

A CLINICAL STUDY ON YASHTIMADHU (*GLYCYRRHIZA GLABRA* LINN.) IN POSTMENOPAUSAL SYNDROME

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ABSTRACT

Ayurveda has adopted holistic approach to maintain healthy and long life. Alterations in the body during puberty, reproductive, menopausal and postmenopausal stages, create affinity towards different diseases in a woman's life. The postmenopausal period is associated with significant increase in the incidence of age where make her prone to more diseases. In *Ayurveda*, menopause is a result of jaravastha caused due to change in time, mostly degenerative in which, Vata dosha is predominant along with depletion of all the seven dhatus. Here Rasayanas help in the Postponement of the ageing process and restore the normal functions of the tissues, through which the decaying is prevented. Here an effort had been made to study the impact of

Yashtimadhu (*Glycyrrhiza glabra* Linn.) in menopausal syndrome by applying the principle of Rasayana Karma and also by its phytoestrogen contents. Charaka has advised milk as anupana to Yastimadhu due to its enhancement effect. The patients suffering from Postmenopausal syndrome were divided into two groups, Group A milk as Anupana and Group B water as Anupana for Yastimadhu. Each group contains 15 patients. All the patients were advised to take 3 grams powdered Yastimadhu roots in three divided doses for a period of 45 days. The result showed that the Yastimadhu root powder showed more significance in patients confined to milk as Anupana due to its Rasayana effect than patients in water as Anupana.

KEYWORDS: Postmenopausal syndrome, Yashtimadhu, Phytoestrogen, Anupana, Rasayana, jaravastha.

INTRODUCTION

The state of women health is indeed completely tied up with the culture in which she lives, her position in it, as well as the way she lives her life as an individual. During her span of existence, she undergoes different changes in her psyche and body. The alterations in her body during puberty, reproductive, menopausal and postmenopausal stages, create affinity towards different diseases.

Aging is a real challenge for women. With increasing life expectancy, women spends one third of her lifetime under postmenopausal period. The postmenopausal period is associated with significant increase in the incidence of age related medical conditions like vasomotor, psychological, genital, locomotors and GIT related symptoms, thus affecting the quality of life (QoL) during climacterium in women.^[1]

Rajonivritti is a marker of aging in women. In Ayurvedic classics, it is mentioned under normal physiology. Age of fifty years is mentioned when there is kshaya of Artava due to kshaya of all dhatus in jaravastha. This age of rajonivritti is classified between praudhavastha i.e forty years and Vriddhavastha i.e fifty years in the division of life span of women.^[2]

As postmenopausal period falls under *Jaravastha*, *svabhavika* dhatukshaya and the dominant *Vata Dosha* of this stage contribute in the occurrence of age related conditions according to Ayurvedic view.^[3] Use of *Rasayana* herbs with *Vatashamaka* and *dhatuwardhana* properties prove to be effective in managing *Rajonivritti Janya Lakshana*.

Yastimadhu has been described in Vedas and Vedic texts. Yastimadhu is used in many simple and compound drug preparations to cure various diseases since time immemorial. Yastimadhu is having several dosage forms used internally as well as externally and number of phytoconstituents are present in it. The chief constituent of Liquorice is a terpenoid saponin known as Glycyrrhizin (Glycyrrhizic acid), which is potassium and calcium salt of Glycyrrhizinic acid. Glycyrrhizinic acid is a glycoside and on hydrolysis yields Glycyrrhetic acid (Glycyrrhetic acid) which has a terpenoid structure. The different varieties are found to contain varying amount of Glycyrrhizin (from 6-14%). Spanish liquorices contain 5-10%, Russian liquorices contain 10%, while Persian liquorices contain

7.5-13% of Glycyrrhizin. Another important chemical aspect of liquorices is the presence of flavonoids which are, yellow in colour, are liquiritin and isoliquiritin. The Indian liquorice roots have shown the presence of 2-methyl isoflavones and a coumarin viz. liquor-coumarin. Carbenoxolone is an oleanane derivative prepared from Glycyrrhiza possesses significant mineralocorticoid activity.^[4] Yashtimadhu is having anxiolytic, anti-depressant, having memory enhancing effect, immunomodulatory, anti-inflammatory, anti-microbial, anti-oxidant and adaptogenic properties. Yashtimadhu consists of many phyto-estrogens as they have beneficial effects, mimicking the critical benefits of estrogen in postmenopausal women.

MATERIALS AND METHODS

Collection and Preparation of medicine

The experiment was conducted at the Department of Dravyaguna, S.V. Ayurvedic College/Hospital, Tirupati.

The Yashtimadhu roots were collected from Hyderabad Market. These were then thoroughly cleaned. The dust from roots was completely removed. About 7 kgs of Yashtimadhu roots were taken. This was put into a machine and small pieces of Yashtimadhu roots were collected. This collected Yashtimadhu pieces/product was again added into another machine for powdery form. The ground and coarsely powdered Yashtimadhu was transferred into a sieve with mesh no. 100 to get fine powder. This powder was then tableted, each weighing 500mg.

Selection of Patients

The patients of Postmenopausal syndrome were selected basing on the following criteria.

Inclusion criteria

- Patients of age group of between 40 – 60 years having cardinal Symptoms of menopausal syndrome ;
- Patients fulfilling the diagnostic criteria which is based on symptomatology commonly associated with menopause and on the basis of post-menopausal rating scale were screened;
- Patients who underwent pan hysterectomy with clinical features of menopausal syndrome;
- Patients willing for the treatment were selected

Exclusion criteria

- Patients above 65 years of age.
- Patients suffering from diabetes, malignant disorders, renal calculi and thyroid related problems.
- Patients who suffered previously from either cardiac or cerebral stroke and also the patients who were seriously ill otherwise.

Diagnostic criteria

Patients were examined clinically and details regarding disease starting from history taking, physical examination, signs and symptoms as mentioned in our classics and allied sciences and relevant lab investigations were recorded in a specially prepared proforma.

Special clinical proforma for the assessment of subjects was prepared, based on criteria of selection and parameters. Special grading was given to chief symptoms/signs of menopausal syndrome. Consent of all the registered subjects was taken prior to the commencement of the treatment.

General investigations

- Routine Haematological:-

Blood

1. TLC
2. DLC
3. ESR(1ST hour)
4. Hb%
5. RBS

Urine

Routine and Microscopic

Specific investigations

pH of vagina

FSH and USG of necessary

Criteria for Assessment

Patients were assessed before and after treatment for subjective and objective parameters.

Subjective Parameters

Assessment was totally based on the changes in the clinical features of *Menopausal syndrome* and improvement in scoring index of *hot flushes, sweating, sleep disturbance, depression, and mood swings etc.* For all these symptoms, the following symptom scores were given depending upon the changes seen before and after the treatment.

Subjective criteria

The result was assessed on the basis of symptoms of post menopause. Quantitative assessment symptoms were carried out by adopting a special scoring pattern.

Table 1: Post-Menopausal Rating Scale.

Parameters	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Hot Flushes	No Flushes	Occasional and very mild hot flushes	Intermittent once In 10-15 days With less duration	Frequent hot Flushes(< once In 5 days)	Severe hot Flushes daily
Night Sweats	No Night Sweats	Occasional and Very Mild night sweats	Intermittent, once In 10-15 days With less duration	Frequent night Sweats (< once In 5 days)	Frequent night Sweats (<once In 5 days)
Fatigue	No Fatigue	Fatigue with Heavy exertion	Fatigue with Exertion	Fatigue with house Hold works	Fatigue with no Work
Bloating Abdomen	No bloating Abdomen	Bloating abdomen But no pain	With mild pain on and off bloating abdomen	Frequent with constipation And Abdominal Pain	Persistent With Unexplaining Bloating/ Stomach Pain and constipation
Veginal dryness (Or) Burning sensation Of Vegina	No veginal Dryness	Burning sensation Of vagina Occasionally	Feels burning sensation/ Dryness When exposed to Unhygienic toilets(climate)	Frequent Veginal Dryness/burning Sensation	Severe burning Sensation/ dryness in Vagina which Is continuous
Insomnia /sleep Disorders	Sound sleep	Occasionally mild Disturbance in Night Sleep with duration Of 6-7 hrs	Frequently disturbed Night sleep with 4-5hrs of duration	Disturbed sleep With Only 2-3 hrs of night sleep	Completely disturbed Night sleep
Arthralgia	No pains	Very mild pains which Occurs Occasionally And can walk/ sit freely Without	Moderate pain and Can freely walk but Feels difficulty in Sitting on floor and On doing works	Moderate bearable Pains with swelling And difficulty on Doing works	Severe unbearable pain associated with swelling and restricted movements

		support			
Incontinence of Urine	No Incontinence	Incontinence with over flow Occasionally	Incontinence with Cough/sneeze	Can't control the Urge	Persistent
Memory lapses	No memory Lapses	Loss / forgot the more recent things	Loss of past thing	Loss of distant past Things	Short and Long Memory Impairment
Depression	No Depression	Sad	Feeling of hopeless	Feeling of alones	Suicidal tendency
Burning micturition	No Burning micturition	With mild pain/burning	With moderate pain/ burning	Severe pain/burning but bearable	Burning micturition with unbearable pain
Hirsutism	No Hirsutism No hair	Appearance of hair on Upper lip/chin/bath	thin hair on Upper lip/chin/ bath and chest	Back thin hair along with grade 2 changes	Abdomen arms, thighs, legs, thick with rapid growth of hair

3.1.2 Objective criteria

Objective	G0	G1	G2	G3
Vaginitis	No vaginitis	Tenderness, soreness +	Doesn't allow speculum/digital examination	Bleeding with examination & tenderness but with negative pap smears

Grouping

30 patients of Postmenopausal syndrome were selected and randomly divided into two groups, each consisting of 15 patients.

1. Group - A: The patients of group A were advised to take Yastimadhu tablet with Milk as Anupana.

2. Group- B: The patients of group B were advised to take Yastimadhu table Water as Anupana.

Duration of treatment

The course of the treatment was fixed for 45 days. All the patients were given digestant drugs like sunthi for 7 days prior to the trail drug administration. During this period, the investigations were carried out and there after the trail drug was administered.

Dose

Each patient under experimentation was administered three grams of powdered Yastimadhu in three divided doses per day.

Follow up

After completion of the treatment, the patients of both the groups were examined during follow ups at the interval of Two weeks for 45 days.

Statistical Evaluation of Results

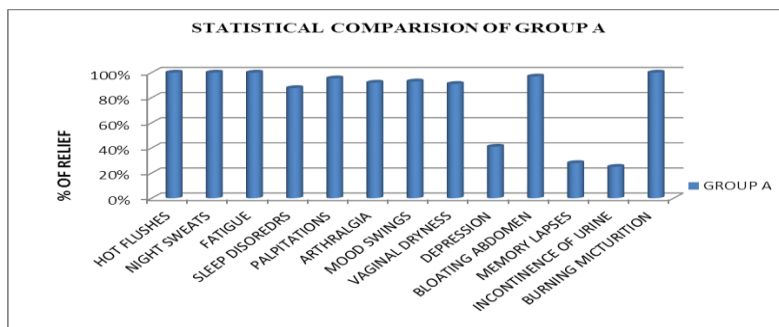
The obtained information was analysed statistically in terms of mean score (x), Standard Deviation (S.D.), Standard Error (S.E.). Paired t-Test was carried out at the level of 0.05, 0.001, and 0.0001 of P levels. For the more effectiveness of therapy paired t-Test is carried out. The results were interpreted as

- a) $P > 0.05$: Insignificant
- b) $P < 0.05$: Significant
- c) $P < 0.001$: Very significant
- d) $P < 0.0001$: Extremely significant

OBSERVATION AND RESULTS**Table 2: Effect of Medicine on Postmenopausal Syndrome of Group-A Patient.**

Parameters	Mean		Mean diff.	S.D.		S.E.		't'	P	Significance
	B.T.	A.T.		B.T.	A.T.	B.T.	A.T.			
Hot flushes	3.00	0.00	3.00	0.60	0.00	0.17	0.00	17.233	<0.0001	Extremely significant
Night sweats	3.20	0.00	3.20	0.42	0.00	0.13	0.00	24.000	<0.0001	Extremely significant
Fatigue	2.42	0.00	2.42	0.51	0.00	0.15	0.00	16.257	<0.0001	Extremely significant
Sleep Disorders	2.36	0.29	2.07	0.63	0.61	0.17	0.16	12.587	<0.0001	Extremely Significant
Palpitations	2.44	0.11	2.33	0.53	0.33	0.18	0.11	5.336	<0.0001	Extremely Significant
Arthralgia	2.64	2.07	2.44	0.50	0.83	0.13	0.22	4.163	0.0011	Very significant
Mood Swings	2.33	0.17	2.17	0.78	0.39	0.22	0.11	10.457	<0.0001	Extremely Significant
Vaginal Dryness/ Burning Sensation	2.67	0.22	2.44	0.50	0.44	0.17	0.15	13.914	<0.0001	Extremely Significant
Depression	2.43	1.43	1.00	0.53	1.27	0.20	0.48	3.240	0.0177	Statistically Significant
Bloating Abdomen	2.92	0.08	2.83	0.79	0.29	0.23	0.08	13.674	<0.0001	Extremely Significant
Memory Lapses	2.25	1.63	0.63	0.46	0.52	0.16	0.18	3.415	0.0112	Statistically Significant
Incontinence of Urine	2.67	2.00	0.67	0.82	0.63	0.33	0.26	2.000	0.1019	Not statistically significant
Burning Micturition	2.70	0.00	2.70	0.48	0.00	0.15	0.00	17.675	<0.0001	Extremely Significant

Above table shows extremely reduction of many Postmenopausal symptoms statistically in Group-A.

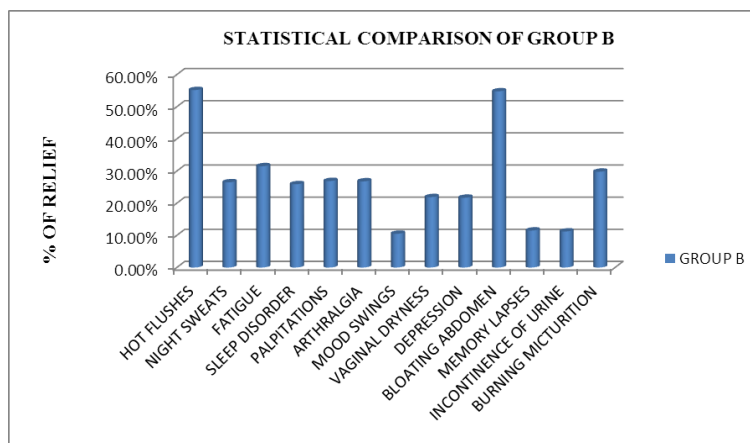


Graph No. 1: Effect of Medicine on Postmenopausal Syndrome of Group - A Patients.

Table 3: Effect of Medicine on Postmenopausal Syndrome of Group-B Patients.

Parameters	Mean		Mean diff.	S.D.		S.E.		't'	P	Significance
	B.T.	A.T.		B.T.	A.T.	B.T.	A.T.			
Hot flushes	3.17	1.42	1.75	0.72	1.08	0.21	0.31	8.0424	<0.0001	Extremely significant
Night sweats	3.09	2.27	0.82	0.70	0.90	0.21	0.27	4.5000	0.0011	Very significant
Fatigue	2.69	1.85	0.85	0.48	0.80	0.13	0.22	4.4296	0.0008	Extremely significant
Sleep disorders	2.58	1.92	0.67	0.51	0.90	0.15	0.26	3.5456	0.0046	Very significant
Palpitations	2.60	1.90	0.70	0.52	0.88	0.16	0.28	2.6888	0.0248	Statistically significant
Arthralgia	2.50	1.83	0.67	0.52	0.94	0.15	0.27	2.9665	0.0128	Statistically significant
Mood Swings	2.55	2.27	0.27	0.69	0.65	0.21	0.19	1.9365	0.0816	Not quite Significant
Vaginal Dryness/Burning Sensation	2.91	2.27	0.64	0.54	0.79	0.16	0.24	4.1833	0.0019	Very significant
Depression	2.67	2.08	0.58	0.49	0.79	0.14	0.23	3.0225	0.0116	Statistically significant
Bloating Abdomen	3.08	1.38	1.69	0.76	1.04	0.21	0.29	6.4409	<0.0001	Extremely Significant
Memory Lapses	2.60	2.30	0.30	0.52	0.67	0.16	0.21	1.9640	0.0811	Not quite Significant
Incontinence of Urine	2.57	2.29	0.29	0.53	0.76	0.20	0.29	1.5492	0.1723	Not statistically significant
Burning Micturition	3.08	2.15	0.92	0.86	0.99	0.24	0.27	12.000	<0.0001	Extremely Significant

Above table shows reduction of Postmenopausal symptoms statistically in Group-B



Graph 2: Effect of Medicine on Postmenopausal Syndrome of Group-B Patients.

Table 4: Over All Result of the Study – % of Relief A. Parameters Wise Result In Group A & Group B/

Parameters	Group A	Group B
Hot flushes	100	55.2
Night sweats	100	26.5
Fatigue	100	31.5
Sleep disorders	87.7	25.9
Palpitations	95.4	26.9
Arthralgia	92	26.8
Mood swings	93	10.5
Vaginal dryness/burning sensation	91	21.9
Depression	41	21.7
Bloating abdomen	96.9	54.8
Memory lapses	28	11.5
Incontinence of urine	25	11.2
Burning micturition	100	29.8
Vaginitis	60	20
pH of Vagina	53	26

The overall result showed that the medicine had shown more effective result in group A patients than in the group B patients.

B. Improvement Wise Result In Group A and Group B.

Overall effect	Group A	Group B
Completely relieved	53.33%	20%
Moderately relieved	26.66%	33.33%
Mildly relieved	20%	20%
Unchanged	0%	26.66%

DISCUSSION

A clinical Study of Yastimadhu (*Glycyrrhiza glabra* Linn.) in Postmenopausal syndrome showed significant result. Yastimadhu is considered to be effective as it could reduce the Postmenopausal symptoms in both the groups of patients. But comparatively the patients belonging to the Group A exhibited a better response.

Probable mode of action of drug

Yastimadhu is having madhura rasa, madhura vipaka, sita virya and guru, Snigdha gunas. It is mainly Vata-pitta shamaka.⁵ Madhura rasa is said to be indriya prasadaneeya and so it uplifts the function of all indriyas including the Manas. On administration, with the help of madhura rasa, sita virya and Madhura vipaka, Yastimadhu is expected to pacify the symptoms of Pitta and by guru, Snigdha gunas and madhura vipaka it normalizes aggravated vata. Vata is the main factor of dhatu kshaya in jaravastha (senility).

Yastimadhu is jivaniya, rasayana and balya. It is one of the best rasayanas as in relation with women due to its vata, pitta shamaka properties and its ability of replenishing dhatus. Such rasayana agents contain in their bulk, high quality of nutrients and as such when administered, they are directly added to the pool of nutrition and in turn help in improved tissue nourishment leading to subsequent Rasayana effect. And also vitalize the metabolic activity resulting in turn improve nutritional status at the level of dhatus. As Rasayana it is said to be having Medhya effect and is meant for improving Medha in particular and helps in psychological functions in jaravasta.

Discussion on phytoestrogens of Yastimadhu

A variety of plant extracts contain compounds, which have activity similar to ovarian steroid hormones and commonly referred to as phytoestrogens.

Among the many plants, Yastimadhu consists of many phyto-estrogens as they have beneficial effects, mimicking the critical benefits of estrogen. The liquorice extracts and its major isoflavan Glabridin acts as estrogen receptor(ER) agonist under in vitro and in vivo conditions. The enzyme creatine kinase is a biomarker for estrogen responsive gene. Liquiritigenin was found to be the principle phytoestrogen of the liquorice extract. Isoliquiritigenin, is the precursor chalcone of liquiritigenin. Glabrene and isoliquiritigenin have a higher affinity for human ER as compared to Glabridin.^[6]

These phytoestrogens have beneficial effects mimicking the critical benefits of estrogen in postmenopausal women

Goksheera

Milk is considered as a complete diet. Among all the jeevaneeya dravyas,ksheera is said to be superior. Regular consumption of milk brings rasayana effect in the body. Ten qualities of milk are similar to those of ojus.⁷ It is the best pathya drug, especially in debilitating conditions. Milk is widely used as food as well as adjuvant. This is highly useful in senile states.

Effect of Yastimadhu with milk

Glabridin is a fat soluble compound native to liquorice. Its molecular structure and lipophilic nature are similar to that of estradiol.

Glabridin, a major active flavonoid in *Glycyrrhiza glabra* Linn. improves memory. Glabridin is clinically used nootropic agent and appears to be a promising drug for memory improvement and it will be worthwhile to explore the potential of glabridin in the management of Alzheimer patients. The combination of antioxidant, neuroprotective and anticholinesterase properties of glabridin may all be responsible for the observed effects.^[8]

RESULTS

The overall effect of the clinical trial on Group A (Yastimadhu with milk) shows that 8 patients (53.33%) were completely cured, 4 patients (26.66%) were cured moderately and 3 patients (20%) were cured mildly.

The overall effect of the clinical trial on Group B (Yastimadhu with water) 3 patients (20%) were completely cured, 5 patients (33.33%) were cured moderately, 3 patients (20%) were cured mildly and 4 patients (26.66%) were not cured.

Subjective Parameters

Interpretation of results in Group A

The therapy has been carried out in total 15 patients in group A

The effect of therapy on Postmenopausal rating scale has shown that there is statistically extremely significant ($P < 0.0001$) relief in Hot flushes by 100% relief, in night sweats by

100%, in sleep disorders by 87.7%, in bloating abdomen by 96.9%, in burning micturition by 100%, in vaginal dryness by 91%, in mood swings by 93%, in palpitations by 95.4%, relief.

The effect of therapy on postmenopausal rating scale has shown that it is statistically very significant ($P < 0.01$) in arthralgia (92%).

The effect of therapy on postmenopausal rating scale has shown significant ($P < 0.05$) results in memory lapses (28%) and depression (41%).

The effect of therapy on postmenopausal rating scale has shown insignificant ($P > 0.05$) results in incontinence of urine (25%).

Interpretation of results in Group B

The therapy has been carried out in total 15 patients in group B.

The effect of therapy on postmenopausal rating scale has shown that there is statistically extremely significant ($P < 0.0001$) result in hot flushes by 55.2%, in bloating abdomen by 54.8%.

The effect of therapy on postmenopausal rating scale has shown that the drug is statistically significant ($P < 0.01$) in night sweats (26.5%), fatigue (31.5%), sleep disorders (25.9%) and vaginal dryness (21.9%).

The effect of therapy on postmenopausal rating scale has shown significant ($P < 0.05$) results in palpitations (26.9%), depression (21.7%) and arthralgia (26.8%).

The effect of therapy on postmenopausal rating scale has shown insignificant ($P > 0.05$) results in incontinence of urine (11.2%), memory lapses (11.5%), and mood swings (10.5%)

OBJECTIVE PARAMETERS

Vaginitis

The effect of therapy on vaginitis has shown significant relief in 53% patients in group A and 20% in group B Patients. Due to estrogenic property good epithelium is developed. Good vaginal epithelium is resistant to infections.

Vaginal PH

Change in PH of vagina is observed in 60% of patients in group A shows and 33.33% in patients of Group B. Due to the same estrogenic property (due to epithelium formation) vaginal pH is maintained. So, pH has shown the reduction change from 7 to 5

Discussion on overall result

The improved variation in the menopausal rating scale especially in hot flushes, night sweats, palpitations, bloating abdomen, burning micturition, vaginal dryness, mood swings may be due to Yastimadhu and its best Rasayana in relation with women due to its vata, pitta shamaka properties and its ability of replenishing dhatus.. Such rasayana agents contain in their bulk, high quality of nutrients and as such when administered, they are directly added to the pool of nutrition and in turn help in improved tissue nourishment leading to subsequent Rasayana effect. As Rasayana it is said to be having Medhya effect and is meant for improving Medha in particular and helps in psychological functions in jaravasta.

Enhanced efficacy of Yastimadhu in Group A over Group B

All the observations related to total effect of therapy suggests that patients of Group A responded better to the therapy than the patients of Group B.

Charaka has advised milk as anupana to Yastimadhu.^[9] So, the same is followed in the patients of Group A. To study the role of anupana, the patients of Group B were advised to take the drug without anupana (that means only with water)

The oushadha becomes more potent when it is given with suitable Anupana by considering the avastha (stage) and bala (strength) of the rogi and roga (patient and disease).

Milk is a media and a conveyer of medicinal properties of Yashtimadhu to the cells. It may act as a fat and water soluble media for the active principles in the herb. Its nutritious qualities support the anti-ageing qualities of the Rasayana medicines.

It is mentioned in Ayurveda that Anupana enhances the assimilation of the drug and further it influences drug pharmacodynamics and pharmacokinetics at various levels. Thus it seems the usage Yastimadhu along with milk as an adjuvant exhibites synergistic affect in this case of postmenopausal syndrome.

The present study also confirms that milk is the best adjuvant in the consumption of Yastimadhu churna in senile time depletion i.e. in post menopausal syndrome

CONCLUSION

The present clinical study proved that Yastimadhu is one of the best Rasyanas and is highly effective in Jarajanya vikaras particularly in menopausal syndrome.

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