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Identifying Frequent Prescription Patterns in Siddha Formulations: A Retrospective Analysis Using Data Mining Techniques

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ABSTRACT Non-communicable diseases (NCDs) are a major global public health risk, with diabetes being a significant challenge. Traditional medicines such as Siddha offer alternative therapeutic approaches to diabetes management, emphasising balance and harmony within the body. An approach, known as reverse pharmacology, involves starting with traditional medicine practices and working towards identifying active compounds responsible for therapeutic effects. Understanding prescription patterns in Siddha medicine can provide a basis for designing effective combination therapies in modern pharmacology, where the recent focus shifts towards synergistic drug combinations rather than individual molecules for enhanced therapeutic outcomes. A grounded theory approach was used to develop a theoretical understanding of prescriptions from Siddha classical texts, specifically from two Siddhars, to understand any common pattern in herbal combinations. R software was used to run the Apriori algorithm, to identify frequent item sets and basic prescription patterns. Confidence and lift for the algorithm were set at 0.75 and 3, respectively. More than half of the diabetes prescriptions in this study were purely herbal remedies, and there is a clear pattern in the prescriptions and that varies between Siddhars. This study paves the way for a paradigm shift in medicine, offering a glimpse into how analysing combinations of natural molecules could unlock new avenues for curing disease with the current problem of resistance to multiple drugs.

INTRODUCTION

Non-communicable diseases (NCDs) pose a significant risk to global public health and are responsible for the majority of deaths worldwide. The World Health Organisation (WHO) reported that 74 percent of global deaths were due to NCDs (Non-Communicable Diseases n.d.). They include conditions such as diabetes, cardiovascular diseases, cancer, and respiratory diseases that impose a substantial economic burden on both individuals and healthcare systems.

In recent years, the prevalence of diabetes mellitus has surged globally, posing a significant challenge to public health. One in eleven adults lives with diabetes, and one out of two adults with diabetes is undiagnosed (Home et al. n.d.). This alarming disclosure indicates that the actual risk of diabetes is likely much higher than the current estimates. As per recent global estimates, 80 percent of global adults with diabetes live in low- and middle-income countries (Home et al. n.d.; Kumar et al. 2023). While conventional allopathic medicine continues to play a pivotal role in diabetes management, there is a growing interest in traditional systems of medicine for alternative therapeutic approaches (Bodeker and Kronenberg 2002; Sarsina et al. 2012; Nasreen et al. 2020).

The Siddha system of medicine, with its roots deeply embedded in ancient Siddha medicine and acknowledged as one of the oldest systems of medicine in the world, encompasses a holistic approach that integrates physical, mental, and spiritual well-being (Subbarayappa 1997; Kanagarathinam and Lourdusamy n.d.; Sathasivampillai et al. 2018; Siddha Medicine—Background and Principles and the Application for Skin Diseases - ClinicalKey n.d.; Thenmozhi et al. 2021). Ancient physicians, who practised Siddha medicine, called Siddhars, have passed down their wisdom through

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an oral tradition, enriching and refining it over generations. Siddha medicine emphasises equilibrium and harmony within the body, seeking to address the root causes of ailments rather than merely treating symptoms (Siddha Medicine-Background and Principles and the Application for Skin Diseases - ClinicalKey n.d.; Subbarayappa 1997).

The essence of Siddha medicine lies in its unique pharmacopoeia, which comprises a diverse array of natural substances derived from herbs, minerals, and metals (Sathasivampillai et al. 2017). The distinguishing feature of Siddha medicine is not only the extensive Materia medica but also the intricate prescription patterns and methodologies employed by different Siddhars (Subbarayappa 1997; Sujatha 2007). Each Siddhar brings to the practice a distinct perspective, influenced by their individual experiences, spiritual insights, and mastery over the subtle energies that govern health and disease (Siddha Medicine—Background and Principles and the Application for Skin Diseases - ClinicalKey n.d.).

Reverse pharmacology is a unique method of finding new drugs that starts with observing the effects of traditional medicine in practice with good effects and then progresses towards isolating and confirming the molecules responsible for the desired effect. The integration of traditional medicine into reverse pharmacology acknowledges the complex synergies present in natural remedies, which include combinations of herbs, minerals, and other elements (Patwardhan and Mashelkar 2009; Hao et al. 2014; Suba 2021). Recent FDA guidelines insist diabetic therapeutics give importance to the cardiovascular system. Traditional medicines around the world are based on compound drugs rather than individual herbs or molecules. Many studies in traditional medicine identify medicinal plants, and the molecules in those herbs were proven to be beneficial for the management of type 2 diabetes mellitus, particularly in lowering blood glucose.

Understanding the prescription patterns in Siddha medicine becomes imperative in this context, offering insights into the unique formulations and treatment modalities employed by the Siddha practitioners. This knowledge is not only crucial for preserving and promoting the heritage of Siddha medicine but also for fostering the identification of synergistic effects of herbs that can help in drug discovery.

Comprehending the prescription patterns within Siddha medicine serves as a foundation for formulating impactful combination therapies in contemporary pharmacology, aligning with the current emphasis on synergistic drug combinations to amplify therapeutic effects. Exploring prescription patterns within Siddha medicine can contribute to bridging these gaps, providing a foundation for evidence-based practices, and promoting the integration of Siddha healthcare into the broader medical landscape. This paper seeks to address the gap in the understanding of prescription patterns within Siddha medicine. By analysing the complex ways Siddha practitioners combine herbs and minerals in their prescriptions, this study will uncover valuable knowledge that can benefit both Siddha healthcare and a broader understanding of traditional medicine.

So far, traditional medicine and modern medicine around the world have used association rule mining only to identify prescription patterns among various physicians for a single disease condition using data provided by patients. This study is the first of its kind to explore the patterns of herb combinations in medicine preparations for a single disease by different Siddhars.

Objectives

This research study aims to systematically examine and analyse prescription patterns in Siddha medicine using a grounded theory approach to identify common formulations, and understanding variations in prescription practices between the Siddhars (Siddhar 1: Agathiyar, Siddhar 2: Therayar).

MATERIAL AND METHODS

The study used qualitative design, which is a grounded theory that enables researchers to understand experiences. Data was collected from published classical text books of Siddha medicine using carefully designed search terms by the expert members from Siddha medicine and linguistics.

Search Terms

After conducting an extensive review of Siddha literature, particularly the writings of Siddhar 1 and Siddhar 2 from the classical texts "*Megham*", "*Madhumegham*", and "*Neerizhilivu*", the terms

used to indicate diabetes have been finalised as a search term (Thenmozhi et al. 2021).

Screened classical textbooks of two *Siddhars* were provided in Supplementary file 1. (Anandakumar 1975; Arangarasan 1984; Aughukudam 1934; Desigar 1887; Mohan 2001;mudaliyar 1936; Nayanar 1931; Pandithar 1958; Ramachandran 1998a; 1998b 1995a; 1995b; Ramachandran 2000a; Ramachandran 2000b; Rathina Nayakar & sons 1921; Rangaswamy Mudaliyar & sons 1982; Rathina Nayakar & sons 2012;sigamani 2022; Thiyagarajan 1974; Thiyagarajan 1976; Thiyagarajan 1997; 1975)

Data Collection

Siddhars wrote their findings and teachings in the form of Tamil poems on palm-leaf manuscripts. The preparations of *Siddhars* in songs refer to the methods and techniques used to create various medicines and substances using their knowledge of alchemy, herbs, minerals, and metals in a particular combination. The preparations of *Siddhars* indicated for specific conditions are termed prescriptions, and two or more herbs together found in a medicine preparation are called combinations. These songs often contain coded or hidden meanings that are difficult to understand without a language expert.

Siddha preparations written as poems in palm-leaf manuscripts are later enhanced to printed material. The explanation of those poems was not accurate because of the writing style and the limited knowledge of the people reading them. Hence, the researchers extracted data directly from the poems rather than the explanation. With the help of a linguistic expert, the data from the poem was validated before entering the data. A data extraction sheet has been created to acquire relevant information on medicinal formulations and treatment principles related to diabetes: The data extracted from those poems include the name of the formulation, book, author (Siddhar) of the book, page number, song number, herbs used in the formulations, parts of the plant, metals and animal products, proportion of each, diseases prescribed, adjuvants, dosage, form of drug (tablet, oil, etc.), and mode (internal/external). This has been validated by a Siddha practitioner and linguistic expert.

The database also included the image of the song, and Supplementary File 2 provides a sample image from the book "Agathiyar Sendooram 300" (Ramachandran 1998) (page number 23, paragraphs 4-5). The subject matter expert coded and categorized some variables to standardize the collected data. Explanation of the song: The first paragraph talks about the ingredients and their quantity, while the second paragraph adds information about the adjuvants, dosage of the medicine, and disease conditions.

Herbals, metals, and minerals in classical texts were mentioned in different local terms, and the same herbs may have different geographically localized names. To standardize this, a separate database has been created based on the Siddha textbook "*Mooligai*". Details regarding vernacular and botanical names for herbs and scientific names for metals and animal products, taste for each part of the herbs, potency, and inherent nature were accumulated in the database.

Herbals in the preparations were converted into a format called transactions for further analysis.

Analysis of Basic Information and the Characteristics of Prescriptions

R software was used to analyse the data statistically. First, a general descriptive analysis was performed on the herbs, metals, animal products, and efficacies of the herbs in the prescriptions. Then the association rule algorithm Apriori was used to identify the core herb combinations with stronger relationships.

Association Rules to Screen Core Prescriptions

Apriori is a general-purpose algorithm usually applied to various types of datasets, making it versatile. It has been successfully employed in diverse domains, including market basket analysis, bioinformatics, and healthcare (IEEE Xplore Full-Text PDF n.d.). Apriori tends to generate strong association rules by considering only those with a support and confidence above predefined thresholds. This ensures that the rules produced are meaningful and have a higher likelihood of reflecting true associations in the data (Lakshmi and Vadivu 2017). In this study, the apriori algorithm was employed to identify frequent item sets. To assess the association rules, individual herbs were considered as item sets, and each formulation as a transaction, with support, confidence and lift as measures.

High confidence values indicate a strong correlation between the pairs of rules. Confidence usually starts with a minimum support of 1 and decreases by 5 percent each time until there are at least 10 rules with a minimum confidence of 0.9 or until the support has reached a lower bound of 0.1, whichever occurs first (Lai et al. 2022). In this study, confidence is fixed at a level of 0.75 so that the rules will be strong enough. Lift is expected to be more than 1 to identify rules that are more significant, and was set at 3 to get strong rules.

RESULTS

Diabetes-related preparations were extracted from 13 books out of 33 books screened, wherein 5 books by Agathiyar (Siddhar 1) provided 35 preparations, and 8 books by Therayar (Siddhar 2) provided 31 preparations, adding up to 66 preparations in total, as shown in Table 1. Almost all the preparations were with some herbs, and more than half (52% of the prescriptions) were purely herbal, without any metals or animal by-products. Metals and minerals appeared in around 24 percent of prescriptions, wherein Siddhar 2 used more metallic preparations (35%) than Siddhar 1 (12%). Similarly, the use of animals and their by-products such as honey, milk, ghee, etc. accounted for 33 percent of the preparations, wherein Siddhar 2 (38%) used more animal products than Siddhar 1 (28%). The median number of herbs in preparations was 4 and ranged between 0 and 34. *Tinospora cardifolia, Cassia auriculata, Syzygium aromaticum, Tirikadugu (Piper longum, Piper nigrum* and *dried Zingiber officinale), Costus speciosus* and *Tiribala (Phyllanthus emblica, Terminalia chebula,* and *Terminalia bellarica)* were the top ten herbals used in diabetic prescriptions. The prescriptions of the Siddhars depict some uniqueness wherein Siddhar 1 used *Tinospora cardifolia* the most, followed by *Elettaria cardamomum, Syzyium aromaticum, Calotropis gigantean,* and *Cuminum cyminum,* while Siddhar 2 used *Cassia auriculata, Tiribala, Costus speciousus, Hemidismus indicus, Sesamum indicum,* and *Tirikadugu,* as shown in Figure 1.

Similarly, in terms of metals and minerals, *Arsenic trisulphidum* was the most commonly used, followed by *potassium nitrate, lead,* and *sulphur* for diabetes. Siddhar 1 used *arsenic* twice as much as Siddhar 2.

The output of the Apriori algorithm, which outlines the predominant prescription patterns associated with diabetes as a whole, was shown in Table 2, and rules by two different Siddhars were given in Table 3. The frequently observed combinations for diabetes involve two and three herbs. The two-herb combination includes *Abies spectabilis* and *Cuminum cyminum* demonstrating a lift value of 9.14, and *Pleactranthus vettiveroides* and *Costus speciousus* exhibiting a lift value of 7. Though *Syzygium aromaticum and Elettaria cardamom* have a lift of 6.4 lesser than the previous two combinations, it is more prevalent (11%). In three-herb combinations, *Tinospora cardifolia* was frequently included (9.5%). Remarkably, 86 percent of prescriptions featuring *Syzygium aromaticum* and *Elettaria cardamom* also incorporated *Tinospora cardifolia* with a lift value of 6.4. While looking at four herb combinations, *Costus speciosus, Syzygium aromaticum, and Tinospora cardifolia* were found significantly along with *Glycyrrhiza glabra* in 6.3 percent of prescriptions, with a lift value of 8.

However, this pattern varies across different Siddhars. In Siddhar 1's prescriptions, the same combination of *Syzygium aromaticum* and *Elettaria cardamom,* along with *Tinospora cardifolia,* was found as two and three herb combinations, respectively, and in 18 percent of the prescriptions, boasting a lift value of 5.3 and a confidence level of 1, while *Tirikadugu* or *Syzgium aromaticum* with *Tinospora cardifolia* and *Elettaria cardamomum* showed a significant association with a

Table 1: Siddhar-specific details of prescriptions

S.No.	*Author/ Siddhar*	*Books*	*Books with prescriptions for diabetes*	*Number of songs*	*Median number of herbs in the preparations*
1	Agathiyar	23	5	35	4 (0-36)
2	Therayar	10	8	31	4 (1-24)
		33	13	66	4 (0-36)

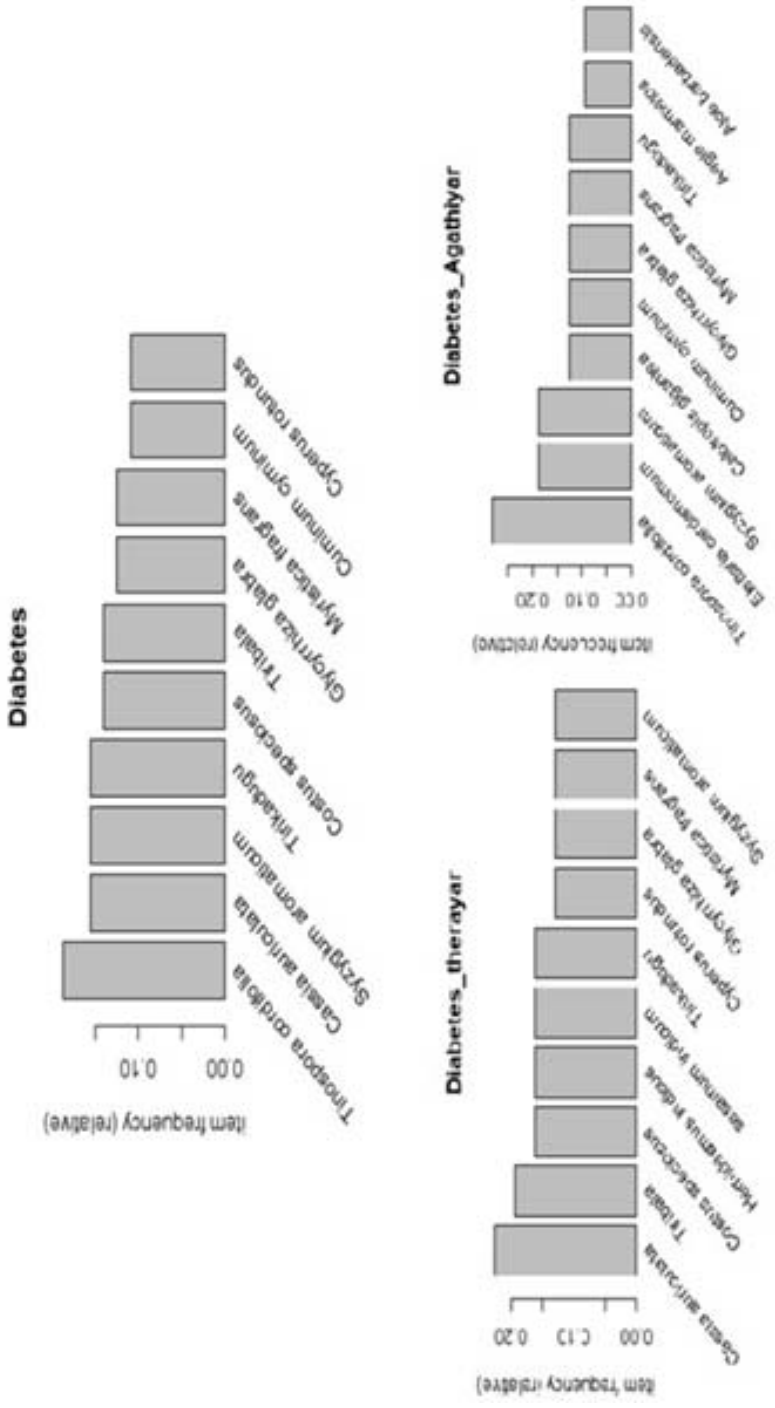

Fig. 1. Top 10 herbs used in Diabetes preparations overall
Source: Authors

Table 2: Top 10 association rules for Diabetes as a whole and by different Siddhars

S.No.	*Left hand side*	*Right hand side*	*Support*	*Confidence*	*Lift*	*Count*
Top Prescription for Diabetes						
[1]	Plectranthus vettiveroides	Costus speciosus	0.0625	1	7.111111	4
[2]	Abies spectabilis	Cuminum cyminum	0.0625	1	9.142857	4
[3]	Elettaria cardamomum	Syzygium aromaticum	0.109375	1	6.4	7
[4]	Elettaria cardamomum	Myristica fragrans, Syzygium aromaticum	0.0625	1	6.4	4
[5]	Costus speciosus	Myristica fragrans, Glycyrrhiza glabra	0.0625	1	8	4
[6]	Myristica fragrans	Tinospora cordifolia, Syzygium aromaticum	0.0625	1	6.4	4
[7]	Cuminum cyminum	Tinospora cordifolia, Syzygium aromaticum	0.0625	1	6.4	4
[8]	Elettaria cardamomum	Tinospora cordifolia, Syzygium aromaticum	0.0625	1	6.4	4
[9]	Elettaria cardamomum	Glycyrrhiza glabra, Syzygium aromaticum	0.0625	1	6.4	4
[10]	Elettaria cardamomum	Tinospora cordifolia, Syzygium aromaticum	0.09375	1	6.4	6

Table 3: Association rules for diabetes by different Siddhar 1 and Siddhar 2

S.No.	*Left hand side*	*Right hand side*	*Support*	*Confidence*	*Lift*	*Count*
Top Prescription for Diabetes						
[1]	Elettaria cardamomum	Syzygium aromaticum	0.1875	1	5.333333	6
[2]	Syzygium aromaticum	Elettaria cardamomum	0.1875	1	5.333333	6
[3]	Elettaria cardamomum	Tinospora cordifolia	0.1875	1	3.555556	6
[4]	Syzygium aromaticum	Tinospora cordifolia	0.1875	1	3.555556	6
[5]	Elettaria cardamomum	Tinospora cordifolia, Syzygium aromaticum	0.1875	1	3.555556	6
[6]	Elettaria cardamomum	Tinospora cordifolia, Syzy gium aromaticum	0.1875	1	5.333333	6
[7]	Syzygium aromaticum	Tinospora cordifolia, Elettaria cardamomum	0.1875	1	5.333333	6
Top Prescriptions of Siddhar 2						
[1]	Limonia acidissima	Cassia auriculata	0.096774	1	4.428571	3
[2]	Plectranthus vettiveroides	Costus speciosus	0.096774	1	6.2	3
[3]	Syzygium aromaticum	Myristica fragrans	0.096774	0.75	5.8125	3
[4]	Myristica fragrans	Syzygium aromaticum	0.096774	0.75	5.8125	3
[5]	Cyperus rotundus	Cassia auriculata	0.096774	0.75	3.32142	3
[6]	Myristica fragrans	Glycyrrhiza glabra	0.096774	0.75	5.8125	3
[7]	Glycyrrhiza glabra	Myristica fragrans	0.096774	0.75	5.8125	3
[8]	Glycyrrhiza glabra	Tirikadugu	0.096774	0.75	4.65	3

lift value of 5.3. Conversely, in Siddhar 2 preparations for diabetes, *Plectranthus vettiveroides and Costus speciousus* emerge as common, with a lift value of 6.2 in 9.6 percent of the prescriptions. *Limonia acidissima* and *Cassia auriculata* stand out as the second most common prescriptions, with a lift value of 4.4 and a confidence level of 1, as shown in Figure 2.

Validation is done using the existing preparations approved by the Siddha formulary of India. For example, "*Avarai choornam*", a preparation for diabetes medication, which uses *Cassia auriculata* and other herbal mixtures that were prepared from dried and powdered plant parts, is commonly used for diabetes and urinary infections (Juan-

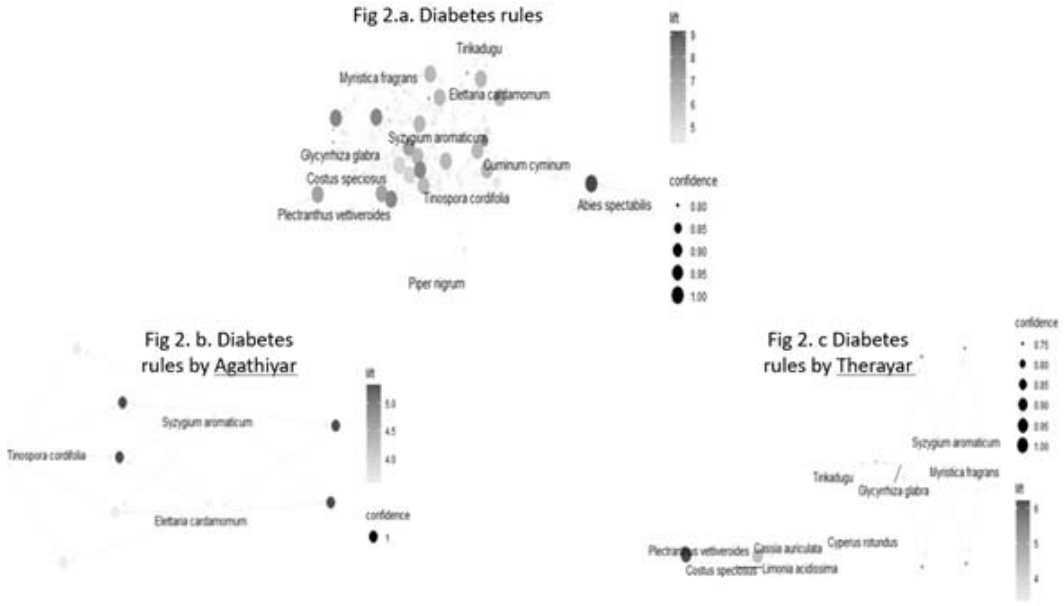

Fig. 2. Prescription rules for diabetes as a whole
Source: Authors

Badaturuge et al. 2011). This preparation by Siddhar 2 containing a combination of *Cassia auriculata* and *Costus speciosus*, is identified as a combination in this study. Another prescription, "*Thetran Vidhai kudineer*" had four herbs, of which *Limonia acidissima* and *Cassia auriculata*, are two ingredients, which are identified as a common pattern in diabetes medicines among Siddhar 2's preparations.

DISCUSSION

Gaining a deeper insight into different methodologies and extracting valuable lessons from past experiences, coupled with crafting a well-suited strategy for the future, is crucial for making a meaningful impact. The Apriori algorithm outlined predominant prescription patterns associated with diabetes, with frequently observed combinations involving two, three, and four herbs, and identified pattern variation among Siddhars. A study by Shu-Rong Yan et al. (2022) found the Apriori algorithm, along with a fuzzy logic, which provided good results in terms of accuracy in prediction and novelty when compared to other cutting-edge methods for huge data sets, and Apriori alone will be sufficient for small datasets.

Siddha medicine has the potential for managing diabetes based on the presence of diverse herbal, mineral, and animal-based medicinal preparations. This study analysed diabetes-related prescriptions in Siddha medicine and identified potential combinations of drugs that occur together. To the researchers' knowledge, this is the first study to explore the herbal combination pattern, in a medicine prescription. Previous studies observed a pattern among the physicians' prescriptions for a single disease condition, whereas in this study, herbal combinations in preparations were explored. A study by Zhang et al. (2005) did not find an association between the diagnostic methods used and the consistency of diagnosis between three different practitioners. Another study by Zhang et al. (2004) found that there was a very mild association with their prescription of herbal formulas for rheumatoid arthritis among the three practitioners.

66 prescriptions were identified, with 35 written by Siddhar 1 and 31 by Siddhar 2. Most of the prescriptions were herbals, with half being purely herbals without any metals or animal by-products.

Metals and minerals appeared in one-fourth of the prescriptions, with Siddhar 2 using one-third of metallic preparations. Animal products were used in 33 percent of the preparations, with Siddhar 2 using 38 percent. The prescriptions were primarily prescribed for diabetes and additionally for some other conditions, as Siddhars provided medicine based on the nature, condition of the patient, and the disease.

The top ten herbs for diabetes were *Tinospora cardifolia, Cassia auriculata, Syzygium aromaticum, Piper nigrum, piper longum, Zingiber officinale, Costus speciosus, Phyllanthus emblica, Terminalia chebula,* and *Terminalia bellarica*. As per Siddha literature, an imbalance in the three basic humours (*Vali, Azhal* and *Aiyam*) of the body will lead to disease (Thenmozhi et al. 2021). Suppressed "digestive fire" was one of the reasons for diabetes, which in turn increases "*Aiyam*". Even in modern concepts, it has been shown that dysbiosis of the gut microbiota is a key factor in the onset and development of a number of metabolic syndromes, including diabetes mellitus (Wu et al. 2011; Xie et al. 2020). So, the drug that decreases the *Aiyam* will be preferred to treat the disease by adding herbs with a bitter and astringent taste to treat diabetes mellitus.

Several phytochemicals, such as alkaloids, glycosides, polysaccharides, peptidoglycans, carbohydrates, and saponin, obtained from herbals have been reported to possess hypoglycaemic activity (Grover et al. 2002). In this study, most of the herbs possess anti-diabetic effects such as antioxidants, hypoglycemic and insulin sensitivity enhancers. *Costus speciousus* is an antidiabetic plant, popularly known as the 'insulin plant', was commonly used by Siddhar 2.

There is some uniqueness found between the two Siddhars in terms of choice of herbals. *Cassia auriculata, Costus speciousus, Sesamum indicum,* and *Hemidesmus indicus* can be seen in use only by Siddhar 2, while *Tinospora cardifolia, Eletteria cardamomum, Calotropis gigantea,* and *Cuminum cyminum* were predominantly used by Siddhar 1.

Siddhar 1 focused on specific botanicals, such as *Tinospora cardifolia, Eletteria cardamomum, Calotropis gigantea,* and *Cuminum cyminum,* which have been scientifically proven to have antidiabetic properties (Grover et al. 2002; Bavarva and Narasimhacharya 2008; Sathasivampillai et al. 2018; Ashokkumar et al. 2020). His herbal medicines aim to reduce blood sugar levels and correct imbalances in the body's *doshas* (humours), using herbs with a bitter and astringent taste preference (Thenmozhi et al. 2021). Siddhar 2, on the other hand, emphasised the healing properties of metals and minerals, such as gold, silver, copper, and sulphur, along with herbals like *Cassia auriculata, Costus speciousus, Sesamum indicum,* and *Hemidesmus indicus,* which are believed to regulate metabolism, enhance pancreatic function, and counteract oxidative stress linked to diabetes (Latha and Pari 2003; Bavarva and Narasimhacharya 2008; Khader et al. 2017; Mohd Fauzi et al. 2017; Maji et al. 2020; Salma et al. 2020). His methods also involve internal alchemy, which involves purifying metals and minerals to restore equilibrium in the body's energies and facilitate healing (Saraswathy 1994; Shrivastava et al. 2015; Arunadevi et al. 2020; Thenmozhi et al. 2021; Paul et al. 2023). Despite their differences, both Siddhar 1 and Siddhar 2's methods converge in their comprehensive understanding of diabetes and prioritisation of natural therapies. Both of their prescriptions used herbals with an astringent and bitter taste, which would reduce the *ayyam* as per Siddha literature.

The combination of *Limonia acidissima* and *Cassia auriculata* identified in Siddhar 2's preparations had enriched fibre, antioxidants, and anthraquinones to provide cues to enhance and sustain reductions in blood glucose levels. This combination also improves insulin sensitivity, facilitates effective glucose utilisation, and manages constipation. The antioxidant and anti-inflammatory properties of these plants may protect pancreatic beta cells, potentially enhancing insulin production. Additionally, the combination may provide extra advantages such as weight management, anti-inflammatory effects, and improved lipid profiles. Some of the herbs in prescriptions had lipid-lowering activity too, and an important feature of diabetes is hyperlipidaemia, which results from the use of lipids instead of glucose (Sugden and Holness 2011; Vesa et al. 2020). When *Costus speciousus* is added to the above combination that possesses anti-hyperglycemic, antihyperlipidemic, and antioxidative effects, this is important in the management of diabetes and its associated effects (Bavarva and Narasimhacharya 2008; Maji et al. 2020). These herbal drugs, as a combined effect, react in different mechanisms and ultimately protect the β-

cells of diabetes patients and reduce the level of glucose in the blood (Gaonkar and Hullatti 2020).

Another combination identified, in Siddhar 2's preparations of *Myristica fragrans* and *Glycyrrhiza glabra* is also important, which is supported by a study done by Sen and Singh (2021) wherein the *Glycyrrhiza glabra* extract is quite effective against hyperglycaemia and the associated free iron-mediated oxidative stress. This combination may lead to improved blood sugar control and increased insulin sensitivity. *Glycyrrhiza glabra* root's glycyrrhizin may mimic insulin effects, aiding in glucose uptake, while *Myristica fragrans* antioxidants could protect pancreatic beta cells, supporting insulin production. Additionally, *Glycyrrhiza glabra* root has anti-inflammatory and immune-modulating benefits, potentially advantageous for individuals with diabetes facing specific complications (Murray 2020).

Antidiabetic compounds with antioxidant properties could be more effective, as free radicals play a role in causing diabetes and its complications (Modak et al. 2007). This study found that Siddhar 1 used more combinations with *Tinospora cordifolia (Guduchi)*, which is known for its hypoglycemic, blood-purifying, and digestive-stimulating properties, as the mainstay of his antidiabetic prescriptions (Grover et al. 2002; Gaonkar and Hullatti 2020). Siddhar 1's approach emphasised not just lowering blood sugar but also restoring balance within the body's doshas (humours). For example, the top rule by Siddhar 1 shows *Tinospora cardifolia, Elettaria cardamomum* (black cardamom) and *Syzygium aromaticum* (cloves), with their digestive-aiding and carminative qualities, complement *Tinospora cardifolia*, action (Grover et al. 2002; Adefegha and Oboh 2012; Sathasivampillai et al. 2018; Ashokkumar et al. 2020; Do et al. 2020; Gaonkar and Hullatti 2020; Cheshmeh et al. 2022).

CONCLUSION

Apriori algorithm identified significant herbal combinations, highlighting synergies potentially responsible for enhanced outcomes. The *Limonia acidissima-Cassia auriculata* combination in Siddhar 2 formulations offers potential for sustained blood sugar reduction, improved insulin sensitivity, and antioxidant protection. Siddhar 1 focuses on restoring *doshic* balance, while Siddhar 2 emphasises on metabolic regulation and oxidative stress defence. Synergistic effect of the combinations identified had an anti-diabetic effect and increased digestive action. This suggests a holistic approach to manage diabetes, addressing both physiological imbalances and cellular damage.

The researchers' results demonstrate the immense value of the Apriori algorithm in finding meaningful frequent rules and association rules. More studies are required to verify the performance and accuracy of this algorithm and its variations, which can enable the use of Apriori algorithm to unlock the pattern in different aspects of Siddha medicine.

RECOMMENDATIONS

The study findings highlight the vast therapeutic potential of Siddha medicine in diabetes management. Further research is needed to confirm the mechanisms of action and efficacy of these unique herbal combinations, which can pave the way for the evidence-based integration of Siddha therapies into mainstream healthcare. In vitro, in vivo and docking studies are recommended to be carried out to confirm the results in the lab.

LIMITATIONS

This study is done with a limited number of books of Agathiyar (Siddhar 1) and Therayar (Siddhar 2) to which the researchers had access from some libraries of siddha institutes. Validation of rules identified with currently approved medicine for treatment is limited. This has to be extended with more books of Agathiyar and Therayar to get more precise and accurate results. Nearly half of the preparations are with metals and inorganic substances, and interactions of herbs and minerals may be different than a prescription with pure herbals, and this needs to be addressed further.

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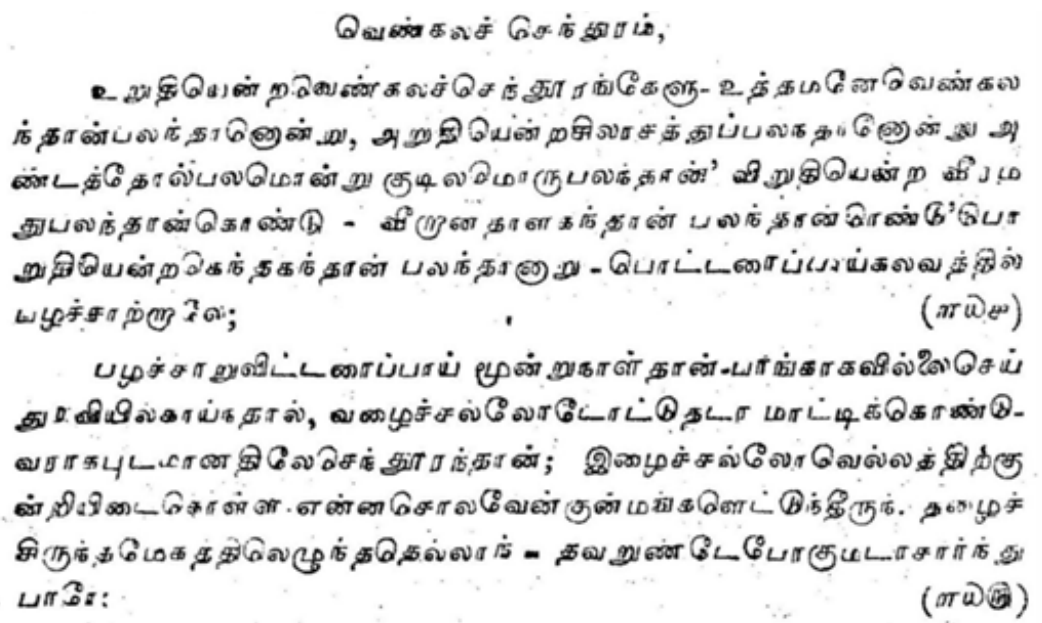
Supplementary file 1: Books considered for the study

Book id (Agathiyar)	*Siddhar 1 (Agathiyar)*	*Siddhar 2 (Therayar)*	*Book id (Therayar)*
Mohan 2001	Agathiyar Vaithya vallathi	Therayar vaithiya kaaviyam 1500	
Ramachandran 1998	*Agathiyar Vaithya rathna surukkam 360*	Therayar Thyila varka surukkam	Pandithar 1958
Rangaswamy Mudaliyar Sons 1936	*Agathiyar idaipagam 400*	Theran karisal	
Agathiyar-Paripashai-thirattu	Therayar maha-karisal	Thiyagarajan 1974	
Desigar 1887	Agathiyar paripooranam 400	Therayar vaagadam	Thiyagarajan 1976
Rathina Nayakar and Sons n.d.	Therayar kappiyam	Anandakumar 1975	
Agathiyar kanma kandam 300	Agathiyar 12000 Volume 1-2	Theran taru 350	Thiyagarajan 1997
Ramachandran 1995a, 1995a, 1995b	Agathiyar poojavithi 200	Therayar venba	Thiyagarajan 1975
	Agathiyar deetcha vithi 200	Therayar vaithiyam	
	Agathiyar Maha diravagam 800	Therayar karisal 300	Nayanar 1931
Sigamani 2022	Agathiyar Ghana amutham		
Arangarasan 1984	Agathiyar Pancha kavya nigandu		
Rangaswamy Mudaliyar Sons 1982	Agathiyar Vaithya sillarai Kovai		
Ramachandran 1998	Agathiyar Sendhooram 300		
Aughukudam 1934	Agathiyar Poorna sooothiram 216		
Ramachandran 2000b	Agathiyar ranavaithiyam Agathiyar vaithiya sinthamani		
Rathina Nayagar Sons (n.d.)	Agathiyar Thailamuraigal		
Ramachandran 2000a	Agathiyar pallu 200		

Supplementary file 2



வெண்கலச் செந்தூரம்,

உறுதியென்றவெண்கலச்செந்தூரங்கேளு- உத்தமனேவெண்கல
ந்தான்பலந்தானென்று, அறுதியென்றசிலாசத்துப்பலந்தானென்று அ
ண்டத்தோல்பலமொன்று குடலேமொருபலந்தான்' விறுதியென்ற வீரம
துபலந்தான்கொண்டு - வீரனதாளகந்தான் பலந்தான்கொண்டுபொ
றுதியென்றகெந்தகந்தான் பலந்தானறு - பொட்டனைப்பாய்கலவத்தில்
பழச்சாற்றிலே; (எண்பது)

பழச்சாறுவிட்டனைப்பாய் மூன்றுகாள்தான்-பார்ங்காகவில்லேசெய்
துவியிலகாய்ந்தால், வழைச்சல்லோடோட்டுதடா மாட்டிக்கொண்டு-
வராகபுடமானதிலேசெந்தூரந்தான்; இழைச்சல்லோவெல்லத்திற்கு
ன்றியிடைசொள்ள.என்னசொலவேன்குன்மங்களைட்டுந்தீருங். தழைச்
சிருந்தமேகத்திலெழுந்தெல்லாங் - தவறுண்டேபோகுமடாசார்ந்து
பாரே: (எண்பத்)