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From Orphan Grain to Multi-Target Nutraceutical: Phytochemical, Mineral, and Amino Acid Mechanisms of *Eleusine coracana* in Type II Diabetes Management

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ABSTRACT

Eleusine coracana (L.) Gaertn., commonly known as finger millet or ragi, is a food security crop across the arid and semi-arid regions of Sub-Saharan Africa and South Asia. Beyond its long history as a subsistence staple, biomedical research is increasingly documenting its exceptional profile of bioaccessible macro- and micronutrients. This review synthesizes the nutritional, chemical, and pharmacological literature on E. coracana, mapping its phytochemical composition, mineral density, and essential amino acid profile. The crop is unusual among cereal grains for its high calcium concentration (294–390 mg/100 g), a robust complement of sulfur-containing amino acids (particularly methionine and cysteine), and a non-starch polysaccharide network that accounts for up to 20% of total dietary fiber. The seed coat also accumulates substantial polyphenolic content, including hydroxybenzoic acids, hydroxycinnamic acids, condensed tannins, and polymeric flavonoids. We evaluate the mechanisms by which these components address the pathophysiological hallmarks of Type II Diabetes Mellitus (T2DM). Bioactive extracts from E. coracana exert multi-targeted glycemic control through non-competitive inhibition of pancreatic α-amylase and intestinal α-glucosidase, suppression of advanced glycation end-products (AGEs), upregulation of peripheral AMP-activated protein kinase (AMPK) signaling, and modulation of the colonic microbiota that promotes short-chain fatty acid (SCFA) synthesis and reduces low-grade systemic inflammation. Taken together, the evidence supports E. coracana as a viable functional food and nutraceutical candidate for the prevention and management of T2DM-associated metabolic complications.

Keywords: Eleusine coracana, Functional Foods, Type II Diabetes, Alpha-Glucosidase, Polyphenols, Glycemic Index, Calcium Bioaccessibility.

INTRODUCTION

Type II Diabetes Mellitus (T2DM) is one of the most pressing global public health concerns of the twenty-first century, marked by chronic, multi-systemic metabolic dysfunction. Its pathogenesis is driven primarily by progressive peripheral insulin resistance combined with an absolute or relative insufficiency of insulin secretion from pancreatic β-cells. The resulting persistent postprandial and fasting hyperglycemia drives downstream complications including microvascular retinopathy, nephropathy, peripheral neuropathy, macrovascular cardiovascular disease, and accelerated macromolecular oxidation. Diabetes-associated dyslipidemia — elevated triglycerides and LDL alongside depressed HDL — further compounds cardiovascular risk in T2DM patients.

Conventional pharmacological strategies, from synthetic biguanides (metformin) to targeted α-glucosidase inhibitors (acarbose), remain standard therapeutic options, but their long-term use is often limited by secondary clinical failure, cost burdens in low- and middle-income countries, and gastrointestinal or hepatic toxicity. Metabolic research has accordingly shifted toward dietary interventions with multi-targeted efficacy and fewer adverse effects. Parallel ethnobotanical research on other traditional antidiabetic plants illustrates this trend:

ISSN 2278-2540 | DOI: 10.51583/IJLTEMAS | Volume XV, Issue VII, July 2026

ethanolic extracts of *Andrographis paniculata* have been shown to improve the lipid profile of alloxan-induced diabetic rats, reducing triglycerides and LDL while raising HDL (Elobisi & Okafor, 2022), reinforcing the broader case for plant-based dietary and phytotherapeutic interventions in metabolic disease management.

Among candidate dietary matrices, the ancient cereal Eleusine coracana (L.) Gaertn. — known as finger millet, ragi, or bird's foot millet — is a strong candidate for functional food development. Native to the highlands of East Africa (Uganda and Ethiopia) and cultivated across the Indian subcontinent for millennia, E. coracana tolerates moisture deficiency, high ambient temperatures, and low-fertility marginal soils (Ramashia et al., 2019). Long regarded as a subsistence crop, it is now recognized for a chemical density that exceeds that of conventional cereals such as wheat, rice, and maize: a complex carbohydrate structure, low lipid content, and a dense mineral and phytochemical profile (Chandra et al., 2016; Kaur et al., 2024). Despite this nutritional advantage, finger millet remains comparatively underutilized and underconsumed relative to major cereals, and processing methods such as malting and fermentation have been identified as key levers for improving its palatability and market appeal without compromising its nutrient density (Simran et al., 2024). Epidemiological surveys in regions with consistent finger millet consumption show an inverse correlation with regional metabolic disease prevalence (Jacob et al., 2024). This review examines the structural chemistry, mineral composition, and proteomic properties of E. coracana, and details the biochemical and molecular pathways through which its constituents act against T2DM.

Structural Carbohydrate Architecture and Dietary Fiber

The therapeutic potential of E. coracana in T2DM management is rooted in its carbohydrate configuration. The grain comprises roughly 65–75% total carbohydrates, structured primarily as non-starch polysaccharides and resistant starch (Kaur et al., 2024). Unlike refined cereals, where endosperm starches undergo rapid enzymatic hydrolysis and release glucose quickly into the bloodstream, the carbohydrate matrix of finger millet resists luminal digestive enzymes (Vidhyalakshmi & Meera, 2024). The total carbohydrate fraction breaks down into free reducing and non-reducing sugars (2–3%), non-starch polysaccharides (15–20%), and starch granules (60–65%). The starch fraction has an amylose-to-amylopectin ratio of roughly 20:80 to 25:75, contained in compact, polygonal, and rhombic granules embedded in a dense protein matrix (Ramashia et al., 2019).

Total dietary fiber content spans 15–22%, well above wheat (~12%) and polished rice (~2%) (Chandra et al., 2016). This fiber matrix consists of insoluble dietary fiber (IDF; 11–18%) and soluble dietary fiber (SDF; 2–4.3%). IDF is concentrated in the pericarp and aleurone layers of the kernel, consisting mainly of cellulose, heteroxylans, hemicelluloses, and small amounts of lignin. SDF comprises mucilages, arabinogalactans, and pectins (Kaur et al., 2024). On ingestion, SDF hydrates quickly in the gastric and upper intestinal lumen, forming a viscous gel layer over the brush-border mucosa. This gel limits the diffusion of luminal enzymes (α-amylase, α-glucosidase) toward their starch substrates, and reduces glucose transport across SGLT-1 and GLUT2 channels (Vidhyalakshmi & Meera, 2024; Wang et al., 2022). As a result, E. coracana products show a low glycemic index (GI ≤ 50–55) and a blunted postprandial glucose curve, which preserves pancreatic β-cell secretory reserve and limits hyperinsulinemic spikes (Vidhyalakshmi & Meera, 2024).

Proteomic Profile and Essential Amino Acids

Total storage protein content in E. coracana ranges from 6.0% to 13.0%, depending on cultivar genotype (white or light-brown varieties tend to show higher concentrations than dark-brown seeds) and nitrogen fertilization regime (Kaur et al., 2024). While overall protein content is comparable to other cereals, the amino acid composition is distinct. Storage proteins fractionate into prolamins (24.6–36.2%), with the remainder made up of albumins, globulins, and glutelins (Chandra et al., 2016). Total essential amino acid content constitutes approximately 44.7% of total amino acid mass — well above the 33.9% FAO reference protein baseline (Jacob et al., 2024).

ISSN 2278-2540 | DOI: 10.51583/IJLTEMAS | Volume XV, Issue VII, July 2026

The most notable feature of the finger millet proteome is its high concentration of sulfur-containing amino acids — methionine (2.5–3.8 g/16g N) and cysteine (1.4–2.2 g/16g N) — which are typically the limiting amino acids in staples like polished rice, wheat, and grain legumes (Chandra et al., 2016; Kaur et al., 2024). It also carries a rich profile of branched-chain amino acids (BCAAs): leucine (6.5–10.1 g/16g N), isoleucine (3.8–5.2 g/16g N), and phenylalanine (4.2–5.8 g/16g N). Methionine is the immediate precursor for glutathione (GSH), the primary intracellular antioxidant tripeptide. T2DM involves chronic intracellular oxidative stress from mitochondrial ROS overproduction during hyperglycemic spikes (Singh et al., 2022); dietary methionine supports the hepatic cystathionine β-synthase and glutathione synthetase pathways, optimizing GSH/GSSG ratios and protecting pancreatic β-cell membranes from ROS-mediated lipid peroxidation and apoptosis. Leucine and isoleucine also modulate the mTOR signaling axis and upregulate insulin-independent GLUT4 translocation into skeletal muscle, directly addressing peripheral insulin resistance (Singh et al., 2022; Shobana et al., 2010).

Mineral and Micromineral Core Architecture

The mineral profile of E. coracana is arguably its most distinctive nutritional feature, with total ash content of 2.5–3.5% — higher than other major and minor cereal grains (Chandra et al., 2016). Calcium concentration ranges from 294 to 390 mg per 100 g, roughly five to eight times that of whole wheat (41 mg/100 g) and up to thirty times that of polished rice (10–12 mg/100 g) (Ramashia et al., 2019; Kaur et al., 2024). The grain also contains substantial magnesium (130–150 mg/100 g), phosphorus (240–283 mg/100 g), iron (3–20 mg/100 g), and zinc (1.8–2.5 mg/100 g) (Chandra et al., 2016).

This mineral density carries clinical relevance for T2DM. Calcium is a critical second messenger governing the biphasic exocytosis of insulin from pancreatic β-cell vesicles: glucose entry via GLUT1/2 raises the intracellular ATP/ADP ratio, closing ATP-sensitive potassium (K_ATP) channels, depolarizing the membrane, and opening voltage-gated calcium channels. The resulting Ca2+ influx activates calmodulin-dependent protein kinase II, driving insulin granule docking and fusion (Singh et al., 2022). Chronic calcium deficiency along this pathway is linked to progressive failure of glucose-stimulated insulin secretion. Magnesium serves as a cofactor for over 300 enzymatic reactions, notably the tyrosine kinase activity of the insulin receptor β-subunit; insufficient magnesium impairs auto-phosphorylation of IRS-1, PI3K, and Akt/PKB, aggravating peripheral insulin resistance (Jacob et al., 2024). Zinc is a structural element in the hexameric storage of insulin, while iron and zinc together support the catalytic efficiency of superoxide dismutase (SOD) and catalase, buffering tissues against diabetes-induced oxidative stress (Chandra et al., 2016; Singh et al., 2022).

Phytochemical and Bioactive Polyphenolic Landscape

E. coracana's standing as a nutraceutical matrix rests substantially on its polyphenol content, and its phytochemical richness is increasingly cited as a defining feature distinguishing it from other minor millets (Singh et al., 2026). Total phenolic content (TPC) ranges from 0.3% to 3.0% (300–3000 mg/100g), exceeding other small millets and standard commercial cereals (Wang et al., 2022). These compounds concentrate in the seed coat/pericarp and exist in free, extractable forms (in the outer cell layers) and bound forms (linked via ester and ether bonds to cell-wall polysaccharides) (Kaur et al., 2024). The polyphenolic profile includes phenolic acids (hydroxybenzoic and hydroxycinnamic derivatives), monomeric and oligomeric flavonoids, condensed tannins (proanthocyanidins), and small amounts of anthocyanins.

HPLC-MS profiling shows the hydroxybenzoic acid group dominated by gallic, protocatechuic, vanillic, and syringic acids, with strong radical-scavenging activity. The hydroxycinnamic acid group includes p-coumaric, ferulic, caffeic, and sinapic acids; ferulic acid is the most abundant bound phenolic, cross-linked into arabinoxylan fibers (Wang et al., 2022). Flavonoid fractions include catechins, epicatechins, quercetin, daidzein, and luteolin. Condensed tannins are polymeric flavan-3-ols responsible for the seeds' brown pigment (Kaur et al., 2024). Once viewed mainly as anti-nutrients for their protein-binding capacity, these polymeric tannins and bound phenolics are now recognized as active agents in metabolic disease management. They remain chemically and thermally

ISSN 2278-2540 | DOI: 10.51583/IJLTEMAS | Volume XV, Issue VII, July 2026

stable through food processing and release slowly in the distal intestine, sustaining bioavailability and biological activity (Wang et al., 2022; Vidhyalakshmi & Meera, 2024).

Synergistic Molecular Mechanisms in Type II Diabetes Management

The anti-diabetic activity of E. coracana operates through several distinct, well-characterized molecular pathways rather than a single metabolic target. Its bioactives address carbohydrate breakdown, peripheral tissue sensitivity, advanced glycation protection, and intestinal microbiota health together.

Table 1: Comprehensive Amino Acid Profile of Eleusine coracana Proteins Compared to FAO/WHO Reference Standards

Amino Acid Species	Conc. in E. coracana (g/100g Protein)	FAO/WHO Standard (g/100g)	Primary Metabolic Regulatory Function in T2DM
Methionine	2.86 – 3.75	2.20	Precursor for glutathione; mitigates β-cell oxidative stress
Cysteine	1.52 – 2.18	1.40	Supports disulfide bond stability; intracellular redox balance
Leucine	6.90 – 9.84	4.20	Activates mTOR path; stimulates skeletal muscle glucose uptake
Isoleucine	3.95 – 4.82	2.80	Upregulates peripheral insulin-independent GLUT4 translocation
Phenylalanine	4.30 – 5.40	2.80	Precursor to catecholamines; modulates neuro-endocrine satiety
Lysine	2.10 – 2.90	4.20	Limiting amino acid; mitigates advanced protein glycation
Threonine	3.10 – 3.85	2.80	Maintains intestinal mucin integrity and mucosal barrier function
Valine	5.20 – 6.10	4.20	Tissue repair; alternative energy substrate during gluconeogenesis

(Adapted from Chandra et al., 2016; Kaur et al., 2024)

Luminal Enzyme Inhibition (α-Amylase and α-Glucosidase)

Postprandial glycemic control depends heavily on the rate of intestinal carbohydrate digestion. Free and bound polyphenols from the E. coracana seed coat produce dose-dependent, non-competitive inhibition of pancreatic α-amylase and intestinal α-glucosidase (maltase and sucrase) (Shobana et al., 2010; Wang et al., 2022). Pancreatic α-amylase hydrolyzes α-(1,4)-glucosidic linkages in amylose and amylopectin into oligosaccharides, which brush-border α-glucosidase then cleaves into free glucose. Polymeric tannins, catechins, and ferulic acid bind to allosteric sites on these enzymes and alter their catalytic conformation (Wang et al., 2022), slowing starch degradation and converting a rapid postprandial glucose spike into a slower, sustained release. This mirrors the action of acarbose but without the associated gastrointestinal side effects, as the fiber content simultaneously moderates colonic gas production (Shobana et al., 2010). Broader comparative reviews across millet species confirm that this enzyme-inhibitory capacity is strongly influenced by processing method — with milling, soaking, and heat treatment generally reducing bound-phenolic inhibitory activity, while germination and fermentation tend to enhance it — underscoring the importance of processing choice in preserving finger millet's glycemic-control properties (Anitha et al., 2024).

ISSN 2278-2540 | DOI: 10.51583/IJLTEMAS | Volume XV, Issue VII, July 2026

Direct in vitro evidence supports this inhibitory activity. In a comparative enzyme assay using aqueous methanolic extracts, E. coracana showed concentration-dependent inhibition of pancreatic α-amylase (IC50 = 5.00 mg/ml) and intestinal α-glucosidase (IC50 = 3.87 mg/ml) — indicating relatively stronger activity against α-glucosidase. For comparison, acarbose achieved IC50 values of 1.28 mg/ml (α-amylase) and 0.30 mg/ml (α-glucosidase), confirming that while finger millet extracts are markedly less potent than the purified pharmaceutical inhibitor, their activity is substantial and dose-responsive (Okafor & Christopher, 2026). The same study found the related small millet Panicum sumatrense to show stronger α-amylase inhibition (IC50 = 3.25 mg/ml) but weaker α-glucosidase inhibition (IC50 = 4.30 mg/ml) than E. coracana, suggesting the two cereals may act complementarily across the two enzymatic checkpoints of carbohydrate digestion (Okafor & Christopher, 2026). Because both extracts remain well below acarbose's potency, their consumption is unlikely to trigger the sudden hypoglycemic episodes associated with pharmaceutical inhibitors, supporting their role as everyday dietary staples rather than acute therapeutic agents (Okafor & Christopher, 2026).

Attenuation of Advanced Glycation End-Products (AGEs)

Persistent hyperglycemia in T2DM drives non-enzymatic glycation of long-lived structural proteins such as vascular collagen and serum albumin, forming advanced glycation end-products (AGEs). Interaction of AGEs with their vascular receptor (RAGE) activates the pro-inflammatory NF-κB pathway, contributing to vascular stiffening, endothelial damage, and diabetic nephropathy (Kaur et al., 2024). Phenolic acids (gallic and ferulic) and flavonoids in E. coracana counter this process in two ways: by scavenging reactive dicarbonyl intermediates such as methylglyoxal and glyoxal, and by competitively blocking the early nucleophilic attack of reducing sugars on protein amino groups — halting the glycation cascade at its origin and limiting chronic macrovascular damage (Wang et al., 2022; Kaur et al., 2024).

Activation of the AMPK Signaling Cascade and Insulin Sensitization

At the cellular level, finger millet bioactives help reverse peripheral insulin resistance. Phenolic extracts activate AMP-activated protein kinase (AMPK) via the upstream kinase LKB1 (Singh et al., 2022). Activated AMPK drives insulin-independent translocation of GLUT4 storage vesicles to the plasma membrane in skeletal muscle and adipose tissue, bypassing defective IRS-1/PI3K signaling and enabling active glucose clearance from the bloodstream (Shobana et al., 2010; Singh et al., 2022). In hepatic tissue, AMPK activation downregulates the rate-limiting gluconeogenic enzymes PEPCK and G6Pase, suppressing hepatic gluconeogenesis — a principal driver of fasting hyperglycemia in advanced T2DM (Singh et al., 2022).

Modulation of the Gut Microbiota and SCFA Generation

Undigested non-starch polysaccharides and bound polyphenols from E. coracana pass intact into the cecum and colon, where they act as prebiotic substrates for the gut microbiota (Singh et al., 2022). Metagenomic analyses show finger millet consumption expanding beneficial saccharolytic microbial populations, including Bifidobacterium, Lactobacillus, Faecalibacterium prausnitzii, and Akkermansia muciniphila. These microbes ferment complex fibers and cross-linked ferulates into short-chain fatty acids (SCFAs) — mainly butyrate, propionate, and acetate (Singh et al., 2022). SCFAs bind GPR41/43 receptors on enteroendocrine L-cells, stimulating release of the incretin hormones GLP-1 and PYY. GLP-1 acts on pancreatic islets to optimize glucose-dependent insulin secretion, reduce glucagon output, and stimulate β-cell proliferation. Butyrate also maintains tight-junction protein integrity (claudin-1, occludin) in the colonic epithelium, preventing translocation of pro-inflammatory bacterial lipopolysaccharides (LPS) and suppressing metabolic endotoxemia and systemic insulin resistance (Singh et al., 2022).

Functional Food Applications and Future Perspectives

Translating E. coracana into accessible functional foods is a key objective for clinical nutrition. Its complete absence of gluten prevents formation of a viscoelastic gluten network, which complicates food processing but

ISSN 2278-2540 | DOI: 10.51583/IJLTEMAS | Volume XV, Issue VII, July 2026

offers a hypoallergenic option for patients with comorbid celiac disease or gluten sensitivity (Vidhyalakshmi & Meera, 2024). Processing techniques such as controlled germination (malting), hydrothermal parboiling, and lactic fermentation improve its functional properties. Controlled germination activates endogenous phytases that hydrolyze phytic acid, an anionic compound that binds divalent cations tightly, increasing bioaccessibility of calcium, iron, and zinc by up to 300% (Ramashia et al., 2019; Vidhyalakshmi & Meera, 2024). Fermentation breaks down cell walls and converts bound phenolic acids into free, more bioavailable forms, enhancing antioxidant and enzyme-inhibiting capacity (Wang et al., 2022). Fermented finger millet products in particular have been highlighted as a distinct nutraceutical category for T2DM management, with fermentation-driven improvements in bioactive compound release and digestibility supporting their proposed role as a dietary tool for glycemic control (Tawde & Jha, 2026).

Current food engineering efforts focus on incorporating processed E. coracana into low-glycemic commercial staples: composite flours blended with legumes to balance essential lysine content, ready-to-eat breakfast flakes, functional pastas, and clinical beverages for diabetic populations (Vidhyalakshmi & Meera, 2024). Composite formulations pairing finger millet with protein-rich legumes such as soybean have also been proposed as next-generation fermented functional foods, combining finger millet's mineral, fiber, and polyphenol density with soybean's complementary protein and bioactive profile (Kokisi et al., 2026). Establishing finger millet as a standard component of medical nutrition therapy will require large-scale, multi-centric, double-blind randomized controlled human trials to quantify its long-term impact on HbA1c, HOMA-IR, inflammatory cytokines (IL-6, TNF-α), and gut microbiome composition (Jacob et al., 2024; Singh et al., 2022). Most existing E. coracana research has focused on glycemic and inflammatory endpoints, leaving lipid profile effects comparatively underexplored — a meaningful gap, given that other traditional antidiabetic botanicals such as Andrographis paniculata have shown that plant-based interventions can address both glycemic control and diabetic dyslipidemia concurrently (Elobisi & Okafor, 2022). Future trials on E. coracana should incorporate lipid panel assessments (LDL, HDL, triglycerides) alongside glycemic markers to more fully characterize its cardiometabolic potential.

A promising translational strategy from recent comparative enzyme-inhibition research is co-formulating E. coracana with complementary ethnomedicinal cereals. Because E. coracana extracts inhibit α-glucosidase more strongly than α-amylase, while Panicum sumatrense shows the inverse potency profile, a composite flour blending the two could achieve more balanced inhibitory coverage across both carbohydrate-digesting checkpoints than either cereal alone (Okafor & Christopher, 2026). Such dual-cereal formulations have been proposed as a practical dietary product for diabetic populations, offering synergistic control of postprandial glucose without the hypoglycemic risk associated with purified pharmaceutical inhibitors like acarbose. Confirming this synergy will require in vivo studies of combined extracts rather than the single-extract in vitro assays reported to date (Okafor & Christopher, 2026).

CONCLUSION

Eleusine coracana is a multi-targeted dietary matrix that connects agronomic resilience with modern clinical nutrition. Its slow-digesting carbohydrate framework and dietary fiber profile support a low glycemic response (Vidhyalakshmi & Meera, 2024), reinforced by a complete essential amino acid profile rich in sulfur-bearing species and a mineral composition rich in calcium and magnesium — both essential for insulin secretion and receptor phosphorylation (Chandra et al., 2016; Kaur et al., 2024). Its seed-coat polyphenol content acts in parallel, inhibiting carbohydrate-splitting enzymes, limiting AGE formation, activating cellular AMPK pathways, and supporting an anti-inflammatory, SCFA-producing gut microbiota (Singh et al., 2022; Wang et al., 2022; Shobana et al., 2010). Direct enzyme-inhibition assays support this multi-target profile in vitro, and further suggest that pairing E. coracana with complementary small millets such as Panicum sumatrense may produce a more balanced, dual-checkpoint inhibitory effect than either cereal alone (Okafor & Christopher, 2026). As the global burden of T2DM continues to rise, integrating whole and processed finger millet into standard diets offers an affordable and sustainable functional food strategy for the prevention and long-term management of T2DM.

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Table 2: Quantitative Inorganic Mineral Density and Specific Molecular Anti-Diabetic Impacts

Mineral Element	Mean Content (mg/100g)	vs. Refined Wheat/Rice	Specific Molecular Target in T2DM Pathophysiology
Calcium (Ca)	344.0	8× to 30× Higher	Regulates Ca2+ influx for biphasic insulin exocytosis in β-cells
Magnesium (Mg)	142.0	3× to 4× Higher	Tyrosine kinase cofactor; critical for IRS-1 auto-phosphorylation
Phosphorus (P)	260.0	2× Higher	Enables ATP/ADP-driven metabolic signaling and cellular energetics
Iron (Fe)	6.5	3× Higher	Cofactor for catalase; preserves oxygen delivery and counters anemia
Zinc (Zn)	2.1	1.5× Higher	Required for zinc-insulin hexamerization and structural stabilization

(Adapted from Chandra et al., 2016; Ramashia et al., 2019)

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