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RESEARCH ARTICLE

Clinical Safety of Selected Ayurvedic Formulations in Diabetes Mellitus–A Pharmaco-epidemiological Perspective

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ABSTRACT

Background: Ayurveda is an ancient system of medicine popularly practiced in India. Many types of researches on various disease conditions have been conducted, but the reporting of clinical safety is negligible. Nowadays, the safety of the drugs is as important as efficacy.

Objective: Reporting of clinical safety of certain Ayurvedic formulations which were trialed in diabetes mellitus (DM) *(Madhumeha*) through four multicentre open-label clinical studies at Research centers of Central Council for Research in Ayurvedic Sciences situated in different geographical regions.

Materials and Methods: The analyzed data of four different clinical studies were critically evaluated to assay the safety profile of Ayurvedic herbal/herbomineral formulations namely, *Saptavimshatika Guggulu* and *Haridra Churna, Nisha Amalaki* and *Chandraprabha Vati, Nisha katakadi kashaya* and *Yashada Bhasma, Gokshuradi Guggulu* and *Guduchi Churna*. In all the studies, the drugs were administered for three months. Safety assessments have been done through analyzing laboratory parameters like Liver function test and renal function test before and after the trial period. Paired sample t-test has been used to compare the mean changes of these parameters from baseline to the end of the trial period. Any adverse drug reaction (ADR)/ adverse events (AE), if any, were noted. Patient compliance was maintained during the study.

Result: The results revealed that all the safety laboratory parameters were within the specified limits and no ADR was reported during the entire study period.

Conclusion: All the trialed drugs used on the subjects of *Madhumeha* are clinically safe and tolerable, in spite of the subjects belonging to different geographical locations, *Prakriti,* gender and age groups.

Significance: Above findings will assure the researchers as well as the public about the safety of these Ayurvedic formulations.

Keywords: Ayurvedic herbal/herbo-mineral formulations, Clinical safety, Diabetes mellitus, *Madhumeha*, Pharmaco-epidemiological study.

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INTRODUCTION

In India out of a population of 1.3 billion, over 60 million patients are suffering from DM. The number of patients of diabetes is expected to increase to 109 million by 2035 out of an estimated population of 1.5 billion.[1]

Diabetes mellitus (DM) appear to have a lot of similarities in etiological factors, classification, clinical symptoms, complications and treatment modalities with *Madhumeha* amongst the twenty types of *Prameha* described in Ayurveda.

Over the time, DM can increase the risk of heart disease and stroke, cause neuropathy, retinopathy, and nephropathy. Morbidity and mortality from cardiovascular disease are two to five times higher in persons with diabetes.[2] Type I DM is managed with insulin injections,[3] and type II DM may be treated with medications. Metformin is generally recommended as a first-line treatment for type II diabetes.[4]

Nowadays with increased reporting of toxicity of drugs have been acknowledged after meta-analysis of multiple clinical trial data[5-7] assurance regarding the safety of drugs is a prime concern for health conscious people. Drug resistance, hypersensitivity with insulin, drug intolerance, and fear to hypo and hyperglycemic episode with drugs are certain setbacks of anti-diabetic modern medicines.[8-11] *Pramehaghna* Ayurveda drugs have *Rasayana* (rejuvinative), *Tridosha Shamaka, Lekhana* properties by which Ayurvedic drugs are efficacious and most importantly safe so as to maintain overall health in people with diabetes. Ayurvedic drugs hence may suffice in the long-term management of DM.[12]

But sometimes sporadic incidences regarding the toxicity of Ayurvedic herbo-mineral drugs are reported[,13] and it is observed that the drugs consumed were usually not standardized. A study reported that one-fifth of both US manufactured and Indian-manufactured Ayurvedic medicines purchased via the Internet contained detectable lead, mercury, or arsenic.[13] In rebuttal through a press release, Ministry of AYUSH (then Department of AYUSH, Ministry of Health and Family Welfare) mentioned that there are many flaws and bias in reporting the study and it was observed that the medicines were sold through the internet, which does not indicate the source of their origin.[14]

Further, a lot of clinical studies conducted so far report mainly on the efficacy of Ayurvedic formulations, but only a few emphasize on the safety of the drugs. The Central Council for Research in Ayurvedic Sciences (CCRAS) has conducted four different clinical studies on DM to study the clinical efficacy and safety of various Ayurvedic formulations viz. *Saptavimshatika Guggulu* and *Haridra Churna, Nisha Amalaki* and *Chandraprabhavati, Nisha Katakadi Kashaya* and *Yashada Bhasma, Gokshuradi Guggulu* and *Guduchi Churna*. This manuscript is envisaged to assess the clinical safety of the mentioned Ayurvedic formulations used on DM.

OBJECTIVE

Critical analysis and presentation of clinical safety outcomes of eight classical Ayurvedic formulations viz. *Saptavimshatika Guggulu* and *Haridra Churna, Nisha Amalaki* and *Chandraprabha Vati, Nisha katakadi kashaya* and *Yashada Bhasma, Gokshuradi Guggulu* and *Guduchi Churna* administered in four multicenter open-label clinical studies on type II Diabetes.

MATERIALS AND METHODS

The detail study protocol, information about the trialed drugs and analyzed data of four clinical studies were assessed. The studies were conducted under IMR (intra mural research) program of CCRAS and they are:
Study 1: "Clinical evaluation of *Saptavimshatika Guggulu* and *Haridra Churna* in the management of type II DM" conducted at three centres;
Study 2: Clinical evaluation of *Nisha Amalaki* and *Chandraprabha Vati* in the management of type II DM (*Madhumeha*)" conducted at four centres;
Study 3: "Clinical evaluation of *Nisha Katakadi Kashaya* and *Yashada Bhasma* in the management of type II DM (*Madhumeha*)" conducted at four centres; and
Study 4: "Clinical evaluation of *Gokshuradi Guggulu* and *Guduchi Churna* in the management of type II DM" conducted at one centre.

Each study was single arm prospective study except study-3 which had three groups. The study protocol and related documents of all the studies were reviewed and approved by the Institutional Ethics committee of all the participating centers. The studies were conducted following Schedule-Y of Drugs and Cosmetics Act, India, amended in 2005 and Indian Council of Medical Research (ICMR) ethical guidelines for biomedical research on human participants, adapted from World Medical Association (WMA)-Declaration of Helsinki. The participants of all the studies were informed about the study procedures. The eligibility criteria were checked precisely, and informed consent forms were also signed by the participants before their enrolment in the study. The formulations fulfilling the physicochemical standards and quality parameters were procured from good manufacturing practice (GMP) certified Ayurveda pharmaceutical companies complying the standard operative procedures for the preparations of the trial drugs mentioned in Ayurvedic pharmacopeia of India. In all the studies the trial drugs were administered for 84 days. All studies have been registered in the Clinical Trial Registry of India (Study 1: CTRI/2012/03/002537; Study 2: CTRI/2016/05/006968; Study 3: CTRI/2014/05/004613 and Study 4: CTRI/2014/09/005048).

Selection Criteria of the Participants

Inclusion Criteria

Participants of either sex aged between 30 to 65 years, who were diagnosed to be type-II DM by either having glycosylated haemoglobin (HbA1c) ≥ 6.5% or fasting blood sugar (BS-F) > 126 mg% or post prandial blood sugar (BS-PP) >200 mg% or diabetics who were on lifestyle modifications (on diet management and physical exercise) or subjects who were on tablet metformin (up to 2 gm/day) and who were willing to participate in the clinical trial for 14 weeks were included in the study.

Exclusion Criteria

Patients suffering from the complications of diabetes like diabetic neuropathy, diabetic nephropathy, and diabetic retinopathy; past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia in the last six months, uncontrolled hypertension (>160/100 mm of Hg); major systemic illness necessitating long term drug treatment (Rheumatoid arthritis, Psycho-Neuro-Endocrinal disorders, etc.); prolonged (> 6 weeks) medication with corticosteroids, antidepressants, anticholinergics, severe renal or hepatic disorders; evidence of malignancy; alcoholics and/or drug abusers; history of hypersensitivity to any of the trial drugs or their ingredients; pregnant and lactating woman, woman on oral contraceptives therapy and who completed participation in any other clinical trial during the past six months or other conditions as per the Investigator may jeopardize the study were excluded from the trial.

A brief description of studies conducted for the management of DM is given in Table 1.

Detailed Profile of Study Interventions

Saptavinshatika Guggulu[15] has detoxifying and antioxidant properties. *Nisha Amalaki*[16] is mentioned as the drug of choice for *Prameha*. *Haridra Churna*[17] and *Amalaki* are *Tridoshashamka*. *Haridra* is a blood purifier while *Amalaki* has a potent *Rasayana* effect. *Chandraprabha Vati*[18] is a rejuvenating compound having hypoglycemic activity. It is *Tridoshashamak, Balya*, and diuretic. It reduces inflammation in the urinary tract. Ingredients like *Musta, Triphala, Shilajita*, and *Guggulu* help to treat dyslipidemia. *Yashad Bhasma*[19] is indicated in *Prameha*. *Nisha katakadi Kashaya*[20] has antihyperglycaemic and antioxidant property. *Yashada Bhasma* contains submicronic or nanoparticles that enhance bioavailability and is known to be effective at very low doses and devoid of toxic effects.[21] *Gokshuradi Guggulu*[22] *is* a commonly used drug for *Mutravaha Srotas*. *Gokshura* is the main ingredient and has *Rasayan*a properties. *Guggulu* is a *Rasayana*, has *Lekhana* and *Tridoshahara* effect. *Guduchi* has hypoglycemic activity, and *Guduchi Churna*[23] is mentioned as a drug of choice in *Prameha*.

Study Procedures

In all the studies, at baseline, the detail demographic data, *Prakriti* (body constitution) of all the enrolled participants were collected in the case record form. The trial medicines were dispensed at each visit and follow up was done every two weeks to record the onset of any adverse drug reaction/adverse events during the 84 days of the treatment period. Clinical assessment through diabetes symptoms score (DSQ) assessed with the help of VAS (0-10), health-related quality of life (HRQoL) recorded at baseline and end of the 84th day by using RAND, 36 items short form health survey (SF-36) questionnaire.

Safety Assessment

Clinical safety was assessed based on the safety laboratory parameters i.e. assessment of liver function and kidney functions at the baseline and end of the intervention period (i.e. 84 days) in each study. Further, the data on

Table 1: Details of the study period, drugs, dose and duration of the studies on diabetes mellitus

Name of the study	*Study period*	*Sample size*	*Study drugs*	*Dosage schedule*
Study 1 Clinical evaluation of *Saptavimshatika Guggulu* and *Haridra Churna* in the management of type-II Diabetes Mellitus	2011–2012	144	*Saptavimshatika Guggulu*	01 gm twice a day with lukewarm water
			Haridra Churna	03 gm twice a day with lukewarm water
Study 2 Clinical evaluation of *Nisha Amalaki* and *Chandraprabha Vati* in the management of type II Diabetes Mellitus *(Madhumeha*)	2013–2014	187	*Nisha Amalaki*	03 gm twice a day lukewarm water
			Chandraprabha Vati	01 gm twice a day with lukewarm water
Study 3 Clinical evaluation of *Nisha Katakadi Kashaya* and *Yashada Bhasma* in the management of type-II Diabetes Mellitus (*Madhumeha*)	2013–2016	189	Group 1 *Nisha Katakadi Kashaya*	15 mL twice a day diluted with 45 ml lukewarm water before food
			Group 2 *Yashada Bhasma*	125 mg thrice a day with lukewarm water
			Group 3 *Nisha Katakadi Kashaya* and *Yashada Bhasma*	15 mL twice a day, diluted with 45 mL lukewarm water, 125 mg thrice a day with lukewarm water
Study 4 Clinical evaluation of *Gokshuradi Guggulu* and *Guduchi Churna* in the management of type II diabetes mellitus	2015–2016	50	*Gokshuradi Guggulu*	01 gm twice a day with lukewarm water
			Guduchi Churna	03 gm twice a day with lukewarm water

adverse drug reaction and adverse drug events reported if any, during the treatment period were also recorded in the case record form.

Statistical Analysis

Safety laboratory parameters were analyzed at the beginning and the end of the trial period. And were compared using a paired t-test. All statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 15.0. (Ref. SPSS Inc. Released 2006. SPSS for Windows, Version 15.0. Chicago, SPSS Inc.)

RESULTS

The data of 144, 187, 189 and 50 participants were analyzed for the study no. 1, 2, 3, and 4 respectively. The demographic profiles viz. gender, education, socio-economic status, dietetic habit, *Prakriti*, etc. of the participants are summarized in Table 2.

Effect of the Drugs on Vital Parameters

The blood pressure, pulse rate, etc. were analyzed and found that there are no abnormal changes in these parameters at the end of the treatment. The details are presented in Table 3.

Effect of the Trial Drugs on Safety Laboratory Parameters

The safety laboratory parameters like liver function test and kidney function tests were carried out in all the studies at baseline and at the end of the treatment to know the clinical safety of trial drugs. The detail data of each study are presented in Tables 4 and 5.

DISCUSSION

The study aimed to assess the safety of Ayurvedic formulations viz. *Saptavimshatika Guggulu* and *Haridra Churna, Nisha Amalaki* and *Chandraprabha Vati, Nisha Katakadi Kashaya* and *Yashada Bhasma, Gokshuradi Guggulu* and *Guduchi Churna* administered on type II diabetes patients of four multicentre open-label clinical studies. From the study, it is observed that all the laboratory safety parameters were found to be within the normal range during the four clinical trials. Significant improvement in clinical symptoms and the patient's well being without any

Table 2: Demographic profile of the patients in all the four clinical trials

Demographic profile	*Study 1(n = 144) n (%)*	*Study 2 (n = 187) n (%)*	*Study 3 (n = 189) n (%)*	*Study 4 (n = 50) n (%)*
Gender				
Male	96 (66.7)	89 (47.6)	89 (47)	40 (80.0)
Female	48 (33.3)	98 (52.4)	100 (52.9)	10 (20.0)
Education				
Not able to read and write	20 (13.96)	21 (11.2)	15 (7.93)	02 (4.0)
Literate	124 (86.1)	166 (88.8)	174 (92.06)	48 (96.0)
Socio-economic status				
Above poverty line	131 (91.0)	166 (88.8)	103 (54.5)	49 (98.0)
Below poverty line	13 (9.0)	21 (11.2)	86 (4.55)	01 (2.0)
Diet				
Vegetarian	68 (47.2)	100 (53.5)	52 (27.51)	31(62.0)
Non-vegetarian	76 (52.8)	87 (46.5)	137 (72.5)	19(38.0)
Prakriti				
Vataja		1 (0.5)	1 (0.5)	
Pittaja		7 (3.7)	12 (6.3)	
Kaphaja			2 (1.0)	
Vata-Pittaja	75 (52.1)	32 (17.0)	47 (24.8)	23 (46.0)
Pitta-Kaphaja	58 (40.3)	139 (73.9)	117 (61.9)	27 (54.0)
Vata-Kaphaja	9 (6.3)	9 (4.8)	8 (4.2)	
Participants completed the trial from different Geographical locations				
Odisha (Bhubaneswar)	54 (37.5)			
Rajasthan (Jaipur)	38 (26.38)			
Himachal Pradesh (Mandi)	52 (36.11)		57 (30.15)	
New Delhi		47 (25.13)		
Assam (Guwahati)		50 (26.73)		
Maharashtra (Nagpur)		41 (21.9)		
Gujarat (Ahmedabad)		49 (26.20%)		
Tamil Nadu (Chennai)			56 (26.69%)	
Andhra Pradesh (Vijayawada)			59 (31.21%)	
Kerala (Cheruthuruthy)			17 (8.99%)	
Madhya Pradesh (Gwalior)				50 (100%)

Table 3: Shows the effect of the drugs on vital parameters

Vital parameters	*Blood pressure*				*Pulse rate*	
	Baseline		*84th Day*			
Study	*Systolic*	*Diastolic*	*Systolic*	*Diastolic*	*Baseline*	*84th Day*
Saptavimshatika Guggulu and *Haridra Churna* (*n* = 144)	124 ± 13.9	80.7 ± 8.5	121.2 ± 9.3	78.6 ± 6.4	78.4 ± 6.1	77.5 ± 5.9
Nisha Amalaki and *Chandraprabhavati* (*n* = 187)	123 ± 11	79.5 ± 4.9	119.6 ± 10.4	79.2 ± 5.1	76.3 ± 6.1	77.8 ± 5.5
Nisha Katakadi Kashaya and *Yashada Bhasma* (*n* = 189)	121.3 ± 8.83	78.9 ± 6.67	119 ± 10.2	77.4 ± 6.5	80.2 ± 4.6	77.4 ± 5.1
Gokshuradi Guggulu and *Guduchi churna* (*n* = 50)	120 ± 7.5	77.7 ± 6.7	119 ± 8.4	77.3 ± 7.4	77.6 ± 5.7	78 ± 5.8

Data: Mean, ± SD

reporting of adverse drug reactions or adverse events by the study participants were observed during the study period. Moreover, no adverse events by metformin interaction with the Ayurvedic formulations *Saptavimshatika Guggulu* and *Haridra Churna* and *Nisha Amalaki* and *Chandraprabha Vati* was reported in the subjects who were on metformin upto 2gm/day during the study.

For *Saptavimshatika Guggulu* and *Haridra churna*, most of the safety parameters were found to be statistically significant. Serum uric acid, creatinine, urea, total protein, and albumin were found to be statistically insignificant. For *Nisha Amalaki* and *Chandraprabha Vati*, serum uric acid and serum cholesterol were found to be statistically significant, and all other safety parameters were in normal range. For *Nisha Katakadi Kashaya* and *Yashada Bhasma*, all the safety parameters were found in the normal range during the study, and there was no significant change observed in Renal function test, Liver function test when compared with baseline data to end of treatment within the group and also in comparison among the three groups. For *Gokshuradi Guggulu* and *Guduchi Churna* Blood sugar and aspartate aminotransferase (AST) is found to be statistically significant while other safety parameters are found to be in normal range.

In the present study, both herbal and herbomineral formulations are administered. *Saptavinshatika Guggulu, Chandraprabha Vati* and *Yashada Bhasma* are herbomineral formulations while *Haridra Churna, Nisha Amalaki, Nisha Katakadi Kashaya, Gokshuradi Guggulu,* and *Guduchi Churna* are herbal formulations. Ayurveda emphasizes mainly on safe treatment and hence factors like *Prakriti* (constitution), *Guna* (properties), *Karma* (actions), *Prabhava* (effect), *Desha* (habitat),[24] *Ritu* (Season/time of collection),[25] Part of plant used for collection,[26] method of collection,[27] storage of collected drugs[28] and afterwards their pharmaceutical processing is considered before preparing herbal formulations. By taking into account all these factors along with enhancement of potency of the drug it is made fit for

Table 4: Shows the effect of the trial drugs of study 1, 2 and 4 on laboratory parameters for safety profile of the participants

	Saptavimshatika guggulu and Haridra Churna (n = 144)		*Nisha Amalaki and Chandraprabha Vati (n = 187)*		*Gokshuradi guggulu and Guduchi Churna (n = 50)*	
Parameters	*Baseline*	*84th day*	*Baseline*	*84th day*	*Baseline*	*84th day*
Liver function test						
AST (IU/L)	26.6 ± 8.2	23.1 ± 9.3	28.5 ± 14.4	26.0 ± 12.33	31.9 ± 3.5	38.83 ± 4.7
ALT (IU/L)	27.8 ± 12.5	25.5 ± 8.2	31.05 ± 20.0	29.16 ± 18.9	35.3 ± 3.0	39.99 ± 5.2
Total protein (gm/dL)	6.9 ± 0.6	6.97 ± 0.4	7.4 ± 0.4	7.69 ± 4.39	7.5 ± 0.1	7.62 ± 0.1
S. albumin (gm/dL)	7.7 ± 41.7	4.4 ± 0.6	4.44 ± 0.3	4.4 ± 0.3	4.6 ± 0.0	4.6 ± 0.04
S. globulin (gm/dL)	2.7 ± 0.44	2.6 ± 0.5	2.98 ± 0.46	2.97 ± 0.44	2.9 ± 0.1	3.02 ± 0.07
Conjugated bilirubin (mg/dL)	0.3 ± 0.25	0.4 ± 0.3	0.25 ± 0.17	0.24 ± 0.19	0.2 ± 0.01	0.2 ± 0.01
Unconjugated bilirubin (mg/dL)	0.5 ± 0.3	0.4 ± 0.3	0.39 ± 0.27	0.37 ± 0.26	0.65 ± 0.04	0.6 ± 0.05
S. alkaline phosphatase (IU/L)	168.1 ± 73.0	193 ± 59.5	87.80 ± 24.1	87.5 ± 24.6	88.9 ± 3.65	85.5 ± 4.1
Renal function Test						
Blood urea (mg/dL)	25.96 ± 6.0	26.33 ± 6.0	20.63 ± 5.8	21.1 ± 7.6	19.62 ± 0.7	20.2 ± 0.7
S. creatinine (mg/dL)	0.93 ± 0.16	0.94 ± 0.1	0.72 ± 0.19	0.75 ± 0.37	0.94 ± 0.03	0.93 ± 0.03
S. uric acid (mg/dL)	4.7 ± 1.2	4.85 ± 1.3	4.88 ± 1.13	4.7 ± 1.12	3.98 ± 0.1	4.0 ± 0.14

Data: Mean, ± SD

Table 5: Shows effect of the trial drugs of Study- 3 on laboratory parameters for safety profile of the participants

	Nisha Katakadi Kashaya (n = 63)		*Yashada Bhasma (n = 62)*		*Nisha Katakadi Kashaya and Yashada Bhasma (n = 64)*	
Parameters	*Baseline*	*84th day*	*Baseline*	*84th day*	*Baseline*	*84th day*
Liver function test						
AST (IU/L)	24.9 ±1.4	23.0 ± 6.0	25.5 ± 8.2	25.35 ± 10.3	26.2 ± 9.5	24.4 ± 8.8
ALT (IU/L)	32.3 ± 2.6	32.8 ± 4.04	32.4 ± 15.1	34.23 ± 14.3	33.3 ± 1.45	35.0 ± 4.2
Total protein (gm/dL)	7.20 ± 0.5	7.0 ± 0.5	7.13 ± 0.5	7.1 ± 0.5	7.2 ± 0.5	7.04 ± 0.5
S. albumin (gm/dL)	4.1 ± 0.34	4.04 ± 0.3	4.01 ± 0.3	3.99 ± 0.3	4.11 ± 0.3	4.07 ± 0.4
S. globulin (gm/dL)	3.1 ± 0.5	2.97 ± 0.5	3.1 ± 0.5	3.1 ± 0.5	3.08 ± 0.5	3.04 ± 0.45
Conjugated bilirubin (mg/dL)	0.2 ± 0.05	0.2 ± 0.05	0.2 ± 0.74	0.2 ± 0.5	0.2 ± 0.06	0.17 ± 0.05
Unconjugated bilirubin (mg/dL)	0.5 ± 0.2	0.5 ± 0.2	0.53 ± 0.2	0.5 ± 0.2	0.5 ± 0.22	0.5 ± 0.15
S. alkaline phosphatase (IU/L)	124.65 ± 63.6	123.22 ± 65.36	123.13 ± 60.01	132.4 ± 56.7	133.3 ± 71.5	134.6 ± 67.5
Renal function Test						
Blood urea (mg/dL)	25.8 ± 6.3	24.4 ± 6.1	25.2 ± 5.1	24.2 ± 5.64	24.4 ± 6.6	25.5 ± 5.6
S. creatinine (mg/dL)	0.94 ± 0.15	0.9 ± 0.2	0.94 ± 0.1	0.95 ±0.15	0.95 ± 0.14	0.94 ± 0.1
S. uric acid (mg/dL)	6.15 ± 6.85	5.05 ± 0.9	4.95 ± 1.1	4.97 ± 1.02	5.04 ± 0.9	5.1 ± 0.9

Data: Mean, ± SD

therapeutic administration.[29] It is by proper processing that even a poisonous or *Tikshna* drug can be converted into an excellent medicine.[30] Description regarding time[31] and route of drug administration[32] are also found in Ayurveda classics which are equally important to obtain maximum benefits without any untoward effects. To ensure and enhance the quality of Ayurveda medicines, the government of India has notified GMP under schedule T of the Drugs and Cosmetics Act, 1940 which also ensures raw materials used in the manufacture of drugs are authentic, of prescribed quality and are free from the pathogen. Medicaments are prepared in Ayurveda after carefully assessing the combined effect, time effect, analytical approach and modification of original qualities. Mineral drugs viz. *Makshika, Yashada, Loha and Shilajita*, in the herbo-mineral formulation administered, are purified and prepared as *Bhasmas* through certain strict procedures such as *Shodhana* (purification and processing) and *Marana* (incineration).[33] The *Bhasmas* prepared are examined as per certain criteria mentioned and then in small doses, are used in Ayurveda formulations. The adverse drug reactions for herbo-mineral formulations (*Bhasmas*) described in Ayurveda appear only if the stringent procedures for manufacturing and certain precautionary measures mentioned in Ayurveda are not followed properly. Any complications could be observed if the drug is too old and reached its expiry date or is not prepared properly or because of improperly given Samskars.[34] Hence the findings of study corroborate that the herbal and herbomineral Ayurvedic formulations assessed in the four clinical studies for the management of DM are clinically safe and effective.

CONCLUSION

The findings of the present study suggest that the Ayurveda formulations viz. *Saptavimshatika Guggulu* and *Haridra Churna, Nisha Amalaki* and *Chandraprabha Vati, Nisha Katakadi Kashaya* and *Yashada Bhasma*, and *Gokshuradi Guggulu* and *Guduchi Churna*, administered in the four clinical trials do not show any adverse events and adverse drug reactions and are clinically safe, effective and tolerable in the management of DM. Hence, it can be concluded that these Ayurvedic formulations are safe therapeutic means in type II DM patients irrespective of their *Prakriti*, gender, age groups, socioeconomic status, and geographic regions.

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हिंदी सारांश

मधुमेह (डायबीटीज मेलाईटस) में चयनित आयुर्वेदिक योगों कि नैदानिक सुरक्षा

शारदा ओता, प्रदीप दुआ, दीप एस साहु, सुरिन्दर के शर्मा, बिनोद के भाराली, विलास व्ही. गांगुर्डे, उदर आर एस नम्बुरी, सीमा जैन, श्रीनिवास पीटा, सुभोष वाराणसी, वलिपरमविल सी दीप, ललीता शर्मा, आरती शीतल, श्रुति खंडुडी, बबीता यादव, भगवान एस शर्मा, नारायणम श्रीकांत

भूमिकाः आयुर्वेद भारत मे प्रचलित एक लोकप्रिय प्राचीन चिकित्सा प्रणाली है। विभिन्न रोग स्थितियों पर कई शोध किए गए हैं परन्तु नैदानिक सुरक्षा का विवरण नगण्य है। आज के परिप्रेक्ष्य में औषध योगों की चिकित्सकीय सुरक्षा उनकी प्रभावकारिता के समान ही महत्वपूर्ण है।

उद्देश्यः विभिन्न भौगोलिक क्षेत्रों में स्थित सी.सी.आर.ए.एस के शोध केन्द्रों पर हुए चार बहुकेन्द्रीय, खुले स्तर के नैदानिक अध्ययनों के माध्यम से डायबीटीज मेलाईटस (मधुमेह) मे प्रयुक्त् कुछ आयुर्वेदिक योगों की नैदानिक सुरक्षा का विवरण प्रस्तुत करना है।

विधिः आयुर्वेदिक औषध योगों नामतः सप्तविंशति गुग्गुलु एवं हरिद्रा चूर्ण; निशा आमलकी एवं चन्द्प्रभा वटी; निशा कतकादी कषाय एवं यशद भस्मग और गोक्षुरादि गुग्गुालु एवं गुडुची चूर्ण का चार अलग–अलग नैदानिक अध्ययनों से प्राप्त हुए आंकडों का विवेचनात्मलक मूल्यांकन के द्वारा नैदानिक सुरक्षा का विश्लेषण किया गया है। सभी अध्ययनों में औषध योगों का तीन माह तक प्रयोग किया गया है। परीक्षण अवधि के प्रारंभ तथा अंत मे प्रयोगशाला मापदंडों जैसे लीवर फंक्शन टेस्ट (एलएफटी) और रीनल फंक्शुन टेस्ट (आरएफटी) द्वारा नैदानिक सुरक्षा का विश्लेगषण किया गया है। युग्मित नमूना टी टेस्ट का प्रयोग मूल अवधि से परीक्षण अवधि के अन्त तक, तुलना करने के लिए किया गया था। पी वैल्यू 0.05 से कम को महत्वलपूर्ण माना जाता है। प्रतिकूल औषध प्रतिक्रिया (एडीआर)/प्रतिकूल घटना (एई) यदि कोई हो, तो नोट किया गया था। अध्ययन के दौरान रोगी अनुपालन बनाए रखा गया था।

परिणामः वर्तमान अध्ययन से स्पष्ट रूप से पता चलता है कि आयुर्वेदिक योग जैसे की सप्तविंशति गुग्गुलु, हरिद्रा चूर्ण, निशा आमलकी, चन्द्र प्रभावटी, निशा कतकादी कषाय, यशद भस्म, गोक्षुरादि गुग्गुलु एवं गुडुची चूर्ण नैदानिक रूप से बहुत सुरक्षित और प्रभावी थे। नियोजित शोध अध्ययनों के परिणाम के माध्यम से समझा जा सकता है की विभिन्न आयु वर्गों, भौगोलिक क्षेत्र और विभिन्न प्रकृति के प्रतिभागियों में भी उक्त औषधियों का उपयोग सुरक्षित पाया गया था तथा सभी सुरक्षात्मकक प्रयोगशाला मापदंड निर्दिष्टं सीमा के भीतर थे।

निष्कर्षः वर्तमान अध्ययन के परिणाम से यह निष्कर्ष निकाला गया है कि मधुमेह के रोगियों पर प्रयुक्त सभी औषध योग, रोगियों के विभिन्न भौगोलिक स्थान, प्रकृति, लिंग और आयु समूहों से संबंधित होने के बावजूद चिकित्सकीय रूप से सुरक्षित एवं सहनीय है।

महत्वः उपरोक्त निष्कर्ष शोधकर्ताओं एवं जनता को इन आयुर्वेदिक योगों की नैदानिक सुरक्षा के बारे में आश्वस्त करेंगे।

मुख्य शब्दः डायबीटीज मेलाईटस, मधुमेह, आयुर्वेदिक औषध/रस–औषधियोग, नैदानिक सुरक्षा, फार्माकोएपिडेमोलॉजिकल अध्ययन।