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A Comprehensive Review on Salacia Oblonga

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Abstract:

(Syn. Comocladia serrata Blanco) (Celastraceae family), a Southern Indian shrub, is an endangered medicinal plant also found in tropical Africa, Sri Lanka, China, Vietnam, and Thailand. *S. oblonga* yields several therapeutic phytocompounds, including salacinol, kotalanol, neokotalanol, neosalacinol, and mangiferin. The plant's components have been employed in Ayurvedic medicine and Southwest Asian nations to cure several diseases. Although *S. oblonga* is well known for treating diabetes, new research have shown its antioxidant, anti-inflammatory, nephroprotective, anti-microbial, and cardiac disorder-treating properties. A complete analysis of *S. oblonga*'s phytomorphology, phytochemistry, and pharmacological activity and safety assessment is presented here.

Keywords: *Salacia oblonga,* diabetes, phytomorphology, pharmacological activities.

INTRODUCTION

Species of the genus Salacia (family Celastraceae) are woody climbers distributed globally in tropical regions, including India, Sri Lanka, China, Southeast Asia, and the tropical zone of Brazil (Jayaweera, 1981; Heywood, 1993; Mabberley, 2005; Matsuda et al., 2005; Singh et al., 2009; He et al., 2009). India is home to 21 species. Fifteen species are documented in Peninsular India (Ramamurthy and Naithani, 2000), with *S. oblonga* and S. reticulata being the main species (Lawerence, 1951). *Salacia oblonga* Wall (Syn. Comocladia serrata Blanco), an indigenous shrub of India, is located in the rainforests of the Western Ghats, extending from Konkan to Kerala (The Plant List, 2013; Anonymous). However, reports indicate that *S. oblonga* and S. reticulata have been classified as endangered species (Prabhuji et al.; C.A.M.P. III, 1997). *S. oblonga* roots and aerial parts have been extensively utilized in traditional Indian Medicine for the treatment of diabetes, as well as rheumatism, gonorrhea, skin and ear diseases, pruritus, and asthma, among other ailments (Rao and Giri, 2010; Chopra et al., 1956; Vaidyaratnam, 1996). Since the 1960s, researchers have investigated the hypoglycemic properties of several extracts from the roots, root bark, and stems of *S. oblonga* in diabetic animals (Soman, 1967; Augusti, 1973; Augusti, 1995). *S. oblonga* exhibits antioxidant, anti-inflammatory,

hypolipidemic, and pancreatic lipase inhibitory properties (Rabbani et al., 2006; Singh et al., 2009). Various bioactive compounds, including salacinol, kotalanol, and mangiferin, serve as effective α-glucosidase inhibitors, while tannins such as epicatechin and sesquiterpene alkaloids have been identified from Salacia species (Rabbani et al., 2006; Duarte et al., 2009). The World Health Organization states that the initial stage in determining the authenticity and purity of plant materials is the macroscopic and microscopic characterization of a medicinal plant, which should be conducted prior to any testing (Gordon and David, 2001). This report thoroughly examined the phytomorphology, phytochemistry, and pharmacological activity of *S. oblonga* to provide a definitive framework for future research.

Phytomorphology

Taxonomical Classification

KINGDOM: *plantae,* PHYLUM: Magnoliophyta, CLASS: Magnoliopsida, ORDER: Celastrales, FAMILY: *Celastracea,* GENUS: *Salacia,* SPECIES: *Salacia oblonga* (GBIF, 2013).

Botanical description

S. oblonga is a robust, climbing shrub characterized by highly warty branchlets. Warts are elongated. Leaves are oblong or oval-lanceolate, measuring up to 21 x 8 cm, green when desiccated, with 8-10 pairs of veins and a 1 cm long petiole. Inflorescence-bearing stalks are short, robust, and multi-flowered. Numerous flowers exhibit a greenish-yellow hue. Sepals measure 1.5 mm in diameter and are round, while petals are 2.5 mm in length and oval. Seeds 1-8, angular, embedded in pulp. The berry is around 4 cm in diameter, exhibiting an orange-red hue and a smooth texture (Fig. 1 A-C). It is located in the evergreen and semi-evergreen forests of South India, namely in the Western Ghats of Maharashtra, Goa, Karnataka, Kerala, and Tamil Nadu, and is seldom observed in the Eastern Ghats of Andhra Pradesh. In Karnataka, it is sometimes observed in the Kodagu district. Commonly found in the districts of Thrissur, Idukki, and Kollam in Kerala. In Tamil Nadu, it has been documented just in Tirunelveli, Coimbatore, and the Nilgiri Hills (Ved et al., 2002).

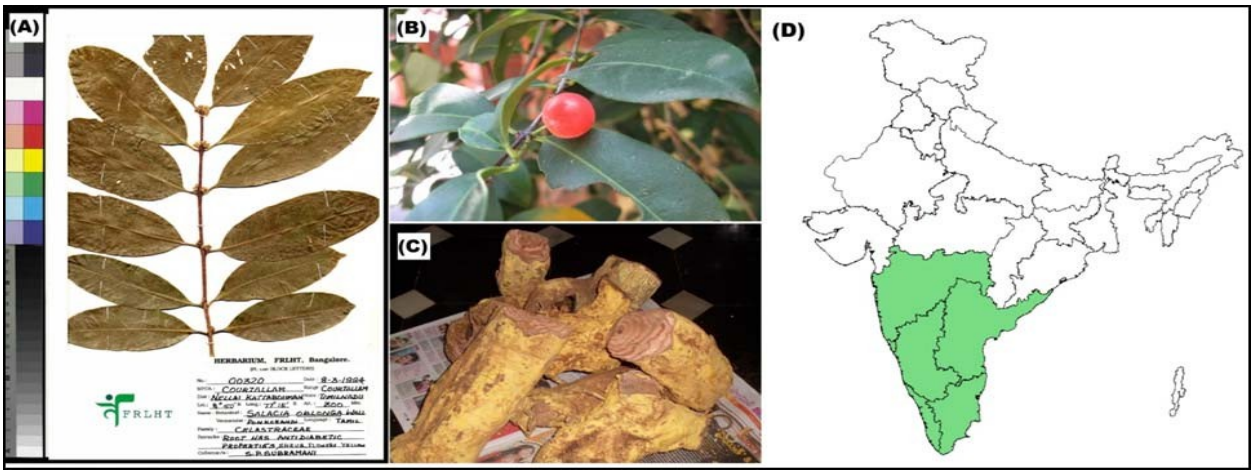

Figure 1 (A-D). (A) Lectotype (B) Fuit (C) Dried root parts and (D) and geographical distribution of *S. oblonga* in India (Ved *et al.,* 2002).

Phytochemistry

Phytochemical and pharmacological methodologies constitute the fundamental basis for assessing medicinal plants, facilitating drug development, a process known as "Natural product screening" (Foye et al., 2008). Qualitative phytochemical screening of the ethanolic, methanolic, and aqueous extracts of the roots and stems of *S. oblonga* indicated the presence of significant quantities of carbohydrates, sterols, phenolic compounds, alkaloids, flavonoids, and tannins. The existence of mangiferin as a significant phytocompound in *S. oblonga* was evidenced by the TLC profile of methanolic and ethanolic extracts (Giron et al., 2009; Basu et al., 2012; Basu et al., 2013). *S. oblonga* comprises two powerful α-Glucosidase inhibitors, Salicinol and Kotalanol, with several recognized phenolic compounds, novel sesquiterpenes (salasols A and B), and triterpenes (kotalagenin 16-acetate, salasones A-E, salaquinones A and B) (Thiruvelan, 2010). Kotalagenin-16-acetate; 26-hydroxy-1,3-friedelanedione; Maytenfolic acid; 3β,22α-dihydroxyolean-12-en-29-oic acid; 19-hydroxyferruginol; Lambertic acid; (-)-4'-O-methylepigallocatechin; glycerol; galactinol; sucrose; D-glucose; dulcitol; D-fructose; raffinose; stachyose; 3-O-α-D-galactopyranosyl-O-β-D-galactopyranosyl-sn-glycerol (Matsuda et al., 1999); and neosalacinol (Minami et al., 2008) are additional significant phytochemicals isolated from *S. oblonga*. GC-MS analysis of the ethanol extracts (neutral and acidic) from the aerial and root parts of *S. oblonga* identified various phytocompounds, including alkanes, alkenes, aliphatic esters, carbonic acid, ketones, aliphatic amines, aliphatic alcohols, benzene rings, phenols, and a novel norfriedelene- I,3-dione, characterized as I5α-hydroxy-24-norfriedel-5-ene- I,3-dione (Anu et al., 2003; Musini et al., 2013).

Pharmacology

The primary pharmacological activities of the Salacia genus include anti-diabetic effects (particularly for type 2 diabetes) (Duke and Ayensu, 1985; Ismail et al., 1997; Yoshikawa et al., 2003; Kishi et al., 2003; Matsuda et al., 2005; Kishino et al., 2009; Muraoka et al., 2011), anti-inflammatory properties (Kishi et al., 2003; Govindaraj et al., 2009), nephroprotective effects (Rana et al., 2010), antioxidant activity (Navneet et al., 2009; Deokate and Khadabadi, 2012), and anti-tumor effects (Guha et al., 1996). The root bark is utilized in the treatment of rheumatism, gonorrhea, pruritus, asthma, thirst, and otological disorders through methods such as boiling in oil, decoction, or powder (Mehra and Handa, 1967; Pullaiah, 2006; Singh and Duggal, 2010; Deokate and Khadabadi, 2012). Additionally, it is significant in addressing hepatitis, cardiac ailments, arthritis (Sanchez et al., 2000), and insulin resistance (Miura et al., 2001). The aerial components, root, and root bark of *S. oblonga* have been widely utilized in Ayurveda and traditional Indian medicine for the management of diabetes (Matsuda et al., 1991), gonorrhea, rheumatism, and dermatological conditions (Chopra, 1956; Marg, 1972; Karunanayake et al., 1984), and exhibit antimicrobial properties (Rao and Giri, 2010; Musini et al., 2013). All examined pharmacological characteristics of this medicinally significant herb to date are included in Table 1.

Table 1: Pharmacological activities of *S. oblonga*

Sn	Activity	Model	Used part/s	Conclusion	Ref. No
1	Anti-diabetic activity	Albino Wister mice	Aqueous extract	Significant decrease in plasma glucose level at a dose of 250 mg/kg/day.	(Savariraj *et al.,* 2011)
2	Anti-diabetic activity	Sucrose- and maltose-loaded rats	Aqueous methanolic extract	Showed inhibitory activities on alpha-glucosidase and aldose reductase, respectively.	(Matsuda *et al.,* 1999)
3	Anti-diabetic activity	KK-Ay/TaJcl type II diabetic model mice and human subjects with premetabolic syndrome	A mixture of extract of *Salacia oblonga* and *IP-PA1* (SI tea)	Significant reduction of plasma glucose levels in mice. Reduction of FPG and HbA1c more rapidly than the control in the HL group, and also significantly improved LDL and HDL levels in the HG group.	(Nakata *et al.,* 2011)
4	Acute-glycemic Activity	Patients with type 2 diabetes	Herbal extract	Significantly lowered the postprandial positive area under the glucose and insulin curve and adjusted peak glucose and insulin response.	(Williams et al., 2007)
5	Anti-hyperglycemic activity and cardiac fibrosis inhibition	Obese Zucker rat (OZR)	Water extract	Markedly improved interstitial and perivascular fibrosis in the hearts of the OZR. It also reduced plasma glucose levels in non-fasted OZR, whereas it had little effect in the fasted animals.	(Li et al., 2004)
6	Postprandial glycemic, insulinemic, and breath hydrogen responses	Non-diabetic adults	480 mL of study beverage (14 g fat, 82 g carbohydrate , and 20 g protein) with	1,000-mg extract dose reduced the plasma glucose and serum insulin incremental areas under the curve (0 to 120 minutes postpr-	(Heacock et al., 2005)

			SO extract.	andial) by 23% (P=.32) and 29% (P=.01), respectively. The other doses did not impact glycemia or insulinemia. Breath hydrogen excretion increased linearly as the dose was advanced.	
7	Postprandial hyperlipidemia and hepatic steatosis in diabetes and obesity	Zucker diabetic fatty rats	Water extract from the root	Lowered plasma triglyceride and total cholesterol (TC) levels, increased plasma high-density lipoprotein levels and reduced the liver contents of triglyceride, non-esterified fatty acids (NEFA) and the ratio of fatty droplets to total tissue. The extract had no effect on plasma triglyceride and TC levels in fasted ZDF rats.	(Huang et al.(1), 2006)
8	Anti-diabetic	Maltose- and sucrose-loaded rat	Isolated salacinol, kotalanol and mangiferin	Inhibited the increase of serum glucose level after administration of maltose or sucrose, but not glucose. The extracts inhibited rat intestinal maltase and sucrase. Salacinol and kotalanol showed inhibitory activities against small intestinal α- glucosidase. Mangiferin inhibited both sucrase and aldose reductase.	Matsuda et al., 2002)
9	Inhibition of diabetic induced renal fibrosis	Zucker diabetic fatty (ZDF) rats	Aqueous extract	SO attenuates diabetic renal fibrosis, at least in part by suppressing anigiotensin II/AT1	He et al., 2009).

				signaling.	
10	Anti-mutagenic and anti-oxidant activity	Sperm abnormality test in Wistar rats	Rootbark extract	Suppressed the changes produced by Mitomycin-C showed significant inhibition in the sperm shape abnormality and sperm count. Improved the status of serum antioxidant enzymes.	(Navneet et al., 2009)
11	Nephro-protective and antioxidant activities	Acetaminop(APAP) APAP-induced toxicity in rats	Ethanol extract (EESO)	APAP significantly increases the levels of serum urea, creatinine and reduces levels of uric acid concentration. The EESO possesses nephroprotective and antioxidant effects against APAP-induced nephrotoxicity in rats.	(Palani et al., 2011)
12	Hypolipidemic activity	Aluminium toxicity induced White Albino Wistar Female Rats	Powder extract-	Significantly lowered the serum alkaline Phosphatase, Serum Aspartate aminotransferase, urea, bilirubin and cratinine at 14th day.	(Kalaiarasi et al., 2011)
13	Anti-microbial Activity	Gram +ve & Gram –ve microbial pathogens	Root, stem and leaf powder	S. oblonga EtOAc acidic & neutral extracts have been active against eleven gram +ve & gram –ve microbial pathogens. EtOAc was the best solvent according to the in vitro results.	(Rao and Giri, 2010)
14	Anti-bacterial activity	Pathogenic bacteria	Stem, leaves and roots extracts	The root extract against Bacillus subtilis showed the highest zone of inhibition than aerial part.	(Rao and Murty, 2010)
15	Postprandial glycemic activity, insulinemic, and breath hydrogen	Healthy adults	Liquid nutritional product containing	Reduction in plasma glucose and insulin areas. Breath hydrogen excretion was 60%	(Collene et al., 2005)

	responses		SO extract	greater (P<0.001) in the SO-containing meals.	
16	Anti-inflammatory activity	Male albino rats	Rootbark powder	Inhibits the transudative, exudative and proliferative components and lower the lipid peroxide content of exudate and liver, gamma-glutamyl transpeptidase activity in the exudate of chronic inflammation. The increased acid and alkaline phosphatase activity and decreased serum albumin in cotton pellet granulomatous were normalized with these drugs.	(Ismail et al., 1997).
17	Hypoglycemic activity	Streptozotocin (STZ) diabetic rats	Rootbark extract	Significant inhibition of the streptozotocin-induced hyperglycemia and hypoinsulinaemia..	(Krishnakumar et al., 1999)
18	Anti-oxidant activity	Streptozotocin (STZ) diabetic rats	Rootbark extract	Increasing the antioxidant activity of enzymes such as superoxide dismutase, catalase, GSHPxase and GSSGRase in the heart tissue of treated STZ diabetic rats.	(Krishnakumar et al., 1999)
19	Anti-hypertriglyceridemic activity	Laying hens	Root extract	Inhibition of the body weight increasing without affecting food intake. However, SOR extract did not induce change in plasma glucose concentration. Moreover, SOR extract did not alter all variables in pullets.	Wang et al., 2012)
20	Obesity and diabetes-associated cardiac hypertrophy	Male Zucker diabetic fatty (ZDF) rats	Water extract	Less cardiac hypertrophy in treated rats. Cardiac overexpression of	(Huang et al., 2008)

				ANP, brain natriuretic peptide (BNP) and AT(1) mRNAs and AT(1) protein suppression. Inhibition of angiotensin II- stimulated [(3) H] thymidine incorpo ration by cardiac fibroblasts.	
21	Cardiac lipid accumulation	Zucker diabetic fatty (ZDF) rats	Oral administrati on	Reduces cardiac triglyceride and fatty acid contents and decreases the Oil red O-stained area in the myocardium. Inhibits cardiac fatty acid oxidation.	(Huang et al(2), 2006)

Anti-diabetic activity

According to the WHO list, 21,000 plant species are utilized for medical reasons globally. Of these, 2,500 species are found in India (WHO, 2002; Modak, 2007). Approximately 800 plant species have been documented to exhibit anti-diabetic properties (Patil et al., 2011). A diverse array of plant-derived active principles, encompassing several bioactive chemicals, has demonstrated potential for application in diabetes therapy (Patil et al., 2011). Salacia species have recently been widely utilized in Japan, the USA, and other nations as dietary supplements for obesity and diabetes prevention, and they have been the focus of substantial research on diabetes management (Patwardhan et al., 2005; Cooper 1, 2008; Cooper 2, 2008). Numerous studies indicate that reducing blood sugar levels diminishes the risk of several diabetes-related problems, including renal disease and neuropathy, as well as ocular impairment. *S. oblonga* interacts with the intestinal enzymes responsible for carbohydrate degradation in the body. These enzymes, known as α-glucosidases, convert carbs into glucose, the sugar that disseminates throughout the body. If the enzyme interacts with the herbal extract instead of a carbohydrate, then diminished glucose enters the bloodstream, leading to reduced blood glucose and insulin levels (Ohio State University, 2005).

Aqueous extracts of S. reticulata and *S. oblonga* significantly reduced postprandial glucose levels in maltose- and sucrose-loaded Wistar rats (Oe and Ozaki, 2008; Matsuda et al., 1999). The oral administration of 'Ilogen-Excel', an Ayurvedic herbal formulation comprising eight medicinal plants, including *S. oblonga* (50 mg/kg and 100 mg/kg), demonstrated anti-hyperglycemic effects by significantly reducing blood glucose levels and enhancing plasma insulin, hepatic glycogen, and total hemoglobin in STZ-induced diabetic rats (Umamaheswari and Mainzen, 2007). Administration of *S. oblonga* root bark extract prevented hyperglycemia and hypoinsulinaemia (Krishnakumar et al., 1999), while a combination of *S. oblonga* extract and IP-PA1 (SI tea) significantly

reduced plasma glucose and lipid levels in KK-Ay/TaJcl type II diabetic model mice (Nakata et al., 2011). Aqueous extracts of *S. oblonga* root have been shown to activate the peroxisome proliferator-activated receptor (PPAR)-α (Huang et al., 2006) and improve postprandial hyperglycemia, hyperlipidemia, hepatic steatosis, cardiac lipid accumulation, and fibrosis in Zucker diabetic fatty (ZDF) rats (Li et al., 2004; Huang et al., 2006; Huang et al., 2008; Huang et al., 2006).

Antioxidant activity

Krishnakumar et al. (1999) assessed the impact of *S. oblonga* (SOB) root bark extract on anti-lipid peroxidative activity in the heart tissue of Streptozotocin (STZ) diabetic rats. SOB markedly suppressed the hyperglycemia and hypoinsulinemia elicited by streptozotocin. SOB resulted in a substantial reduction in peroxidation products, namely thiobarbituric acid reactive compounds, conjugated dienes, and hydroperoxides. The antioxidant activity of enzymes, including superoxide dismutase, catalase, GSHPxase, and GSSGRase, was demonstrated to be elevated in the cardiac tissue of STZ diabetic rats administered SOB, indicating the antioxidative properties of SOB. The antioxidant efficacy of *S. oblonga* root bark was assessed by quantifying blood concentrations of superoxide dismutase (SOD) and catalase (CAT) in Wistar rats, revealing a significant increase ($p<0.01$) in serum antioxidant enzyme levels (Navneet et al., 2009). The extract of *S. oblonga* elevated blood urea and creatinine levels while decreasing uric acid concentration via enhancing antioxidative responses, as evaluated through biochemical and histological markers in rats subjected to APAP-induced nephrotoxicity (Palani et al., 2011).

Cardiovascular agent

The oral administration of *S. oblonga* root extract (SOE) diminishes cardiac triglyceride and fatty acid (FA) concentrations and reduces the Oil Red O-stained area in the myocardium, corresponding with the effects on plasma triglyceride and FA levels. This study suggests that the enhancement of excessive cardiac lipid buildup and elevated cardiac fatty acid oxidation in diabetes and obesity results from a decrease in cardiac fatty acid absorption, consequently influencing cardiac PPAR-alpha-mediated fatty acid metabolic gene transcription (Huang et al., 2006). Chronic treatment of *S. oblonga* extract significantly inhibited α-glucosidase activity in vitro, alleviated interstitial and perivascular fibrosis in the hearts of obese Zucker rats, and lowered plasma glucose levels in non-fasted OZR (Li et al., 2004). The possible cardioprotective function of *S. oblonga* was validated by a decrease in ventricular hypertrophy, at least partially through the inhibition of cardiac angiotensin II type 1 (AT(1)) receptor upregulation (Huang et al., 2008).

Anti-microbial activity

By comparing the anti-microbial efficacy of root, stem, and leaf powdered extracts of *S. oblonga* against pathogenic strains of gram positive and gram negative bacteria Rao et al. (2010) have revealed Rao and Murty, (2010) who had used pathogenic bacteria including gram positive bacteria Staphylococcus epidermidis, Enterococcus faecalis, Bacillus subtilis and gram negative bacteria Escherichia coli, Salmonella typhi, Klebsiella pneumonia, Enterobacter cloacae, Pseudomonas aeruginosa confirmed the anti-bacterial activity of the aerial parts (stem and leaf) and root extracts of *S. oblonga*. Against Bacillus subtilis, the root extract of *S. oblonga* had the best zone of inhibition than aerial portion.

Other important activities

Efficacy against obesity In both in vivo and in vitro studies, chronic oral administration of *S. oblonga* root water extract to Zucker diabetic fatty rats activated PPAR-alpha, which may improve postprandial hyperlipidemia and hepatic steatosis in diabetes and obesity. *S. oblonga* rootbark powder and A. tetracantha leaf powder have anti-inflammatory properties that suppress chronic inflammation, with increased acid and alkaline phosphatase activity and decreased serum albumin normalized after treatment. These medicines may stabilize lysosomal membranes, inhibit proliferation, and reduce oxidative damage (Ismail et al., 1997). *S. oblonga* root bark extract (SOB) inhibited sperm abnormalities in Wistar rats, according to Navneet et al. (2009). They showed that SOB therapy inhibited MMC alterations. At 1.0 gm/kg bw, SOB significantly reduced sperm shape abnormalities and count in both time periods. Biochemical and histological studies showed that *S. oblonga* protects the kidneys in APAP rats, according to Palani et al. (2011).

Safety evaluation

Salacia plant extracts have been shown to be safe in in vitro genotoxicity experiments. *S. oblonga* extract (SOE) was tested for genotoxicity and safety using a standard battery of tests (reverse mutation assay, chromosomal aberrations assay, mouse micronucleus assay) recommended by the US Food and Drug Administration for food ingredients (Flammang et al., 2006). SOE did not cause general organ or systemic toxicity when fed to rats at 2500 mg/kg/day for at least 90 days based on mortality. A hot water extract of *S. oblonga* supplemented to or processed into a medical food consumed for two weeks in male Sprague-Dawley rats at 10-fold higher doses than recommended for humans showed no clinical chemistry or histopathologic toxic effects (Wolf and Weisbrode, 2003).

Conclusions

Although several biological active chemicals have been identified from *S. oblonga*, previous research gave less attention to this field than to other medicinal plant species. Isolating novel phytoconstituents from this therapeutic plant requires more work. The plant and its extracts have been used for centuries to treat various disorders, but only the anti-diabetic mechanism (α-glucosidase inhibitory activity) has been studied. Further scientific evaluation and quality control measures are needed to ensure the authenticity and content of the active constituents in these products.

Many toxicological tests have proven the plant's safety, although repeatability remains a worry and requires additional toxicity study and clinical trials. Mechanistic investigations are needed to understand medication interactions with other therapies. This plant is endangered by improper cultivation, habitat degradation, and excessive and indiscriminate collecting of these vital medicinal herbs to meet worldwide demand, notably for its anti-diabetic properties. Therefore, sustainable harvesting and conservation need agronomic growing approaches. Proper in vitro propagation strategies using sophisticated plant biotechnological methods of growing plant cells and tissues are also needed.

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