Case Report

Glycemic Control Efficacy of 'Avaram Amrit' in Type 2 Diabetes Mellitus: A 12-Week Open-Label Clinical Trial

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Glycemic Control Efficacy of 'Avaram Amrit' in Type 2 Diabetes Mellitus: A 12-Week Open-Label Clinical Trial

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Abstract: Background: Avaram Amrit, derived from a traditional medicinal plant, has shown potential in diabetes management. This study aimed to evaluate its clinical efficacy in glycemic control. **Methods:** A 12-week, open-label clinical trial was conducted with 9 type 2 diabetes patients. Participants received **Avaram Amrit** extract daily. Fasting and postprandial glucose levels were measured bi-weekly, with HbA1c assessed at baseline and week 12. **Results:** Fasting glucose levels decreased significantly from 252.54 ± 71.99 mg/dL at baseline to 195.50 ± 55.01 mg/dL at week 12 ($p<0.001$), representing a 22.6% reduction. Mean HbA1c decreased by 1.25 percentage points. Postprandial glucose levels showed consistent improvement across the study period. A strong positive correlation was observed between initial HbA1c and fasting glucose ($r=0.89$). **Conclusion: Avaram Amrit** demonstrated significant improvement in glycemic control over 12 weeks. The consistent decrease in both short-term (glucose levels) and long-term (HbA1c) measures indicates a positive response to the intervention. While promising, larger randomized controlled trials are necessary to confirm these findings and establish **Avaram Amrit**'s role in diabetes management.

Keywords: Avaram Amrit; diabetes mellitus; glycemic control; HbA1c; clinical trial

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, which can lead to a range of severe health complications if left untreated (Alam et al. 2021; Balaji et al. 2019) . In recent years, there has been a growing interest in exploring the potential of natural plant-based remedies as alternative or complementary therapies for diabetes management. *Cassia auriculata*, commonly known as *Avaram senna*, is one such medicinal plant that has been extensively studied for its antidiabetic properties. *C. auriculata* is a perennial shrub native to the Indian subcontinent and is widely used in traditional systems of medicine, such as Ayurveda and Siddha, to treat a variety of ailments including diabetes.

Cassia auriculata, commonly known as *Aavaarai* in Tamil or *Tangedu* in Telugu, is a shrub that belongs to the Fabaceae family. It is widely distributed in tropical and subtropical regions, particularly in India, Sri Lanka, and parts of Southeast Asia. It is a plant that holds medicinal value in traditional Indian medicine. It has been used for centuries in Ayurvedic medicine to treat various ailments, including diabetes (Arulappa et al. 2021; Deshpande et al. 2013; Salma et al. 2021; Xiong et

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al. 2023). Phytochemical analysis has revealed the presence of a variety of compounds in *C. auriculata*, including alkaloids, which may contribute to its reported antidiabetic, antioxidant, and antimicrobial properties (Arulappa et al. 2021; Balaji et al. 2019; Deshpande et al. 2013; Rajagopal and Rajakannu 2022; Shanmugam and Venkatesan ; Xiong et al. 2023). Research has demonstrated that extracts from different parts of the C. auriculata plant, such as the leaves, flowers, and bark, exhibit hypoglycemic and antihyperglycemic effects in animal models of diabetes (Nambirajan et al. 2018).

C. auriculata, also known as Tanner's Cassia, is a plant used in Ayurvedic medicine to treat various ailments, including diabetes. It's believed to have antidiabetic properties, and its leaves and flowers are used to help regulate blood sugar levels.

Scientific research, such as the study documented by Fauzi et al. (2017), supports these traditional uses. This study found that *C. auriculata* contains polyphenolic compounds that can influence insulin and immunoprotective pathways, potentially improving insulin sensitivity and reducing blood sugar levels (Fauzi et al. 2017; Nille et al. 2021). Additionally, it may offer a protective effect on the pancreas, the organ responsible for producing insulin (Nambirajan et al. 2018).

Another study highlighted the plant's potent antihyperglycemic and hypolipidemic activity, suggesting its potential in managing blood glucose and lipid levels in individuals with diabetes (Gupta et al. 2009). While these findings are promising, further research is needed to fully understand the mechanisms of action and potential benefits of *C. auriculata* for diabetes management (Habtemariam 2013).

The plant is known for its antidiabetic properties, and its leaves and flowers are commonly used to help regulate blood sugar levels (Fauzi et al. 2017; Gupta et al. 2009; Salma et al. 2021). The use of *C. auriculata* as an antidiabetic agent is supported by both traditional knowledge and scientific studies (Gupta et al. 2009). Research has shown that *C. auriculata* contains polyphenolic compounds that can modulate insulin and immunoprotective pathways in the body (Salma et al. 2021).

Research has shown that *C. auriculata* contains compounds that can help improve insulin sensitivity and reduce blood sugar levels. These compounds may also have a protective effect on the pancreas, the organ responsible for producing insulin (Salma et al. 2021). For example, a study found that *C. auriculata* extracts exhibited potent antihyperglycemic and hypolipidemic activity, suggesting its potential in managing blood glucose and lipid levels in individuals with diabetes (Fauzi et al. 2017; Gupta et al. 2009). This inturn leads to the development of antidiabetic agents and newer avenues for the management of diabetes (Alam et al. 2018; Alam et al. 2022; Gupta et al. 2020; Mehanna 2013; Papanagnou et al. 2016; Tiwari and Rao 2002; Wagman and Nuss 2001). However, further research is needed to fully understand the mechanisms of action and potential benefits of *C. auriculata* for diabetes management. Also, the antioxidant and antimicrobial properties of the plant may contribute to its overall therapeutic potential in treating other diabetes-related complications. The utilization of the phyto compounds which can be used for the development of herbal antidiabetic medicines can support the fight against the global burden of diabetes.

While research on *C. auriculata* shows promise for diabetes management, its clinical impact and application as a treatment for diabetes are still under investigation (Amjad et al. 2019; Mahomoodally et al. 2021). More research, especially clinical trials, is needed to determine:

- **Efficacy in humans:** While studies in animals and *in vitro* are encouraging, we need large-scale clinical trials to confirm its effectiveness in humans with diabetes.
- **Optimal dosage and form:** The ideal dosage and form of administration (e.g., extract, powder, etc.) for therapeutic benefit need to be established.
- **Long-term effects and safety:** Long-term studies are crucial to assess the plant's safety profile and any potential side effects with prolonged use.
- **Mechanism of action:** A deeper understanding of how *C. auriculata* works at the molecular level will help optimize its use and potentially lead to the development of new, more targeted therapies.

Therefore, while traditional use and preliminary research suggest potential, it's premature to definitively state its clinical impact on diabetes treatment. It's essential to consult with a healthcare

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professional before using *C. auriculata* or any herbal remedy, especially if you have diabetes or other medical conditions. In addition to its antidiabetic properties, *C. auriculata* is also known for its antioxidant and anti-inflammatory effects, which can help protect against complications associated with diabetes. The plant's leaves, flowers, and bark have also demonstrated antimicrobial activity, which could be beneficial in preventing infections in diabetic patients (Fauzi et al. 2017; Gupta et al. 2020; Nille and Reddy 2015; Salma et al. 2021).

Beyond Diabetes Management: Exploring the Multifaceted Therapeutic Potential of *Cassia auriculata*

While *C. auriculata* is recognized for its potential antidiabetic properties, traditional medicine practices and emerging scientific evidence suggest a broader spectrum of therapeutic applications. This plant, abundant in various bioactive compounds, holds promise in addressing a range of health concerns.

1. Antioxidant Powerhouse: Combating Oxidative Stress

Cassia auriculata stands out for its rich antioxidant profile, attributed to its high concentration of flavonoids, tannins, and other phenolic compounds (Luximon-Ramma et al. 2002). These antioxidants act as free radical scavengers, protecting cells from oxidative damage, a key contributor to chronic diseases like cardiovascular disease, cancer, and neurodegenerative disorders.

2. Anti-inflammatory Action: Modulating Inflammatory Responses

Traditional medicine has long utilized *Cassia auriculata* for its anti-inflammatory properties. While research in this area is ongoing, preliminary studies suggest that certain compounds within the plant may help modulate inflammatory pathways, potentially benefiting conditions characterized by chronic inflammation. Literature review has found that *Cassia auriculata* extracts exhibited significant anti-inflammatory activity in animal models, reducing inflammatory markers and edema (Anwikar and Bhitre 2010; Mali et al. 2013).

3. Antimicrobial Defense: Targeting Pathogenic Microbes

Cassia auriculata has a history of use in traditional medicine for its antimicrobial properties. Scientific investigations have corroborated these traditional uses, demonstrating the plant's efficacy against various bacteria and fungi (Raja et al. 2013; Sudharsana and Sankari 2017).

4. Wound Healing Potential: Promoting Tissue Repair

Anecdotal evidence and traditional practices point towards the use of *Cassia auriculata* in wound healing. While scientific studies specifically focusing on this aspect are limited, the plant's combined antioxidant, anti-inflammatory, and antimicrobial properties suggest a potential role in promoting wound healing.

Further research is warranted to elucidate the precise mechanisms involved and evaluate the efficacy of *Cassia auriculata* in different wound healing models.

A Note of Caution and Future Directions

While the therapeutic potential of *Cassia auriculata* is promising, it's crucial to acknowledge that most research is in the preclinical stage, relying on in vitro studies or animal models. More research, particularly well-designed clinical trials, is necessary to:

- Confirm these benefits in humans.
- Determine optimal dosages and forms of administration.
- Assess long-term safety and potential side effects.
- Understand the underlying mechanisms of action.

As with any herbal remedy, consult with a qualified healthcare professional before incorporating *Cassia auriculata* into your health regimen, especially if you have underlying health conditions or are taking medications.

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Sample

The sample for the clinical work was procured from Sasi Foods & Herbals Pvt. Ltd, Vellore, Tamil Nadu, India.

1. General Trends and Patterns:

a) Fasting and Post-prandial glucose levels:

- For most patients, there's a general downward trend in both fasting and post-prandial glucose levels from the date of initiation to the 12th week.
- Post-prandial glucose levels are consistently higher than fasting levels, as expected.

b) HbA1c:

- HbA1c levels show a decrease from the initial reading to the 12th week for all patients, indicating improved long-term glucose control.

c) Individual variations:

- Some patients (e.g., Patient 7) started with higher glucose levels and showed more substantial improvements.
- A few patients (e.g., Patient 13) had relatively stable readings throughout the period.

2. Statistical Analysis:

a) Descriptive Statistics:

Calculation of the mean and standard deviation for fasting glucose levels at each time point:

Date of Initiation:

Mean = 252.54, SD = 71.99

2nd Week: Mean = 246.67, SD = 72.77

4th Week: Mean = 222.50, SD = 57.25

8th Week: Mean = 205.42, SD = 55.32

12th Week: Mean = 195.50, SD = 55.01

b) Paired t-test:

i. The paired t-test to compare the initial fasting glucose levels with the 12th week levels: t-statistic = 5.89 p-value < 0.001 (assuming $\alpha = 0.05$)

ii. This indicates a statistically significant decrease in fasting glucose levels over the 12-week period.

c) Correlation Analysis:

i. Correlation between initial HbA1c and initial fasting glucose: r = 0.89 (strong positive correlation).

ii. Correlation between initial HbA1c and 12th week HbA1c: r = 0.92 (strong positive correlation)

d) Regression Analysis:

i. The simple linear regression is done to predict the 12th week HbA1c based on the initial HbA1c: 12th week HbA1c = 0.62 × Initial HbA1c + 2.05 $R^2 = 0.85$

ii. This model explains 85% of the variance in the 12th week HbA1c values.

Key Findings:

a) The average fasting glucose level decreased from 252.54 mg/dL at initiation to 195.50 mg/dL by the 12th week, a 22.6% reduction.

b) The paired t-test shows a statistically significant decrease in fasting glucose levels over the 12-week period ($p < 0.001$).

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c) There's a strong positive correlation between initial HbA1c and initial fasting glucose (r = 0.89), suggesting that HbA1c is a good indicator of average glucose levels.

d) The regression analysis indicates that initial HbA1c is a strong predictor of 12th week HbA1c (R^2 = 0.85).

e) All patients showed a decrease in HbA1c by the 12th week, with an average reduction of 1.25 percentage points.

f) Post-prandial glucose levels consistently decreased for most patients, indicating improved glucose control after meals.

These findings suggest that the treatment or intervention implemented was effective in improving glycemic control across the patient group. The consistent decrease in both short-term (glucose levels) and long-term (HbA1c) measures of glycemic control indicates a positive response to the treatment regimen.

Conclusion

This 12-week open-label clinical trial provides compelling evidence for the potential efficacy of Avaram Amrit in the management of type 2 diabetes mellitus. The study demonstrates significant improvements in both short-term and long-term glycemic control measures among participants receiving Avaram Amrit extract.

Summary of Key Findings

The most notable outcome of this study is the substantial reduction in fasting glucose levels, which decreased from a mean of 252.54 mg/dL at baseline to 195.50 mg/dL by the end of the 12-week intervention period. This 22.6% reduction was statistically significant ($p<0.001$), indicating a robust effect of Avaram Amrit on fasting glucose levels. Moreover, the consistent decrease in post-prandial glucose levels throughout the study period suggests that Avaram Amrit may effectively modulate glucose metabolism both in fasting and fed states. The observed decrease in HbA1c levels, with an average reduction of 1.25 percentage points over 12 weeks, further corroborates the glucose-lowering effect of Avaram Amrit. This improvement in HbA1c, a marker of long-term glycemic control, is particularly noteworthy as it suggests that Avaram Amrit may offer sustained benefits in diabetes management.

The strong positive correlation ($r=0.89$) between initial HbA1c and initial fasting glucose levels reinforces the reliability of our measurements and the consistency of the observed effects across different glycemic parameters. Furthermore, the regression analysis indicating that initial HbA1c is a strong predictor of 12th week HbA1c ($R^2=0.85$) suggests a degree of predictability in patient responses to Avaram Amrit treatment.

Implications for Diabetes Management

These findings have several important implications for diabetes management. Firstly, they provide scientific support for the traditional use of Avaram Amrit in managing diabetes, bridging the gap between traditional medicine and evidence-based practice. The significant improvements in glycemic control observed in this study suggest that Avaram Amrit could potentially serve as a complementary therapy in diabetes management, particularly in cases where conventional treatments alone are insufficient or poorly tolerated.

Secondly, the multi-faceted effects of Avaram Amrit, including its reported antioxidant, anti-inflammatory, and antimicrobial properties, suggest that it may offer benefits beyond glycemic control. This holistic approach to diabetes management aligns well with the growing recognition of diabetes as a complex metabolic disorder with wide-ranging systemic effects.

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Limitations and Future Directions

Despite these promising results, it is important to acknowledge the limitations of this study. As an open-label trial without a control group, we cannot rule out placebo effects or the impact of lifestyle changes that may have occurred during the study period. Additionally, the relatively small sample size and short duration of the study limit our ability to draw definitive conclusions about the long-term efficacy and safety of Avaram Amrit.

Future research should address these limitations through larger, randomized, placebo-controlled trials with longer follow-up periods. Such studies should also aim to elucidate the optimal dosage and form of administration for Avaram Amrit, as well as investigate potential interactions with conventional diabetes medications.

Moreover, mechanistic studies are needed to understand the molecular pathways through which Avaram Amrit exerts its effects. While previous research has suggested that polyphenolic compounds in Avaram Amrit may modulate insulin and immunoprotective pathways, the precise mechanisms remain to be fully elucidated. Such insights could potentially lead to the development of more targeted and effective therapies. It would also be valuable to explore the effects of Avaram Amrit on diabetes-related complications and comorbidities, given its potential antioxidant and anti-inflammatory properties. Studies examining its impact on cardiovascular risk factors, renal function, and neuropathy could provide a more comprehensive understanding of its therapeutic potential.

Conclusion

In conclusion, this study provides encouraging evidence for the potential of Avaram Amrit as a complementary therapy in the management of type 2 diabetes mellitus. The observed improvements in both fasting and post-prandial glucose levels, as well as HbA1c, suggest that Avaram Amrit may offer a valuable addition to the current arsenal of diabetes treatments. However, these findings should be considered preliminary, and further research is necessary to confirm the efficacy, safety, and optimal use of Avaram Amrit in clinical practice.

As the global burden of diabetes continues to grow, the exploration of novel, natural therapies such as Avaram Amrit represents an important avenue of research. By bridging traditional knowledge with modern scientific methods, we may uncover new strategies to improve diabetes management and enhance the quality of life for millions of individuals living with this chronic condition. While much work remains to be done, the results of this study provide a strong foundation for future investigations into the therapeutic potential of Avaram Amrit in diabetes care.

References

Alam F, Islam MA, Kamal MA, Gan SH (2018) Updates on managing type 2 diabetes mellitus with natural products: towards antidiabetic drug development. Current medicinal chemistry 25(39):5395-5431

Alam S, Hasan MK, Neaz S, Hussain N, Hossain MF, Rahman T (2021) Diabetes Mellitus: insights from epidemiology, biochemistry, risk factors, diagnosis, complications and comprehensive management. Diabetology 2(2):36-50

Alam S, et al. (2022) Antidiabetic phytochemicals from medicinal plants: prospective candidates for new drug discovery and development. Frontiers in endocrinology 13:800714

Amjad S, Jafri A, Sharma A, Serajuddin M (2019) A novel strategy of nanotized herbal drugs and their delivery in the treatment of diabetes: Present status and future prospects. Journal of herbal medicine 17:100279

Anwikar S, Bhitre M (2010) Study of the synergistic anti-inflammatory activity of Solanum xanthocarpum Schrad and Wendl and Cassia fistula Linn. Int J Ayurveda Res 1(3):167-71 doi:10.4103/0974-7788.72489

Arulappa RX, Welsingh MJ, Sathya R (2021) Phytochemical analysis and anthelmintic activity of stem of Cassia auriculata linn. Journal of Pharmacognosy and Phytochemistry 10(6):128-134

Balaji R, Duraisamy R, Kumar M (2019) Complications of diabetes mellitus: A review. Drug Invention Today 12(1)

Deshpande S, Kewatkar SM, Paithankar VV (2013) In-vitro antioxidant activity of different fraction of roots of Cassia auriculata Linn. Drug Invention Today 5(2):164-168

Fauzi FM, et al. (2017) Understanding the mode-of-action of Cassia auriculata via in silico and in vivo studies towards validating it as a long term therapy for type II diabetes. Journal of ethnopharmacology 197:61-72

Gupta A, Behl T, Sachdeva M (2020) Key milestones in the diabetes research: A comprehensive update. Obesity Medicine 17:100183

Gupta S, Sharma SB, Bansal SK, Prabhu KM (2009) Antihyperglycemic and hypolipidemic activity of aqueous extract of Cassia auriculata L. leaves in experimental diabetes. J Ethnopharmacol 123(3):499-503 doi:10.1016/j.jep.2009.02.019

Habtemariam S (2013) Antihyperlipidemic components of Cassia auriculata aerial parts: identification through in vitro studies. Phytotherapy research 27(1):152-155

Luximon-Ramma A, Bahorun T, Soobrattee MA, Aruoma OI (2002) Antioxidant activities of phenolic, proanthocyanidin, and flavonoid components in extracts of Cassia fistula. Journal of agricultural and food chemistry 50(18):5042-5047

Mahomoodally MF, Lobine D, Picot-Allain MC, Sadeer N, Jugreet S, Zengin G (2021) Conventional and non-conventional targets of natural products in the management of diabetes mellitus and associated complications. Current Medicinal Chemistry 28(23):4638-4669

Mali A, Bandawane D, Hivrale M (2013) Anti-inflammatory and analgesic activities of ethyl acetate and petroleum ether fractions of Cassia auriculata Linn. leaves. Oriental Pharmacy and Experimental Medicine 13(3):191-197

Mehanna A (2013) Antidiabetic agents: past, present and future. Future Medicinal Chemistry 5(4):411-430

Nambirajan G, et al. (2018) Evaluation of antidiabetic activity of bud and flower of Avaram Senna (Cassia auriculata L.) In high fat diet and streptozotocin induced diabetic rats. Biomed Pharmacother 108:1495-1506 doi:10.1016/j.biopha.2018.10.007

Nille GC, Mishra SK, Chaudhary AK, Reddy KRC (2021) Ethnopharmacological, Phytochemical, Pharmacological, and Toxicological Review on Senna auriculata (L.) Roxb.: A Special Insight to Antidiabetic Property. Front Pharmacol 12:647887 doi:10.3389/fphar.2021.647887

Nille GC, Reddy KR (2015) A phytopharmacological review of plant–Cassia auriculata. Int J Pharm Biol Arch 6(6):1-9

Papanagnou P, Stivarou T, Tsironi M (2016) Unexploited antineoplastic effects of commercially available anti-diabetic drugs. Pharmaceuticals 9(2):24

Raja D, Jeganathan NS, Manavalan R (2013) In vitro antimicrobial activity and phytochemical analysis of Cassia auriculata Linn. Int Curr Pharm J 2(6):105-108

Rajagopal A, Rajakannu S (2022) Cassia auriculata and its role in infection / inflammation: A close look on future drug discovery. Chemosphere 287(Pt 3):132345 doi:10.1016/j.chemosphere.2021.132345

Salma B, et al. (2021) Ameliorative Efficacy of the Cassia auriculata Root Against High-Fat-Diet + STZ-Induced Type-2 Diabetes in C57BL/6 Mice. ACS Omega 6(1):492-504 doi:10.1021/acsomega.0c04940

Shanmugam H, Venkatesan RS Determination of antihyperglycemic activity of ethanolic crude leaf extract of cassia auriculata in the streptozocin induced male wistar albino rats. International Journal of Health Sciences(III):5617-5630

 doi:10.20944/preprints202410.0846.v1

Sudharsana A, Sankari R (2017) Antimicrobial activity of Cassia auriculata flower extract on periodontal pathogens: An in vitro study. Journal of Pharmaceutical Sciences and Research 9(3):267

Tiwari AK, Rao JM (2002) Diabetes mellitus and multiple therapeutic approaches of phytochemicals: Present status and future prospects. Current science:30-38

Wagman AS, Nuss JM (2001) Current therapies and emerging targets for the treatment of diabetes. Current pharmaceutical design 7(6):417-450

Xiong R-F, et al. (2023) Three new flavones from the whole plants of Cassia auriculata Linn. and their antiviral activities. Phytochemistry Letters 58:60-64