10.5005/jp-journals-10064-0026

RESEARCH ARTICLE

Selected Ayurvedic Formulations in Gynecological Disorders: A Clinical Safety and Pharmacoepidemiological Perspective

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ABSTRACT

Background: Nowadays, safety of a drug is a major challenge than its efficacy. As the demand for Ayurvedic drugs is increasing day by day, the reporting of safety is essential.

Objective: To review the clinical safety of Ayurvedic formulations, viz., *Rajahpravartini vati Kanchanara Guggulu, Varunadi Kashaya*, *Ashokarishta*, *Ashvagandha Churna,* and *Pravala Pishti,* which were trialed in 3 clinical trials on women's health to assess their efficacy and also clinical safety.

Materials and methods: The analyzed data of 03 clinical studies on *Kastartava* (dysmenorrhea), menopausal syndrome, and polycystic ovary syndrome (PCOS) were collected from the Central Council for Research in Ayurvedic Sciences (CCRAS) database. These studies were conducted at 9, 3, and 2 centers on 359, 115, and 60 cases respectively, at the CCRAS institutes. The data have been critically evaluated to assay the clinical safety of the named six drugs trialed in these studies. All the studies were approved by the Institutional Ethics Committee conducted following the guidelines of good clinical practice. Written consent was obtained from the participants before their enrolment. Safety assessments were done by analyzing the laboratory parameters like liver function test and kidney function test before and after the trial periods. Paired sample t-test was used to compare the mean score. Any adverse drug reactions (ADRs) and side effects were also critically monitored.

Results: In all the studies, it is observed that the safety laboratory parameters were within the normal range after drug administration in the participants, who were from different age groups, habitats, and prakriti. No cases of any ADR or drug intolerability were reported during the treatment period.

Conclusion: From the results, it may be concluded that all the trial drugs are safe to use and can be used for a long period.

Clinical significance: The results of the present study support the notion that if any Ayurvedic formulation has been manufactured as per good manufacturing practices (GMP) and administered at the recommended dose and duration, it is safe for human use.

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Keywords: Ashokarishta, Ashvagandha Churna, Clinical safety, Kanchnar Guggulu, Pravala Pishti, Rajahpravartini vati, Varunadi Kashaya.

How to cite this article: Ota S, Srikanth N, Dhiman KS, Sheetal A, Sharma L. Selected Ayurvedic Formulations in Gynecological Disorders: A Clinical Safety and Pharmacoepidemiological Perspective. J Res Ayurvedic Sci 2017;1(4):254-262.

Source of support: Nil

Conflict of interest: None

BACKGROUND

Established researchers and people, in general, have turned out to be progressively mindful of and legitimately worried about the wellbeing of women, and there is ensuing expanding interest to assess the potential health risk factors of women. In India, the life expectancy of females is lacking, which further indicates the absence of orderly issues in the women's health care.[1] Women and men in India have nearly the same life expectancy at birth, whereas as age advances better health status and life expectancy are not seen in females, which reflects the poor health of women in India. Due to high mortality rates amid the adolescent and reproductive years, care for women's health is a pivotal issue.[2] A woman's reproductive organs are constantly showing signs of change. The anatomical, physiological, and emotional changes occur drastically in the body of women at different stages right from the pubescence stage to menopause. In Ayurveda, *Prasutitantra,* which deals with the Obstetrics and Gynecology section, describes the major health issues in a woman's reproductive system as *Yoni vyaapad,* which are health problems related to menstruation and the female genital organs, and they are 20 in number.[3] The rest of the problems related to a woman's reproductive system, such as complications occurring in pregnancy, during labor, after delivery, and during lactation have been described separately.

The awareness of the benefits in using Ayurvedic medicines is growing in India and also across the globe. Therefore, with the increasing use of Ayurvedic medicines, the concerns of safety are being raised accordingly.[4]

It is highly accepted that clinical trials are the most ideal approach to assess the efficacy of any treatment. It has been observed that although emphasis has been

given on the reporting of the clinical efficacy of Ayurvedic drugs, positive outcomes like clinical safety, improvement in quality-of-life, easy availability of medicines, and lower costs have been underreported.

Although safety is an intrinsic strength of the Ayurvedic system of medicine, a better safety/tolerability assessment framework is constantly required to measure the extent of safe use of these medicines. Ayurveda has always stressed upon or focused on safe treatment, which includes alleviation of a disease condition and not stimulating occurrence any other disease due to the treatment.[5]

Any new intervention/drug, when introduced, is then expected to match the efficacy of the standard intervention/drug or existing drugs. In some instances, it may happen that the new intervention/drug may demonstrate additional advantages too i.e. convenience in use, cost effectiveness, or more safety than the existing drug. There needs to be a combined and integrative approach when evaluating the efficacy and safety of a drug, and due importance should be assigned to safety.

From the literature review, it has been revealed that although a number of clinical studies with classical Ayurvedic formulations have already been conducted from time-to-time, and reports on their efficacy by researchers have been performed, establishing the clinical safety of the medicines is very negligible. It may be assumed that as the drugs have been in use for a long period and they are mostly plant-based, they are safe to use without any adverse reaction or due importance may not be given to this issue.

Considering the importance of reporting the safety of Ayurvedic formulations, the aim of this manuscript is to report the clinical safety of some classical Ayurvedic formulations, which were trialed in 3 clinical trials on women's health. This study aimed to assess their safety along with the efficacy at research centers located at different geographical regions of the country.

OBJECTIVE

To report the clinical safety of Ayurvedic formulations, viz., *Rajahpravartini vati*,[6] *Kanchanara Guggulu*,[7] *Varunadi Kashaya*,[8] *Ashokarishta*,[9] *Ashvagandha Churna*,[10] and *Pravala Pishti*,[11] which were studied in 3 clinical trials on women's health.

MATERIALS AND METHODS

The analyzed data of 3 clinical studies (single arm study), with the above-mentioned 6 clinical Ayurvedic formulations conducted at different centers and periods under the intramural research (IMR) program of the CCRAS, were collected from the data repository of the organization. The study protocol and related documents of all the studies were reviewed and approved by the Institutional Ethics Committee of each participating center. The studies were conducted in accordance with the Schedule-Y of Drugs and Cosmetics Act, India, amended in 2005 and the Indian Council of Medical Research ethical guidelines for biomedical research on human participants, adopted from the 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. All three studies were also registered in the Clinical Trial Registry of India (CTRI). The efficacy has already been reported for two studies, whereas efficacy data of one study are under publication.[12,13] The name of the study, study period, and CTRI number are presented in Table 1.

Study Participants

Inclusion and Exclusion Criteria

Study 1: Women aged between 16 and 35 years suffering from painful menstruation for at least three consecutive regular menstrual cycles (21–35 days) and having normal bleeding were included in the study. Patients of secondary dysmenorrhea, abnormal reproductive system, pelvic inflammatory disease, or any serious systemic disorders likely to influence the menstrual cycle, history of malignancy, hypo and hyperthyroidism, diabetes mellitus, hypertension, women using intrauterine device/oral contraceptive pills, and participating in any other

Table 1: The details of the study, study period, and CTRI number

Name of the study	*Study period*	*No. of study participants*	*CTRI No.*
Multicentric open clinical trial of Rajahpravartini vati in kastartava (dysmenorrhea)	October 2013 to October 2015	368	CTRI/2015/01/005429
Clinical evaluation of efficacy and safety of Ashokarishta, Ashvagandha churna, and Pravala pishti in the management of menopausal syndrome	2011–2012	116	CTRI/2015/03/005649
Clinical evaluation of the efficacy of Rajahpravartini Vati, Kanchanar Guggulu, and Varunadi Kashaya in the management of PCOS	March 2011–August 2012	60	CTRI/2012/03/002538

interventional study were excluded from the study. Pregnant and lactating women were also excluded.

Study 2: Women aged between 40 and 55 years, amenorrhea for ≥12 months, Kupperman menopausal index score ≥15, follicle-stimulating hormone ≥20 IU/L, and thickness of endometrium ≤5 mm, and those who agreed to participate were included in the study.

Exclusion criteria included history of surgical menopause; evidence of malignancy; established cases of mental illness, diabetes mellitus, hypertension, rheumatoid arthritis, coronary heart disease, hepatic disorder, chronic obstructive pulmonary disease, and hypothyroidism; the women on prolonged (>6 weeks) medication with corticosteroids, antidepressants, anticholinergics, or any other drugs that might have an influence on the outcome of the study; alcoholics and/or drug abusers, and who have participated in any other clinical trial in the past 6 months of screening.

Study 3: Women aged between 18 and 40 years with PCOS, as defined by Rotterdam 2003 criteria, having hyperandrogenism clinically (hirsutism)/or biochemically (elevated serum testosterone concentrations), hnovulation/or oligomenorrhea (cycles of 35 days or longer), or amenorrhea (no menses in the last 6 months) after negative screening pregnancy test and polycystic ovary (more than 10 follicles in a ovary/or one cyst more than 10 mm in size), who were able to comply with the requirements of the study and willing to provide signed informed consent were included in the study.

Women who were younger than 18 years or older than 40 years; having history of primary amenorrhea and secondary amenorrhea due to lactation; who were pregnant/or have planned pregnancy during the treatment period; women having any organic reproductive system abnormalities (diagnosed clinically and radiologically), pelvic inflammatory disease, hydrosalpinx, endometriosis, adenomyosis, fibroid uterus, and carcinoma of reproductive organ; subjects with metabolic and endocrinal disorders like diabetes mellitus, chronic liver disease, renal disorder, high blood pressure, hypo and hyperthyroidism; subjects having history of current or previous (within the last 3 months) use of oral contraceptives, glucocorticoids, antiandrogens, ovulation-induction agents, antidiabetic and antiobesity drugs, or other hormonal drugs; subjects who had ingested any investigational drug within 4 weeks prior to the recruitment in the study, and subjects who had no uterine bleeding in the progesterone challenge test were excluded from the study.

Details of Study Interventions in These Three Clinical Trials

Totally, six classical Ayurvedic formulations were studied for their safety and efficacy in the said clinical trials. All the formulations were procured from the GMP-certified manufacturing companies following the standard operative procedures for preparation and standards laid down in the Ayurvedic Pharmacopoeia of India (API). The ingredients and textual references of each formulation are presented in Table 2. The duration of drug administration, dose, dosage form, and vehicle are presented in Table 3.

Table 2: Details of ingredients of each formulation

Formulations, references, and ingredients	*Botanical name*	*Parts used*
Kanchnara Guggulu|The Ayurvedic Formulary of India (AFI, Part 1) 5:1		
Kanchara	*Bauhinia Variagata* Linn.	Stem, bark
Haritaki	*Teminalia chebula* Retz.	Pericarp
Vibhitaka	*Terminalia bellirica* Roxb.	Pericarp
Amalaki	*Emblica officinales* Gaertn.	Pericarp
Shunthi	*Zingiber officinale Rosc.*	Rhizome
Maricha	*Piper Nigrum* Linn.	Fruit
Pippali	*Piper longum* Linn.	Fruit
Varuna	*Crataeva nurvala* Buch ham.	Stem, bark
Ela (Sukshmaila)	*Elettaria cardamomum* Maton	Seed
Tvak	*Cinnamomn zeylanicum Blume*	Stem, bark
Patra (Tejapatra)	*Cinnamomn tamala* Nees & Eberm.	Leaf
Guggulu	*Commiphora wighiti* (arn.) Bhandari	Exudate
Varunadi kashayam|Sahasra yoga		
Varuna	*Crataeva nurvala* Buch ham.	Stem, bark
Saireyak (Rakta, Sweta)	*Barleria Cristata* Linn.	Whole plant, specially leaf
Sarieyak (Peeta)	*Barleria prionitis* Linn.	Whole plant, specially leaf
Shatavri	*Asparagus racemosus* Wild.	Root
Chitrak	*Plumbago zeylanica* Linn.	Root
Murva	*Marsdenia tenacissima* Wight and Arn.	Root
Bilwa	*Aegle marmelos* Corr.	Fruit pulp
Meshshringi	*Gymnema sylvestre*	Leaf and root
Vrihati	*Solanum indicum* Linn.	Root
Sahijan	*Moringa pterygosperma* Lam.	Leaf
Bhllatak	*Semecarpus anacarduim* Linn. F.	Fruit
Karanj	*Pongamia pinnata* (Linn.) Merr.	Seed
Lata Karanj	*Caesalpinia crista* Linn.	Seed
Jayanti	*Sesbenia sesban* (Linn.) Merr.	Leaf
Darbh	*Imperata cylindrica* Beauv.	Root
Rajahpravartini Vati|The Ayurvedic Formulary of India (AFI Part 1) 12:25		
Kanyasara (Kumari)	*Aloe barbadensis* Mill.	Leaf
Kasisa-suddha	Green vitrol	
Ramatha (Hingu)	*Ferula narthex*	Exudate
Tankana Suddha	Borax (ore)	
Kanya (Kumari) Swarasa	*Aloe barbadensis* Mill.	Leaf

(Cont'd…)

(Cont'd…)

Formulations, references, and ingredients	*Botanical name*	*Parts used*
Ashokarishta|The Ayurvedic Formulary of India (AFI-Part-1) 1:5		
Asoka	*Saraca asoca* (Roxb.) De.Wilde	Stem, bark
Jala	Water	
Dhataki	*Woodfordia fruticosa* Kurz.	Flower
Guda		
Ajaji	*Cuminum cyminum* Linn.	Fruit
Mustaka	*Cyperus rotundus* Linn.	Rhizome
Sunthi	*Zingiber officinale* Rosc.	Rhizome
Darvi	*Berberis aristata* DC	Stem
Utpala	*Nymphae stellata* Wild.	Flower
Haritaki	*Terminalia chebula* Retz.	Pericarp
Bibhitaki	*Terminalia belerica* Roxb.	Pericarp
Amalaki	*Emblica officinalis* Gaertn.	Pericarp
Amrasthi	*Mangifera indica* Linn.	Endosperm (Bija majja)
Jiraka (Svetajiraka)	*Cuminum cyminum* Linn.	Fruit
Vasa	*Adhatoda vasica* Nees.	Root
Candana (Sveta chandana)	*Santanum album* Linn.	Heart wood
Ashwgandha churna|The Ayurvedic Pharmacopoeia of India, Part-1, Vol. 1		
Ashwgandha	*Withania Sominifera* Dunal	Root
Pravala pishti|The Ayurvedic Formulary of India (AFI-Part-1) 17:2		
Pravala	Tubispora muscia (Coral)	
Gulab arka	*Rosa centifolia* Linn.	Flower

Study Procedures

At screening visit, subject's demographic profile, medical history, family history, history particularly related to gynecological disorders, menstrual history, *Prakriti* (body constitution), and vital parameters were recorded. At each visit, i.e., baseline, 30th, 60th, 90th day, etc. study medications were dispensed and clinical assessments were performed. Safety laboratory assessments were done at the beginning and at the end of the intervention period. Subject's compliance was monitored by keeping up a regular follow-up by personal contact or telephonic/electronic communication. The investigators checked the medicine packaging for its compliance at each visit.

On each follow-up visit, subject's general and systemic examinations were also carried out. The ADRs (e.g., headache, dizziness, nausea, vomiting, etc) or adverse events, if any, reported during the treatment period were also recorded during each follow-up as per the protocol of the studies.

Safety Assessment

The clinical safety of the participants was assessed through safety laboratory parameters like blood urea, serum creatinine, serum alkaline phosphatase, aspartate aminotransferase , serum alanine aminotransferase, and total bilirubin. These were assessed at baseline and at the end of the intervention period in each study.

All the subjects were specifically questioned as per a predetermined list of common symptoms that may have occurred during treatment period (anorexia, nausea, vomiting, diarrhea, constipation, dysuria, skin rash, giddiness, oral mucous ulcers, dyspepsia, and abdominal discomfort and pain) based on the experiences in clinical practice and previous trials. Participants were also encouraged to voluntarily report information that they considered to be adverse events or a side effect.

STATISTICAL ANALYSIS

The clinical safety parameters were analyzed according to the intention-to-treat analysis. Missing values were imputed by the last-observation carried-forward method. Statistical analysis was performed using Statistical Packages for Social Sciences version 15.0. Statistical significance was defined as $p < 0.05$. Baseline characteristics were reported as mean [standard deviation (SD)] and frequency (%). Pairwise comparison and within subject

Table 3: Details on schedule of drug administration

Name of study	*Name of trial drug*	*Dosage schedule*	*Intervention period*
Multicentric open clinical trial of *Rajahpravartini vati* in *kastartava* (Dysmenorrhea).	*Rajahpravartini vati*	250 mg BD with lukewarm water	90 days
Clinical evaluation of efficacy and safety of *Ashokarishta*, *Ashvagandha churna*, and *Pravala pishti* in the management of menopausal syndrome	*Ashokarishta*	25 mL BD with water in equal quantity (i.e., 25 mL)	84 days
	Ashvagandha churna	3 gm BD 1 hour before meal with milk	
	Pravala pishti	250 mg BD an hour before meal with milk	
Clinical evaluation of the efficacy of *Rajahpravartini Vati*, *Kanchanar Guggulu*, and *Varunadi Kashaya* in the management of PCOS	*Rajahpravartini Vati*	250 mg (1 tablet twice a day) orally with lukewarm water after lunch and dinner	180 days
	Kanchanar Guggulu	500 mg (2 tablets twice a day (morning and evening after food) orally with Varunda kashaya	
	Varunadi Kashaya	20 mL mixed with 40 mL lukewarm water	

effects of outcome measures were done by using repeated measures analysis of variance.

RESULTS

In the study 1, 2, and 3, the data of 359, 115, and 60 subjects have been analyzed by imputation for intension-to-treat analysis for safety and efficacy evaluation. The baseline values of different variables viz. age, marital status, and other demographic profiles, etc., of these subjects are given in Table 4, and data on vital parameters and body mass index (BMI) are presented in Table 5.

Effect of the Trial Drugs on Safety Parameters

As the trial drugs were administered in combination for 3 months continuously and also for 6 months, for assessment of their clinical safety, laboratory safety parameters, i.e., renal and liver functions test, were carried out at baseline and at the end of the treatment in all the studies. From the data, it is observed that though some variations are found in the data (mean ± SD) of both ends, all were in the normal range and no statistically significant changes were observed. This finding helps establish the safety of the drug for human use. The details are presented in Tables 6, 7, and 8. Further, it is also observed that none of the study subjects withdrew due to any adverse event or drug-related toxicity.

DISCUSSION

The primary objective of the manuscript is to evaluate the safety of 6 Ayurvedic formulations trialed in 3 different

Table 4: Demographic profile of the study population in three clinical studies

Demographic profile	*Study 1 (n %)*	*Study 2 (n %)*	*Study 3 (n %)*
Total subjects	359	115	60
Age (in years)	16–20 years—177 (49.3)	46–50 years—50 (43.5)	18–24 years—39 (65.0)
	21–25 years—101 (28.13)	51–55 years—46 (40.0)	25–30 years—15 (25.0)
Educational status			
Illiterate	11 (3.1)	10 (8.7)	01 (1.7)
Up to primary/middle	48 (13.4)	104 (90.4)	01 (1.7)
Up to 10th/college or above	297 (82.7)	01 (0.9)	58 (96.7)
Marital status			
Married	91 (25.3)	98 (85.2)	17 (28.3)
Unmarried	268 (74.7)	–	43 (71.7)
Nonsmoker and nonalcoholic	359 (100)	115 (100)	60 (100)
Prakriti (predominant)			
Pittaja-kaphaja	202 (56.3)	59 (51.3)	35 (58.3)
Vata-pittaja	87 (24.2 0	46 (40.0)	19 (31.7)

Table 5: Baseline vital data of the study subjects of three clinical trials

Baseline vital data	*Study 1 (mean ± SD)*	*Study 2 (mean ± SD)*	*Study 3 (mean ± SD)*
BMI (kg/m^2)	20.63 ± 4.06	25.21 ± 4.19	27.2 ± 5.49
Body vitals			
Pulse rate	74.1 ± 5.4	75.88 ± 6.544	77.68 ± 8.34
Respiration rate	17.0 ± 1.9	18.44 ± 1.75	16.98 ± 1.05
Blood pressure (mm Hg)			
Systolic	109.1 ± 8.3	118.90 ± 11.25	114.73 ± 11.09
Diastolic	71.71 ± 7.7	76.70 ± 7.35	75.07 ± 6.84

Table 6: Effect of the drugs on safety laboratory parameters in study 1

Laboratory safety parameters	*Baseline (mean ± SD)*	*90th day (mean ± SD)*
Kidney function test		
Blood urea (mg/dL)	17.56 ± 5.2	18.28 ± 4.78
Serum creatinine (mg/dL)	0.70 ± 0.5	0.69 ± 0.16
Liver function test		
Asparate transaminase (IU/L)	19.99 ± 6.27	20.27 ± 6.3
Alanine transaminase (IU/L)	18.56 ± 9.92	18.49 ± 9.69
Total bilirubin (mg/dL)	0.53 ± 0.23	0.63 ± 2.19

Table 7: Effect of the drugs on safety laboratory parameters in study 2

Laboratory safety parameters	*Baseline (mean ± SD)*	*84th day (mean ± SD)*
Kidney function test		
Blood urea (mg/dL)	22.87 ± 6.27	21.97 ± 4.99
Serum creatinine (mg/dL)	0.76 ± 0.15	0.75 ± 0.13
Liver function test		
Aspartate transaminase (IU/L)	23.13 ± 7.57	23.35 ± 7.27
Alanine transaminase (IU/L)	24.20 ± 9.49	24.14 ± 11.31
Total bilirubin (mg/dL)	0.58 ± 0.35	0.73 ± 2.1

Table 8: Effect of the drugs on safety laboratory parameters in study 3

Laboratory safety parameters	*Baseline (mean ± SD)*	*90th day (mean ± SD)*	*180th day (mean ± SD)*
Kidney function test			
Serum creatinine (mg/dL)	0.8 ± 0.1	–	0.81 ± 0.1
Serum urea (mg/dL)	21.23 ± 6.0	–	21.18 ± 6.05
Liver function test			
Aspartate transaminase (IU/L)	20.8 ± 6.3	22.02 ± 7.4	22.9 ± 8.3
Alanine transaminase (IU/L)	22.6 ± 11.3	22.98 ± 14.02	24.13 ± 14.35
Total bilirubin (mg/dL)	0.6 ± 0.2	0.6 ± 0.23	0.57 ± 0.2

clinical trials. Pharmacovigilance[14] plays an utmost important role in optimizing the safety of drugs and bring the desired improvement in treatment outcomes. The scattered information related to drug safety and ADR, such as drug overdose, drug interaction, drug intolerance among patients, idiosyncrasy, and drug allergy[15] is being found in various Ayurvedic texts. Though the term ADR is not found, the concept of the same and safety issues are profoundly mentioned at full length in the Ayurvedic texts.

The Ayurveda system of medicine, since its inception, has given utmost importance to the safety and benefit of the patient during the entire period of the management of diseases, and includes raw drug selection, raw drug collection, the processing methods, and the administration of drug in appropriately diagnosed patient. The ADR can be minimized if one uses medicines of good quality and perform assessments by *Dashavida pareeksha* (ten-fold examination of diseased person),[16] viz., *Prakriti* (body constitution), *Vaya* (Age), *vikruti* (any pathological condition), *satmya* (tolerance), *vyayamshakti* (capacity of exercise), *Saara* (tissue quality), *samhanana* (physical proportion), and *bala* (strength); *by Trividha praeeksha*[17] (three-fold examination of diseased person), *Chaturvidha pareeksha (*four-fold examination of patients),[18] *Shadvidha preeksha*[19] (six-fold examination), and *Ashtavidh pareeksha* (eight-fold examination).[20] As mentioned in texts, if the drug administered is stronger than the disease, then it produces another disease after pacifying the present one, and if the strength is lower, then the drug becomes ineffective stating importance of administration of drug in appropriate strength.[21]

Ayurvedic formulations are mainly of herbs and herbo-mineral/metal compositions. Ayurveda states that every *Aushadha* (single/compound formulations), be it herbal or herbo-mineral/metal, if, not used judiciously may cause harm to the body, which may be mild-to-severe or unpredictable. There are many studies reporting on the drug interactions also, i.e., bleeding tendency after intake of phenproprocoumon[22] along with ginger; the activity of lithium is decreased when consumed along with herbal diuretics like *Tribulus terrestris, Syzigium cumini*;[23] phenytoin along with *Convolvulus plucaulis (Sankhpushpi)* causes loss on seizure control.[24]

The formulations having metals and minerals as *Bhasmas* (incinerated mineral formulations) or as herbo-minerals are to be prescribed and manufactured under given guidelines, and the portrayals of adverse reactions are found, if safety measures are not taken care of while manufacturing and administering these formulations. The manufacturing procedures are also very stringent (as mentioned in the *vishesha shodhana* and *marana*[25] methods for all minerals and metals) to weaken or negate the toxic effects of drugs.

So, nonreporting of any ADR/adverse drug event after administration of these drugs could be because of use of each ingredient after appropriate *sanskaras* (*samnaya Shodhana, vishesh shodhana, Marna*, etc.) described in Ayurvedic classics. It might have contributed in modifications of the adverse property of metals, minerals, or toxic medicinal plants, resulting in the elimination of toxicity and, at the same time, retaining the pharmacological properties of the drugs.

Further, studies have also been conducted on the purification and detoxification (*shodhan prakriya*) methods of toxic herbal plants, such as *Vacha*[26] (*Acorus calamus* Linn.), *Langli*[27] (*Gloriosa* superb Linn.), and *Gunja*[28] (*Abrus precatorius* Linn). Various *shodhan prakriyas* have shown results regarding the detoxification or decrease of the toxic components, such as colchicines, aconitine, β-asarone, and polyphenols due to the treatment medium used or multiple processes of heating with different media or other purification methods described in the Ayurvedic classics.

Rajahpravartini Vati having *kasisa* (purified green vitriol) and *Kanchanar Guggulu* were manufactured after purification following the methods mentioned in texts for *kasisa*[29] and *guggulu*.[30] All the ingredients had been taken as per API standards and the finished products were also manufactured following the standards laid in the API at GMP-certified pharmaceutical companies.

As shown in Table 2, the said formulations were successfully administered in different centers across the country covering different geographical regions but no

adverse effects/reactions were reported. Thus, it proves the safety profile of the formulations administered.

To summarize this, the Ayurveda system of medicines supports the fact of "safe administration" of medicine stating that "even a strong poison can become an excellent medicine if administered properly and on the contrary even the most useful drug can act like a poison if handled carelessly."[31]

CONCLUSION

The Ayurvedic formulations, viz., *Rajahpravartini vati, Kanchanara Guggulu, Varunadi Kashaya, Ashokarishta, Ashvagandha Churna, and Pravala Pishti,* are found clinically safe as no ADRs and no significant changes in biochemical parameters of liver and kidney function were reported during the treatment period in all three studies.

The results of the present studies support the notion that if any Ayurvedic formulation has been manufactured as per GMP following the standard operative procedures laid down in the classics and administered at the recommended dose and duration, it is safe for human use.

ACKNOWLEDGMENTS

Authors would like to thank the principal investigators and coinvestigators of the reported studies, viz., Dr Krishna Kumari, Dr Rajesh Sannd, Dr Kiran V Kale, Dr Rinku Tomar, Dr MN Subhashree, Dr K Pramila Devi, Dr P Madhavi Kutty, Dr Anu Bhatnagar, Dr Seema Jain, Dr Sushmita Priyadarshini Ota, Dr Indira Kumari, Dr Savita Sharma, and Dr Vilas Gangurde for data collection and to Dr Rakesh Kumar Rana (Statistical Officer) and Dr Richa Singhal (Statistical Assistant), for data analysis. Authors are also thankful to Miss Meera Verma and Mr Pradeep Kumar for their secretarial assistance while preparing the manuscript.

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हिन्दी सारांश

"स्त्रीरोगों में चयनित आयुर्वेदिक योगों/औषधियों की नैदानिक सुरक्षा एवं फार्माकोएपिडेमोलोजिकल दृष्टिकोण का अध्ययन"

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भूमिका: वर्तमान समय में किसी भी औषधी की नैदानिक सुरक्षा (clinical safety) उसकी प्रभावकारिता (efficacy) की तुलना में एक बड़ी चुनौती है और दिन–प्रतिदिन बढ़ रही आयुर्वेदिक दवाओं की मांग को देखते हुए इनकी नैदानिक सुरक्षा की रिपोर्टिंग अत्यंत आवश्यक है।

उद्देश्य: महिलाओं के स्वास्थ्य पर "केंद्रीय आयुर्वेद अनुसंधान परिषद" द्वारा प्रभावकारिता और नैदानिक सुरक्षा का आंकलन करने के लिए 03 नैदानिक परीक्षणों में 06 आयुर्वेदिक योगों जैसे की रजःप्रवर्तिनी वटी, अशोकारिष्ट, अश्वगंधा चूर्ण, प्रवाल पिष्टि, कांचनार गुग्गुलु एवं वरुणादी कषाय की नैदानिक सुरक्षा का आंकलन/समीक्षा करना।

सामग्री एवं विधि: केंद्रीय आयुर्वेद अनुसंधान परिषद की देखरेख में 03 नैदानिक अध्ययनों जो की – कष्टआर्तव (डिस्मेनोरिया) के प्रबंधन में रजःप्रवर्तिनी वटी के प्रभाव पर नैदानिक अध्ययन, मेनोपौसल सिंड्रोम के प्रबंधन में अशोकारिष्ट, अश्वगंधा चूर्ण & प्रवाल पिष्टि की नैदानिक प्रभावकारिता एवं सुरक्षा पर किया गया अध्ययन एवं पोली सिस्टिक ओवेरियन सिंड्रोम (PCOS) के प्रबंधन में रजःप्रवर्तिनी वटी, कांचनार गुग्गुलु एवं वरुणादी कषाय की प्रभावकारिता का नैदानिक मूल्यांकन क्रमशः 09 केंद्रों में 359 प्रतिभागियों में; 03 केंद्रों में 115 प्रतिभागियों में एवं 02 केंद्रों में 60 प्रतिभागियों पे सम्पन्न हुए थे। उपरोक्त 03 नैदानिक परीक्षणों से प्राप्त आंकड़ों से बतायी गई 06 आयुर्वेदिक योगों की नैदानिक सुरक्षा की जाँच करने के लिए मूल्यांकन किया गया था। यह तीनों चिकित्सीय परीक्षण बहु–केंद्रीय स्तर पर किए गए थे एवं संस्थागत नैतिकता समिति (Institutional Ethics Committee) द्वारा अनुमोदित था।

सुरक्षा आंकलन परीक्षण अवधि के पहले और बाद में प्रयोगशाला पैरामीटर जैसे यकृत कार्य परीक्षण (L.F.T.), किडनी फंक्शन टेस्ट (K.F.T.) के विश्लेषण के माध्यम से किया गया। पेयरड सैम्पल टी–टेस्ट का उपयोग औसत स्कोर की तुलना करने के लिए किया गया था। किसी भी प्रतिकूल प्रतिक्रियाओं, जटिलताओं और दुष्प्रभाव को ठीक से नोट किया गया था।

परिणाम: नियोजित सभी नैदानिक शोध अध्ययनों में स्पष्ट रूप से पता चलता है कि विभिन्न आयु वर्गों, भौगोलिक क्षेत्रों और प्रकृति के प्रतिभागीयों में आयुर्वेदिक योगों के तीन से छह महीने की अवधि तक प्रयोग के बाद भी नैदानिक सुरक्षा मूल्यांकन के लिए किए गए प्रयोगशाला के निष्कर्ष सामान्य स्तर में पाये गए थे। उपचार की अवधि के दौरान प्रयोग हुई औषधियों की प्रतिकूल प्रतिक्रिया या असहिष्णुता का एक भी मामला दर्ज नहीं किया गया था।

निष्कर्ष: इन शोध अध्ययनों के नतीजे से यह निष्कर्ष निकाला जा सकता है कि सभी 06 आयुर्वेदिक औषधियां चिकित्सीय उपयोग करने के लिए सुरक्षित हैं और इन औषधियों का इस्तेमाल लंबी अवधि के लिए किया जा सकता है।

महत्व: वर्तमान अध्ययन के परिणाम, इस धारणा का समर्थन करते हैं कि अगर किसी भी आयुर्वेदिक औषधी/योग का निर्माण "गुड मेन्युफेक्चरिंग प्रेक्टिस" (G.M.P.) के अनुसार किया जाता है और उस आयुर्वेदिक औषध/योग को अगर संस्तुत मात्रा एवं अवधि के लिए उपयोग किया जाता है तो वह औषधी चिकित्सीय उपयोग के लिए सुरक्षित होती है।

संकेत चिन्ह: नैदानिक सुरक्षा, रजःप्रवर्तिनी वटी, अशोकारिष्ट, अश्वगंधा चूर्ण, प्रवाल पिष्टि, कांचनार गुग्गुलु एवं वरुणादी कषाय।