

A Review on Antidiabetic and Antioxidant Potential of Macrotyloma Uniflorum Seed Extract: A Correlative Study of Disease Pathways

Mohd Tahseen, Shiv Dev Singh*

Department of Pharmacy, M J P Rohilkhand University, Bareilly– 243006, Uttar Pradesh, India

ARTICLE INFO

Article History:

Accepted : 11 Jan 2025

Published: 13 Jan 2025

Publication Issue :

Volume 12, Issue 1

January-February-2025

Page Number :

95-100

ABSTRACT

Macrotyloma uniflorum (horse gram) has emerged as a nutraceutical with promising antidiabetic and antioxidant properties. This review offers a novel integrative analysis of the seed extract's bioactive compounds and their dual role in targeting oxidative stress and dysregulated glucose metabolism—key drivers of diabetes progression. By bridging phytochemistry with metabolic disease pathway, we propose a system biology perspective that highlights the potential of M. uniflorum to act as both therapeutic agent and metabolic modulator. This correlative study not only underscores its pharmacological benefits but also opens avenues for developing multifunctional interventions to prevent diabetes and its oxidative complications.

Keywords: Macrotyloma uniflorum, Oxidative stress, Antioxidant, Antidiabetic, Bioactive Phytoconstituents.

I. INTRODUCTION

Diabetes mellitus

Diabetes mellitus is one of the metabolic diseases which is diagnosed by raised body fluid sugar levels, increased triglycerides in the blood (hypertriglyceridemia), and higher levels of cholesterol (hypercholesterolemia). These conditions arise due to malfunctions in insulin production, function, or both.¹ Insulin, a protein hormone synthesized by the pancreatic β cells to stimulate glucose.² It might be immune-related, as in type 1 diabetes, or be caused by a concomitant resistance to insulin & depletion as observed in type 2 diabetes or caused by carbohydrate intolerance as in Gestational

diabetes mellitus (GDM).^{3,4} Long term hyperglycemia can disrupt normal bodily functions by damaging organs and leads to serious problems for example retinopathy, neuropathy, nephropathy, and cardiovascular conditions in affected individuals.^{5,6}

Free radicals, their production and their biological role

Free radicals are short-lived, reactive species with unpaired electrons.⁷ Free radicals, though often damaging, play essential role in life's evolution and cellular processes. They activate signaling pathways like Mitogen activated protein kinase (MAPK) and extracellular- signal-regulated kinase (ERK), influence gene expression, and work with superoxide dismutase to start cell death.⁸ Free radicals are produced

internally and externally in cells and their environment through reactions between organic compounds and oxygen, ionizing radiation,⁹ and mitochondrial oxidative phosphorylation.

Oxidative stress and antioxidants

Oxygen, essential for aerobic life, also limits lifespan by generating reactive species that can lead to cell necrosis and death. Oxidative stress occurs when the synthesis of ROS overcomes the tendency of antioxidant protection systems of the body. Oxidative stress has been implicated in the etiology of over 50 diseases including diabetes and its associated complications.^{10,11} An antioxidant inhibits or delays oxidation, even in small amounts. Endogenous as well as exogenous antioxidants, like glutathione, vitamins E and C, and cystine, act like defenses and biomarkers of oxidative stress.^{12,13}

Role of ROS in diabetes mellitus

Oxidative stress is a key factor in the progress of vascular difficulties associated to type 2 diabetes.⁹ Increased ROS levels in diabetes may arise from diminished neutralization or enhanced generation by antioxidant systems for example, superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px). Fluctuations in the activity of these enzymes elevate tissue vulnerability to oxidative damage, fostering the onset of diabetic problems.¹⁴ Epidemiological evidence suggests that vascular diseases, rather than hyperglycemia, are significant contributors to diabetes-related mortality.⁹

Role of oxidative stress in pathophysiology of diabetes

The function of oxidative stress in the onset of type 1 and type 2 diabetes is highlighted by current research. Non-enzymatic protein glycation, glucose oxidation, and elevated lipid peroxidation cause oxidative damage in diabetes, which hinders enzymatic function, damages cellular structures and exacerbates insulin resistance.¹⁵ Studies reveal that oxidative aggregation of LDL, driven by hydroxyl radical-mediated cross-linking of apo-B monomers, plays a role in diabetic complications.⁹ ROS/RNS influence insulin signaling by enhancing physiological functions in response to

insulin but also by negatively regulating signaling pathways, leading to insulin resistance, which is a key contributor for type 2 diabetes.¹⁶ Oxidative stress triggers multiple disorders, including rheumatoid arthritis, diabetes mellitus, and cancer. In diabetes, it leads to complications such as cardiovascular disease, nerve damage, kidney dysfunction, vision impairment, and cerebrovascular events.¹⁷⁻¹⁹

Macrotyloma uniflorum

Macrotyloma uniflorum (Horse gram), also called as Kulthi in Hindi, Gahot in Kumaon and Garhwal, Gahot refers to the process of destroying stone at its first stage.^{20,21} Farmers grow horse gram all over India. It grows well in dry, slightly warm climates. The prime planting season for horse gram runs from late August to November.²² People in India consume horse gram in various forms, including whole seeds, sprouts, or as a complete meal.²³ It also contains iron and molybdenum in abundance. Horse gram contains slowly digestible starch, causing a slight increase in blood sugar levels after meals for people with diabetes.²⁴ The National Institute of Nutrition (ICMR)'s food composition table shows that horse gram seeds contain almost double the protein content as compared to other cereal grains.²⁵ Horse gram is a rich source of diverse nutrients, including carbohydrates, proteins, amino acids, lipids, fatty acids, phenolic acids, flavonoids, tannins, saponins, anthocyanidins, phytosterols, and essential minerals like calcium, iron, and molybdenum.²⁶ In ancient Indian books like Charak Samhita and Sushruta Samhita it is mentioned that the seeds of horse gram are well-known to heal abdominal lumps, bronchial asthma, hiccups, piles, and also in controlling sweating.²⁷

Phytochemicals in *Macrotyloma uniflorum*

Plant seeds are rich in flavonols, minerals, essential fatty acids, myricetin, kaempferol, and quercetin, as well as arachidic, stearic, linoleic, oleic, gadoleic, and lignoceric acids.²⁸ Additionally, Tannin, flavonoid, alkaloid, triterpenoid, steroid, saponin, carbohydrate,

phenolics, glycoside, amino acid, and mucilage phytoconstituents were detected in plant extract. The acetone extract had a high level of total polyphenols and tannins, but the methanol extract had a significant flavonoid content.²⁹ It has a high protein content (22-24%), a significant quantity of soluble fibers (57.2%), fat (1.1%), vitamins, and minerals (3.2%). These seeds extract exhibits strong anti-adipogenic, anti-hyperglycemic, and anti-hypercholesterolemic properties. It works to counteract oxidative stress.³⁰ Mome inositol, stigmaterol, n-hexadecanoic acid, ethyl derivatives, ethyl alpha-d-glucopyranoside, Vitamin E, linoleic acid and its esters, and 3-beta-stigmast-5-en-3-ol were the principal components discovered.³¹

Antioxidant potential of *Macrotyloma uniflorum*

Mathaiyan et al. (2022) evaluated the antioxidant properties of *M. uniflorum* seeds against ferric complexes, DPPH, hydroxyl radicals, and phosphomolybdenum complexes. Their findings revealed that *M. uniflorum* seeds possess remarkable antioxidant activity, primarily due to their free radical scavenging ability, which helps suppress oxidative processes.³² Subsequently, they prepared seed extracts using various solvents, including hexane, ethyl acetate, and methanol, and concluded that *M. uniflorum* seeds were highly effective in treating methanol-induced liver damage. This therapeutic potential was attributed to the presence of phytocompounds present in it, which likely played a significant role in providing antioxidant protection against alcohol-induced liver tissue damage. Furthermore, histological analysis confirmed the hepatoprotective properties of *M. uniflorum* seeds.³³

Faujdar et al. (2022) prepared ethanolic extract of leaves of *Bryophyllum pinnatum* (BPE) and methanolic extract of *M. Uniflorum* seeds. Researchers evaluated both extracts for their antioxidant, antiurolithiatic, and injury healing capabilities. Researchers determined the antioxidant activity using DPPH and ABTS assays. The extracts underwent testing to assess their capacity for reducing

Vero cell damage induced by calcium oxalate monohydrate (COM) crystals. The wound healing capability was tested using a scratch assay. They determined that the extract contain phytochemicals with antioxidant, cell defending, and injury healing activities.³⁴

Parasuraman et al. (2021) evaluated the free radical scavenging activity of ethanolic and methanolic extracts of *Macrotyloma uniflorum* seeds using DPPH and hydroxyl radical scavenging assays. Their findings revealed that the ethanolic extract contained a higher phenolic content compared to the methanolic extract. Both extracts demonstrated antioxidant activity, with dose dependent manner in both assays.³⁵

Bharathi et al. (2018) prepared ethanolic extract of seeds and suggested that *M. uniflorum* possess antioxidant and anti-inflammatory potential, which protected the body against the negative effects of obesity induced by a high fat diet in albino Wistar rats. The results proved that a HFD elevated liver enzymes and depleted antioxidants.³⁶

Panda et al. (2015) prepared *M. uniflorum* seeds extract with 80:20 v/v ethanol: water mixture. The research aimed to investigate if a hydroalcoholic extract of *M. uniflorum* seeds and ferulic acid could protect rats from hyperlipidemia and cardiac irregularities associated with metabolic syndrome. Researchers found that *M. uniflorum* seed extract protects against hyperlipidemia and cardiac abnormalities linked to the Metabolic Syndrome. The antioxidant activity of phenolic phyto constituents, especially ferulic acid.³⁷

Sanjeev et al. (2014) examined the hepatoprotective effect of methanolic extract of seeds of *M. uniflorum* in CCl₄-induced hepatotoxicity in rats seems to be associated with its ability to decrease lipid peroxidation and prevent depletion of GSH.³⁸

Antidiabetic potential of *Macrotyloma uniflorum*

Allenki et al (2019) elaborated the anti-diabetic effects of *M. uniflorum* stem and seeds extract on alloxan-induced diabetic rats. The finding of their study demonstrated that the extract restored blood glucose

levels to normal in diabetes-induced rats, indicating its hypoglycemic activity. The mode of action of extracts in reducing diabetes is unknown.³⁹

Gupta et al. (2011) The *M. uniflorum* seeds were extracted with normal saline. Researchers observed that extract inhibited both the mouse pancreatic and human salivary α -amylase in a non-competitive manner. It lowered the serum glucose levels in the treated diabetic mice.³¹

II. CONCLUSION

This review highlights the substantial therapeutic potential of *Macrotyloma uniflorum* seeds extract in addressing diabetes and its associated oxidative stress, emphasizing its significance as a natural and sustainable remedy. The bioactive compounds present in the seeds, particularly polyphenols, flavonoids, and other phytoconstituents, contribute to its potent antidiabetic and antioxidant effects by targeting critical pathways involved in hyperglycemia, insulin resistance, and oxidative damage. These dual actions not only support glycemic control but also protect against diabetes-induced complications by scavenging free radicals and boosting the body's antioxidant defenses. Many studies support the extract's therapeutic potential, highlighting the significant ability of *M. uniflorum* to alleviate inflammation and oxidative stress in obese rats. Furthermore, the plant extract has been demonstrated to inhibit α -amylase and α -glucosidase, effectively lowering glucose levels, enhancing the lipid profile, and preventing weight loss in diabetic mice. It has been observed that *M. uniflorum* improves insulin sensitivity by regulating signaling pathways, enhancing cellular responsiveness to insulin, and reducing blood glucose levels. Overall, *M. uniflorum* emerges as a valuable candidate for developing novel, plant-based therapeutic strategies for diabetes management, potentially contributing to the growing demand for natural alternatives in pharmaceutical interventions. While the current findings are promising, further studies are essential to

fully characterize its bioactive compounds, optimize extraction processes, and explore its molecular mechanisms. Additionally, preclinical studies using laboratory animals can further elucidate the pharmacologic potential, safety, and mode of action of these compounds, enabling their integration into diverse drug delivery systems, including oral tablets, capsules, and functional food supplements.

REFERENCES

- [1]. Tenpe, C.R.; Yeole, P.G.; Comparative evaluation of antidiabetic activity of some marketed polyherbal formulations in alloxan induced diabetic rats. Int J Pharm. Res. 2009, 1(1), 43-49.
- [2]. Joshi, S.; Parikh, R.; Insulin-History, Biochemistry, Physiology and Pharmacology. J. of the Assoc. of Phys. of India, 2007, 55, 19-25.
- [3]. Kebir, N.E.; Zahzeh, T.; Magnesium Deficiency Associated with Stress, Systemic Inflammation, and Insulin Resistance in Diabetes Mellitus: a review. Egypt Acad J Biol. Sci. C Physiol. Mol. Biol. 2022, 14(1), 31-46.
- [4]. Ricart, W.; Lopez, J.; Mozas, J.; Potential impact of American Diabetes Association (2000) criteria for diagnosis of gestational diabetes mellitus in Spain. Diabetologia, 2005, 48(6), 1135-1141.
- [5]. Mohammad, M.Y.; Yaheya, M.; Ismail, M.; Clinical Evaluation of Antidiabetic Activity of Trigonella Seeds and Aegle marmelos Leaves. World Appl Sci J, 2009, 7(10), 1231-1234.
- [6]. Sagoo, M.K.; Gnudi, L.; Diabetic nephropathy: Is there a role for oxidative stress? Free Radical Bio. Med. 2018, 116, 50-63.
- [7]. Bansal, A.K.; Bilaspuri, G.S.; Impacts of oxidative stress and antioxidants on semen functions. Vet Med Int. 2010, 2011, 1-7.
- [8]. Cho, K.H.; Wolkenhauer, O.; Analysis and Modelling of Signal Transduction Pathways in Systems Biology. Bi. Soc. Trans. 2003, 31, 1503-1509.

- [9]. Pham-Huy, L.; He, H.; Pham-Huy, C.; Free Radicals, Antioxidants in Disease and Health. Int J of biomed sci, 4(2), 2008, 89-96.
- [10]. Nespolo, M.; Free Radicals in Biology and Medicine. Acta Cryst Section D 2017, 73, 384-385.
- [11]. Asmat, U.; Abad, K.; Ismail, K.; Diabetes mellitus and oxidative stress-A concise review. Saudi Pharma J, 2016, 24(5), 547-553.
- [12]. Somogyi, A.; Rosta, K.; Pusztai, P.; Tulassay, Z.; Nagy, G.; Antioxidant measurements. Physiol Meas., 2007, 28(4), 41-55.
- [13]. Khanna, S.; Thiol antioxidants: Protection against oxidative stress and redox regulation of cellular responses. Kuopio uni pub C natural and envi sci 2000, 109, 1-76.
- [14]. Lipinski, B.; Pathophysiology of Oxidative Stress in Diabetes Mellitus. J of Diab and Its Comp., 2001, 15, 203-210.
- [15]. Maritim, A.C.; Sanders, R.A.; Watkins J.B.; Diabetes, oxidative stress, and antioxidants: A review. J Biochem Mol Toxicol. 2003, 17(1), 24-38.
- [16]. Erejuwa, Omotayo, O.; Oxidative Stress in Diabetes Mellitus: Is There a Role for Hypoglycemic Drugs and/or Antioxidants? Oxidative Stress and Diseases, 2012, 217-246.
- [17]. Asfandiyarova, N.; Kolcheva, N.; Ryazantsev, I.; Ryazantsev, V.; Risk factors for stroke in type 2 diabetes mellitus. Diabetes Vasc Dis Res, 2006, 3, 57-60.
- [18]. Phillips, M.; Cataneo, R.N.; Cheema, T.; Greenberg, J.; Increased breath biomarkers of oxidative stress in diabetes mellitus. Clinica Chimica Acta., 2004, 344(1-2), 189-194.
- [19]. Elfaramawy, S.M.; Rizk, R.A.; Spectrophotometric Studies on Antioxidants-Doped Liposomes. J of American Sci 2011, 7(7), 363-369.
- [20]. Patel, V.B.; Acharya, N.; Effect of M. uniflorum in ethylene glycol induced urolithiasis in rats. Heliyon, 2020, 6(6), 1-7.
- [21]. Sudheer, A.; Reddy, K.S.; Naidu, R.J.; Horse gram a traditional food medicine protects the kidney from the cisplatin-induced nephrotoxicity in albino rats. Indian J of Trad Know., 2023, 22(4), 746-754.
- [22]. Rao, S.; Sharma, A.; Review on medicinal and traditional importance of horse gram. World J of Bio Pharm Health Sci., 2022, 12(3), 9-13.
- [23]. Lavudi, K.; Harika, V.S.; Kokkanti, R.R.; 2-Dimensional in vitro culture assessment of ovarian cancer cell line using cost effective silver nanoparticles from M. uniflorum seed extracts. Front Bioeng Biotechnol, 2022, 10, 1-15.
- [24]. Siddhuraju, P.; Maheshu, V.; Loganayaki, Nataraj.; Manian, Sellamuthu.; Antioxidant Activity and Free Radical Scavenging Capacity of Dietary Phenolic Extracts from Processed Indigenous Legumes, M. Uniflorum (Lam.) Verdc. and Dolichos Lablab L. Food Global Sci Books 2008, 2(2), 159-167.
- [25]. Longvah, T.; Ananthan, R.; Bhaskarachary, K.; Venkaiah, K.; Indian Food Composition Tables. Indian Council of Med Res, 2017, 1-505.
- [26]. Chirania, A.; Sharma, D.; Pharmacological Activity of M. uniflorum-A Review. Int J Phar & Biomed Rese, 2021, 8(4) 1-5.
- [27]. Kaundal, S.; Sharma, A.; Kumar, R.; Kumar, V.; Exploration of medicinal importance of an underutilized legume crop, M. uniflorum (LAM.) horse gram: A review. Int J pharm sci rese, 2019, 10(7), 3178-3186.
- [28]. Morris, J.B.; Wang, M.L.; Grusak, M.A.; Tonnis, B.; Fatty acid, flavonol, and mineral composition variability among seven m. uniflorum accessions. Agriculture (Switzerland), 2013, 3(1), 157-169.
- [29]. Papiya, B.; Sourabh, V.; Alok, S.; Chandra Shekhar, S.; Pharmacognostic and Physico-chemical standardization of M. uniflorum edible seed. Pharmacognosy Communication. 2014, 4(1), 16-24.

- [30]. Sandamalie, R.; Ediriweera, E.R.H.S.S.; Medicinal and Nutritional Values of *M. uniflorum*: A Conceptual Study. *Global J Pharm & Pharm Sci*. 2017, 1(2), 1-10.
- [31]. Gupta, L. H.; Badole, S. L.; Bodhankar, S. L.; Sabharwal, S. G.; Antidiabetic potential of α -amylase inhibitor from the seeds of *M. uniflorum* in streptozotocin-nicotinamide-induced diabetic mice. *Pharm Biol.*, 2011, 49(2), 182-189.
- [32]. Mathaiyan, M.; Muthukrishnan, S.; Eswaran, A.; Pradeep K. S.; Ganesan, T.; The Free Radicals Scavenging Potential of Methanol Extract of Seeds of *M. Uniflorum*. *Neuro Quantology*, 2022, 20(11), 8476-8483.
- [33]. Mathaiyan, M.; Pradeep K. S.; Ganesan, T.; Muthukrishnan, S.; Hepatoprotective effect of *M. uniflorum* seed Aqueous extract in Alcohol Induced Liver Damage in Rats (ALD). *Neuro Quantology* 2022, 20(15), 5062-5073.
- [34]. Faujdar, C.; Priyadarshini; Comparative study of hydroalcoholic extracts of *Bryophyllum pinnatum* and *M. uniflorum* for their antioxidant, antiurolithiatic, and wound healing potential. *J Appl Biol Biotechnol*, 2022, 10(1), 196-205.
- [35]. Parasuraman, S.; Raipan, V. A.; In vitro Antioxidant Activity of Methanolic and Ethanolic Extracts of seeds of *M. uniflorum*. *Free Radicals and Antioxidants*. 2021;11(1):24-26.
- [36]. Bharathi, V.; Rengarajan, R.L.; Radhakrishnan, R.; Effects of a medicinal plant *M. uniflorum* (Lam.) Verdc.formulation (MUF) on obesity-associated oxidative stress-induced liver injury. *Saudi J Biol Sci*, 2018, 25(6), 1115-1121.
- [37]. Panda, V.; Protective effects of *M. uniflorum* seeds (horse gram) in abnormalities associated with the metabolic syndrome in rats. *J Diabetes Obes*, 2015, 2(2), 1-10.
- [38]. Panda, V.; Kharat, P.; Sudhamani, S.; Hepatoprotective Effect of the *M. uniflorum* Seed in Ethanol-Induced Hepatic Damage in Rats. *J Bio Pro Nat*, 2015, 5(3), 178-191.
- [39]. Allenki, V.; Vasantha, G.; Venkatesham, A.; Dayakar, C. H.; Anti-diabetic effect of leaf and stem extract of *m. uniflorum* in alloxan induced diabetic rats. *Int J Pharm Sci Res*, 2021, 12(4), 2428-2437.