Journal of Ayurveda & Holistic Medicine

https://jahm.co.in

eISSN-2321-1563

CLINICAL RESEARCH- PILOT STUDY **OPEN ACCESS**

MANAGEMENT OF *SHWETA PRADARA*(ABNORMAL VAGINAL DISCHARGE) WITH *KUKKUTANDA TWAK BHASMA* AND *PIPPALYADI YONI VARTI*: A PILOT STUDY

ANAGHA SIVANANDAN[1*] PARMAR BHAKTIBA L.[2]

[1*]Assistant Professor, Department of Prasutitantra and Streeroga,Murlidhar Ayurved College, Rajkot, Gujarat, India.

[2]Final year BAMS Student, Murlidhar Ayurved College, Rajkot, Gujarat,India.

Corresponding Author Email: anaghasivanandan1@gmail.com **Access this article online: https://jahm.co.in**

Submitted on- 02-12-24	Revised on- 06-12-24	Accepted on-07-12-24

ABSTRACT:

Introduction-Abnormal and excessive white discharge per vagina is termed as *Shweta Pradara*(NAMC code- EL 5) in Ayurvedic classics. It is a very a common complaint reported by the women of reproductive age group.In this trial, a protocol combining both systemic and topical approaches has been implemented for the management of *Shwetapradara.* **Material and methods**: 17 patients fulfilling the inclusion criteria were selected from the OPD of Prasuti tantra and Stree Roga, of the concerned college. *Kukkutanda Twak Bhasma* in a dose of 250 mg twice a day with honey was administered for 30 days and *Pippalyadi yoni varti* was kept per vagina (for 3 hours daily) after the completion of bleeding phase of menstrual cycle for 7 days. The effect of therapy was assessed by change in the scores of assessment criteria and vaginal pH. **Result:** Statistically highly significant ($p<0.001$) results were obtained in amount and consistency of discharge *(Yonisrava)* and *Yonikandu*. Significant($p<0.05$) results were obtained in *Katishoola.* **Discussion:** *Shweta Pradara* can be considered as *Kapha-vata pradhana Tridoshaja Vyadhi* and its line of treatment should be *Kapha-vatahara, Yoni vishodhana* and *Krimighna*. *Sthanika Chikitsa* is having great role when combined with the systemic approach in the management of *Shwetapradara*. The *Kaphahara and Yonivishodhana* action of *Pippalyadi Varti* was supported by the systemic effect *of Kukkutanda Twak Bhasma* leading to appreciable results. **Conclusion:** Oral administration of *Kukkutanda Twak Bhasma* along with local application of *Pippalyadi Yoni Varti* was found to be effective in the management of *Shweta Pradara* and recommended for further research.

Key Words: *Shwetapradara,* Abnormal vaginal discharge, *Kukkutandatwak Bhasma*, *Pippalyadi Varti*, *Sthanika Chikitsa*

INTRODUCTION

Abnormal Vaginal discharge is the most common complaint among women in the reproductive age group. The term "leucorrhoea" being used even in common language nowadays, actually means "a running flow of white substance". It usually refers to the condition where the normal vaginal secretion is increased in amount and the discharge is non-purulent and non-offensive. Even though it is included in abnormal vaginal discharge, it is a physiological one which account for 1/3rd of abnormal vaginal discharges. This is related to general health condition of the women like nutritional factors, hormonal factors and psychological factors. The other types of abnormal vaginal discharges may be considered based upon the colour, consistency, odour etc. Most of them are the results of reproductive tract infections (RTIs) which occupy the second position in public health problems[1]. In 2019, WHO has published estimates of new cases of reproductive tract infections showing total estimated incident cases of 376.4 million among people 15–49 years old in 2016[2].In India, there are no recent data to determine the magnitude of reproductive tract infections including STIs, but a few prevalence surveys among key populations are reported[3]. As per the current estimates, one among four women in the reproductive age group has any one type of reproductive tract infection[4]. The prevalence rate of abnormal vaginal discharge due to reproductive tract infection ranges from 19% to 71% in various states of India [5].

In *Ayurvedic* literature, excessive white vaginal discharge is called as *Shweta Pradara*(NAMC code-EL 5) which is quoted as a symptom in multiple gynaecological disorders. Acharya *Chakrapani* has mentioned the term *Shweta Pradara* while describing the *Chiktisa* of "*Pandura Asrigdara"*[6]. In Sanskrit language, "*Shweta*" means "white" and *"Pandu varn*a" refers to slightly yellowish white colour. The word "*Pradara*" refers to excessive secretion/ discharge from vagina. It is considered as a complication of the disease "*Pandu*" (anaemia) which is caused by vitiation of *Rasa dhatu*. The presentation of *Shweta Pradara* may be due to some pelvic pathologies which are having either inflammatory or non-inflammatory origin which include cervicitis, cervical erosion, polyp etc. *Shweta pradara* may not be considered as a disease, but a symptom of so many diseases. However, sometimes this symptom is so severe that it overshadows the other symptoms of the actual disease and women approach the physician for the treatment of this irritating symptom only.

Conventional medical therapy includes the use of systemic or topical antibiotics and antifungal preparations which may temporarily reduce infection but often disrupt the balance of normal vaginal flora, leading to recurrent infections. Most of the antibiotics and antifungal medicines and their injudicious administration leads to many systemic side effects including gastrointestinal upset like nausea, vomiting, abdominal pain, diarrhoea, skin rash, headache, dizziness, depression, paraesthesia, vertigo etc.

In Ayurveda, *Sthanika Chikits*a(specialized local therapy) has great role in *Stree Roga*(gynaecological conditions) which includes *Yoni Dhavana*(vaginal douche), *Yoni Pichu Dharana* (application and retention of medicine in vaginal cavity using a cotton ball)*, Yoni Dhupana* (Fumigation of vagina), *Yoni Varti*(Vaginal suppositories) etc. These are highly beneficial in curing the infections and maintaining the normal health of vagina. However, Ayurveda always emphasizes a holistic approach considering the root cause of any disease ie, the imbalance in *Tridosha*. Especially in case of *Shweta pradara*, vitiation of *Kapha Dosha* and *Rasadhatu* is predominant along with the vitiation of *Vata Dosha*. Also, there may be some local pathological conditions of infective or non-infective origin which contribute to the manifestation of this symptom. In this trial, the term "*Shweta pradara*" is taken as a general term for excessive white discharge per vagina due to both intrinsic and extrinsic factors and a common protocol addressing both the systemic as well as local domains is adopted for managing *Shweta Pradara.*

MATERIALS AND METHODS:

Study design: Pilot study

IEC approval letter: Ref No.006/MURLI-AYU/IEC/2024, dated 23/02/2024.

Study Population: Female patients attending the OPD of Murlidhar Ayurved College Rajkot, Gujarat, India.

Study Sample: Married women of age group 20-35 years complaining of excessive/abnormal white discharge per vagina who were willing to participate in the clinical trial and provided the informed written consent signed.

Sample Size : Total 17 patients were enrolled for the study. Among them, 16 patients completed the treatment protocol along with follow up and one patient discontinued due to personal reasons.

Diagnostic Criteria: The female patients complaining of excessive/abnormal white discharge per vagina with or without associated symptoms like *Yoni kandu* (itching in vaginal area), *Yoni-daurgandhya* (foul smell),*Yoni Vedana*(pain in vagina), *Kati shoola* (low back pain),*Udara shoola* (pain in lower abdomen) etc.

Inclusion Criteria: Only married women belonging to the age group of 20-35 years and satisfying the diagnostic criteria were included for the study.

Exclusion Criteria: Unmarried women**,** pregnant women, lactating mothers, diagnosed cases of any sexually transmitted diseases(STDs), HIV, genital TB, or any malignant conditions were excluded.

Intervention: The intervention includes oral administration of *Kukkutanda twak Bhasma* for a period of 30 days and intra-vaginal application of *Pippalyadi Yoni Varti* for 7 days (in proliferative phase of menstrual cycle-after the stoppage of menstrual bleeding).*Varti* retention time was advised to be minimum 3 hours or up to next urge of micturition. The details of the trial drugs are given in table no:01 and table no:02.

Table no.01: Dose, Anupana and duration of trial drugs.

Sl.No	Name of Drug	Dosage Form	Dose	Anupana	Duration
1	Kukkutanda tvak Bhasma	Bhasma	250 mg twice a day	Madhu	30 days
2	Pippalyadi Varti[7]	Yoni varti	1 Varti/day (≈2.5g varti)	Dipped in Tila Taila(sesame oil)	7 days

Table no. 02: Ingredients of *Pippalyadi Varti*

Drugs	B.N	Useful part	Form	Quantity
Pippali	Piper longum	Fruit	Choorna	1part
Maricha	Piper nigrum	Fruit	Choorna	1part
Masha	Vigna mungo	Seed	Choorna	1part
Kushta	Saussurea lappa	Root	Choorna	1part
Shatahva	Antheum graveolens	Seed	Choorna	1part
Saindhava	Rock salt	-	-	Qty.suffiecient
Guda	Jaggery	-	-	Qty.suffiecient

Follow up: Follow up was done during every 15 days for a period of 1 month after completion of the treatment protocol.

Assessment Scale: Effect of therapy was assessed based on the grading (0-3) of subjective parameters as per the assessment criteria given in table no:03, as well as change in vaginal pH before and after treatment was also considered as an objective criteria.

Table no.03: Assessment Criteria

Sl No.	Criteria	Grading
1	**Amount of Vaginal Discharge (*Yonisrava*)**	No c/o discharge - 0 Slight discharge(Occasional, vulval moistness)- 1 Moderate discharge (Staining of undergarments but area of staining is less than 10 cm square)- 2 Heavy discharge (Staining area more than 10-20 cm square or patient needs to use a sanitary pad)- 3
2	**Consistency of Vaginal Discharge (*Yonisrava*)**	No discharge-0 Clear watery or mucoid discharge-1

		Thick Curdy or milky discharge-2 Yellowish/ Muco-purulent discharge-3
3	***Yoni Kandu*** **(Itching vulva)**	No itching-0 Occasional(Mild, feeling of irritability, No need of medicine)-1 Moderate(Disturbs daily routine, Need of medicine and relief after medicine,Increase after specific factors like menstruation)-2 Constant(Severe, Affects routine activity, No relief after taking medicine)-3
4	***Kati Shoola*** **(Low back pain)**	No pain-0 Occasional (mild pain, Only feeling of discomfort)-1 Moderate pain(relief after taking medicine, do not interference with daily routine)-2 Severe pain(No relief after taking medicine, Interfere daily routine)-3
5	***Udara Shoola*** **(Lower Abdominal pain)**	No pain-0 Occasional or mild-1 Moderate-2 Severe-3
6	***Yoni Vedana*** **(local tenderness)**	Absent-0 Mild tenderness-1 Moderate tenderness-2 Severe (patient resist for per vaginal examination)-3
7.	***Yoni Daurgandhya*****(foul smell)**	Non offensive-0 Mild foul smell felt only while performing P/S examination-1 Moderate foul smell felt from a short distance-2 Severe foul smell, observer is unable to stand near the patient-3

RESULT

The data of total 16 patients who had completed the treatment protocol along with follow up were considered for statistical analysis of the effect of therapy. The effect of therapy in terms of percentage of relief from different signs and symptoms of *Shwetapradara* is shown in table no. 04.

Table no.04 : Effect of therapy on chief complaints and associate complaints (n=16)

N*	**Assessment Criteria**	**Mean Score**		**Mean Difference**	**Percentage of Relief**
		BT	**AT**		
16	Amount of Vaginal discharge (*Yonisrava*)	2.06	0.5	1.56	75.75%

16	Consistency of Vaginal discharge (*Yonisrava*)	1.93	0.62	1.31	67.74%
15	*Yonikandu*	1.5	0.06	1.44	95.83%
13	*Katishoola*	1.125	0.125	1	88.88%
5	*Udarashoola*	0.315	0.125	0.187	60%
8	*Yoni vedana*	0.56	0.31	0.25	44.44%
6	*Yoni daurgandhya*	0.5	0.185	0.315	62.5%

Wilcoxon Signed Rank test was applied to find out the significance of difference between the scores given to the symptoms before treatment (BT) and after treatment (AT) as per the assessment criteria. Statistically highly significant ($p<0.001$) results were obtained in amount of discharge (*Yonisrava*), consistency of discharge (*Yonisrava*) and *Yonikandu* in comparison of BT and AT Scores in the assessment criteria. Significant($p<0.05$) results were obtained in *Katishoola*. The differences were insignificant in the scores of *Udarashoola, Yonivedana* and *Yoni daurgandhya*.

Student's paired t-test was applied for comparing the values of vaginal pH before and after treatment and the results were statistically insignificant which is shown in table no.05.

Table no. 05: Effect of therapy on pH of vaginal canal

Mean± SD		**Mean Difference**	**T**	**P**	**Significance**
BT	**AT**				
5.044±0.572	4.894±0.330	0.15±0.51	1.162	0.263	IS

Overall effect of therapy : 81.25% of patients got marked improvement (>75 % relief) and 18.75% of patients got moderate improvement (≥50 -75 % relief) in symptoms of *Shwetapradara* as a result of the treatment protocol.

DISCUSSION

An abnormal vaginal discharge is a frequent manifestation of reproductive tract infections, including sexually transmitted infections, so it will be more prevalent among the ladies of reproductive age where there are more chances of getting exposed to pathogenic organisms. A recent study has reported that abnormal vaginal discharge for women of age 35 and less was 5.1 times higher than women of the age of more than 35 years[8].

In this study, excessive use of *Madhura Rasa* and *Katu Rasa*, faulty dietary habits like *Samashana*(eating wholsome and unwholsome food items together), *Vishamashana*(un-timely eating)and *Adhyashana*(over-eating), irregular bowel habits and micturition frequency, psychological stress, faulty intimate hygiene practices, and multiparity were identified as risk factors for manifestation of *Shweta pradara.* Excessive use of Madhura rasa can lead to increase in Kapha Dosha. Recent research works indicted

that sugars can increase Chamydia Trachomatis infectivity and virulence, by modulating the expression/exposure of chlamydial membrane ligands[9]. A previous study reported that the risk of severe bacterial vaginosis(BV) was more than twice as high in women with high fat intake and there was significantly lower risk of severe BV in women with high intakes of folate, vitamin E, and calcium [10].

Majority of the patients enrolled in this study reported irregular bowel habits and 17.64% reported hard stools. Increased frequency of micturition was reported by some patients. A previous study suggested that women with incomplete defecation, dysuria, burning micturition, incomplete urination, urgency and increased frequency of urination had elevated the risk of developing reproductive tract infection[8].

A systematic review reported a significant association between unhygienic sanitary methods performed especially during menstruation and the risk of urogenital infections[11]. Soap or shampoo use for vaginal washing in particular can alter the vaginal microbiota, leading to a higher risk of vaginal symptoms compared to the use of water only for cleaning[12].82.35% of patients enrolled in this study reported psychological stress due to family, work related and personal issues. A previous study also mentioned acute stress as a factor in the mechanism of development of vulvovaginitis[13].

Probable mode of action of *Kukkutanda Twak Bhasma:*_Kukkutanda twak_ has properties which can subside the vitiation of *Kapha* and *Vata* in *Shwetapradara*. It also has the properties of *Rasayana, Balya,* and *Shakti Vardhaka*[14]. Being a good source of calcium, *Kukkutanda twak Bhasma* can improve the overall health status as well as vaginal health in patients of *Shwetapradara*. A previous study had shown that vitamin D plus calcium supplementation is effective in improving vaginal health[15]. The *Rasapanchaka*(Ayurvedic pharmacodynamic parameters) of *Kukkutanda Twak* is also suitable for breaking the *Samprapti*(pathogenesis)of *Shwetapradara*. Being *Kashaya*(astringent) *Rasa*(taste) predominant, it drives of *Kleda*(liquid waste materials)by virtue of *Sangrahi*(absorbent), *Soshana* (drying) and *Shlesma Prashamana* (*Kapaha* pacifying) properties. *Kukkutanda tvak bhasma* is having *Sheeta Virya* (cold potency). *Sheeta virya* drugs can act in *Srortas*(bodily channels) and cause *Stambhana*(arresting the excessive flow) .A previous study has proven that the oral administration of *Kukkutanda Twak Bhasma* 500 mg. twice daily for 3 months is safe and effective in *Shwetapradara* [16].

Probable mode of action of *Pippalyadi Varti:*The mode of action of *Yoni Varti* (vaginal suppository) is yet to be proven scientifically, the hypothetical probability is that vaginal epithelium absorbs water soluble/liophilic active principle. The drugs may help restoring acidic pH of vagina which is protective shield against infection.Generally, Yoni Varti are meant for *Shodhana*(cleansing) purpose. As they are hygroscopic in nature, they absorb the excess *Yoni Srava* (vaginal discharge). The action of the *Varti* depends up on the ingredient drugs. The main action of *Pippalyadi Varti* is referred as "*Yoni vishodhana*"(cleansing the vaginal canal) in classics.

The ingredient drugs are having predominantly *Katu*(pungent) and *Tikta* (bitter) *Rasa*(taste)*, Ruksha Guna* (dry property)and *Ushna Veerya* (hot potency) which will antagonistically act on vitiated *Kapha*. The drugs are also having *Krimihara*(antimicrobial) property. Most of the drugs have proven antimicrobial, antifungal and anti-inflammatory actions. And also, the *Varti* is advised to be inserted into vagina after smeared with *Taila* (oil) .Taila is referred as *Yoni Vishodhana*. Taila is *Sukshma*(subtle) and *Vyavayi* (spreading)so provides a medium to drugs for easy penetration in vaginal epithelium. Drugs administered through vaginal route have a higher bio-availability compared to the oral mute as it bypasses the hepatic circulation. The high vascularity of vaginal wall and the pelvic tissues enables faster absorption of drugs than oral administration. The anatomical position of vagina also enhances the drug action in situ for a period of approximately 3 hours[17]. In vaginal application, generally the lipophilic molecules are transported by the transcellular route, while hydrophilic substances are absorbed by paracellular diffusion. It was found that low molecular weight lipophilic drug molecules undergo better absorption than the larger ones or hydrophilic compounds[18].

The normal pH value of vaginal discharge ranges from 3.4 to 6.4, with an average pH at 4.7[19]. In this study, the mean vaginal pH before treatment was 5.04 which was reduced to 4.89 after treatment. The acidity of the vaginal environment is controlled by the constant secretion of lactic acid by Lactobacillus spp.Bacteria [20]. The treatment protocol may have an effect on correcting the vaginal microbiota by influencing the pH and maintaining a good vaginal health.

CONCLUSION

Shwetapradara can be considered as *Kapha-vata pradhana Tridoshaja Vyadhi* with or without the involvement of *Agantuja*(external) factors like *Krimi*(micro-organisms).

Sthanika Chikitsa (local therapeutic procedures)is having great role when administered along with the systemic approach in the management of *Shwetapradara*.The line of treatment of *Shwetapradara* should be mainly *Kapha-vatahara*, *Yoni vishodhana* and *Krimighna.* The treatment protocol of oral administration of *Kukkutanda Twak Bhasma* along with local application of *Pippalyadi Yoni Varti* is found to be effective in the management of *Shweta Pradara* and recommended for further multi-center trials with large sample size.

REFERENCES

1.National Guidelines on Prevention, Management and Control of Reproductive tract Infections including Sexually Transmitted Infections. National AIDS Control Organization, MOHFW, Govt. of India. 2007:1–2.

2.WHO. Guidelines for the management of symptomatic sexually transmitted infections Geneva: World Health Organization, 2021.

3.Dhabhai N, Chaudhary R, Wi T. et. al, Prevalence of reproductive tract infections including sexually transmitted infections among married women in urban and peri-urban mid to low socioeconomic neighbourhoods of Delhi, North India: an observational study protocolBMJ Open 2022;12:e059583. doi: 10.1136/bmjopen-2021-059583.

4. Sri Devi B, Swarnalatha N. Prevalence of RTI/STI among reproductive age women (15-49 years) in urban slums of Tirupati Town, Andhra Pradesh. Health Popul Perspect Issues.2007;30:56–70.

5. Urai V, Varadharajan S, Muthuthandavan AR. Reproductive tract infections in rural India- A population-based study. J Family Med Prim Care. 2019 Nov 15;8(11):3578-3583.doi: 10.4103/jfmpc.jfmpc_703_19. PMID: 31803656; PMCID: PMC6881949.

6. Yadavaji Trikamaji (editor). Charaka Samhita of Charaka, Chikitsasthana, chapter30, verse no.116.1st edition, Varanasi; Chowkhambha Sanskrit Sansthan;2000:639.

7. K.Shasthri(editor).Charaka Samhita of Charaka, Chikitsasthana, chapter30, verse no.73.8th edition,Varanasi; Chowkhambha Sanskrit Sansthan;2004:761.

8.Durai V, Varadharajan S, Muthuthandavan AR. Reproductive tract infections in rural India - A population-based study. J Family Med Prim Care. 2019 Nov 15;8(11):3578-3583. doi: 10.4103/jfmpc.jfmpc_703_19. PMID: 31803656; PMCID: PMC6881949.

9.Marziali G, Marangoni A, Foschi C, Re MC, Calonghi N. Effect of Sugars on Chlamydia trachomatis Infectivity. Pathogens. 2020 Apr 17;9(4):298. doi: 10.3390/pathogens9040298. PMID: 32316668; PMCID: PMC7237991.

10.Neggers YH, Nansel TR, Andrews WW, Schwebke JR, Yu KF, Goldenberg RL, Klebanoff MA. Dietary intake of selected nutrients affects bacterial vaginosis in women. J Nutr. 2007 Sep;137(9):2128-33. doi: 10.1093/jn/137.9.2128. PMID: 17709453; PMCID: PMC2663425.

11.Alaa Daher, Obey Albaini, Lauren Siff, Stephanie Farah, Karl Jallad,Intimate hygiene practices and reproductive tract infections: A systematic review,Gynecology and Obstetrics Clinical Medicine,Volume 2, Issue 3,2022,Pages 129-135,ISSN 2667-1646,https://doi.org/10.1016/j.gocm.2022.06.001.

12. K.K. Baker, B. Padhi, B. Torondel, et al.From menarche to menopause: a population- based assessment of water, sanitation, and hygiene risk factors for reproductive tract infection symptoms over life stages in rural girls and women in India, PLoS One, 12 (12) (2017), Article e0188234.

13. Istiana Asrari Bansu, Nurdiana Lante, Psychosocial Stress With Vaginal Discharge Of Adolescent Women In The New Normal Era, Science Midwifery, Vol 10, No. 2, April 2022. ISSN 2086-7689.

14. Sashtri Vaidya Shri Laxmipati, Shastri Bhisagratna Pandit Sri Brahma Sankar., editors. Yogaratnakar with Vidyotini Hindi Commentary, Varanasi: Chaukhambna Sanskrit Sansthan; 2004.

15.Mucci M, Carraro C, Mancino P, Monti M, Papadia LS, Volpini G, et al. Soy isoflavones, lactobacilli, Magnolia bark extract, vitamin D3 and calcium. Controlled clinical study in menopause. Minerva Ginecol. 2006;58:323—334.

16.Panda G, Mohapatra KB. Clinical effect of Kukkutanda Tvak Bhasma in the management of Swetapradara. Ayu. 2011 Jul;32(3):370-4. doi: 10.4103/0974-8520.93917. PMID: 22529653; PMCID: PMC3326885.

17.Trisha Moni Das, Yamiben Humtose, Efficacy of pippalyadi yoni varti in kaphaja Yoni vyapad(Vulvovaginal Candidiasis):A case study .World journal of Pharmaceutical research Volume 11 Issue 8,668-673 ISSN2277-7105.

18.Machado R.M., Palmeira-de-Oliveira A., Gaspar C., Martinez-de-Oliveira J., Palmeira- de-Oliveira R. Studies and methodologies on vaginal drug permeation. Adv. Drug Deliv.Rev. 2015;92:14—26. doi: 10.1016/j.addr.2015.02.003.

19.Valea, F.A. Reproductive Anatomy Gross and Microscopic, Clinical Correlations. In Comprehensive

Gynecology; Lobo, R.A., Gershenson, D.M., Lentz, G.M., Valea, F.A., Eds.; Elsevier: Philadelphia, PA, USA, 2017; pp. 48—77. ISBN 978-0-323-32287-4.

20.Miller, E.A.; Beasley, D.A.E.; Dunn, R.R.; Archie, E.A. Lactobacilli dominance and vaginal pH: Why is the human vaginal microbiome unique? Front. Microbiol. 2016, 7, 1936.

CITE THIS ARTICLE AS

Anagha Sivanandan, Parmar Bhaktiba L. Management of *Shweta Pradara*(abnormal vaginal discharge) with *Kukkutanda Twak Bhasma* and *Pippalyadi Yoni Varti*: A Pilot Study. *J of Ayurveda and Hol Med (JAHM)*. 2024;12(11):1-10

Conflict of interest: None

Source of support: None