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Effect of *kanyasara* (solidified *Aloe vera* exudate) on high fat diet letrozole induced polyendocrine metabolic ovarian syndrome in rats

V Porchezhiyan[1], K Buvanesvaragurunathan[1], B Premkumar[2], G C Leela Priyanka[2], T S Subha[1]*, P Pandikumar[3]* & S Ignacimuthu[3]*

[1]PG and Research Department of Botany, Bharathi Women's College, Broadway Road, George Town, Chennai, Tamil Nadu 600108, India

[2]Department of Pharmacology, K. K. College of Pharmacy, Gerugambakkam Main Road, Chennai, Tamil Nadu 600122, India

[3]Xavier Research Foundation, St Xavier's College, Palayamkottai, Tamil Nadu 627002, India

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Polyendocrine metabolic ovarian syndrome (PMOS) is a prevalent hormonal disorder that affects approximately one in eight women of reproductive age. In Indian systems of traditional medicine, *kanyasara* (solidified exudate of *Aloe vera* Burm.f.) has been used for treating PMOS. This study evaluated the anti-PMOS effect of *kanyasara* using a preclinical model. *Kanyasara* was standardised by quantifying the aloin content using HPLC. PMOS was established by feeding Sprague Dawley rats with a high fat diet for eight weeks and orally administering letrozole (1 mg/kg) for three weeks. *Kanyasara* (25 to 50 mg/kg) treatment was given consecutively for 28 days; metformin (120 mg/kg) was used as a positive control. *Kanyasara* used in this study contained 37.58% of aloin. Compared to the HFD-letrozole animals, *kanyasara-treated* animals (50 mg/kg) showed 54.94% reduction in blood glucose. The treatment significantly lowered total cholesterol (28.28%) and triglyceride (25.72%) levels at 50 mg/kg concentration. The treatment also lowered the levels of plasma FSH (50.06%) and LH (59.16%). Histological examination showed normal follicles, corpus luteum, and ovarian stroma by *kanyasara* treatment. This study supported the use of *kanyasara* for the treatment of PMOS; detailed investigations are needed to establish its efficacy and safety.

Keywords: *Aloe barbadensis*, *Anthraquinones*, *Kariabolam*, *Musabhar*, PCOS, Siddha

Polyendocrine metabolic ovarian syndrome (PMOS) is a common endocrine disorder that affects approximately one in eight women of reproductive age. It is characterised by imbalances in several hormones; its clinical features are diverse and include metabolic abnormalities (e.g. hyperglycemia, obesity), reproductive dysfunction (irregular menstrual cycles), psychological (depression, anxiety) and dermatological (acne, hirsutism) manifestations. Formerly it was known as polycystic ovary syndrome (PCOS); it was renamed by expert consensus to reflect the multisystem involvement, ease early diagnosis and timely management[1]. A systematic review and meta-analysis indicated that the global prevalence of PMOS is ~12%; high prevalences were noted in the Eastern Mediterranean region, followed by the South-East Asian region[2]. In India, the pooled prevalence of PMOS was predicted as 5.8-10%[3].

*Correspondence:
E-mail: subhatss@gmail.com;
pandikumarperumal@gmail.com; xrfsxc@gmail.com

Lifestyle modification is recommended as the first line therapy for achieving mental well-being, healthy body composition and weight. Combined oral contraceptives, metformin, clomid citrate, spironolactone, orlistat, etc., are some of the pharmacotherapies prescribed for the management of PMOS[4]. Dipeptidyl peptidase IV inhibitors, sodium-glucose cotransporter 2 inhibitors, and Glucagon-like peptide-1 receptor agonists have also been repurposed for managing PMOS[5]. Various vitamins (B12, D, E, and K), minerals (chromium picolinate), antioxidants (α-lipoic acid), probiotics, and omega-3 fatty acids have been used as supplements for the management of PMOS[6]. Various medicinal plants like pomegranate, cinnamon, mint, ginger, etc. have also been used traditionally as supplements[7,8].

Aloe vera Burm.f. (synonym: *A. barbadensis* Mill., *Ghrit Kumari* in Sanskrit) belongs to the family Asphodelaceae and is widely used for the treatment of PMOS[8]. *A. vera* is considered native to the Arabian Peninsula and has been used in Indian systems of traditional medicine for many centuries. In Indian

traditional medicine, *A. vera* has been used to treat many gynecological conditions[9]. Previous preclinical studies have reported the beneficial effects of *A. vera* gel in PMOS, using letrozole-induced rodents as an animal model[10-13]. Non-polar constituents such as lupeol, β-sitosterol, stigmasterol, and campesterol acetate were identified as responsible for the beneficial effects of *A. vera* against PMOS, acting through modulation of key enzymes like 3β-hydroxy steroid dehydrogenase[10,14,15].

Solidified *A. vera* exudate has been widely used in the Indian system of traditional medicines to treat PMOS; it is known as *kanyasara* in Sanskrit, *musabhar* in Hindi, and *kariabolam* in Tamil. *Kanyasara* serves as a key ingredient in *Rajahpravartini vati*, an *Ayurvedic* formulation prescribed for the treatment of dysmenorrhea and PMOS. In a small-scale clinical study involving 53 women with PMOS, the administration of four *Ayurvedic* formulations, including *Rajahpravartini vati*, resulted in significant improvements in Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and estradiol levels after three months of treatment. Furthermore, the treatment alleviated symptoms such as oligomenorrhea and hirsutism, ultimately enhancing the overall quality of life[16]. In another study, 40 PMOS patients were treated with *Moosambara mezhugu*, a *Siddha* formulation containing the *A. vera* exudate, which showed significant reductions in the PMOS clinical features[17]. This study highlights the beneficial effects of *kanyasara*, the traditionally solidified *A. vera* exudate, in the context of High Fat Diet (HFD) - letrozole induced PMOS.

Materials and methods

Procurement of *kanyasara* and botanical confirmation

The traditional manufacturers of *kanyasara* in Virudhunagar district were consulted, and one of their team was taken to the field where *kanyasara* is usually prepared. The exudate of *A. vera* was collected, and *kanyasara* was prepared in accordance with the traditional method. This *kanyasara* was used in this study, and a voucher specimen was deposited in our herbarium (XCH 40453) for future reference.

HPLC quantification of aloin in *kanyasara*

Kanyasara sample and the standard aloin were dissolved in 0.1% acetic acid in methanol. HPLC analysis was done using Agilent 1200 module with photodiode array detector; the column was an ODS column (100 × 4.6 mm, 3 µm). The mobile phases were 0.1% acetic acid in water (A) and 0.1% acetic acid in methanol at a flow rate of 1.5 mL per min; the separation was done at 30 °C, and the detector wavelength was set at 357 nm. A gradient method was used, starting from 83% A up to 12 min, linearly changed to 0% A for 5 min, maintained at 0% A for 3 min, linearly changed to 83% A for 3 min and equilibrated for another 5 min under the initial condition; the total run time was 28 min. The standard aloin was run at five concentrations, and the concentration of aloin in *kanyasara* sample was estimated using linear regression analysis.

Animals

Thirty female Sprague Dawley rats obtained from Mass Biotech, Chengalpattu were used in this study. The rats were acclimatised for 10 days before the start of the experiments. Throughout the study, the rats were kept under standard conditions of ambient temperature, humidity, and light/dark cycles. They were provided with *ad libitum* access to food and water, except during fasting periods. Physiological fasting was implemented for six hours between 7.00 a.m. and 1.00 p.m. For this study, a purified High Fat Diet (HFD) was utilised, following a previously established method[18]. All protocols adhered to the regulations and recommendations set forth by the Committee for Control and Supervision of Experiments on Animals and approved by the Institutional Animal Ethics Committee (Clearance number: KKCP/2022/03).

Fixation of the dosage

The recommended dosage of *kanyasara* for humans ranged between 125 and 500 mg, as specified by the API[19]. Conversion of the human dose to rats yielded 20 and 80 mg/kg body mass, in accordance with an established method[20]. For this study, the doses were selected as 25 and 50 mg/kg, which were within the recommended dose limits. The dose of metformin used was 150 mg/kg[21]. To prepare the test drugs, they were finely powdered, weighed, and suspended in a vehicle composed of 0.9% NaCl, 0.5% carboxy methyl cellulose, and 0.2% Tween-80 in distilled water. The control animals were administered the vehicle only, and all treatments were administered once daily through oral gavage.

Establishment of HFD-letrozole induced PMOS in rats

PMOS was induced by following the method described by Wang and colleagues[22], with certain

modifications. All animals except those in the normal control group were fed a High Fat Diet (HFD) for 56 days before the initiation of the treatment, and this diet was continued throughout the study. On the 36th day, the rats received a daily oral dose of letrozole (1 mg/kg) for a period of 21 days. On the 56th day, serum levels of FSH, LH, and blood glucose were measured, and the rats were randomly divided into five groups, each consisting of six animals.

Group I consisted of normal control animals, while Group II included negative control animals (HFD-letrozole + vehicle treated). Group III comprised positive control animals (HFD-letrozole + metformin 120 mg/kg). Groups IV and V consisted of HFD-letrozole-induced animals treated with *kanyasara* at concentrations of 25 mg/kg and 50 mg/kg, respectively. The treatments were administered once daily for 28 days through oral gavage.

End of the study

Daily feed and water intake measurements were conducted at 9:00 a.m. On the 85th day, the rats were euthanised under isoflurane anaesthesia, and blood was collected. It was then centrifuged at 3500 rpm, and the resulting serum was preserved for subsequent analyses. Ovary, uterus, and liver tissues were stored in a 10% PBS buffered formalin solution for histological examinations. Blood glucose levels were determined using a one-touch glucometer (Apollo, India). Serum lipid profile measurements were performed on the same day as euthanasia using commercially available spectrophotometric kits (Erba Transasia). FSH and LH levels were also measured on the day of euthanasia using the ELISA method.

Statistics

The results were expressed as the mean ± standard deviation (SD) from six replicates. Statistical analysis was performed using one-way ANOVA followed by Tukey's HSD, utilising GraphPad Prism (Version 8). Statistical significance was considered at a level of $P \leq 0.05$.

Results

HPLC quantification of aloin in *kanyasara*

HPLC quantification showed that the *kanyasara* used in this study had 37.58% of aloin A and B (Fig. 1).

Effect of *kanyasara* treatment on the estrus cycle of the HFD-letrozole induced PMOS

At the proestrus stage, many small nucleated cells were found in normal and treated animals; similarly,

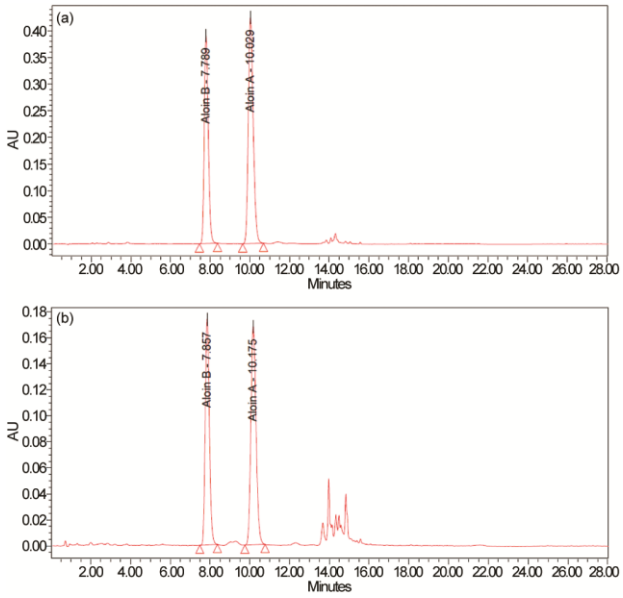

Fig 1 — HPLC chromatograms of a) aloin standard and b) *kanyasara*

at the estrus and metestrus stages, many anucleated epithelial cells were found. At the diestrus stage, many neutrophils were found in the normal and treated animals; such cell types were absent in the disease control animals (Fig. 2).

Effect of *kanyasara* treatment on body and organ masses of the HFD-letrozole induced PMOS

The body mass of disease control animals was increased remarkably from the baseline values. Compared to the disease control group, the treatment with *kanyasara* reduced body mass by 20.76 and 12.22% at 25 and 50 mg/kg concentrations, respectively; these reductions were highly significant ($P < 0.005$) (Table 1). The treatment did not alter the feed and water intake (data not shown). Similarly, the treatment significantly reduced the ovary, uterus and liver masses (Table 2).

Effect of *kanyasara* treatment on the blood glucose level of the HFD-letrozole induced PMOS

The HFD-letrozole administered animals showed a slight but significant increase in blood glucose levels before treatment. In the disease control animals, hyperglycemia was aggravated by 50.46% at the end of the study, while comparing the baseline values. The treatment with *kanyasara* lowered blood glucose levels by 42.01 and 54.94%, compared to the disease control group, at 25 and 50 mg/kg concentrations, respectively; these reductions were highly significant ($P < 0.005$) and comparable with that of metformin (Table 3).

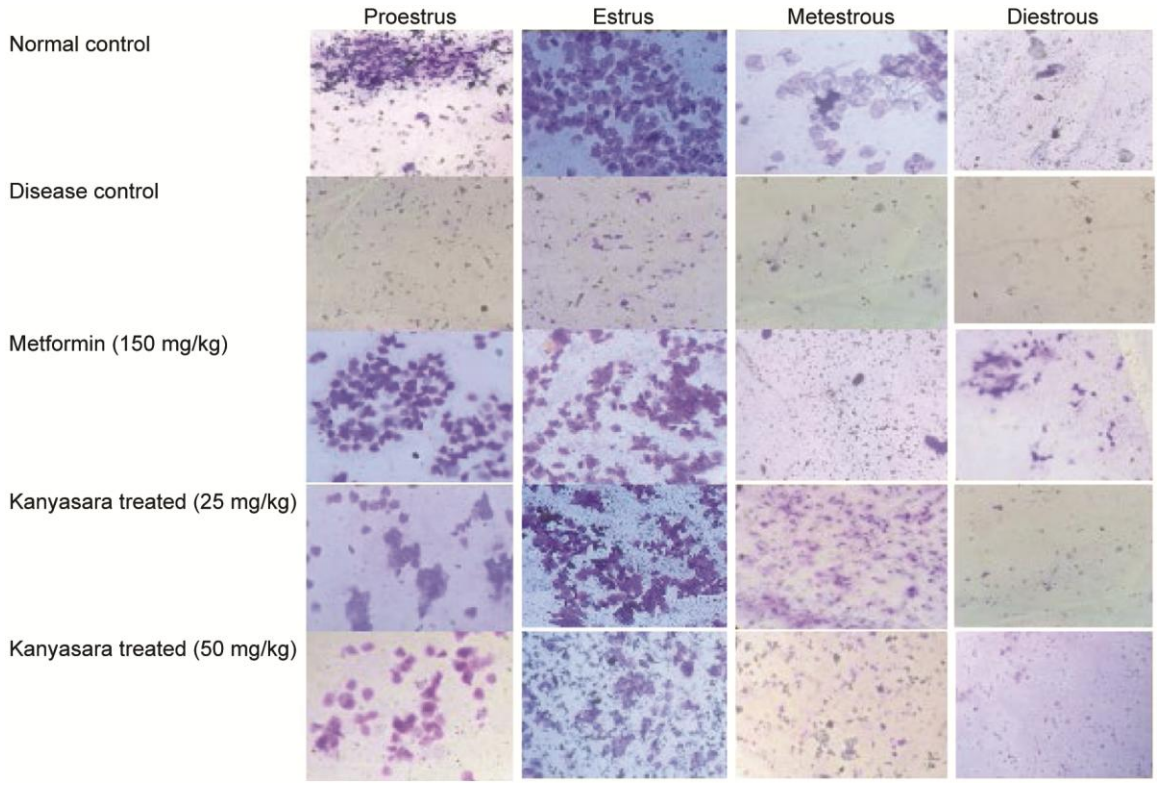

Fig 2 — Representative images showing vaginal smear of HFD-letrozole induced PMOS animals after 28 days of treatment with *kanyasara*

Table 1 — Effect of *kanyasara* treatment on the body mass of HFD-letrozole induced PMOS animals before and after treatment for 28 days

Groups	Initial body mass	Final body mass
Normal control	135.2 ± 7.85[a]	187.5 ± 5.96[a]
Disease control	191.3 ± 14.85[b]	297.0 ± 15.17[b]
Metformin (150 mg/kg)	200.3 ± 17.59[b]	225.3 ± 5.31[c]
Kanyasara (25 mg/kg)	181.3 ± 9.51[b]	228.8 ± 11.13[c]
Kanyasara (50 mg/kg)	186.7 ± 9.02[b]	212.7 ± 14.30[c]

Values (in g.) indicate mean ± SD for six animals; values having same alphabet in a column did not vary significantly (Tukey's HSD; $P \leq 0.05$)

Effect of *kanyasara* treatment on serum lipid profile of the HFD-letrozole induced PMOS

The treatment with *kanyasara* also ameliorated the deranged lipid profile induced by HFD-letrazole administration; the treatment with *kanyasara* at 25 mg/kg concentration lowered total cholesterol level by 18.42%, and this reduction was significant ($P < 0.05$); at 50 mg/kg concentration, it lowered total cholesterol level by 28.28% in a highly significant manner ($P < 0.005$). The treatment with *kanyasara* also lowered triglyceride levels by 23.64 and 25.72% at 25 and 50 mg/kg concentrations, respectively, in a highly significant manner ($P < 0.005$). Similarly,

Table 2 — Effect of *kanyasara* treatment on the organ masses of HFD-letrozole induced PMOS animals after treatment for 28 days

Groups	Ovary	Uterus	Liver
Normal control	0.053 ± 0.009[a]	0.447 ± 0.016[a]	4.85 ± 0.54[a]
Disease control	0.157 ± 0.011[b]	0.155 ± 0.015[b]	9.96 ± 0.85[b]
Metformin (150 mg/kg)	0.061 ± 0.048[c]	0.405 ± 0.033[c]	5.61 ± 0.35[a]
Kanyasara (25 mg/kg)	0.066 ± 0.014[c]	0.407 ± 0.017[c]	5.22 ± 0.11[a]
Kanyasara (50 mg/kg)	0.066 ± 0.023[c]	0.402 ± 0.022[c]	4.81 ± 0.13[a]

Values (in g./100 g. bw) indicate mean ± SD for six animals; values having the same alphabet in a column did not vary significantly (Tukey's HSD; $P \leq 0.05$)

Table 3 — Effect of *kanyasara*treatment on the blood glucose levels of HFD-letrozole induced PMOS animals before and after treatment for 28 days

Groups	Initial blood glucose	Final blood glucose
Normal control	84.00 ± 3.03[a]	88.24 ± 3.57[a]
Disease control	91.83 ± 2.31[b]	185.39 ± 35.37[b]
Metformin (150 mg/kg)	95.83 ± 2.56[b]	94.16 ± 2.56[a]
Kanyasara (25 mg/kg)	94.16 ± 3.65[b]	107.50 ± 9.91[a]
Kanyasara (50 mg/kg)	95.83 ± 3.06[b]	83.52 ± 3.61[a]

Values (in mg/dL) indicate mean ± SD for six animals; values having the same alphabet in a column did not vary significantly (Tukey's HSD; $P \leq 0.05$)

treatment with *kanyasara* lowered LDL and VLDL cholesterol levels in a highly significant manner (Table 4).

Effect of *kanyasara* treatment on FSH and LH levels of the HFD-letrozole induced PMOS

In the disease control group, FSH and LH levels were higher than those of normal animals; the treatment with *kanyasara* lowered FSH levels by 32.05 and 50.06% at 25 and 50 mg/kg concentrations, respectively; these reductions were in a highly significant manner ($P < 0.005$). Similarly, LH levels were reduced in a highly significant manner ($P < 0.005$) by 40.87 and 59.16% by *kanyasara* treatment at 25 and 50 mg/kg concentrations, respectively. There was no significant variation between normal control and metformin and *kanyasara*-treated animals. The treatment also reduced the LH to FSH ratio, but this reduction was not significant (Table 5).

Effect of *kanyasara* treatment on the histology of the ovaries, uterus and liver in the HFD-letrozole induced PMOS

In the normal control group, the histology of the ovaries showed preantral and antral follicles; the corpus luteum and ovarian stroma were normal. In the disease control group, the presence of many atretic follicles was noted with atrophy of ovarian stroma. In metformin-treated animals, the follicles, corpus luteum and the ovarian stroma were normal. In *kanyasara*-treated animals at 25 mg/kg concentration, cystic preantral follicles were noted, while the corpus luteum and the ovarian stroma were normal. At 50 mg/kg concentration, *kanyasara*-treated animals showed antral follicles; the corpus luteum and the ovarian stroma were normal (Fig. 3).

The histology of the uterus in the normal control group showed normal agglomerates of endometrial glands in the stroma and myometrium. In the disease control group, the uterus had increased endometrial stroma with less scattered endometrial glands; considerable myometrial hyperplasia was found in all the animals. In metformin-treated animals, the uterine sections were normal. In *kanyasara*-treated animals at 25 mg/kg concentration, the number of endometrial glands was low, while the myometrium appeared normal. At 50 mg/kg concentration, *kanyasara*-treated animals showed agglomerates of endometrial glands with normal myometrium (Fig. 4).

The liver histology of the normal control animals showed normal hepatocytes, sinusoids and portal triads; in the disease control group, the hepatocytes had cytoplasmic vacuolations and a peripherally pushed nucleus; the sinusoids were dilated and had periportal inflammation. These changes were mild in metformin and *kanyasara*-treated animals (Fig. 5).

Discussion

This study validated the use of *kanyasara* – a major ingredient of famous traditional Indian medicinal formulations like *Rajahpravartini vati* and *Moosambara mezhugu*, using an HFD-fed letrozole-treated animal model. In several traditional medical systems, *A. vera* occupies a significant place in the treatment of PMOS. Previous studies demonstrated the efficacy of non-polar constituents from *A. vera* gel[15]. This study reported the beneficial effect of anthraquinone-rich *A. vera* exudate, since it is an essential raw drug of Indian traditional medicine for the treatment of PMOS.

Table 5 — Effect of *kanyasara* treatment on plasma FSH and LH levels of HFD-letrozole induced PMOS animals after treatment for 28 days

	LH (mIU/mL)	FSH (mIU/mL)	LH/FSH
Normal control	9.83 ± 1.69^{a}	4.66 ± 1.03^{a}	2.20 ± 0.60^{a}
Disease control	27.33 ± 1.86^{b}	8.33 ± 1.21^{b}	3.33 ± 0.51^{b}
Metformin (150 mg/kg)	$12.02 \pm 1.26^{a,d}$	4.83 ± 0.75^{c}	$2.52 \pm 0.38^{a,b}$
Kanyasara (25 mg/kg)	16.16 ± 3.11^{c}	5.66 ± 0.51^{c}	$2.90 \pm 0.77^{a,b}$
Kanyasara (50 mg/kg)	$11.16 \pm 0.75^{c,d}$	4.16 ± 0.98^{c}	$2.81 \pm 0.72^{a,b}$

Values (in mg/dL) indicate mean ± SD for six animals; values having the same alphabet in a column did not vary significantly (Tukey's HSD; $P \leq 0.05$)

Table 4 — Effect of *kanyasara*treatment on serum lipid profile of HFD-letrozole induced PMOS animals after treatment for 28 days

	TC	TG	LDL-c	HDL-c	VLDL-c
Normal control	117.02 ± 3.74^{a}	131.66 ± 13.99^{a}	32.67 ± 2.58^{a}	41.33 ± 3.62^{a}	38.23 ± 2.52^{a}
Disease control	150.17 ± 8.75^{b}	279.83 ± 41.28^{b}	70.83 ± 3.50^{b}	17.67 ± 1.03^{b}	65.83 ± 3.43^{b}
Metformin (150 mg/kg)	116.13 ± 20.8^{a}	130.17 ± 5.07^{a}	58.17 ± 3.19^{c}	32.17 ± 1.47^{c}	$42.17 \pm 4.26^{a,c}$
Kanyasara (25 mg/kg)	122.5 ± 19.42^{a}	213.67 ± 8.76^{c}	55.17 ± 4.02^{c}	23.83 ± 2.48^{d}	47.33 ± 2.58^{c}
Kanyasara (50 mg/kg)	107.7 ± 13.37^{a}	207.83 ± 1.94^{c}	43.16 ± 4.26^{d}	27.83 ± 1.16^{e}	$42.83 \pm 3.06^{a,c}$

Values (in mg/dL) indicate mean ± SD for six animals; values having the same alphabet in a column did not vary significantly (Tukey's HSD; $P \leq 0.05$)

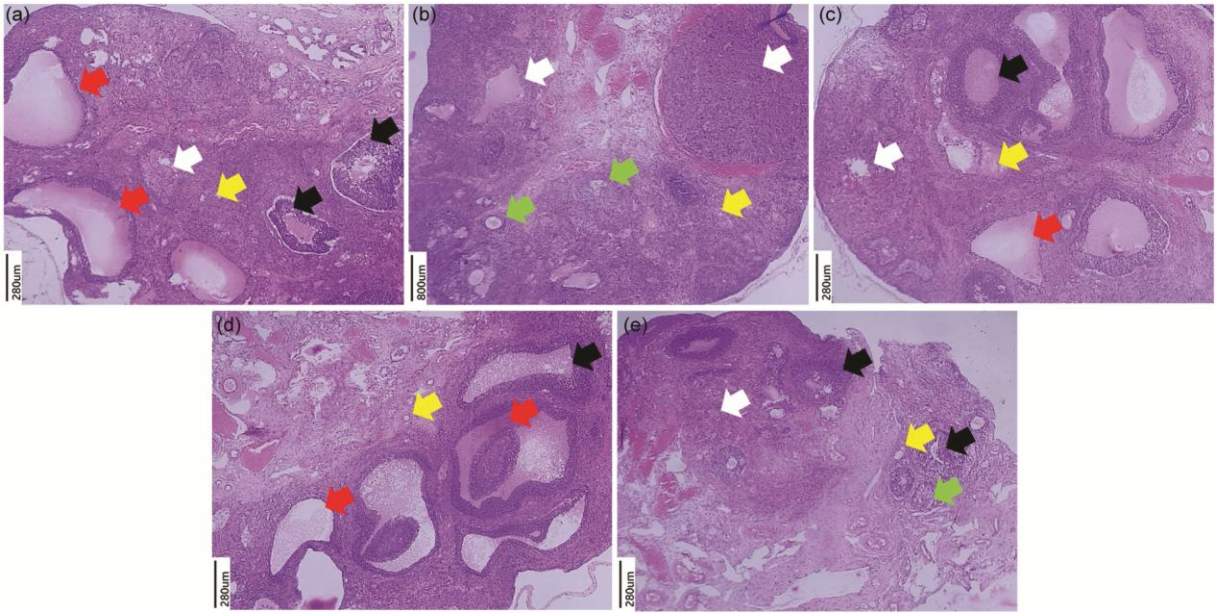

Fig 3 — Representative images of histological sections of the ovary of HFD-letrozole induced PMOS animals after 28 days of treatment with *kanyasara.* Sections were stained with haematoxylin and eosin; (a) normal control, (b) disease control, (c) metformin (150 mg/kg), (d) *kanyasara* treated (25 mg/kg) and (e) *kanyasara* treated (50 mg/kg); preantral follicle (red), antral follicles (black), atretic follicles (green), corpus luteum (white) and ovarian stroma (yellow) were shown with arrows of different colour

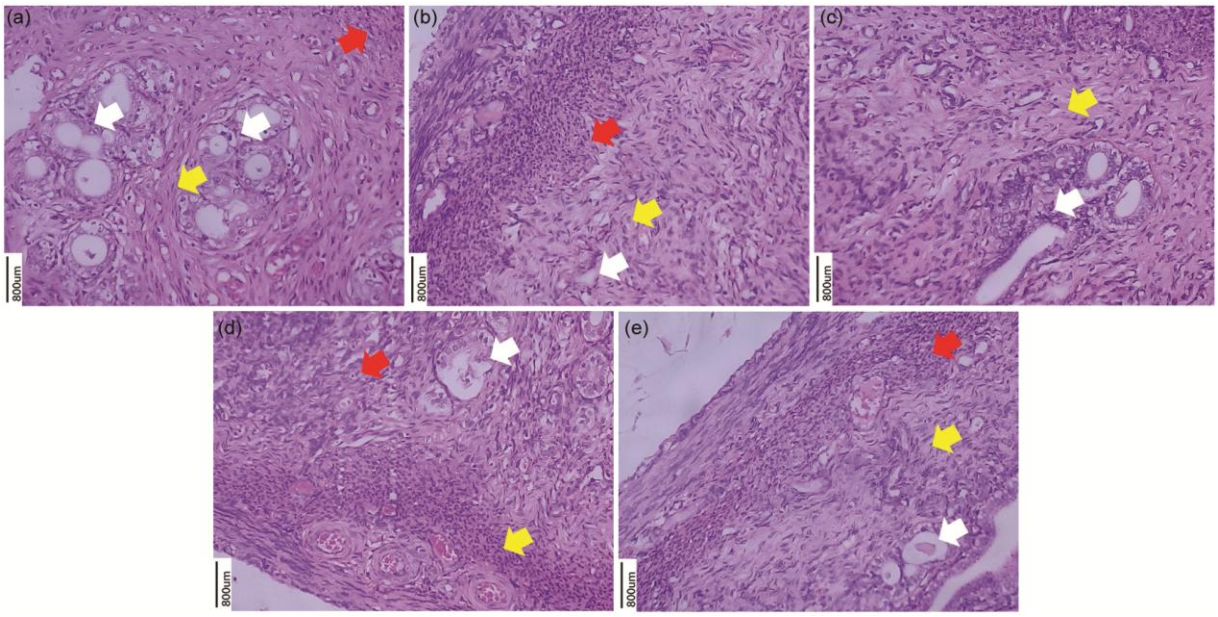

Fig 4 — Representative images of histological sections of the uterus of HFD-letrozole induced PMOS animals after 28 days of treatment with *kanyasara.* Sections were stained with haematoxylin and eosin; (a) normal control, (b) disease control, (c) metformin (150 mg/kg), (d) *kanyasara* treated (25 mg/kg) and (e) *kanyasara* treated (50 mg/kg); endometrial glands (white), stroma (yellow) and myometrium (red) were shown with arrows of different colour

PMOS is a complex metabolic disorder and is strongly linked to insulin resistance, hyperglycemia, abdominal obesity, dyslipidemia, steatohepatitis, and cardiovascular abnormalities[23]. To mimic these metabolic abnormalities, various genetic, hormone- and chemical-induced animal models have been developed for studying PMOS[24]. HFD supplementation triggers insulin resistance[25]; co-administration of letrozole or androgens to the animals induces PMOS with other associated metabolic abnormalities that closely mimic human PMOS[26]. In this study, HFD-letrozole administration

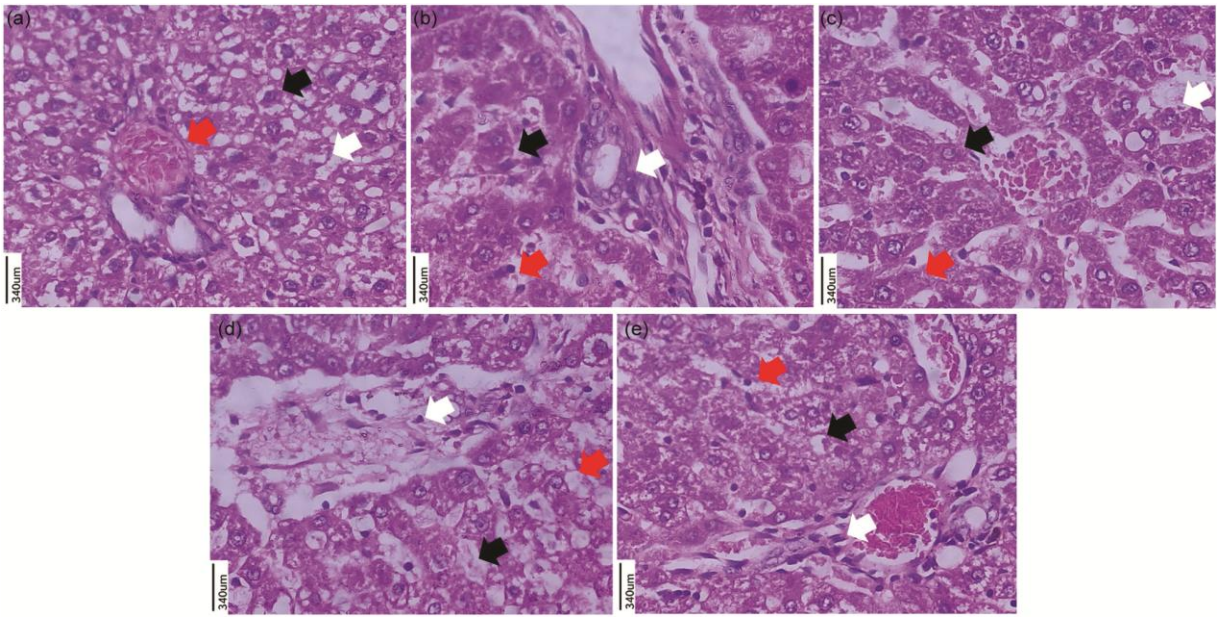

Fig 5 — Representative images of histological sections of the liver of HFD-letrozole induced PMOS animals after 28 days of treatment with *kanyasara*. Sections were stained with haematoxylin and eosin; (a) normal control, (b) disease control, (c) metformin (150 mg/kg), (d) *kanyasara* treated (25 mg/kg) and (e) *kanyasara* treated (50 mg/kg); hepatocytes (black), sinusoids (red) and portal traid (white) were shown with arrows of different colour

exhibited hyperglycemia, dyslipidemia, and steatohepatitis along with PMOS.

HFD-letrozole animals exhibited a significant elevation in blood glucose levels; the treatment with *kanyasara* significantly lowered it by 54.94% at 50 mg/kg concentration, and this effect was comparable to that of metformin. The treatment with *kanyasara* also lowered triglyceride, total cholesterol, and LDL cholesterol levels in a significant manner. Though it was not dose-dependent, the treatment with *kanyasara* lowered the body mass of the animals, without altering feed intake (data not shown). Previous studies demonstrated the adverse effects of hyperglycemia and hyperlipidemia in PMOS and the importance of their control for better management of PMOS[27,28]. The antihyperglycemic, antihyperlipidemic, and hepatoprotective effects of *A. vera* had been previously reported[29]. Several anthraquinones including chrysophanol and emodin exhibited antihyperglycemic effects[30]. The antihyperglycemic effect of aloin was reported in the literature[31]; it was also shown to ameliorate non-alcoholic steatohepatitis[32]. The findings of this study were also in concordance with the previous findings.

In this study, HFD-letrazole animals had elevated levels of LH, a characteristic feature of PMOS. The treatment with *kanyasara* significantly reduced the LH levels; this effect was comparable to that of metformin. The investigation also revealed an elevated LH/FSH ratio in the disease control group, indicating dysregulation in the hypothalamic-pituitary-gonadal axis. Nevertheless, treatment with *kanyasara* reduced this ratio.

The histopathological and histo-morphological analyses confirmed the observed changes in ovarian function in the PMOS rats compared to normal animals. Rats with PMOS exhibited an increased number of follicular cysts and a reduced or absent corpus luteum, along with fewer antral follicles. Additionally, there was hyperplasia of theca cells and thickened ovarian capsules. In contrast, the examination of *kanyasara* treatment revealed distinct stages of follicular development and the presence of corpus luteum, suggesting the restoration of ovarian morphology. Furthermore, this treatment led to the reversal of the typical uterine architecture in rats with PMOS[21].

Feeding a HFD for five weeks resulted in morphological changes in the ovaries. However, when the HFD was supplemented with letrozole in the treated animals, it led to elevated testosterone levels and insulin resistance, exacerbating the PMOS morphology in the ovaries[33]. Similarly, in our study, the mass of the ovaries increased, and histological examination of the ovaries from the HFD-letrozole-treated animals revealed the presence of numerous

atretic follicles and atrophied ovarian stroma. However, in the treated animals, these abnormalities were reduced, and the follicles, corpus luteum, and ovarian stroma exhibited normal characteristics.

HPLC analysis of *kanyasara* indicated that it majorly contained anthraquinones, aloin A and B. Anthraquinones are a group of phytochemicals known for their diverse biological activities. Certain anthraquinones, such as emodin and 2,6-dihydroxyanthraquinone, have been reported to possess estrogenic properties[34,35]. Studies have shown that anthraquinones like emodin can bind to Estrogen Receptor α as isoflavones, with a comparable distance between the two hydroxyl substituents of estradiol and emodin[36]. Diacerin, an anthraquinone derived from aloin and used in the treatment of osteoarthritis, had shown significant improvement in letrozole-induced PMOS in rats in preclinical experiments[37]. These reports were also supportive of the results of this study.

Despite the positive results, certain naturally occurring anthraquinones, including those found in *A. vera*, have been associated with toxicity[38]. Prolonged usage of *A. vera* exudate was shown to be associated with diarrhoea, abdominal issues, hypokalemia, cathartic colon, and cancer[39]. This preliminary study validated the use of *kanyasara* for treating PMOS in a sub-acute preclinical model. However, deeper investigations are required to examine the long-term efficacy and safety of *kanyasara* in the treatment of PMOS.

Conclusion

This study communicates the ameliorative effect of aloin-rich *kanyasara* on PMOS induced by HFD-letrozole in rats. The treatment with *kanyasara* significantly reduced the body mass of HFD-letrozole induced rats with PMOS without altering feed and food intake. The treatment also lowered the blood glucose and serum lipid profile. The treatment with *kanyasara* lowered the FSH and LH levels in a highly significant manner. This study provides validation for the utilisation of *kanyasara* in the treatment of PMOS and warrants the need for further studies.

Ethical statement

The animal studies were approved by the Institutional Animal Ethics Committee at K. K. College of Pharmacy, Chennai (Clearance number: KKCP/2022/03).

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Conflict of interest

The authors declare that they have no competing interests.

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