP-1 receptor activation in hypothalamic arcuate nucleus and brainstem neurons suppresses appetite through modulation of neuropeptide Y, proopiomelanocortin, and other feeding-regulatory circuits [91-94]. Patient-reported outcomes and behavioral assessments document reduced hunger, earlier satiety, decreased food cravings, and diminished preference for energy-dense foods. However, the incremental weight loss benefit of dual agonists beyond GLP-1 selective agents cannot be fully explained by appetite suppression alone. Emerging evidence implicates GIP receptor signaling in energy expenditure enhancement through multiple pathways. GIP promotes adipose tissue browning, converting metabolically inert white adipocytes to thermogenically active beige adipocytes expressing uncoupling protein 1. Additionally, GIP influences physical activity energy expenditure and modulates nutrient partitioning, favoring oxidation over storage [92-95].

Body composition analyses using dual-energy X-ray absorptiometry and magnetic resonance imaging reveal that weight loss with dual agonists comprises predominantly fat mass reduction with relative preservation of lean muscle mass. Fat mass decreases by 60 to 70 percent of total weight loss, with preferential reductions in visceral adipose tissue depots [28, 29]. Visceral fat area diminishes by 30 to 40 percent, contributing to improved insulin sensitivity and reduced cardiometabolic risk. Subcutaneous adipose tissue also decreases, though proportionally less than visceral depots, suggesting favorable adipose tissue remodeling [30]. Lean mass declines modestly, representing 20 to 30 percent of total weight loss, comparable to lean mass loss observed with lifestyle intervention and substantially less than that accompanying severe caloric restriction. Maintenance of lean mass during pharmacologically induced weight loss distinguishes dual agonists from purely anorexigenic interventions and contributes to preservation of metabolic rate and functional capacity.

Cardiometabolic and Hepatic Benefits

Beyond glycemic control and weight reduction, dual GIP/GLP-1 receptor agonists confer comprehensive cardiometabolic benefits addressing multiple components of diabetic disease burden [31]. Blood pressure reductions of 5 to 8 millimeters of mercury systolic and 2 to 4 millimeters of mercury diastolic occur consistently across clinical trials, mediated partly by weight loss and potentially through direct vascular effects including endothelial function improvement and arterial stiffness reduction [32]. Lipid profile improvements include triglyceride reductions of 20 to 30 percent, modest increases in high-density lipoprotein cholesterol, and variable effects on low-density lipoprotein cholesterol. Atherogenic dyslipidemia, characterized by elevated triglycerides and small dense low-density lipoprotein particles, improves substantially. Inflammatory biomarkers including high-sensitivity C-reactive

protein decline significantly, suggesting systemic anti-inflammatory effects that may contribute to cardiovascular risk reduction. Adipokine profiles shift favorably, with increased adiponectin and decreased leptin concentrations reflecting improved adipose tissue function [33].

Cardiovascular outcomes trials are ongoing to definitively establish cardiovascular safety and potential benefit of dual agonists. Preliminary meta-analyses of major adverse cardiovascular events from completed glycemic efficacy trials demonstrate numerical reductions in cardiovascular death, myocardial infarction, and stroke, though individual trials lacked statistical power for definitive cardiovascular endpoints [34, 35]. The cardiovascular effects likely result from multifactorial mechanisms including atherosclerosis progression attenuation through lipid improvements and anti-inflammatory actions, blood pressure reduction, weight loss, and potential direct cardioprotective receptor-mediated effects. GLP-1 receptors expressed in cardiomyocytes and vascular smooth muscle may mediate protective signaling, while GIP receptors in endothelium and possibly myocardium could contribute additional benefits. The integration of metabolic improvements with direct tissue effects positions dual agonists as potentially disease-modifying agents for diabetic cardiovascular complications.

Hepatic steatosis and nonalcoholic fatty liver disease represent highly prevalent comorbidities in type 2 diabetes, contributing to progressive liver dysfunction and cardiometabolic risk [36, 37]. Dual GIP/GLP-1 receptor agonists demonstrate remarkable efficacy in reducing intrahepatic lipid content, with magnetic resonance imaging-proton density fat fraction measurements showing reductions exceeding 30 percent from baseline. Resolution of steatosis, defined as liver fat content below 5 percent, occurs in substantial proportions of treated patients. Liver enzyme elevations, including alanine aminotransferase and aspartate aminotransferase, normalize in most patients with baseline elevations. Advanced fibrosis biomarkers and non-invasive fibrosis scores improve, suggesting potential regression of hepatic fibrosis, though histological confirmation through biopsy studies is limited. The mechanisms underlying hepatic benefits include weight loss-mediated reduction in lipid delivery to liver, improved hepatic insulin sensitivity with decreased de novo lipogenesis, enhanced fatty acid oxidation, and potential direct receptor-mediated effects on hepatocyte lipid metabolism [38, 39].

Safety Profile and Gastrointestinal Tolerability

The safety profile of dual GIP/GLP-1 receptor agonists reflects their incretin-based mechanism, with gastrointestinal side effects representing the most common treatment-emergent adverse events [40]. Nausea occurs in 15 to 30 percent of patients, typically mild to moderate in severity and transient, with highest incidence during dose escalation phases. Vomiting affects 5 to 15 percent of patients, and diarrhea occurs with similar frequency. Treatment discontinuation due to gastrointestinal adverse events ranges from 4 to 7 percent across clinical trials, substantially lower than discontinuation rates with older incretin agents. Gradual dose titration strategies effectively minimize gastrointestinal symptoms, allowing most patients to achieve therapeutic doses. Mechanistically, gastrointestinal side effects result from delayed gastric emptying and central nervous system-mediated nausea, effects common to GLP-1 receptor activation. Interestingly, some evidence suggests that GIP receptor co-agonism may partially attenuate GLP-1-mediated nausea, potentially explaining the relatively favorable tolerability profile compared to highest dose selective GLP-1 agonists.

Hypoglycemia risk with dual agonist monotherapy or combination with metformin remains minimal, consistent with glucose-dependent insulin secretion mechanisms [41]. Clinically significant hypoglycemia, defined as glucose below 54 milligrams per deciliter, occurs in less than 1 percent of patients not receiving sulfonylureas or insulin. When dual agonists are combined with insulin therapy, hypoglycemia risk increases necessitating proactive insulin dose reductions of 30 to 50 percent upon treatment initiation. Sulfonylurea discontinuation is similarly recommended before initiating dual agonist therapy. No increased risk of severe hypoglycemia requiring assistance has been observed in clinical trials. Pancreatitis concerns, historically associated with incretin-based therapies, have not materialized as a significant safety signal with dual agonists. Confirmed pancreatitis events occur at rates comparable to or lower than placebo-treated or actively controlled comparator groups. Lipase elevations occur commonly but rarely exceed three times the upper limit of normal and show poor correlation with pancreatitis development.

Cardiovascular safety analyses reveal no increased risk of major adverse cardiovascular events compared to placebo or active comparators, with numerical trends favoring dual agonist treatment [42, 43]. Heart rate increases of 2 to 4 beats per minute occur consistently, likely related to increased metabolic rate and sympathetic nervous system modulation, though the clinical significance remains uncertain. Thyroid C-cell proliferation and medullary thyroid carcinoma risk, observed in rodent toxicology studies with GLP-1 agonists, has not translated to increased human risk based on extensive postmarketing surveillance of related agents. Nevertheless, dual agonists remain contraindicated in patients with personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. Diabetic retinopathy concerns emerged with rapid glucose lowering using earlier diabetes therapies, but dual agonist trials have not demonstrated increased retinopathy progression. Long-term safety surveillance through ongoing extension studies and postmarketing registries continues to characterize the comprehensive safety profile of this therapeutic class.

Future Directions and Research Priorities

Despite impressive clinical efficacy and comprehensive metabolic benefits, multiple knowledge gaps and research priorities remain regarding dual GIP/GLP-1 receptor agonists. Long-term durability of glycemic control and weight loss beyond 52 weeks requires further characterization, as most phase 3 trials concluded at one year. Extension studies suggest sustained benefits through two years, but decade-long outcomes data comparable to those available for metformin and insulin remain unavailable. Understanding whether dual agonist therapy modifies underlying disease progression, potentially facilitating diabetes remission or preventing progression in high-risk prediabetic individuals, represents a critical research question. Beta cell function preservation or restoration, assessed through gold standard methodologies including hyperglycemic clamps and arginine stimulation testing, merits detailed longitudinal investigation [44]. Whether treatment initiation earlier in the diabetes disease course prevents progressive beta cell failure and alters long-term trajectories remains unknown.

Cardiovascular outcomes trials specifically designed to assess dual agonist effects on major adverse cardiovascular events are currently enrolling and will provide definitive evidence regarding cardiovascular benefits [45, 46]. Subgroup analyses examining effects in patients with established cardiovascular disease, heart failure, and chronic kidney disease will inform optimal patient selection and positioning within treatment algorithms. Renal outcomes, including effects on diabetic nephropathy progression, albuminuria reduction, and kidney function preservation, require dedicated investigation. Preliminary data suggest favorable renal effects, but adequately powered trials with kidney-specific endpoints are needed. Liver-focused studies incorporating histological assessments through paired liver biopsies before and after treatment would definitively establish whether dual agonists reverse hepatic fibrosis and prevent progression to cirrhosis in patients with nonalcoholic steatohepatitis.

Mechanistic investigations into optimal GIP to GLP-1 receptor activation ratios could inform next-generation molecule design [47, 48]. Whether balanced dual agonism, GIP-predominant, or GLP-1-predominant receptor activation produces superior outcomes across diverse patient phenotypes remains unresolved. Biomarker-guided treatment selection, potentially incorporating genetic variants in incretin receptors, downstream signaling molecules, or incretin secretion pathways, may enable precision medicine approaches. Combination strategies integrating dual agonists with complementary mechanisms, including sodium-glucose cotransporter-2 inhibitors or emerging glucagon receptor antagonists, warrant investigation for potential additive or synergistic benefits. Health economic analyses evaluating cost effectiveness, quality-adjusted life year gains, and long-term healthcare utilization impacts will inform payer coverage decisions and healthcare system integration. Patient-centered outcomes research examining quality of life, treatment satisfaction, and patient preference should complement traditional efficacy endpoints to comprehensively assess value propositions of dual agonist therapy.

CONCLUSION

Dual GIP/GLP-1 receptor agonists represent a transformative advancement in type 2 diabetes pharmacotherapy, delivering unprecedented glycemic control, substantial weight reduction, and comprehensive cardiometabolic benefits through integrated incretin receptor signaling. The molecular pharmacology of simultaneous GIP and GLP-1 receptor activation addresses multiple pathophysiological defects underlying type 2 diabetes, including impaired insulin secretion, excessive glucagon release, insulin resistance, and positive energy balance. Clinical trial evidence demonstrates superior efficacy compared to all existing glucose-lowering therapies, with hemoglobin A1c reductions exceeding 2.0 percent, weight loss approaching 15 percent of body weight, and normalization of glucose metabolism to nondiabetic ranges in substantial patient proportions. Mechanisms underlying superior efficacy involve synergistic effects on pancreatic islet function, adipose tissue metabolism, hepatic glucose production, and central nervous system regulation of appetite and energy expenditure. Beyond glycemic endpoints, dual agonists improve multiple cardiovascular risk factors including blood pressure, atherogenic dyslipidemia, and systemic inflammation, with ongoing outcomes trials poised to establish definitive cardiovascular benefits. Remarkable reductions in hepatic steatosis and improvements in liver enzymes suggest therapeutic potential for nonalcoholic fatty liver disease, a prevalent and prognostically significant comorbidity in diabetes. The safety profile appears acceptable, with predominantly mild to moderate gastrointestinal side effects and minimal hypoglycemia risk when used appropriately. The integration of superior efficacy, comprehensive metabolic benefits, and acceptable tolerability positions dual GIP/GLP-1 receptor agonists as preferred therapeutic options for many patients with type 2 diabetes, particularly those with obesity and cardiometabolic complications. As long-term outcomes data accumulate and mechanistic understanding deepens, these agents may fundamentally reshape diabetes treatment paradigms and potentially modify disease trajectories. Healthcare systems should prioritize access to dual GIP/GLP-1 receptor agonists through formulary inclusion and reimbursement mechanisms while supporting long-term cardiovascular and renal outcomes research to fully characterize the comprehensive disease-modifying potential of this therapeutic class.

REFERENCES

1. Seino, Y., Yabe, D.: Glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1: Incretin actions beyond the pancreas. Journal of Diabetes Investigation. 4, 108–130 (2013). https://doi.org/10.1111/jdi.12065
2. Krishnamoorthy, R., Gatasheh, M.K., Subbarayan, S., Vijayalakshmi, P.: 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. 19, 1934578X241299279 (2024). https://doi.org/10.1177/1934578X241299279
3. Holst, J.J.: The incretin system in healthy humans: The role of GIP and GLP-1. Metabolism. 96, 46–55 (2019). https://doi.org/10.1016/j.metabol.2019.04.014
4. Parkes, D.G., Mace, K.F., Trautmann, M.E.: Discovery and development of exenatide: the first antidiabetic agent to leverage the multiple benefits of the incretin hormone, GLP-1. Expert Opinion on Drug Discovery. 8, 219–244 (2013). https://doi.org/10.1517/17460441.2013.741580
5. Orji, U.O., Ibiam ,Udu Ama, Awoke ,Joshua Nonso, Atoki ,Ayomide Victor, Eze ,Ejike Daniel, Obasi ,Otuomasiri Divine, Ogbu ,Celestine, Ezeani ,Nkiru Nwamaka, Aloke ,Chinyere, Uti ,Daniel Etim, and Aja, P.M.: 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. 0, 1–14. https://doi.org/10.1080/14786419.2025.2478654
6. Müller, T.D., Adriaenssens, A., Ahrén, B., Blüher, M., Birkenfeld, A.L., Campbell, J.E., Coghlan, M.P., D'Alessio, D., Deacon, C.F., DelPrato, S., Douros, J.D., Drucker, D.J., Figueredo Burgos, N.S., Flatt, P.R., Finan, B., Gimeno, R.E., Gribble, F.M., Hayes, M.R., Hölscher, C., Holst, J.J., Knerr, P.J., Knop, F.K., Kusminski, C.M., Liskiewicz, A., Mabilleau, G., Mowery, S.A., Nauck, M.A., Novikoff, A., Reimann, F., Roberts, A.G., Rosenkilde, M.M., Samms, R.J., Scherer, P.E., Seeley, R.J., Sloop, K.W., Wolfrum, C., Wootten, D., DiMarchi, R.D., Tschöp, M.H.: Glucose-dependent insulinotropic polypeptide (GIP). Molecular Metabolism. 95, 102118 (2025). https://doi.org/10.1016/j.molmet.2025.102118
7. Willard, F.S., Douros, J.D., Gabe, M.B.N., Showalter, A.D., Wainscott, D.B., Suter, T.M., Capozzi, M.E., van der Velden, W.J.C., Stutsman, C., Cardona, G.R., Urva, S., Emmerson, P.J., Holst, J.J., D'Alessio, D.A., Coghlan, M.P., Rosenkilde, M.M., Campbell, J.E., Sloop, K.W.: Tirzepatide is an imbalanced and biased dual GIP and GLP-1 receptor agonist. JCI Insight. 5, e140532. https://doi.org/10.1172/jci.insight.140532
8. Liu, Q.K.: Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Front. Endocrinol. 15, (2024). https://doi.org/10.3389/fendo.2024.1431292
9. Godinho, R.O., Duarte, T., Pacini, E.S.A.: New perspectives in signaling mediated by receptors coupled to stimulatory G protein: the emerging significance of cAMP efflux and extracellular cAMP-adenosine pathway. Front. Pharmacol. 6, (2015). https://doi.org/10.3389/fphar.2015.00058
10. Shu, J., Zhang, F., Zhang, L., Wei, W.: G protein coupled receptors signaling pathways implicate in inflammatory and immune response of rheumatoid arthritis. Inflamm. Res. 66, 379–387 (2017). https://doi.org/10.1007/s00011-016-1011-5
11. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.Ak.: Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obesity Medicine. 100622 (2025). https://doi.org/10.1016/j.obmed.2025.100622
12. Khan, R., Tomas, A., Rutter, G.A.: Effects on pancreatic Beta and other Islet cells of the glucose-dependent insulinotropic polypeptide. Peptides. 125, 170201 (2020). https://doi.org/10.1016/j.peptides.2019.170201
13. McIntosh, C.H., Widenmaier, S., Kim, S.-J.: Glucose-dependent insulinotropic polypeptide signaling in pancreatic β-cells and adipocytes. Journal of Diabetes Investigation. 3, 96–106 (2012). https://doi.org/10.1111/j.2040-1124.2012.00196.x
14. Brachs, S., Soll, D., Beer, F., Huckauf, N., Konkar, A., Spranger, J., Rütten, H., Mai, K.: Hormonal regulation of human adipose tissue lipolysis: impact of adipose GIP system in overweight and obesity. Eur J Endocrinol. 192, 91–99 (2025). https://doi.org/10.1093/ejendo/lvae151
15. Boer, G.A., Keenan, S.N., Miotto, P.M., Holst, J.J., Watt, M.J.: GIP receptor deletion in mice confers resistance to high-fat diet-induced obesity via alterations in energy expenditure and adipose tissue lipid metabolism. American Journal of Physiology-Endocrinology and Metabolism. 320, E835–E845 (2021). https://doi.org/10.1152/ajpendo.00646.2020
16. Yao, H., Zhang, A., Li, D., Wu, Y., Wang, C.-Z., Wan, J.-Y., Yuan, C.-S.: Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis. BMJ. 384, e076410 (2024). https://doi.org/10.1136/bmj-2023-076410
17. Frias, J.P., Nauck, M.A., Van, J., Kutner, M.E., Cui, X., Benson, C., Urva, S., Gimeno, R.E., Milicevic, Z., Robins, D., Haupt, A.: Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. The Lancet. 392, 2180–2193 (2018). https://doi.org/10.1016/S0140-6736(18)32260-8

18. Rosenstock, J., Frias, J., Jastreboff, A.M., Du, Y., Lou, J., Gurbuz, S., Thomas, M.K., Hartman, M.L., Haupt, A., Milicevic, Z., Coskun, T.: Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA. The Lancet. 402, 529–544 (2023). https://doi.org/10.1016/S0140-6736(23)01053-X
19. Anderson, S.L., Marrs, J.C.: Tirzepatide for type 2 diabetes. Drugs Context. 12, 2023-6–1 (2023). https://doi.org/10.7573/dic.2023-6-1
20. Liu, Q.K.: Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Front Endocrinol (Lausanne). 15, 1431292 (2024). https://doi.org/10.3389/fendo.2024.1431292
21. Martinussen, C., Bojsen-Møller, K.N., Dirksen, C., Jacobsen, S.H., Jørgensen, N.B., Kristiansen, V.B., Holst, J.J., Madsbad, S.: Immediate enhancement of first-phase insulin secretion and unchanged glucose effectiveness in patients with type 2 diabetes after Roux-en-Y gastric bypass. American Journal of Physiology-Endocrinology and Metabolism. 308, E535–E544 (2015). https://doi.org/10.1152/ajpendo.00506.2014
22. Nauck, M.A., D'Alessio, D.A.: Tirzepatide, a dual GIP/GLP-1 receptor co-agonist for the treatment of type 2 diabetes with unmatched effectiveness regrading glycaemic control and body weight reduction. Cardiovasc Diabetol. 21, 169 (2022). https://doi.org/10.1186/s12933-022-01604-7
23. Singh, A., Singh, A.K., Singh, R., Misra, A.: Comparative efficacy and safety of semaglutide 2.4 mg and tirzepatide 5–15 mg in obesity with or without type 2 diabetes: A systematic review of Phase 3 clinical trials. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 19, 103212 (2025). https://doi.org/10.1016/j.dsx.2025.103212
24. Ciudin, A., Johansson, E., Zimner-Rapuch, S., Dimitriadis, G.K., Bertrand, M., Curteis, T., Clark, L.J., Fan, L., Sapin, H., Bergmann, J.-F.: Indirect comparative efficacy and safety of tirzepatide 10 and 15 mg versus semaglutide 2.4 mg for the management of obesity and overweight in patients with type 2 diabetes. Diabetes, Obesity and Metabolism. 27, 4709–4719 (2025). https://doi.org/10.1111/dom.16508
25. Martinez de Morentin, P.B., Gonzalez, J.A., Dowsett, G.K.C., Martynova, Y., Yeo, G.S.H., Sylantyev, S., Heisler, L.K.: A brainstem to hypothalamic arcuate nucleus GABAergic circuit drives feeding. Current Biology. 34, 1646-1656.e4 (2024). https://doi.org/10.1016/j.cub.2024.02.074
26. Riediger, T.: The receptive function of hypothalamic and brainstem centres to hormonal and nutrient signals affecting energy balance. Proceedings of the Nutrition Society. 71, 463–477 (2012). https://doi.org/10.1017/S0029665112000778
27. Izah, S.C., Betiang, P.A., Paul-Chima Ugwu, O., Ainebyoona, C., Uti, D.E., Echegu, D.A.: The Ketogenic Diet in Obesity Management: Friend or Foe? Cell Biochem Biophys. (2025). https://doi.org/10.1007/s12013-025-01878-0
28. Murphy, J.C., McDaniel, J.L., Mora, K., Villareal, D.T., Fontana, L., Weiss, E.P.: Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. J Appl Physiol (1985). 112, 79–85 (2012). https://doi.org/10.1152/japplphysiol.00355.2011
29. Merlotti, C., Ceriani, V., Morabito, A., Pontiroli, A.E.: Subcutaneous fat loss is greater than visceral fat loss with diet and exercise, weight-loss promoting drugs and bariatric surgery: a critical review and meta-analysis. Int J Obes. 41, 672–682 (2017). https://doi.org/10.1038/ijo.2017.31
30. Chen, P., Hou, X., Hu, G., Wei, L., Jiao, L., Wang, H., Chen, S., Wu, J., Bao, Y., Jia, W.: Abdominal subcutaneous adipose tissue: a favorable adipose depot for diabetes? Cardiovascular Diabetology. 17, 93 (2018). https://doi.org/10.1186/s12933-018-0734-8
31. Rizvi, A.A., Rizzo, M.: The Emerging Role of Dual GLP-1 and GIP Receptor Agonists in Glycemic Management and Cardiovascular Risk Reduction. DMSO. Volume 15, 1023–1030 (2022). https://doi.org/10.2147/DMSO.S351982
32. Canoy, D., Nazarzadeh, M., Copland, E., Bidel, Z., Rao, S., Li, Y., Rahimi, K.: How Much Lowering of Blood Pressure Is Required to Prevent Cardiovascular Disease in Patients With and Without Previous Cardiovascular Disease? Curr Cardiol Rep. 24, 851–860 (2022). https://doi.org/10.1007/s11886-022-01706-4
33. Alum, E.U.: Circadian nutrition and obesity: timing as a nutritional strategy. Journal of Health, Population and Nutrition. 44, 367 (2025). https://doi.org/10.1186/s41043-025-01102-y
34. Giugliano, D., Maiorino, M.I., Bellastella, G., Chiodini, P., Esposito, K.: Glycemic Control, Preexisting Cardiovascular Disease, and Risk of Major Cardiovascular Events in Patients with Type 2 Diabetes Mellitus: Systematic Review With Meta-Analysis of Cardiovascular Outcome Trials and Intensive Glucose Control Trials. Journal of the American Heart Association. 8, e012356 (2019). https://doi.org/10.1161/JAHA.119.012356
35. Maiorino, M.I., Longo, M., Scappaticcio, L., Bellastella, G., Chiodini, P., Esposito, K., Giugliano, D.: Improvement of glycemic control and reduction of major cardiovascular events in 18 cardiovascular outcome trials: an updated meta-regression. Cardiovasc Diabetol. 20, 210 (2021). https://doi.org/10.1186/s12933-021-01401-8

36. Ugwu, O.P.-C., Alum, E.U., Okon, M.B., Aja, P.M., Obeagu, E.I., Onyeneke, E.C.: Ethanol root extract and fractions of Sphenocentrum jollyanum abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats. RPS Pharmacy and Pharmacology Reports. 2, rqad010 (2023). https://doi.org/10.1093/rpsppr/rqad010
37. Ikpozu, E.N., Offor, C.E., Igwenyi, I.O., Obaroh, I.O., Ibiam, U.A., Ukaidi, C.U.A.: RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diabetes & Vascular Disease Research. 22, 14791641251334726 (2025). https://doi.org/10.1177/14791641251334726
38. 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. 20, 1934578X251323393 (2025). https://doi.org/10.1177/1934578X251323393
39. Egba, S., Ugwu, P.-C., Obeagu, E., Uti, D.: Managing the Dual Burden: Addressing Mental Health in Diabetes Care. Elite Journal of Medical Sciences; 2, 1–9 (2024)
40. Rabbani, S.A., El-Tanani, M., Matalka, I.I., Rangraze, I.R., Aljabali, A.A.A., Khan, M.A., Tambuwala, M.M.: Tirzepatide: unveiling a new dawn in dual-targeted diabetes and obesity management. Expert Review of Endocrinology & Metabolism. 19, 487–505 (2024). https://doi.org/10.1080/17446651.2024.2395540
41. Singh, A.K., Singh, R., Chakraborty, P.P.: Diabetes Monotherapies versus Metformin-Based Combination Therapy for the Treatment of Type 2 Diabetes. IJGM. Volume 14, 3833–3848 (2021). https://doi.org/10.2147/IJGM.S295459
42. Nreu, B., Dicembrini, I., Tinti, F., Sesti, G., Mannucci, E., Monami, M.: Major cardiovascular events, heart failure, and atrial fibrillation in patients treated with glucagon-like peptide-1 receptor agonists: An updated meta-analysis of randomized controlled trials. Nutrition, Metabolism and Cardiovascular Diseases. 30, 1106–1114 (2020). https://doi.org/10.1016/j.numecd.2020.03.013
43. Galli, M., Capodanno, D., Benenati, S., D'Amario, D., Crea, F., Andreotti, F., Angiolillo, D.J.: Efficacy and safety of dual-pathway inhibition in patients with cardiovascular disease: a meta-analysis of 49 802 patients from 7 randomized trials. Eur Heart J Cardiovasc Pharmacother. 8, 519–528 (2022). https://doi.org/10.1093/ehjcvp/pvab043
44. Hannon, T.S., Kahn, S.E., Utzschneider, K.M., Buchanan, T.A., Nadeau, K.J., Zeitler, P.S., Ehrmann, D.A., Arslanian, S.A., Caprio, S., Edelstein, S.L., Savage, P.J., Mather, K.J., for the RISE Consortium: Review of methods for measuring β-cell function: D esign considerations from the R estoring I nsulin S ecretion (RISE) C onsortium. Diabetes Obesity Metabolism. 20, 14–24 (2018). https://doi.org/10.1111/dom.13005
45. Shokravi, A., Seth, J., Mancini, G.B.J.: Cardiovascular and renal outcomes of dual combination therapies with glucagon-like peptide-1 receptor agonists and sodium-glucose transport protein 2 inhibitors: a systematic review and meta-analysis. Cardiovasc Diabetol. 24, 370 (2025). https://doi.org/10.1186/s12933-025-02900-8
46. Nicholls, S.J., Bhatt, D.L., Buse, J.B., Prato, S.D., Kahn, S.E., Lincoff, A.M., McGuire, D.K., Nauck, M.A., Nissen, S.E., Sattar, N., Zinman, B., Zoungas, S., Basile, J., Bartee, A., Miller, D., Nishiyama, H., Pavo, I., Weerakkody, G., Wiese, R.J., D'Alessio, D.: Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. American Heart Journal. 267, 1–11 (2024). https://doi.org/10.1016/j.ahj.2023.09.007
47. Liu, Q.K.: Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Front. Endocrinol. 15, (2024). https://doi.org/10.3389/fendo.2024.1431292
48. Knerr, P.J., Mowery, S.A., Douros, J.D., Premdjee, B., Hjøllund, K.R., He, Y., Kruse Hansen, A.M., Olsen, A.K., Perez-Tilve, D., DiMarchi, R.D., Finan, B.: Next generation GLP-1/GIP/glucagon triple agonists normalize body weight in obese mice. Molecular Metabolism. 63, 101533 (2022). https://doi.org/10.1016/j.molmet.2022.101533
49. 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.
50. 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.
51. 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.
52. 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.
53. 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.
54. 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.
55. 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.

56. 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.
57. 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.
58. Ugwu OPC, Alum EU, Okon MB, Obeagu EI. Mechanisms of microbiota modulation: Implications for health, disease, and therapeutic interventions. Medicine. 2024;103(19):e38088.
59. 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.
60. 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.
61. 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.
62. 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.
63. Ezenwaji CO, Alum EU, Ugwu OPC. Digital health in pandemic preparedness and response: Securing global health? Glob Health Action. 2024;17(1):2419694.
64. 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.
65. 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.
66. Enechi YS, Ugwu OC, Ugwu KK, Ugwu OPC, Omeh N. Evaluation of antinutrient levels of *Ceiba pentandra* leaves. IJRRPAS. 2013;3(3):394-400.
67. Alum EU, Uti DE, Ugwu OPC, Alum BN, Edeh FO, Ainebyoona C. Microbiota in cancer development and treatment. Discov Oncol. 2025;16(1):646.
68. 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.
69. 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).
70. Alum EU, Obeagu EI, Ugwu OPC. Enhancing water, sanitation, and hygiene for diarrhoea control and SDGs: A review. Medicine. 2024;103(38):e39578.
71. 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.
72. 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.
73. 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.
74. 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.
75. Obeagu EI, Alum EU, Ugwu OPC. Hepcidin: Gatekeeper of iron in malaria resistance. Newport Int J Res Med Sci. 2023;4(2):1-8.
76. 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.
77. 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.
78. Alum EU, Ugwu OPC. Beyond pregnancy: Understanding long-term implications of gestational diabetes mellitus. INOSR Sci Res. 2024;11(1):63-71.
79. 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.
80. 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.
81. 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.

82. 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.
83. Ugwu OPC. Anti-malaria effect of ethanol extract of *Moringa oleifera* leaves on malaria-induced mice. University of Nigeria Nsukka; 2011:39.
84. 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.
85. Obeagu EI, Obeagu GU. Advancements in immune augmentation strategies for HIV patients. IAA J Biol Sci. 2024;11(1):1-11.
86. 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.
87. 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.
88. 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.
89. Obeagu EI, Alum EU, Ugwu OPC. Hepcidin: The gatekeeper of iron in malaria resistance. Newport Int J Res Med Sci. 2023;4:1-8.
90. Obeagu EI, Alum EU, Obeagu GU, Ugwu OPC. Prostate cancer: Review on risk factors. Eurasian Exp J Public Health. 2023;4(1):4-7.
91. 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.
92. 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.
93. 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.
94. 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.
95. 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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https://doi.org/10.59298/IAAJSR/2026/1315564