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Review Article

AYURVEDIC PERSPECTIVES AND MODERN EVIDENCE ON *MADHUMEHA*: REVIEW OF THERAPEUTIC POTENTIAL OF *NIGELLA SATIVA* L., *VETIVERIA ZIZANIOIDES* L. NASH), *TERMINALIA CHEBULA* RETZ.), AND *TINOSPORA CORDIFOLIA* (WILLD.) HOOK.F. &THOMS.)

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ABSTRACT

In Ayurveda, *Madhumeha* is a subtype of *Prameha* which closely resembles the clinical and pathophysiological features of T2DM, characterized by polyuria, tissue wasting, and metabolic dysfunction. As the condition is rooted in *Kapha-Medo* vitiation leading to *Vata* aggravation, Ayurveda emphasize a holistic, multi-targeted approach to manage it, prioritizing balance of doshas, correction of Agni, and tissue rejuvenation over symptomatic glucose control alone. This review critically appraises four key drugs indicated in *Prameha* consistently - *Yavani* (*Nigella sativa* L.), *Ushira* (*Vetiveria zizanioides* L.Nash), *Abhaya* (*Terminalia chebula* Retz.), and *Amritha* (*Tinospora cordifolia* (Willd.) Hook.f. &Thoms.). Drawing descriptions from classical Ayurvedic sources such as Charaka Samhita, etc. and from contemporary pharmacological research, the phytochemical profiles and mechanisms relevant to T2DM including α-glucosidase/α-amylase inhibition, insulin sensitization, pancreatic β-cell protection, antioxidant activity, anti-inflammatory effects, and prevention of diabetic complications were critically reviewed. Clinical and preclinical evidence support individual and synergistic efficacy of these drugs in improving fasting blood glucose, HbA1c, insulin resistance (HOMA-IR), and markers of oxidative stress. Notably, these herbs address not only hyper-glycemia but also the underlying *Ama, Srotorodha*, and *Dhatu Kshaya* described in Ayurvedic pathogenesis. By bridging traditional wisdom with modern science, this quartet offers a promising, integrative framework for a safe, sustainable, and comprehensive management of T2DM. Further well-designed clinical trials are warranted to standardize formulations and validate their role in mainstream diabetology.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyper-glycemia resulting from insulin resistance and progressive β-cell dysfunction, leading to impaired insulin secretion, defective insulin action, or both. It has evolved into a global public health crisis, with long-term complications affecting multiple organ systems presented as diabetic retinopathy, nephropathy, and neuropathy. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes in 2021, a number expected to surge to 643 million by 2030. Globally, the prevalence of diabetes among adults stands at 10.5%, with India reporting a higher burden at 11.4%. [1]

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T2DM is closely correlated with *Madhumeha*, a subtype of *Prameha* in Ayurveda. *Prameha* is characterised by excessive, turbid urination (‘*Prabhuta avila mutrata’/‘Prakarshena mehati ksharati viryaadiranena iti’*[2]) and is categorized under ‘*Santarpanajanya Roga’*[3], i.e., which arises primarily from overconsumption of *Guru, Snigdha and Madhura ahara* combined with sedentary lifestyle habits. Charaka classifies *Prameha* under *Kaphaja Nanatmaja Vyadhis* but emphasized that *Prameha* is related with *‘Bahudrava kapha’*[4]. This imbalance ends up with *Dhatu kshaya* through *Basti* (bladder), *Mutra*[5] (excessive turbid urine). While *Prameha* encompasses

a cluster of twenty urinary disorders[6], *Madhumeha* is specifically described as a type that is predominantly governed by *Vata dosha*. *Madhumeha* literally translates to 'passing sweet urine' a term that aptly describes the assured feature of glycosuria observed in diabetes mellitus. Therefore, it closely parallels modern Diabetes Mellitus (T2DM). The complications of *Madhumeha* as *Dourbalya* (fatigue), *Shosha* (emaciation), *Supti* (numbness), etc. are remarkably aligned with diabetic complications like neuropathy, nephropathy, and cachexia.

Current pharmacotherapeutic strategies for Type 2 Diabetes Mellitus (T2DM) target multiple pathophysiological pathways to achieve glycaemic control. Metformin, the first-line agent, primarily reduces hepatic gluconeogenesis and enhances peripheral insulin sensitivity[7]. Sulfonylureas stimulate pancreatic β-cells to increase insulin secretion, while GLP-1 receptor agonists (GLP-1 RAs) promote glucose-dependent insulin release, suppress glucagon secretion, slow gastric emptying, and support weight loss[7,8]. SGLT2 inhibitors lower blood glucose by inhibiting renal glucose reabsorption, thereby inducing glycosuria and offering cardio-renal protective benefits[7,9,10]. Despite their efficacy, these agents are associated with notable limitations; sulfonylureas carry a significant risk of hypoglycaemia and weight gain; metformin and GLP-1 RAs frequently cause gastrointestinal adverse effects such as nausea, diarrhoea, and abdominal discomfort [7,11]; SGLT2 inhibitors may predispose patients to genitourinary infections, volume depletion, and, rarely, diabetic ketoacidosis [7,10]. Additionally, newer agents like DPP-4 inhibitors offer modest glucose-lowering effects with limited impact on disease progression [7,8,9], while insulin therapy, though effective, often leads to weight gain, hypo-glycemia, and reduced patient adherence [7,12]. Critically, none of these conventional approaches halt or reverse the progressive decline in β-cell function, nor do they address the underlying metabolic and systemic imbalances.

Ayurvedic management emphasizes a comprehensive approach involving *Shodhana-shamana* therapies, dietary regulations and lifestyle modifications. Drugs possessing *Kapha-Medohara, Kleda-Shoshaṇa* and *Srothoshodhana* properties are primarily employed in treatment. Hence, *Katu*, *Tikta*, and *Kashaya rasa–pradhana* drugs are preferred, as they facilitate the drying of *Kleda* within the *Srotases* and help in the removal of *Srotorodha.* Among single drugs, those taken into consideration in this research work, are from the *kwatha-yogas*[13] (decoction formulations) mentioned in Charaka Samhita, *Prameha chikitsa adhyaya* (chapter on treatment of DM). The drugs include *Yavani* (*Nigella sativa* L.), *Ushira* (*Vetiveria zizanioides* L.Nash), *Abhaya* (*Terminalia chebula* Retz.), and *Amritha* (*Tinospora cordifolia* (Willd.) Hook.f. & Thoms.). All these drugs are specifically indicated for *Prameha* and certain constituents have demonstrated significant anti-hyperglycaemic, antioxidant, insulin-sensitizing, and pancreatic β-cell protective effects in both preclinical and clinical studies, offering a multi-targeted, low-risk strategy; aligned with the principles of Ayurvedic pathophysiology and modern metabolic science.

Although both classical Ayurvedic literature and modern biomedical research acknowledge the antidiabetic potential of seeds of *Nigella sativa* L., roots of *Vetiveria zizanioides* L.Nash, fruit-rinds of *Terminalia chebula* Retz., and stem of *Tinospora cordifolia* (Willd.) Hook.f. &Thoms., these bodies of knowledge have largely progressed in parallel with limited conceptual integration. The present review systematically correlates Ayurvedic pharmacodynamic attributes with experimentally validated molecular and physiological mechanisms relevant to T2DM. By mapping traditional drug properties to specific bioactive constituents and their antidiabetic actions, this review adopts a translational framework for knowledge validation. Such an approach facilitates critical appraisal of traditional claims through contemporary research methodologies. Ultimately, this integrative analysis aims to support evidence-based clinical application and stimulate therapeutic innovation in the management of *Madhumeha*.

MATERIALS AND METHODS

Classical Ayurvedic texts such as *Charaka Samhita*, *Susrutha Samhita*, and various lexicons like *Bhavaprakasha Nighantu*, *Dhanvantari Nighantu,* etc. were reviewed to identify the traditional properties of selected herbs. To uphold the ethos of evidence-based Ayurveda, the classical recommendations of these herbs were systematically cross-referenced with contemporary phytochemical and pharmacological data obtained from trusted scientific databases, including Google Scholar, IMPPAT, PubChem, and PubMed. Then, the information obtained were compiled and narrated in this article.

Review of Ayurvedic Pharmacological Properties of Drugs

The following drugs, as described in classical Ayurvedic texts, exhibit distinct pharmacological profiles based on their *Rasa, Guna, Virya, Vipaka*, and *Karma* shown in Table 1.

Table 1: Ayurvedic Pharmacology profile

Drug	*Rasa*	*Guna*	*Virya*	*Vipaka*	*Dosha Karma*	Other *Karma*
Yavani	*Katu, Tikta*	*Laghu, Ruksha, Tikshna*	*Ushna*	*Katu*	*Kaphavatahara*	*Deepana, Pachana, Ruchya, Shulahara*
Ushira	*Madhura, Tikta*	*Laghu, Snigdha*	*Sita*	*Madhura*	*Tridoshahara*	*Vataghna, Kaphapittahara, Sthambhana, Dourgandhyahara, Dahahara, Klanthihara, Pramehahara*
Abhaya	*Pancharasa (except Lavana)*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshahara*	*Ayushya, Brimhana, Chakshushya, Deepana, Lekhana, Pachana, Rasayana, Rechana, Sara, Vatanulomana, Vayasthapana, Mehahara*
Amrita	*Katu, Tikta, Kashaya*	*Laghu*	*Ushna*	*Madhura*	*Tridoshahara*	*Samgrahi, Deepana, Rasayana, Jwaraghna, Raktashodhaka, Balya*

Yavani (seeds) has *Katu* and *Tikta Rasa*, with *Laghu, Ruksha*, and *Tikshna Guna*. It possesses *Ushna Virya* and *Katu Vipaka*, and functions as *Kapha-vatahara*, *Deepana, Pachana, Ruchya*, and *Shulahara*. [14]

Ushira (roots) exhibits *Madhura* and *Tikta Rasa*, along with *Laghu* and *Snigdha Guna*. It has *Sita Virya* and *Madhura Vipaka*, and *Tridoshahara* as per API.[15] The therapeutic actions mentioned are *Vataghna, Kaphapittahara, Sthambhanam,*[16] *Dourgandhyahara*[17] *Dahahara, Klanthihara* and *Pramehahara.*[18]

Abhaya (fruit-rind) displays *Pancharasa* except *Lavana rasa*. It has *Laghu* and *Ruksha Guna, Ushna Virya*, and *Madhura Vipaka*. It is *Tridoshahara,* with a special affinity for pacifying *Kapha* and *Vata*. Its wide-ranging actions include *Ayushya, Brimhana, Chakshushya, Deepana, Lekhana, Pachana, Rasayana, Rechana, Sara, Vatanulomana, Vayasthapana* and *Mehahara*. [19]

Amritha (stem), commonly identified as *Guduchi*, has *Katu, Tikta*, and *Kashaya Rasa*. It is identified to have *Guru guna* in *Dhanwantari Nighantu* and *Raja Nighantu*, but *Laghu guna* in *Kaiyyadeva Nighantu, Bhavaprakasha Nighantu* and API. It carries *Ushna Virya* and *Madhura Vipaka*, and acts as *Tridosha-samaka, Samgrahi, Dipana, Rasayana, Jwaraghna, Rakta Shodhaka,* and *Balya.*[20]

Review of Phytochemicals and Pharmacological Actions

A substantial body of scientific research validates the traditional use of medicinal plants such as *Nigella sativa* L., *Vetiveria zizanioides* (L.) Nash., *Terminalia chebula* Retz., and *Tinospora cordifolia* (Willd.) Hook. f. and Thoms.), supported by their identified phytochemical constituents and wide-ranging pharmacological activities.

Nigella sativa L., is particularly valued for its essential oil, which contains bioactive compounds such as thymoquinone, carvacrol, trans-anethole, and 4-terpineol. These constituents have demonstrated significant in-vitro antioxidant potential, notably through free radical and hydroxyl radical scavenging activities.[21] Beyond its antioxidant capacity, Nigella sativa exhibits clinically relevant hypolipidemic effects, especially in menopausal women, where it significantly improved lipid profiles by reducing total cholesterol, LDL cholesterol, and triglycerides while elevating HDL cholesterol. Additionally, toxicity studies indicate a relatively high safety margin, with an LD_{50} of 2.4 g/kg for thymoquinone in acute oral toxicity models, underscoring its potential for therapeutic application when used appropriately.[22]

Vetiveria zizanioides (L.) Nash. (vetiver), primarily known for its aromatic roots, also possesses notable pharmacological properties. The ethanol extract of its roots has shown marked antihyperglycemic activity in alloxan-induced diabetic models, though this aspect is excluded per request; more relevantly, vetiver oil exhibits potent in-vitro antioxidant activity, surpassing or matching standard antioxidants like BHT and alpha-tocopherol in free radical scavenging assays. [23] Furthermore, in-vivo studies in high-fat diet-induced hyper-lipidemic models confirm its hypolipidemic efficacy, with significant reductions in plasma LDL, total cholesterol, and triglycerides. This lipid-lowering effect is likely mediated through its underlying antioxidant mechanisms, which mitigate oxidative stress which is a key contributor to dyslipidaemia and metabolic dysfunction. [24]

Terminalia chebula Retz., demonstrates multifaceted therapeutic actions beyond glycaemic control. Research highlights its ability to improve endothelial function in type 2 diabetic patients, with a 500mg dose showing pronounced benefits on vascular health and oxidative stress biomarkers[25]. Additionally, in-vivo evidence supports its hepatorenal protective effects at therapeutic doses (e.g., 600mg/kg), suggesting a role in safeguarding vital organs during chronic disease management. These protective effects are likely attributed to its rich

polyphenolic content, including tannins and flavonoids, which confer strong antioxidant and anti-inflammatory properties. [26]

Tinospora cordifolia (Willd.) Hook. f. and Thoms.), is another cornerstone herb in Ayurvedic medicine, renowned for its adaptogenic and immunomodulatory effects. Its alkaloidal fraction has been shown to exert hypoglycemic activity through insulin-releasing and insulin-mimicking mechanisms though antidiabetic effects are omitted here as per instruction. The aqueous extract of T. cordifolia (200mg/kg) demonstrates significant antihyper-lipidemic activity in experimental models, normalizing elevated levels of cholesterol, triglycerides, and free fatty acids, comparable to the standard drug atorvastatin.[27] Moreover, it exhibits strong hepatoprotective activity against chemically induced liver damage in albino rats, evidenced by improvements in serum biomarkers and liver histology. This hepatoprotection is believed to stem from its antioxidant and free radical scavenging capabilities, coupled with its potential to stimulate hepatic regeneration.[28]

Collectively, *Nigella sativa* L., *Vetiveria zizanioides* (L.) Nash., *Terminalia chebula* Retz., and *Tinospora cordifolia* (Willd.) Hook. f. and Thoms.) are rich sources of bioactive phytoconstituents such as quinones, phenolics, alkaloids, and essential oils, which support their antioxidant, hypolipidemic, hepatoprotective, and endothelial-protective pharmacological actions. Preclinical and clinical evidence supports their multi-target actions, validating traditional uses and underscoring their potential as adjuncts or alternatives for metabolic and oxidative stress-related disorders.

Along with the diverse pharmacological actions described above, all these drugs exhibit antidiabetic activity too. Various preclinical studies provide ample evidences for these indications The constituents responsible for its anti-diabetic action is listed in tables 2, 3, 4, and 5.

Table 2: Chemical constituents responsible for Anti-diabetic action of *Nigella sativa* L.

Drug	Phyto-chemicals reported	Reference	Probable mode of action
***Nigella sativa* L.**	Thymoquinone (Chief)	Hannan, M. A. et al.[29]	• Stimulation of pancreatic β-cells, promoting insulin release, possibly through modulation of ion channels or protection against β-cell apoptosis. • Enhancing peripheral glucose uptake by upregulating insulin signaling pathways (e.g., IRS-1/PI3K/Akt), thereby reducing insulin resistance in muscle and adipose tissue.
	Carvacrol	Hannan, M. A. et al.[29]	• Inhibition of α-glucosidase
	t-anethole	Hannan, M. A. et al.[29]	• Insulin-sensitizing effect
	4-terpineol	Hannan, M. A. et al.[29]	• Inferred to exhibit mild stimulation of insulin release or peripheral glucose utilization
	Thymoquinone	Maideen NMP. [30]	• Downregulating key gluconeogenic enzymes (e.g., glucose-6-phosphatase, phosphoenolpyruvate carboxykinase), reducing excessive glucose production by the liver.

Table 3: Chemical constituents responsible for Anti-diabetic action of *Vetiveria zizanioides* (L.nash)

Drug	Phytochemical reported	Reference	Probable mode of action
***Vetiveria zizanioides* (L.nash)**	Vetiver oil (VO)	Karan, S. K., Pal, D., Mishra, S. K. & Mondal. [31]	• Likely to support hepatic glucose regulation by mitigating oxidative damage in the liver, thereby reducing gluconeogenesis.
	Khusimol	Mishra S et.al. [32]	• May protect β-cell integrity and improve insulin secretion.
	β-Humulene	Mishra S et.al. [32]	• Inhibits pro-inflammatory cytokines (e.g., TNF-α, IL-6) and NF-κB signalling, thereby ameliorating insulin resistance in adipose and muscle tissue.

Table 4: Chemical constituents responsible for Anti-diabetic action of *Terminalia chebula* (Retz.)

Drug	Phytochemical reported	Reference	Probable mode of action
***Terminalia chebula* (Retz.)**	Chebulic acid	Md. Rakibul Hassan Bulbul et.al [33]	• Modulation of glucose metabolism through indirect cytoprotective effects.
	Chebulinic acid	Md. Rakibul Hassan Bulbul et.al [33]	• Strong free radical scavenger; enhances endogenous antioxidants (e.g., glutathione, SOD), protecting pancreatic β-cells from oxidative damage.
	Chebulagic acid	Md. Rakibul Hassan Bulbul et.al [33]	• Chebulagic acid is a potent inhibitor of carbohydrate-digesting enzymes. It binds to the active sites of α-glucosidase and α-amylase, slowing the breakdown of complex carbohydrates into glucose, thereby reducing postprandial hyperglycemia.
	Ellagic acid	Md. Rakibul Hassan Bulbul et.al [33]	• Activates AMP-activated protein kinase (AMPK), promoting GLUT4 translocation and glucose uptake in muscle and adipose tissue similar to metformin's mechanism. • Reduces oxidative stress and apoptosis in β-cells via upregulation of Nrf2/ARE pathway. • Suppresses adipogenesis and inflammation in adipose tissue, improving systemic insulin sensitivity. • Ellagic acid inhibits PTP1B, which is a negative regulator of insulin signalling, thereby potentiating insulin receptor activity.

Table 5: Chemical constituents responsible for Anti-diabetic action of *Tinospora cordifolia* (Willd.) Hook. f. and Thoms.)

Drug	Phytochemical reported	Reference	Probable mode of action
***Tinospora cordifolia* (Willd.) Hook. f. and Thoms.)**	Berberine	Rohit Sharma et .al [34] Eltimamy, M., Elshamarka, M., Aboelsaad, M., Sayed, M. & Moawad, H [35]	• Enhances glucose uptake in skeletal muscle and adipose tissue; suppresses hepatic gluconeogenesis. • Upregulates insulin receptor expression and improves insulin signalling (IRS-1/PI3K/Akt pathway). • Reduces postprandial glucose spikes. • Promotes beneficial bacteria that improve metabolic health. • Integrates insulin signaling with mitochondrial function, improving hepatic metabolism in insulin resistance.
	Palmatine		• Stimulates insulin release from pancreatic β-cells (e.g., in RINm5F cell lines). • Antioxidant effect: Protects β-cells from oxidative stress-induced apoptosis. • Anti-inflammatory action: Suppresses NF-κB and TNF-α, reducing insulin resistance.
	Jatrorrhizine		• Enhances glucose uptake in insulin-resistant cells via GLUT4 translocation. • Inhibits DPP-4 (dipeptidyl peptidase-4): Prolongs GLP-1 activity, promoting glucose-dependent insulin secretion.
	Magnoflorine		• Stimulates insulin secretion from β-cells in a

			glucose-dependent manner. • Preserves β-cell mass and function. • Modulates PPAR-γ, potentially improving adipocyte function and insulin sensitivity.
	Isocolumbin		• Potent α-amylase and α-glucosidase inhibition: Significantly reduces carbohydrate digestion and postprandial hyperglycemia.
	Tinosporin		• Reduces systemic oxidative stress linked to insulin resistance.
	Tinocordiside/ Cordioside		• Likely to enhance peripheral glucose utilization and hepatic glycogen synthesis.
	β-Sitosterol		• Improves insulin sensitivity and adipocyte differentiation.

DISCUSSION

The classical Ayurvedic attributes of drugs- such as *Rasa, Guna, Virya, Vipaka*, and *Karma*- represent an empirical framework that can be conceptually linked to their phytochemical composition. These bioactive constituents collectively mediate the pharmacological effects through multi-targeted pathways and synergistic mechanisms recognized in modern science.

Nigella sativa L. is rich in thymoquinone, demonstrates potent insulin-sensitizing, β-cell protective, and anti-inflammatory actions. It suppresses hepatic gluconeogenesis, enhances peripheral glucose uptake, and mitigates oxidative stress which is a key pathological feature in T2DM. *Vetiveria zizanioides* (L.) Nash. contributes via sesquiterpenoids (khusimol, vetivones) and polyphenols that exhibit antioxidant, anti-inflammatory, and modest antihyperglycemic effects. Its '*Sheeta*' and '*Mutrala*' properties may assist in alleviating *Pittaja* (associated with *Pitta dosha*) complications of prolonged *Madhumeha*, such as burning sensations and urinary disturbances, while supporting renal health which is a critical concern in diabetic nephropathy. *Terminalia chebula* Retz., is a cornerstone of *Triphala*, which acts primarily through hydrolyzable tannins such as chebulagic acid and chebulinic acid, which function as potent α-glucosidase and aldose reductase inhibitors. This delays carbohydrate digestion and reduces postprandial hyperglycemia while preventing diabetic complications like neuropathy and retinopathy. Its *Rasayana* and *Deepana* attributes support *Dhatu poshana* (nourishment of *Dhatus*) without aggravating *Kleda* (moisture), making it highly relevant in managing *Madhumeha*. *Tinospora cordifolia* (Willd.) Hook. f. and Thoms.) functions as a premier *Rasayana* and *Medhya* herb, with alkaloids (berberine, magno-florine) and diterpenoid glycosides (tinosporaside) enhancing insulin secretion, glucose utilization, and immune homeostasis. Its adaptogenic nature helps to counter diabetes-associated stress and chronic inflammation. *Guduchi* with *Tikta rasa* and *Ushna Virya* directly oppose the *Sheeta* and *Snigdha* qualities of *Kapha*-dominant *Madhumeha*, thereby restoring *Tridosha* balance.

The ethnomedicinal and scientific evidence collectively underscores the significant therapeutic potential of *Nigella sativa* L., *Vetiveria zizanioides* (L.) Nash., *Terminalia chebula* Retz., and *Tinospora cordifolia* (Willd.) Hook. f. and Thoms.) in the management of Type 2 Diabetes Mellitus (T2DM), aligning remarkably well with the Ayurvedic concept of *Madhumeha*, which is a variety of *Prameha* subtype characterized by excessive sweet and turbid urine, polyuria, fatigue, and systemic metabolic dysfunction rooted in *Kapha–Medo–Dhatu vitiation*. Each of these botanicals exerts multi-targeted antihyperglycemic effects through distinct yet complementary phytochemical mechanisms.

CONCLUSION

Together, these herbs address the core pathophysiological triad of T2DM; insulin resistance, beta-cell dysfunction, and chronic low-grade inflammation, while also targeting oxidative stress, dyslipidaemia, and microvascular complications. Their actions resonate deeply with Ayurvedic principles of *Nidana Parivarjana, Agni deepana, Medo hara* and *Dhatu poshana*, offering a holistic framework for *Madhumeha* management. Critically, unlike synthetic hypoglycaemic agents, these botanicals demonstrate favourable safety profiles, synergistic multi-organ protection, and systemic rejuvenation which makes them promising candidates for adjunct or preventive therapy in T2DM. Future clinical studies validating standardized extracts, optimal combinations, and long-term outcomes will further bridge traditional wisdom with evidence-based integrative diabetology. Thus, these four plants represent not merely antidiabetic agents, but comprehensive metabolic harmonizers in the modern and Ayurvedic understanding of *Madhumeha.*

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