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Review Article

CHANDRAKALA GUTIKA IN THE MANAGEMENT OF *PRAMEHA* (DIABETES MELLITUS TYPE 2): A CLASSICAL DRUG REVIEW WITH EVIDENCE-BASED ANALYSIS OF ACTIVE PRINCIPLES

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ABSTRACT

Chandrakala Gutika is a traditional Ayurvedic polyherbomineral formulation *(Kharaliya Rasayana)* highly regarded in classical texts like Bhaishajya Ratnavali for treating *Madhumeha* (Type 2 Diabetes Mellitus). This chronic metabolic disease is particularly prevalent in South Asian populations. The formulation consists of eleven key ingredients- four minerals and seven herbs- processed by levigating them with *Guduchi* and *Shalmali Kwatha* before rolling them into pills *(Gutika).* A comprehensive review of classical literature like the Charaka Samhita and the Ayurvedic Pharmacopoeia of India, alongside modern pharmacological databases like PubMed, reveals that *Chandrakala Gutika* works through multi-targeted cellular and molecular pathways. Its energetic profile *(Rasa Panchaka)* is predominantly characterized by *Sheeta Veerya* (cooling potency, 55%), *Laghu Guna* (light attribute, 40%), and *Katu Rasa* (pungent taste, 35%). At a systemic level, the formulation breaks down disease pathogenesis *(Samprapti Vighatana)* and clears metabolic channels *(Srotoshodhana).* Modern scientific evidence shows its active components achieve this through multiple mechanisms: inhibiting alpha-glucosidase, sensitizing insulin via PPARγ and AMPK activation, protecting pancreatic beta-cells, and restoring vital antioxidant enzyme activities. Key active principles driving these effects include berberine from *Guduchi*, fulvic acid from *Shilajitu*, emblicanin-A/B and gallic acid from *Amalaki*, and nano-particulate tin oxide from *Vanga Bhasma*. Together, these ingredients work synergistically to address diabetes at molecular and cellular levels. However, validating these promising mechanisms requires future rigorous, randomized controlled clinical trials using fully standardized formulations.

INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a major 21st-century global health burden characterized by insulin resistance and chronic hyperglycemia. The International Diabetes Federation estimates that 589 million adults worldwide live with diabetes, with India ranking second globally at 89.8 million cases[1]. While conventional medications are effective, they often cause weight gain, hypoglycemia, gastrointestinal issues, and long-term liver or kidney damage, driving interest in integrated therapies [2].

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In Ayurveda, Type 2 DM corresponds closely to *Madhumeha*, the most severe of twenty types of *Prameha*. It is characterized by *Prabhoota-avila mutrata* (excessive, turbid urine), sweet honey-like urine, and a loss of *Ojas* (vital essence). Classical texts like the *Charaka Samhita* and *Sushruta Samhita* attribute its pathogenesis (*Samprapti*) to *Kapha-Medas* vitiation, channel obstruction (*Srotodushti*), and tissue depletion (*Dhatu kshaya*).[3,4,5]

Chandrakala Gutika, recorded in the *Bhaishajya Ratnavali*, is a traditional *Kharaliya Rasayana* formulation used clinically to treat this condition.[6] Prepared via trituration in a *Khalvayantra*, it combines eleven active ingredients- seven herbs and four refined minerals (*Bhasmas*)- levigated with *Guduchi* and *Shalmali* decoctions (*Kwatha*).

Despite its extensive historical and clinical use, peer-reviewed pharmacological data for *Chandrakala*

Gutika remains absent. This review bridges the gap for researchers, clinicians, and regulatory agencies by providing a comprehensive analysis of the formulation. It details the anti-diabetic mechanisms of individual ingredients, maps its Ayurvedic pharmacodynamic profile (*Rasa Panchaka*), analyzes how it interrupts pathogenesis (*Samprapti Vighatana*), and outlines a standardized preparation flowchart to support evidence-based integration.

METHODS

Literature Search Strategy

A thorough study of the literature was done using both modern pharmaceutical databases and traditional Ayurvedic texts. *Bhaishajya Ratnavali, Charaka Samhita, Sushruta Samhita, Ashtanga Hridayam,* and the Ayurvedic Pharmacopoeia of India (API) were among the classical sources considered. The following search terms were used to obtain current pharmacological literature from PubMed, Scopus, Google Scholar, and ScienceDirect:

RESULT AND DISCUSSION

Classical Formulation

एला सकर्पूरशिला सधात्रीजातीफलं केशरशाल्मली च ।
सूताभ्रवङ्गायसभस्म सर्वमेतत्समानं परिभावयेत्तु ।।६७।।
गुडूचिकाशाल्मलिकाकषायैर्निष्काद्धमानां मधुना ततश्च ।
बद्ध्वा गुडीं चन्द्रकलेतिसंज्ञां मेहेषु सर्वेषु नियोजयेच्च ।।६८।।

Bhaishajya ratnavali, Prameha Chikitsa, Verses 67–68

Rasa Panchaka of *Chandrakala Gutika*

Table 1 presents the Ayurvedic pharmacodynamic profile of all thirteen ingredients based on classical references and the API. [7,8]

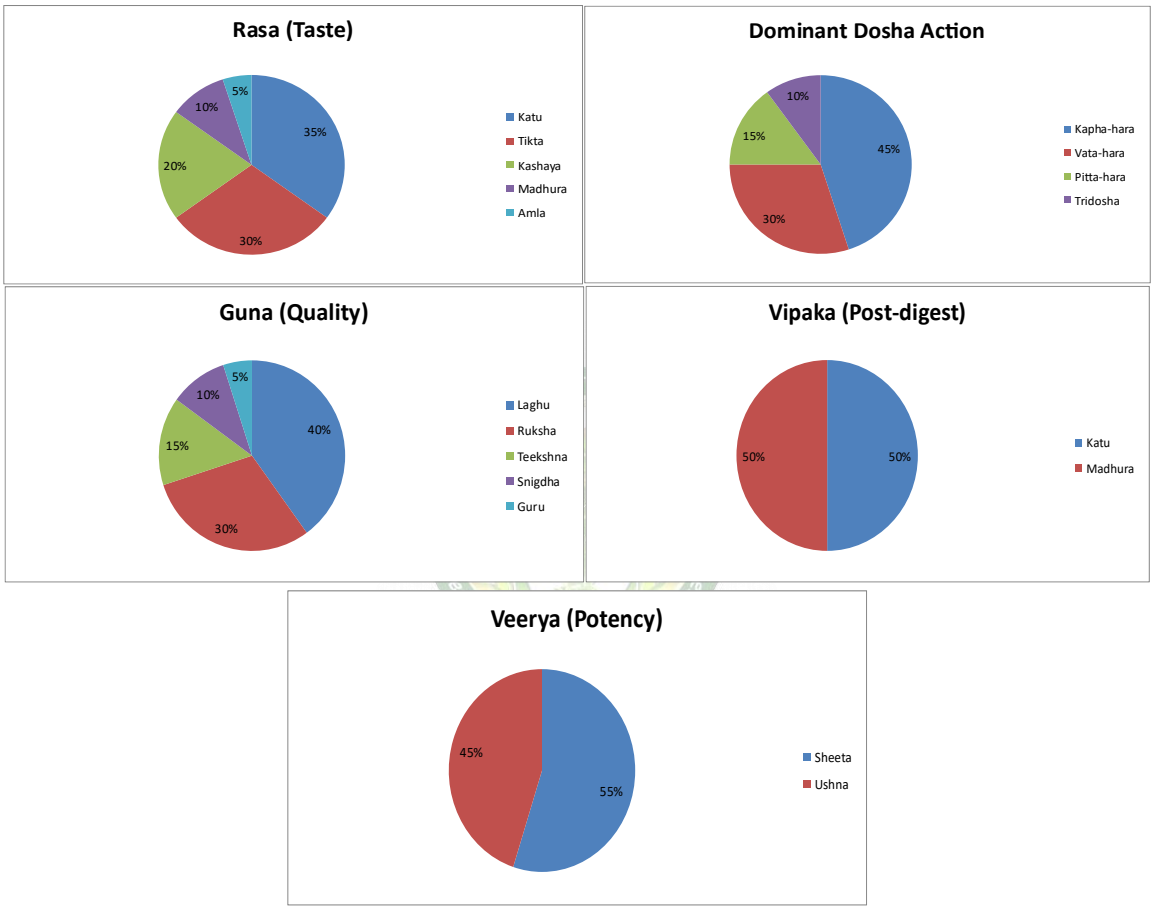
Table 1: *Rasa Panchaka* of *Chandrakala Gutika* Ingredients

Ingredient	*Rasa*	*Guna*	*Veerya*	*Vipaka*	*Doshagnata*	*Key Karma*
Ela (Elettaria cardamomum)	*Katu, Madhura*	*Laghu, Ruksha*	*Sheeta*	*Katu*	*KV-hara*	*Deepana, Pachana, Pramehaghna*
Karpura (Cinnamomum camphora)	*Tikta, Katu, Madhura*	*Laghu, Ruksha*	*Sheeta*	*Katu*	*KP-hara*	*Chedana, Lekhana, Medohara*
Amalaki (Phyllanthus emblica)	*Pancharasa (all 5)*	*Laghu, Ruksha*	*Sheeta*	*Madhura*	*Tridoshahara*	*Rasayana, Pramehaghna, Chakshushya*
Jayaphala (Myristica fragrans)	*Katu*	*Guru, Ruksha, Teekshna*	*Ushna*	*Katu*	*KV-hara*	*Grahi, Deepana, Pachana*
Nagakesara (Mesua ferrea)	*Tikta, Kashaya*	*Laghu, Ruksha, Teekshna*	*Ushna*	*Katu*	*KP-hara*	*Vishahara, Sophahara, Amapachana*
Shalmali (Bombax ceiba)	*Kashaya*	*Laghu, Snigdha*	*Sheeta*	*Madhura*	*VP-shamaka*	*Grahi, Shukravardhini, Pramehaghna*
Shuddha Shilajitu	*Katu, Tikta, Kashaya*	*Teekshna*	*Na ati Ushna*	*Katu*	*Tridoshahara*	*Rasayana, Yogavahi, Mehahara*
Shuddha Parada (Kajjali)	*Pancharasa*	*Snigdha, Guru, Sara*	*Ushna*	*Madhura*	*Tridoshahara*	*Yogavahi, Rasayana, Deepana*
Abhraka Bhasma	*Madhura, Kashaya*	*Laghu, Snigdha*	*Sheeta*	*Madhura*	*Tridoshahara*	*Rasayana, Balya, Medhya, Ojavardhaka*
Vanga Bhasma	*Tikta, Kashaya*	*Laghu, Sara, Ruksha*	*Sheeta*	*Madhura*	*V-hara, Sarva Meha-nashana*	*Chakshushya, Balya, Pramehaghna*
Loha Bhasma	*Madhura, Amla, Katu, Tikta,*	*Laghu, Ruksha,*	*Ushna*	*Madhura*	*KPV-hara*	*Raktavardhaka, Rasayana, Balya*

Ingredient	*Rasa*	*Guna*	*Veerya*	*Vipaka*	*Doshagnata*	*Key Karma*
	Kashaya	*Teekshna*				
Guduchi (Tinospora cordifolia)	*Tikta, Kashaya*	*Laghu*	*Ushna*	*Madhura*	*Tridosha shamaka*	*Rasayana, Deepana, Balya, Jwaraghna*
Shalmali Kwatha	*Kashaya, Madhura*	*Guru, Grahi, Sheetala*	*Sheeta*	*Madhura*	*VP-shamaka*	*Stambhana, Grahi, Pramehaghna*

Abbreviations: KV = Kapha-Vata; KP = Kapha-Pitta; VP = Vata-Pitta; KPV = Kapha-Pitta-Vata (Tridosha)

Chart 1: Percentage Distribution of Major *Rasa, Guna, Veerya*, and *Vipaka* in *Chandrakala Gutika*



Evidence-Based Analysis of Active Principles in components of *Chandrakala gutika*

***Vanga Bhasma* (Calcined Tin- Stannum Oxide)**

Vanga Bhasma is the primary *Pramehaghna* (anti-diabetic) mineral in this formulation. In a clinical trial by Patgiri et al., 250mg of *Vanga Bhasma* combined with *Guduchi Ghana* demonstrated moderate anti-hyperglycemic effects in 64 *Madhumeha* (Type 2 DM) patients over 28 days.[9] Jawanjal et al. recorded 14 traditional *Marana* (calcination) techniques for *Trivanga Bhasma*, confirming *Madhumeha* as its primary classical indication.[10] The traditional *Marana* method yields bio-reactive nano-particulate tin oxide particles (50–300nm), validated via TEM/SEM.[10,11] Mechanistically, its *Tikta Rasa* (bitter taste) and *Sheeta Veerya* (cooling potency) directly eliminate *Kleda* (excess tissue fluid/stickiness) and rectify *Dhatushaithilya* (tissue laxity)- the twin pathological drivers of *Prameha*. Furthermore, its *Vatahara* property addresses diabetic neuropathy symptoms.

***Guduchi* (*Tinospora cordifolia* (Wild.) Miers)**

Serving as both an ingredient and a *Bhavana Dravya* (levigation medium), *Guduchi's* anti-diabetic action is well-documented. Hussain et al. demonstrated that *Tinospora cordifolia* stem extract significantly inhibits alpha-glucosidase, salivary amylase, and pancreatic amylase, flattening post-prandial glucose spikes.[12] Its key alkaloids- berberine, palmatine, tinosporine, and isocolumbin- exert multi-targeted anti-diabetic effects.[13,14,15] Lee et al. showed that berberine activates AMP-activated protein kinase (AMPK) in 3T3-L1 adipocytes and L6 myotubes, enhancing GLUT4 translocation independently of PI3-kinase and reducing lipid accumulation.[16] Xu et al.

confirmed that berberine increases glucose uptake in HepG2 and C2C12 cells via both AMPK-dependent and independent pathways.[17] Additionally, Cicero et al. noted that berberine and palmatine accelerate glycolysis, decrease adipogenesis, inhibit gluconeogenesis, and boost glucokinase activity.[14]

***Amalaki* (*Phyllanthus emblica* L.)**

Amalaki is a rich source of Vitamin C and polyphenols (emblicanin-A, emblicanin-B, punigluconin, pedunculagin, and gallic acid).[18,19] Majeed et al. showed that a standardized fruit extract (Saberry®) strongly inhibits alpha-amylase, alpha-glucosidase, and DPP-4, acting as a triple-target anti-diabetic agent.[18] Variya et al. reported that *Amalaki's* antioxidant components (gallic acid, gallotannin, ellagic acid, corilagin) mitigate hyperglycemia and long-term complications like cardiomyopathy, nephropathy, neuropathy, and cataractogenesis.[19] Its component beta-glucogallin selectively inhibits aldose reductase, preventing polyol pathway-driven neuropathy and retinopathy.[19] In Ayurveda, its *Pancharasa* (five tastes) and *Tridoshahara* nature make it a premier *Rasayana* that rejuvenates exhausted tissues (*Dhatus*).

***Nagakesara* (*Mesua ferrea* Linn.)**

The active principles of *Mesua ferrea* include mesuaxanthone-A and -B, mammeisin, mammeigin, and flavonoids (mesuol, mesuprenol).[20] Kyaw et al. [21] showed that *Mesua ferrea* extracts increased glucose uptake in 3T3-L1 adipocytes and showed alpha-glucosidase and alpha-amylase inhibitory action ($IC_{\bullet}^{1}$ =128.8µg/mL and 146.8µg/mL, respectively). In rats with alloxan-induced diabetes, M. ferrea stamens caused a dose-dependent decrease in blood glucose at 150 and 300mg/kg.[21] The persistent low-grade inflammation that underlies insulin resistance in Type-2 diabetes is addressed by the anti-inflammatory action of *Mesua ferrea* xanthones, which inhibit COX-2 and suppress the NF-κB pathway.[22] Its *Kapha-Pittahara* action targets inflammatory and secretory excesses in *Prameha*, while its *Ushna Veerya* (hot potency) and *Amapachana* (toxin-digesting) activity clear metabolic endotoxins (*Ama*) that compromise insulin receptors.

***Shuddha Shilajitu* (*Asphaltum punjabianum*)**

Shilajitu is a humic mineral exudate rich in fulvic acid (60–80%), dibenzo-alpha-pyrones, triterpenes, and trace minerals. Ghosal et al. proved that processed *Shilajitu* enhances the hypoglycemic action of insulin and prevents STZ-induced beta-cell damage in rats.[23] Vemuri et al. showed that 200mg/kg of *Shilajitu* reduced blood glucose by over 50%, reversed pancreatic beta-cell degeneration, and suppressed hemoglobin glycation more effectively than glibenclamide.[24] Its main bioactive, fulvic acid, stimulates ATP consumption and glucose uptake in C2C12 muscle cells, mimicking exercise-like metabolic effects and enhancing mitochondrial membrane potential.[25] Rajpoot et al. (2025) confirmed that Shilajitu significantly lowers serum glucose, HOMA-IR, and increases insulin sensitivity.[26] Its *Yogavahi* (bioavailability enhancer) property accelerates the action of co-formulated *Bhasmas*.

***Ela* (*Elettaria cardamomum* Maton)**

Cardamom contains phenolics (quercetin, gallic acid, luteolin) and volatile oils, primarily 1,8-cineole (50–60%). Daneshi-Maskooni et al. confirmed that 1,8-cineole reduces adipose tissue mass and improves glycemic control by inhibiting NF-kB and fatty acid synthesis, while upregulating gamma (PPARy) expression- the molecular target of thiazolidinediones.[27] A systematic review by Zamani et al. showed that 3gm/day of cardamom improves insulin sensitivity in pre-diabetic patients.[28] Paul and Bhattacharjee demonstrated the fasting hypoglycemic effects of its 1,8-cineole extract in diabetic rats.[29] Ayurvedically, Ela's *Deepana-Pachana* action restores *Agni* (metabolic fire) and prevents *Ama* formation.

***Jayaphala* (*Myristica fragrans* Houtt.)**

Nutmeg contains myristicin, elemicin, safrole, eugenol, and macelignan. Nguyen et al. identified two non-competitive PTP1B inhibitors in nutmeg, meso-dihydroguaiaretic acid and otobaphenol.[30] Inhibiting PTP1B (a negative regulator of insulin signaling) increases insulin receptor tyrosine phosphorylation, enhancing insulin sensitivity.[30] Morikawa et al. showed that macelignan exhibits strong (PPARy) binding affinity (-8.3kcal/mol), and its co-administration with glimepiride significantly outperforms monotherapy in diabetic mice.[31] Its *Grahi* (absorbent) and *Pachana* (digestive) properties correct tissue hyperlipidemia and malabsorption.

***Karpura* (*Cinnamomum camphora*)**

Camphor's constituents (borneol, camphene, terpineol) exert *Medohara* (lipolytic) activity, reducing the visceral fat accumulation that triggers insulin resistance.[32] Its suppression of the COX/LOX pathways addresses systemic inflammation, while its vasodilatory properties enhance microcirculation to combat peripheral vascular disease. This lipolytic effect correlates to its classical *Lekhana* (scraping) property, helping resolve the *Kapha-Medas* excess.

***Shuddha Parada - Kajjali* (Purified Mercury)**

Kajjali (black sulfide of mercury), prepared via prolonged trituration of purified mercury (*Parada*) and sulfur (*Gandhaka*), acts as a premier *Yogavahi* agent. It enhances the cellular penetration, bioavailability, and therapeutic potency of all co-formulated ingredients.[33] When prepared via classical *Ashtasamskara* protocols, it is distinct from inorganic mercuric compounds and is non-toxic within classical

dosage limits (125–250mg/day). Its *Rasayana* and *Tridoshahara* traits support systemic renewal.

***Abhraka Bhasma* (Calcined Mica)**

Kantak et al. identified *Abhraka Bhasma* as square-shaped crystalline nano-particles (mean size 92.3nm) composed of Si, Mg, O, Fe, Ca, and K.^34 Sarkar et al. demonstrated that it significantly upgrades superoxide dismutase (SOD) and catalase (CAT) activities in liver tissue, providing direct enzymatic defense against beta-cell-depleting oxidative stress.[35] As an *Ojavardhaka Rasayana*, it replenishes lost *Ojas* (vital essence) and enhances mitochondrial ATP production, corresponding to *Dhatwagnivardhana* (tissue-level metabolic optimization).[35]

***Loha Bhasma* (Calcined Iron Oxide)**

The nano-particulate iron oxide in *Loha Bhasma* helps restore enzymatic antioxidant defenses. Shafiq et al. demonstrated that metallic nanoparticles successfully restore critically depleted SOD and CAT activities under diabetic conditions, intercepting free-radical damage at multiple steps.[36] Its *Raktavardhaka* (hematopoietic) and *Balya* (strengthening) properties specifically counter the *Dhatu Kshaya* (tissue wasting) and *Panduta* (anemia) characteristic of advanced *Madhumeha*.

***Shalmali* (*Bombax ceiba* L.)**

The root bark of *Shalmali* contains flavonoids, phenolics, and anti-inflammatory sesquiterpenoids (shamimicin, bombamalosides) that reduce vascular inflammation, while its hepatoprotective traits address insulin-resistance-associated fatty liver. Its *Kashaya Rasa* (astringent taste) and *Grahi* properties rectify *Dhatusaithilya* and dry up excess *Kleda*.[6,7] Utilizing it as a *Bhavana Kwatha* ensures its bioactive compounds are thoroughly integrated into the matrix, amplifying the overall anti-diabetic efficacy of the *Gutika*.

Preparation Method: Standardized Flowchart

The traditional *Kharaliya Rasayana* procedure, which includes sequential cleansing (*Shodhana*), calcination (*Marana*), trituration (*Bhavana*), and tablet manufacture (*Vati Nirmana*), is used to prepare *Chandrakala Gutika*. A step-by-step, preparation flowchart is shown in Figure 1.

Figure 1: Standardised Preparation Flowchart for *Chandrakala Gutika* (*Kharaliya Rasayana* Method)

Step 1: Raw Material Procurement & Authentication

Collect all herbal ingredients (*Ela*, *Karpura*, *Amalaki*, *Jayaphala*, *Nagakesara*, *Shalmali*, *Shilajitu*) and metallic ingredients (*Parada*, *Abhraka*, *Vanga*, *Loha Bhasma*). Authenticate via morphological and organoleptic parameters per API standards.

Step 2: *Shodhana* (Purification)

Shuddha Parada: Triturate with lemon juice or *Haritaki Kwatha* following *Ashtasamskaras*. *Shuddha Shilajitu*: Purify by dissolving in warm water, filtering through cloth, and drying in sunlight. *Bhasmas* (*Abhraka*, *Vanga*, *Loha*): Prepared via traditional *Shodhana-Marana* process.

Step 3: *Bhasma* Preparation

Abhraka, *Vanga*, and *Loha* undergo *Shodhana* (quenching in herbal juices), *Marana* (calcination in *Musha*/crucible at defined temperatures), and *Amritikarana* (final purification), producing nanoparticulate *Bhasmas* conforming to classical quality tests (*Rekhapurnata*, *Varitara*, *Apunarbhava*).

Step 4: *Kajjali* Preparation

Triturate equal parts of *Shuddha Parada* (purified mercury) with *Gandhaka* (sulphur) in a *Khalva yantra* (mortar) until a fine, lustrous, homogeneous black powder (*Kajjali*) forms. This is the foundation of *Kharaliya Rasayana* preparations.	 KAJJALI
Step 5: Mixing of all Ingredients	
Combine all herbal powders (*Ela*, *Karpura*, *Amalaki*, *Jayaphala*, *Nagakesara*, *Shalmali*) with *Kajjali* and all three *Bhasmas* (*Abhraka*, *Vanga, Loha*) in equal proportions. Mix thoroughly using *Khalvayantra* until homogeneous.	
Step 6: *Bhavana* (Levigation) with *Kwatha*	
Prepare *Guduchi Kwatha* (1:16 decoction of *Tinospora cordifolia* stems reduced to 1:4). Prepare *Shalmali Moola Kwatha* similarly. Levy the mixed powder with *Guduchi Kwatha* until proper consistency is achieved. Repeat with *Shalmali Kwatha* for additional *Bhavana* cycles.	
STEP 7: TABLET FORMATION (VATI NIRMANA)	
Roll the mass into tablets of 500mg each (or 250mg as per institutional protocol). Shape into round, uniform tablets using traditional hand-rolling or mechanical compression consistent with classical *Vati Kalpana*.	
Step 8: Drying & Quality Control	
Dry tablets at room temperature in shade for 3–7 days. Conduct quality control checks: organoleptic parameters, weight uniformity, disintegration time, moisture content, and heavy metal safety assays per API/Ayurvedic Pharmacopoeia standards.	
Step 9: Storage & Dispensing	
Pack in airtight amber glass containers. Label with batch no., date of preparation, and expiry. Dose: 500mg (1 tablet) twice daily with lukewarm water, before meals. Duration: 90 days for *Prameha* management.	

CONCLUSION

Chandrakala Gutika is a pharmacologically complex, scientifically coherent polyherbo-mineral formulation. Its traditional use for all forms of *Prameha* (diabetes) is strongly validated by modern pharmacological data. The formulation's thirteen components work synergistically through seven distinct therapeutic pathways:

- **Carbohydrate Modulation:** *Vanga Bhasma*, *Nagakesara*, *Ela*, and *Amalaki* inhibit alpha-glucosidase and alpha-amylase enzymes.

- **Insulin Sensitization:** *Ela*, *Shilajitu*, and *Guduchi* stimulate AMPK pathways and activate PPARγ.
- **Beta-Cell Protection:** *Amalaki*, *Guduchi*, and *Abhraka Bhasma* offer vital antioxidant and anti-apoptotic defense.
- **Anti-Glycation:** *Amalaki* actively reduces HbA1c levels.
- **Channel Cleansing (*Srotovishodhana*):** *Vanga Bhasma*, *Karpura*, and *Shilajitu* clear blocked metabolic pathways.
- **Tissue Rebuilding:** *Guduchi*, *Abhraka Bhasma*, and *Shilajitu* deliver restorative *Rasayana* effects to depleted *Dhatus*.
- **Bioavailability Enhancement:** *Kajjali* and *Shilajitu* act as *Yogavahi* agents to improve ingredient absorption.

Its *Rasa Panchaka* profile- dominated by *Katu–Tikta Rasa*, *Laghu–Ruksha Guna*, *Sheeta Veerya*, and *Katu–Madhura Vipaka*- perfectly counters *Prameha*. It clears *Srotas*, reduces excess *Kapha–Meda*, restores metabolic fire (*Agni*), rebuilds tissues, and addresses Pitta-driven inflammation via its cooling potency (*Sheeta Veerya*).

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