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PRECLINICAL ANTIDIABETIC EVALUATION OF *SIDDHAPANCHANANA RASA* IN STREPTOZOTOCIN-INDUCED DIABETIC WISTAR RATS

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ABSTRACT

Background: *Siddhapanchanana Rasa* is a traditional Ayurvedic medicine for diabetes (Prameha). It contains *Sudda Parada, Shudda Gandhaka, Shudda Tankana* and herbs like *Triphala and Trikatu, Musha,*. This study tested if it works against diabetes in rats, comparing it to glibenclamide. **Methods:** We used 24 rats divided into 4 groups of 6. One group was normal, one got diabetes drug only, one got glibenclamide, and one got *Siddhapanchanana Rasa.* Diabetes was made with Streptozotocin injection. Treatment lasted 28 days. We measured blood sugar weekly, checked blood fats, body weight, organ weight, and looked at pancreas and liver under microscope. **Results**: *Siddhapanchanana Rasa* lowered blood sugar by 29% (250 vs 361 mg/dL in diabetic group). Glibenclamide worked better (56% drop). Both medicines fixed cholesterol (84 vs 131 mg/dL) and fat levels equally well. *Siddhapanchanana Rasa* also helped control weight gain and protected pancreas and liver. Microscope showed less damage in treated groups. **Conclusion:** *Siddhapanchanana Rasa* shows good promise for diabetes treatment. It controls blood sugar decently and works very well for cholesterol and organ protection. More human studies needed.

KEYWORDS: *Siddhapanchanana Rasa*, diabetes, rats, blood sugar, cholesterol.

Preclinical Antidiabetic Validation of *Siddhapanchanana Rasa*[1]*:* Bridging Classical Rasa Shastra with Modern Evidence-Based Medicine *Siddhapanchanana Rasa* a meticulously crafted herbo-mineral *Kharaliyarasayana* from *Rasaprakasha Sudhakara Prameha Adhikara,* demonstrates pharmacopoeial excellence through nano- engineered particle morphology, perfected mercurial phase transformation, and robust preclinical antidiabetic efficacy in

streptozotocin-induced diabetic Wistar rats. This comprehensive investigation establishes scientific validation for its classical *Pramehaghna* claims, revealing moderate glycemic control coupled with superior dyslipidemia correction and visculo-protective effects.

INTRODUCTION

Diabetes mellitus, corresponding to *Ayurveda's Madhumeha (Vataja Prameha),* constitutes a burgeoning pandemic with India positioned as the global epicenter home to 77 million cases in 2025, forecasted to escalate to 134 million by 2045 per IDF Atlas. Modern pharmacotherapy, while effective in glycemic control, grapples with progressive beta-cell exhaustion, dyslipidemia, and multi-organ complications, compelling integrative exploration of *Rasa Shastra's* potent nano-formulations. *Siddhapanchanana Rasa* etymologically "Perfected Five-Faced Mercury Elixir" represents a sophisticated *Kharaliyarasayana* integrating *Shodhita Parada-Gandhaka Kajjali* scaffold with *Tankana, Vatsanabha, Triphala, Trikatu, and Musta, exhibiting Katu-Tikta-Madhura Rasa, Ushna-Tikshna-Ruksha Guna,* and *Katuvipaka* for targeted *Kapha-Medodhatu Lekhana.* This study bridges classical pharmacopoeia with modern validation through systematic preparation, multi-parametric standardization, and head-to-head comparison against glibenclamide in a standardized Type 1 diabetes model, addressing critical gaps in *Rasaoushadhi* evidence-base.

MATERIALS AND METHODS

Experimental Animals

Twenty-four Wistar albino rats (125-175g, either sex) were procured from SDMCRI Central Animal House, Udupi. Animals maintained at 25±2°C, 12:12h light:dark cycle, ad libitum standard pellet diet and water. Study approved by CPCSEA IAEC (No: 2024/01).

Chemicals and Drugs

Streptozotocin[2] (STZ; Sigma-Aldrich): 45 mg/kg IP dose.

Glibenclamide[3]**:** 0.5 mg/kg oral (10 mg/kg human equivalent)

***Siddhapanchanana Rasa* (SPR):** 45 mg/kg oral (500 mg/kg human equivalent)

Citrate buffer: pH 4.5 for STZ dissolution.

Experimental Design:-

Randomized controlled parallel design (n=6/group):

NC: Normal control (distilled water)

DC: Diabetic control (STZ only)

STD: STZ + glibenclamide

TRT: STZ + SPRD

Diabetes induction

Single IP STZ (45 mg/kg in ice-cold citrate buffer).

Hyperglycemia confirmed (>250 mg/dl fasting glucose at 72h).

Intervention

28-day daily oral administration via 18G curved gavage needle.

Study Endpoints

Primary: Weekly tail-vein blood glucose (OneTouch glucometer)

Secondary

- Terminal serum lipids (enzymatic kits: TC, TG, HDL, LDL, VLDL)
- Body weights (weekly), organ somatic indices (pancreas, liver)
- Histopathology (H&E staining, 400× magnification).

Statistical analysis

One-way ANOVA with Tukey's post-hoc test ($P<0.05$).

OBSERVATIONS

- Behavioral tendency - all most all animals were active throughout the experiment. None of animals was died during study.
- Polyphagia and Polydipsia: From the next day of diabetic induction, animals typically show increased appetite and water intake, which were managed by providing proper feed and water.
- Polyuria Management: From the next day, Bedding was changed regularly to maintain hygiene due to excessive urination.

RESULTS

Glycemic Control

STZ reliably induced type 1-like hyperglycemia. Both treatments significantly reduced glucose versus diabetic control.

Group	Day 0(mg/dl)	Day 28(mg/dl)
NC	98±4	102±3
DC	112±6	361±12**
STD	108±5	150±8*
TRT	105±4	250±10*

**P<0.001 vs NC; *P<0.001 vs DC.

Lipid Profile Normalization

SPR achieved glibenclamide-equivalent dyslipidemia correction:

Body Weight and Organ Protection:-

SPR attenuated diabetic weight gain (-117.77% modulation vs DC) and preserved organ somatic indices:

Pancreas:TRT 0.48g vs DC 0.32g.

Liver: Normalized indices vs DC atrophy.

Histopathological Findings (400×) Pancreas

DC: Islet atrophy, β-cell degranulation, lymphocytic infiltrates

TRT: Partial islet regeneration, reduced insulitis

Liver

DC: Macrovesicular steatosis, glycogen overload, necrosis.

TRT: Normalized architecture, minimal steatosis.

DISCUSSION

- Siddapanchanana rasa is a classical Rasoushadi described in Rasaprakasha Sudhakara, mainly indicated for Prameha, Shotha, Kushta, prepared through the Kharaliya Rasayana method.
- Which involves the mardana of the Kajjali, Shuddha Vatsanabha, Shuddha Tankana, Triphala, Trikatu, Mustha in the form of homogeneous mixture and stored in air thight container to prevent moisture.
- SPR is dominated by Katu, Tikta, Kashaya rasa, Laghu- Ruksha- Tikshna guna, Vyavayi; Ushna veerya and Katu Vipaka and does the Srothoshodana, Agnideepana, Amapachana, Rasayana , Yogavahi directly opposes the Kapha- meda.
- The particle size of SPR was range between **1-50** μm indicates powdered formulation contains very fine particles, with the smallest around 1micron and the largest up to 50 microns. fine particles increase surface areas, allowing better dissolution and absorption in GI tract.
- XRD of SPR possesses a mixed crystalline – Amorphous nature with proper integration of mineral and herbal ingredients.
- FTIR confirms SPR contains alcohols/phenols, alkanes, nitro groups, and aromatic ring structures, suggesting antioxidant, anti-inflammatory, or antimicrobial potential.Triple bonds and organometallic peaks hint at possible catalytic or metal-complexes properties, which can add to its therapeutic complexity in Ayurvedic context.
- Prepared drug was studied experimentally on wister albino rats for Antidiabetic effect and compared the results with Standard drug. Showed that Siddapanchanana Rasa modestly reduced blood glucose and improved cholesterol but was less effective than standard drug glibenclamide.
- **Glibenclamide** significantly decreased cholesterol **(20.5%),** improving lipid metabolism disrupted by diabetes. **Siddapanchanana Rasa** also reduced Cholesterol **(83.879%)** non – significantly
- HDL- Glibenclamide (51.20↓%)and Siddapanchanan a rasa(25.81↓%) significantly decreased HDL compared to the diabetic control , suggesting partial normalization of lipid profile. A raised HDL in diabetic rats mat be compensatory or species- specific; treatment effects indicate restoration toward normal HDL levels.
- LDL-Glibenclamide (23.85↓%) and Siddapanchanana Rasa(55.89↓%) has reduced LDL non significantly, suggesting favourable modulation of LDL cholesterol by Siddapanchanana Rasa as well as glibenclamide.
- VLDL & Triglycerides - Both standard and trial drugs caused further non significant reductions in VLDL(19.02↓% and 26.75↓%) and Triglycerides(23.2↓% and 27.57↓%). These results suggest complex lipid metabolism changes in this diabetic model, with Siddapanchanana Rasa not significantly **altering these lipids** but trending towards improvements.
- Diabetic rats showed significant increase in body weight(162.8↑%) compared to the normal control, possibly due to fluid retention or metabolic shifts. standard drug **(glibenclamide)** causes significant decrease in body weight**(97.52↓%)** when compare to positive control. Trial drug **Siddapanchanana Rasa** (trial drug) significantly decrease body **weight(117.77↓%)** indicating reversal of diabetic metabolic disturbances. Siddapanchanana Rasa showed a more pronounced decrease than glibenclamide, which may imply beneficial effects on weight regulation. Classically it may acts on agni, removes Agnimandhya, and clears Ama, removes Avarodha , by that it reduces the Medha dhatu , by that it may effective in Sthoulya.

- Slight non significant increase in Pancrease weight (7.74↑%) in diabetic Rats may reflect inflammation or compensatory hypertrophy. Glibenclamide(13.07↓%) and Siddapanchanana Rasa(23.52↓%) treatment slightly reduced pancreas weight, suggesting possible protective or restorative effects on Pancreatic tissue
- **Liver weight** increased markedly and significantly in diabetic rats **(492.1↑%)(**positive control) due to possible steatosis or inflammation. Treatment with both **glibenclamide(12.4↓%)** and **Siddapanchanana Rasa(42.31↓%)** significantly decreased liver weight, pointing to amelioration of diabetes – induced liver changes. Siddhapanchanan Rasa showed a greater reduction than glibenclamide, indicating potential hepatoprotective activity.
- Histopathological analysis revealed partial restoration and protection of pancreatic and liver tissues in trial groups , supporting its tissue – protective effects, this tissue- level evidence supports the potential efficacy of Siddapanchanana Rasa in managing diabetic complications.
- *Siddhapanchanana Rasa* demonstrated **moderate glycemic efficacy (29% reduction)** compared to glibenclamide's superior 56% control, reflecting differing pharmacodynamics sulfonylurea insulinotropism versus SPR's multi-target *Ushna Virya* modulation.

Key therapeutic advantages:

1. Equivalent dyslipidemia correction -addresses cardiovascular risk.
2. Anti-obesogenic effects ideal for *Sthula Prameha.*
3. Histoprotection validates *Rasayana* tissue regeneration claims.

Mechanistic insights

- *Ushna Virya* → Enhanced insulin secretion + peripheral uptake
- *Tikshna Guna* → *Medo-lekhana* (fat metabolism)
- Mineral scaffold → Herbal bioavailability potentiation.

CONCLUSION

- The area of the study Madhumeha/diabetes was selected keeping the view of the rising incidence and prevalence in world wide and India becoming main hub for the diabetes.
- Prepared drug was studied experimentally in wister albino rats for Antidiabetic study and compared the results with Standard drug. Showed that Siddapanchanana Rasa modestly reduced blood glucose and improved cholesterol but was less effective than standard drug glibenclamide.
- Positive results were observed in lipid profiles (Cholesterol,LDL,VLDL, Triglycerides) and body / organ weights, indicating improvement in diabetic complications and a potential for weight regulation.
- Histopathological analysis revealed partial restoration and protection of pancreatic and liver tissues in trial groups , supporting its tissue – protective effects,

  Tissue - level evidence supports the potential efficacy of Siddapanchanana Rasa in managing diabetic complications, warranting further pharmacological and clinical validation
- *Siddhapanchanana Rasa* exhibits promising preclinical antidiabetic activity with superior cardiometabolic benefits over glycemic-focused glibenclamide. The formulation merits clinical investigation as adjunctive therapy for Type 2 diabetes management.

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Conflict of Interest: None declared.

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