

Evaluation of the efficacy and safety of Menosan in the management of postmenopausal syndrome with special reference to improvement in the quality of life: A prospective, double blind, randomized, placebo-controlled, phase III clinical trial

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ABSTRACT

Ovarian senescence is accompanied by physical changes and psychological changes, and life stressors, surgical menopause and poor health exacerbate these menopausal symptoms. Recent studies have cast doubt on the cardioprotective effects of HRT, as the combination of HRT has been shown to lead to increased risks of CADs, CVAs, pulmonary embolism, in addition to increased risks of vaginal bleeding and breast cancer. These adverse events have given fillip to effective and safer alternative approaches; and phytoestrogens are currently heralded

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ABBREVIATIONS

BSO	:	Bilateral surgical oophorectomy
CVA	:	Cerebrovascular accident
CVD	:	Cardiovascular disease
ECG	:	Electrocardiograph
HERS	:	Heart and estrogen/progesterone replacement study
HRT	:	Hormone replacement therapy
HS	:	Highly significant
LDL	:	Low density lipoprotein
LDL-C	:	Low density lipoprotein-cholesterol
NS	:	Not significant
NYHA	:	New York Heart Association
PMO	:	Postmenopausal osteoporosis
QOL	:	Quality of life
S	:	Significant
UTI	:	Urinary tract infection
WHI	:	Women Health Initiative
WHO	:	World Health Organization
WHODAS	:	World health organization disability assessment schedule
WHOQOL	:	World health organization quality of life

as the potential therapy for estrogen-dependent diseases. Menosan is a polyherbal formulation, which is a rich source of phytoestrogens and this study was planned to evaluate the efficacy and safety of Menosan in postmenopausal syndrome, with special reference to improvement in the QOL.

This study was a prospective, double blind, randomized, placebo-controlled, phase III clinical trial, conducted as per the ethical guidelines of Declaration of Helsinki. A total of 40 female patients who underwent total abdominal hysterectomy with BSO, and were suffering from surgical menopause were included in the trial. At the randomization visit, a detailed medical history was obtained

to ascertain the presence of postmenopausal symptoms. Thereafter, all the patients underwent complete physical and gynecological examination and laboratory investigations. The hormonal level assessment was done at baseline and at the end of the study. Radiological examination, ECG, bone densitometry and mammography were also done for all the patients. All the patients were evaluated for QOL status by using 2 scales i.e. the WHO-QOL-BREF and WHODAS questionnaires. All the patients were randomly divided into the drug and placebo groups, and each group had 20 patients. All the patients, from both the groups received the respective drugs, from the 7th postoperative day till completion of the next 3 months, in

a dose of 1 tablet twice daily, orally. All the patients were followed up for a total period of 3 months. The predefined primary efficacy endpoints were improvement in the mean postmenopausal symptom score and improvements in laboratory parameters. The predefined secondary safety endpoints were reduced incidence of adverse events and overall patient compliance to the drug therapy. All the adverse events either reported or observed by the patients were recorded with information about severity, date of onset, duration and action taken regarding the study drug. Statistical analysis was done according to intent-to-treat principles.

This study observed highly significant improvement in the "Physical health", "Psychological health" and "Social relationships" domains, in the Menosan group, as compared to the placebo group, at the end of the study period. Also, there were no clinically significant changes in the hematological and biochemical parameters and there were no clinically significant adverse reactions, which is reflected in the excellent patient compliance. These effects might be due to the phytoestrogens and calcium present in Menosan. Therefore, it may be concluded that Menosan is clinically effective and safe in the management of postmenopausal syndrome, and for improving QOL in postmenopausal patients.

INTRODUCTION

The loss of estrogen and progesterone production is the hallmark of "ovarian senescence" (the process of aging) and subsequent menopause. This hormonal decline is accompanied by ubiquitous changes throughout the body. This transition to menopause is frequently accompanied by significant physical changes (vasomotor symptoms, sleep pattern disruption and sexual dysfunction) and psychological changes (mood disturbances, depression, irritability and cognitive dysfunction).¹⁻³ Certain factors like life stressors, surgical menopause and poor health exacerbate these menopausal symptoms.^{4,5}

Recent years have witnessed remarkable research in menopause

management and currently, several treatment options are available for perimenopause management. However, recent studies (e.g. HERS trial)⁶ have cast doubt on the cardioprotective effects of HRT,⁷ and these concerns have been further accentuated after mid-term results of the WHI trial. (The WHI study, which was initiated in 1992, involved 16,000 postmenopausal women and was planned to run through the 2007, but was stopped in July 2002 because of its shocking results.⁸ Based on the interim analysis, it was concluded that the combination of HRT led to increased risks of CADs, CVAs, pulmonary embolism,⁹ vaginal bleeding¹⁰ and breast cancer.¹¹ These short- and long-term adverse events have given fillip to clinically effective and much safer alternative approaches, and phytoestrogens (plant-derived estrogens) are currently heralded as the potential therapy for estrogen-dependent diseases (postmenopausal syndrome, cancer, CVAs and PMO).

Menosan is a polyherbal formulation and is a rich source of phytoestrogens. Menosan is recommended for the management of postmenopausal syndrome and it contains the extracts of *Asparagus racemosus*, and *Saraca indica*, and the powders of *Centella asiatica*, *Terminalia chebula*, *Glycyrrhiza glabra*, *Sida cordifolia*, *Kuk-kutandativak bhasma* and *Zaharmohara bhasma*. This study was planned to evaluate the efficacy and safety of Menosan in postmenopausal syndrome, with special reference to improvement in the QOL.

Aim of the study

This clinical trial was planned to evaluate the efficacy and safety (short- and long-term) of Menosan in postmenopausal syndrome, with special reference to the improvement in the QOL.

Study design

This study was a prospective, double blind, randomized, placebo-controlled, phase III clinical trial, conducted at the Outpatient clinic of the Department of Obstetrics and Gynecology, Lady Hardinge Medical College and SSK Hospitals, New

Delhi, India as per the ethical guidelines of Declaration of Helsinki. The study protocol, case record forms, regulatory clearance documents, product related information and informed consent forms were submitted to the institutional ethics committee, and were approved by the same.

MATERIALS AND METHODS

Inclusion criteria

A total of 40 female patients who underwent total abdominal hysterectomy with BSO, and were suffering from surgical menopause were included in the trial.

Exclusion criteria

Patients on treatment with estrogenic drugs, calcium building drugs (bisphosphonates and calcitonin), corticosteroids or those patients consuming any herbal supplement/s [including dehydroepiandrosterone (DHEA)] within 3 months prior to enrollment in the study, and those patients, who were not willing to give informed consent were excluded from the study.

Study procedure

At the randomization visit, a detailed medical history was obtained to ascertain the presence of postmenopausal symptoms (hot flushes, night sweats, pruritus vulvae, dryness of vagina, backache, insomnia, headache, fatigue, anxiety, irritability and depression). Thereafter, all the patients underwent complete physical and gynecological examination and laboratory investigations (hematological, microbiological and biochemical). The hormonal level assessment was done at baseline and at the end of the study. Radiological (USG abdomen and pelvis) examination, ECG, bone densitometry and mammography were also done for all the patients.

All the patients were evaluated for QOL status by using 2 different scales i.e. the "WHOQOL-BREF"¹² and the "World Health Organization Disability Assessment Schedule (WHODAS)"¹³ questionnaires.

All the patients were randomly divided into the drug and placebo groups, and each group had 20 patients. All the patients from both the

Table 1: Improvement in the mean score for "Physical health" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	10.26	11.51	15.35	10.26	10.35	10.4
SD	0.3545	0.9824	2.277	0.3545	0.4894	0.5026
SEM	0.07927	0.2197	0.5092	0.07927	0.1094	0.1124
Lower 99% CI	10.03	10.88	13.89	10.03	10.04	10.08
Upper 99% CI	10.49	12.14	16.8	10.49	10.66	10.72
ANOVA summary	F=63.61, R ² =0.77; p<0.0001; HS			F=1.264, R ² =0.0624, p=0.2940; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-1.25	2.66	p<0.05	-2.650 to 0.1503	-0.09	1.009	p>0.05	-0.3559 to 0.1759
Baseline vs. 3 month	-5.085	10.82	p<0.001	-6.485 to -3.685	-0.14	1.569	p>0.05	-0.4059 to 0.1259

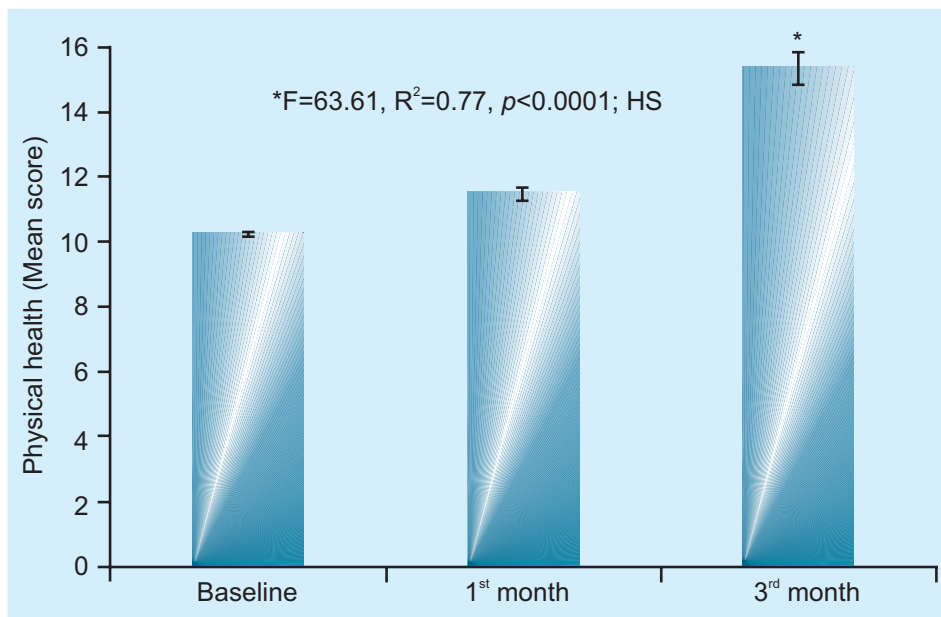


Figure 1: Improvement in the mean score for "Physical health" with Menosan treatment

groups received the respective drugs, from the 7th postoperative day till completion of the next 3 months, in a dose of 1 tablet twice daily, orally.

Follow-up and assessment

All the patients were followed up for a total period of 3 months and at each follow-up visit, a complete clinical examination, gynecological examination and QOL assessment was done.

Primary and secondary endpoints

The predefined primary efficacy

endpoints were improvement in the mean postmenopausal symptom score and improvements in laboratory (hematological and biochemical) parameters. The predefined secondary safety (short- and long-term) endpoints were reduced incidence of adverse events and overall patient compliance to the drug therapy.

Adverse events

All the adverse events reported or observed by patients were recorded with information about severity, date

of onset, duration and action taken regarding the study drug. Relation of adverse events to the study medication were predefined as "Unrelated" (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), "Possible" (follows a known response pattern to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), and "Probable" (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state).

Patients were allowed to voluntarily withdraw from the study if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Noncompliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure and reasons for non-compliance were noted.

Statistical analysis

Statistical analysis was done according to intent-to-treat principles. "Repeated Measures ANOVA Test"

Table 2: Improvement in the mean score for "Psychological health" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	10.26	11.2	15.35	10.26	10.26	10.27
SD	0.3545	1.077	2.277	0.3545	0.3817	0.4196
SEM	0.07927	0.2407	0.5092	0.07927	0.08535	0.09383
Lower 99% CI	10.03	10.51	13.89	10.03	10.02	9.997
Upper 99% CI	10.49	11.89	16.8	10.49	10.5	10.53
ANOVA summary	F=66.99, R ² =0.779, p<0.0001; HS			F=0.002005, R ² =0.0001055, p=0.9980; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-0.94	2.011	p>0.05	-2.333 to 0.4533	0	0	p>0.05	-0.2718 to 0.2718
Baseline vs. 3 months	-5.085	10.88	p<0.001	-6.478 to -3.692	-0.005	0.05483	p>0.05	-0.2768 to 0.2668

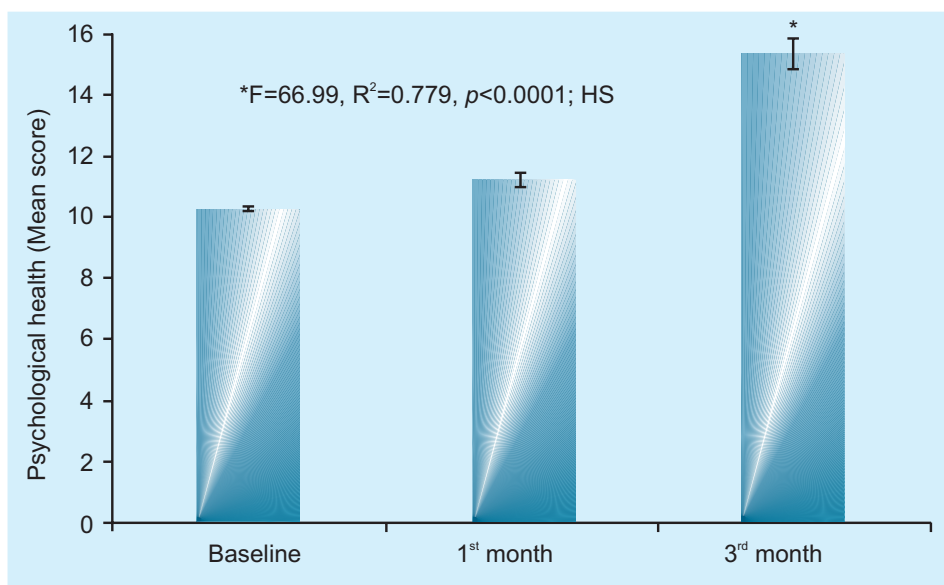


Figure 2: Improvement in the mean score for "Psychological health" with Menosan treatment

and "Bonferroni's Multiple comparison test" evaluated the changes in the baseline values and the values after 6th, 9th and 12th month. The minimum level of significance was fixed at 99% confidence limit and a two-sided "p" value of <0.0001 was considered as highly significant.

RESULTS

There was a highly significant improvement in the 'physical' 'psychological' and 'social relationships' domains in the Menosan group, as compared to the placebo group, at the end of the treatment.

In the "Physical domains", the mean scores for Menosan improved from baseline of 10.26 to 15.35 at the end of 3 months (F=63.61, R²=0.77, p<0.0001; HS) (Table 1 and Figure 1). The mean symptom score for "Psychological domains" improved from baseline of 10.26 to 15.35 at the end of 3 months (F=66.99, R²=0.779, p<0.0001; HS) (Table 2 and Figure 2). In the "Social relationships domain", the mean scores for Menosan improved from baseline of 10.26 to 14.20 (F=133.3, R²=0.8753, p<0.0001; HS) (Table 3 and Figure 3).

The mean symptom score for

"Understanding and communication" improved from baseline of 10.26 to 12.56 at the end of 3 months (F=82.67, R²=0.8131, p<0.0001; HS) (Table 4 and Figure 4). Similarly, the mean symptom score for "Getting along with people" improved from baseline of 7.87 to 12.19 at the end of 3 months (F=158.3, R²=0.8928, p<0.0001; HS) (Table 5 and Figure 5). The mean symptom score for "Participation in society" improved from baseline of 10.26 to 14.05 at the end of 3 months (F=104.9, R²=0.846, p<0.0001; HS) (Table 6 and Figure 6). The mean symptom score for "Life activities" increased from a baseline of 8.78 to 10.26 at the end of three months (F=17.51, R²=0.4795, p<0.0001; HS) (Table 7 and Figure 7). However, there was no improvement in the 'environment' domain, in both the groups at the end of the treatment.

There were no clinically significant changes in the hematological and biochemical parameters. There were no clinically significant adverse reactions, either reported by patients, or observed by the investigators and the overall compliance to the treatment was excellent.

DISCUSSION

The WHO defines health as "a state of complete physical, mental and social well-being and not merely as the

Table 3: Improvement in the mean score for "Social relationships" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	10.26	12.71	14.20	10.26	10.22	10.26
SD	0.3545	0.2269	1.325	0.3545	0.3602	0.3872
SEM	0.07927	0.05073	0.2964	0.07927	0.08055	0.08657
Lower 99% CI	10.03	12.56	13.35	10.03	9.985	10.01
Upper 99% CI	10.49	12.86	15.05	10.49	10.45	10.51
ANOVA summary	F=133.3, R ² =0.8753, p<0.0001; HS			F=0.5236, R ² =0.02682, p=5966; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-2.45	10.06	p<0.001	-3.176 to -1.724	0.045	0.8863	p>0.05	-0.1063 to 0.1963
Baseline vs. 3 months	-3.94	16.17	p<0.001	-4.666 to -3.214	0	0	p>0.05	-0.1513 to 0.1513

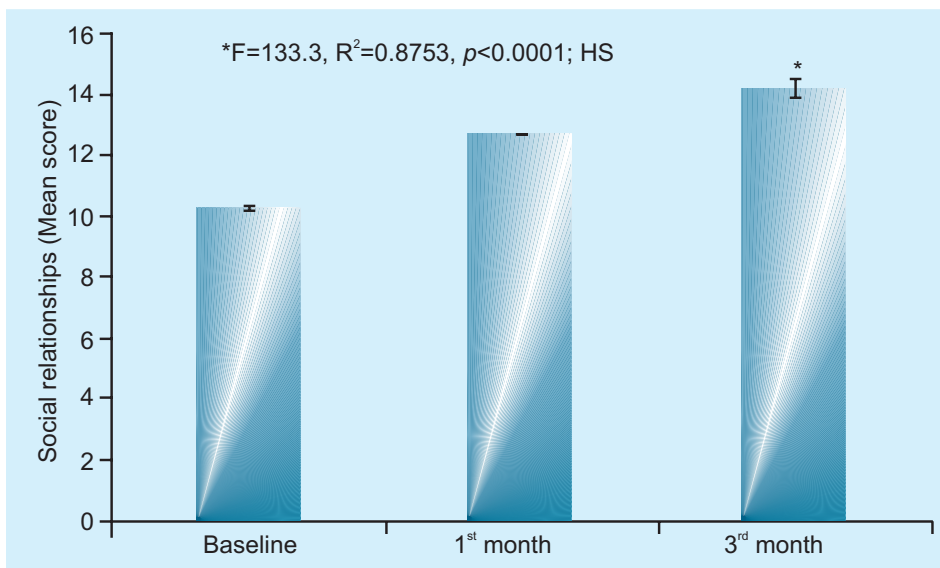


Figure 3: Improvement in the mean score for "Social relationships" with Menosan treatment

absence of disease or infirmity", and it follows that the measurement of health and the effects of health care must include an estimation of improvement in the QOL. World Health Organization has therefore developed 2 instruments for measuring the QOL, which can be used in a variety of cultural settings (while allowing the results from different populations and countries to be compared).^{14,15}

World Health Organization defines QOL as individuals' perception of their position in life in the context of the culture and value systems in

which they live, and in relation to their goals, expectations, standards and concerns. It is a broad concept influenced by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to the environment. The full instrument (WHOQOL-100)¹⁴ has been rigorously tested to assess its validity and reliability (The WHOQOL-BREF is an abbreviated 26-item version of the WHOQOL-100, and all items are rated on a 5 point scale.). The structure of the WHOQOL reflects the issues from the 6 broad domains of QOL:

"Physical health", "Psychological health", "Level of independence", "Social relationships", "Environment" and "Spirituality/religion/personal beliefs".¹⁵

Most assessments in clinical practice are obtained by clinical examinations and laboratory tests, but the WHOQOL instruments provide a new perspective on disease, by focusing on individuals' own views of their well-being. In clinical practice, the WHOQOL instruments can be used with other forms of assessment, to obtain valuable information that can help the practitioner to make the best choices in patient care. In addition, they can be used to measure the change in QOL over the course of treatment. The physician's increased understanding of how disease affects a patient's QOL can change and improve the interaction between the patient and the doctor. It also helps in assessing the effectiveness and relative merits of different treatments.¹⁶

Various researchers have documented wide ranges of symptoms of menopause. A "hot flush" is the most uncomfortable sign of approaching menopause and 8% of women experience hot flushes within the first 3 months of natural or surgical menopause. Hot flushes can be accompanied by other symptoms, which include tachycardia, headache,

Table 4: Improvement in the mean score for "Understanding and communicating" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	10.26	10.68	12.56	10.26	10.36	10.04
SD	0.3545	0.5684	0.7265	0.3545	0.407	1.981
SEM	0.07927	0.1271	0.1625	0.07927	0.09102	0.443
Lower 99% CI	10.03	10.31	12.09	10.03	10.1	8.772
Upper 99% CI	10.49	11.04	13.02	10.49	10.62	11.31
ANOVA summary	F=82.67, R ² =0.8131, p<0.0001; HS			F=0.441, R ² =0.02269, p=0.6466; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-0.415	2.182	p>0.05	-0.9819 to 0.1519	-0.1	0.2869	p>0.05	-1.139 to 0.9390
Baseline vs. 3 months	-2.295	12.07	p<0.001	-2.862 to -1.728	0.22	0.6311	p>0.05	-0.8190 to 1.259

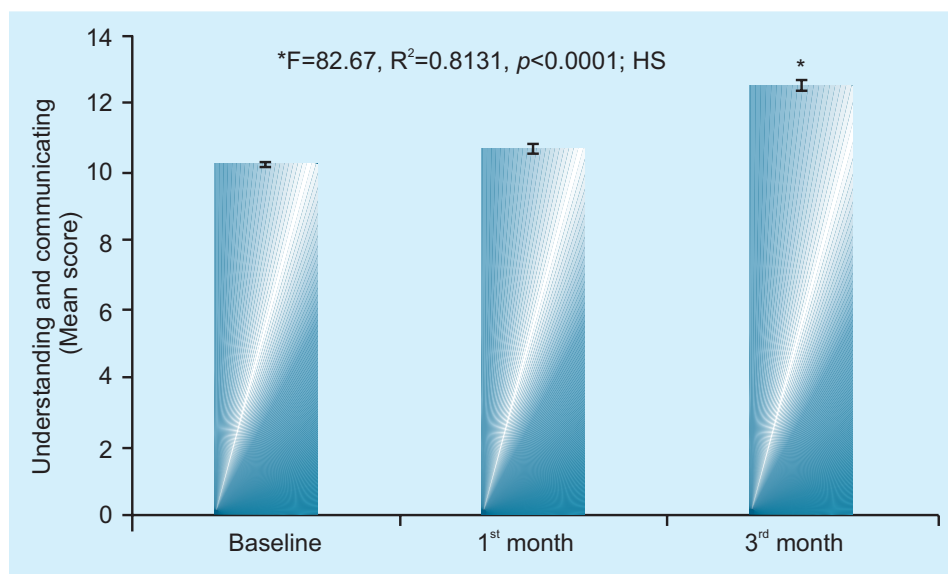


Figure 4: Improvement in the mean score for "Understanding and communicating" with Menosan treatment

dizziness, weight gain, fatigue and insomnia. After menopause, the vaginal lining becomes atrophic, which results in the breakdown of the natural defense mechanisms against bacterial growth in the urinary tract and subsequently, women experience an increased susceptibility to UTIs and about 15% of menopausal women experience frequent bladder infections.¹⁷

This study observed highly significant improvement in the "Physical health", "Psychological

health", and "Social relationships" domains, in the Menosan group, as compared to the placebo group, at the end of the study period. Also there were no clinically significant changes in the hematological and biochemical parameters and there were no clinically significant adverse reactions, which is reflected in the excellent patient compliance. These effects might be due to the phytoestrogens and calcium present in the Menosan. Menosan also has cardio protective actions and hence helps in the

prevention of CADs, which are commonly associated with postmenopausal women and Menosan also has a high amount of natural calcium that helps in PMO.

In the recent years, phytoestrogens have kindled a great deal of interest due to their beneficial effects in menopause management. It is well documented that Asian populations who consume more phytoestrogen in the form of isoflavones (as compared with women in Western countries), have less menopausal symptoms. Phytoestrogens are estrogen like compounds from plants and they act as natural selective estrogen receptor modulators. Phytoestrogens are structurally related to estrogens and have a diphenolic ring in their structure similar to endogenous estrogens. Phytoestrogens bind to estrogen receptors, acting as either "partial agonists" or "antagonists" in different tissues. Phytoestrogens exhibit weak estrogenic activity in the order of 10⁻²-10⁻³ of that of 17β-estradiol, but may be present in the body in concentrations 100-fold higher than endogenous estrogens.¹⁸⁻²² Phytoestrogens have a higher binding affinity for estrogen-receptor [β] than for estrogen-receptor [α].²³

The principle active triterpene glycoside of *Glycyrrhiza glabra* is

Table 5: Improvement in the mean score for "Getting along with people" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	7.875	8.735	12.19	7.875	7.9	7.93
SD	0.6155	1.149	0.4295	0.6155	0.5849	0.6845
SEM	0.1376	0.257	0.09605	0.1376	0.1308	0.1531
Lower 99% CI	7.481	8	11.91	7.481	7.526	7.492
Upper 99% CI	8.269	9.47	12.46	8.269	8.274	8.368
ANOVA summary	F=158.3; R ² =0.8928, p<0.0001; HS			F=1.00, R ² =0.05, p=0.3774; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-0.86	3.354	p<0.01	-1.624 to -0.09579	-0.025	0.6419	p>0.05	-0.1411 to 0.09107
Baseline vs. 3 months	-4.31	16.81	p<0.001	-5.074 to -3.546	-0.055	1.412	p>0.05	-0.1711 to 0.06107

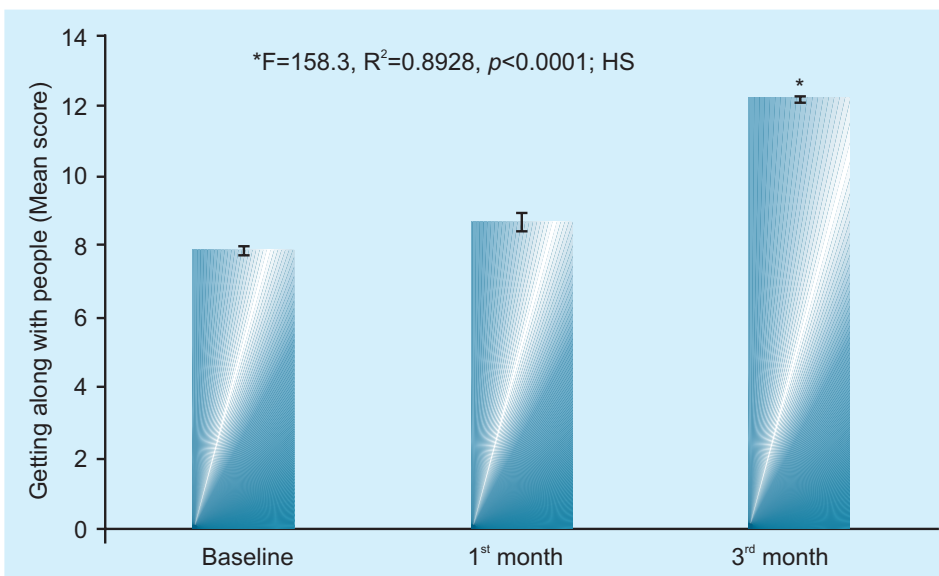


Figure 5: Improvement in the mean score for "Getting along with people" with Menosan treatment

glycyrrhizin (glycyrrhizic or glycyrrhizinic acid) and the other compounds are isoflavonoid derivatives (isoflavonol, kumatakenin, licoricone, glabrol), glabridin, hisglabridin A, hisglabridin B, 4'-O-methylglabridin, 3'-hydroxy-4'-O-methylglabridin, chalcones and coumarins; which have potent antioxidant activity. Shihata et al. and Van et al. observed the estrogenic activity of *Glycyrrhiza glabra*.^{24,25}

Asparagus racemosus is also a rich source of phytoestrogens (isoflavones) and the active compounds in

Asparagus racemosus are steroidal saponins (shatavarins I-IV). Shatavarin I is the glycoside, whereas shatavarin IV contains isoflavones (8-methoxy-5, 6,4'-trihydroxyisoflavone-glucopyranoside), asparagamine (alkaloid), racemosol (9,10-dihydrophenanthrene) and polysaccharides.²⁶⁻²⁸ Thatte et al. observed that *Asparagus racemosus* acts as an immunomodulator and produced leucocytosis, and neutrophilia with increased phagocytic activity of macrophages.^{29,30} Furthermore,

Asparagus racemosus prevented myelosuppression by reducing cyclophosphamide-induced leucopenia.³¹ Rao et al. documented that *Asparagus racemosus* inhibited drug-induced mammary carcinogenesis, drug-induced suppression of chemotactic activity, and the production of interleukin-1 (IL-1) and tumour necrosis factor- α (TNF- α).³²

The active ingredients of *Terminalia arjuna* are glycosides (arjunetin, and arjunosides I-IV), flavones, tannins, oligomeric proanthocyanidins and acids (arjunic acid, terminic acid). *Terminalia arjuna* is a potent antioxidant agent (comparable to vitamin E) and also has a remarkable hypocholesterolemic effect.³³ *Terminalia arjuna* has anti-ischemic properties, which are beneficial in patients with ischemic heart disease. Gupta et al. reported that *Terminalia arjuna* was a potent hypolipidemic agent and induced partial inhibition of atheroma.³⁴ Arjunolic acid in *Terminalia arjuna* has been shown to prevent the decrease the levels of superoxide dismutase, catalase, glutathione peroxidase, ceruloplasmin, alpha-tocopherol, and to reduce glutathione, lipid peroxide, and hence enhance cardioprotection. In a study done amongst the patients with angina

Table 6: Improvement in the mean score for "Participation in society" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	10.26	11.07	14.05	11.07	11.12	11.12
SD	0.3545	0.7604	1.348	0.7604	0.7481	0.7492
SEM	0.07927	0.17	0.3014	0.17	0.1673	0.1675
Lower 99% CI	10.03	10.58	13.18	10.58	10.64	10.64
Upper 99% CI	10.49	11.55	14.91	11.55	11.6	11.59
ANOVA summary	F=104.9, R ² =0.846, p<0.0001; HS			F=2.742, R ² =0.1261, p=0.0772; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-0.805	2.924	p<0.05	-1.626 to 0.01561	-0.055	2.118	p>0.05	-0.1324 to 0.02241
Baseline vs. 3 months	-3.785	13.75	p<0.001	-4.606 to -2.964	-0.05	1.925	p>0.05	-0.1274 to 0.02741

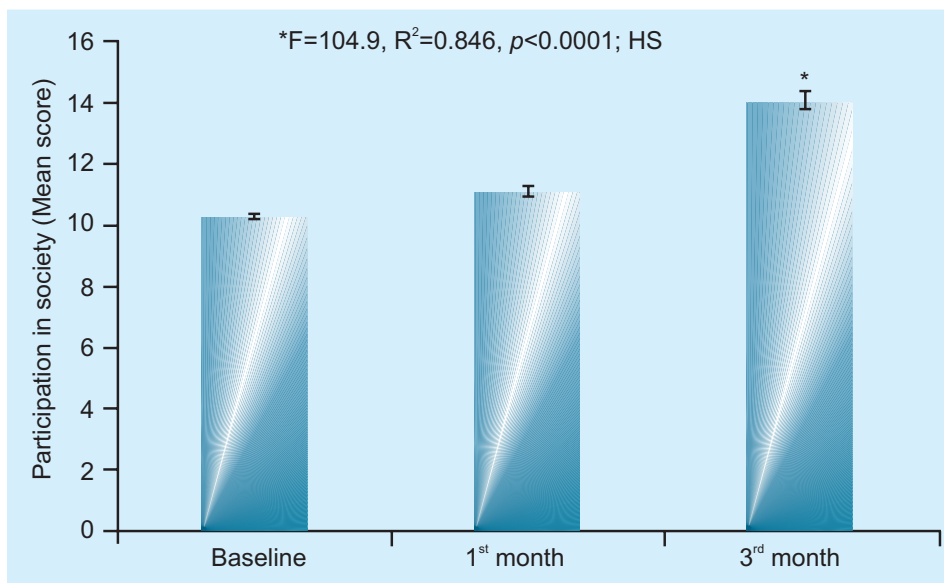


Figure 6: Improvement in the mean score for "Participation in society" with Menosan treatment

pectoris, congestive cardiac failure and left ventricular hypertrophy, significant improvement in left ventricular ejection fraction and reduction in left ventricular mass was documented, and the patients with ischemic cardiomyopathy showed significant symptomatic relief in coronary heart failure from NYHA class III to NYHA class I.³⁵

Epidemiological studies have implicated postmenopausal estrogen deficiency for increased lower urinary tract disorders, including UTI. The various ingredients of Menosan have

potent antimicrobial activity against commonly involved pathogens responsible for UTI. *Terminalia chebula* is microbicidal against a wide range of Gram-positive and -negative bacteria.^{36,37} *Terminalia arjuna* has significant antimicrobial activity against *Escherichia coli*, *Klebsiella aerogenes*, *Proteus vulgaris* and *Pseudomonas aerogenes*.³⁸ *Saraca indica* is a potent antimicrobial agent³⁹ and *Asparagus racemosus* also has considerable antimicrobial activity against *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus*.⁴⁰

Menopause is frequently associated with psychological symptoms like mood swings, anxiety, depression, irritability and insomnia. Menosan contains *Centella asiatica*, which has an anxiolytic and sedative effect. In a study, *Centella asiatica* produced a marked increase in the time spent in the open arms of the plus maze and potentiation of pentobarbitone-induced sleeping time. In another study, the effect of triterpenes from *Centella asiatica* on the immobility time in forced swimming mice and concentration of amino acids in mice brain tissue was observed; and the investigators reported potent antidepressant activity. Other studies have documented the 'adaptogenic' and immunostimulatory effect of *Asparagus racemosus* (plant adaptogens are defined as "smooth pro-stressors", which reduce reactivity of the host defense systems and decrease the damaging effects of various stressors due to increased basal level of chemomediators involved in the stress response). This adaptogenic effect helps the postmenopausal women to adapt to the changes in the neurotransmitter levels, which is responsible for the resultant postmenopausal anxiety and depression.⁴¹⁻⁴⁴

The incidence of CVDs among postmenopausal women has been

Table 7: Improvement in the mean score for "Life activities" with Menosan and placebo

Parameter	Mensosan			Placebo		
	Base-line	1st Month	3rd Month	Base- line	1st Month	3rd Month
Mean	8.785	9.38	10.26	8.785	8.89	8.89
SD	1.269	0.9534	0.3545	1.269	1.389	1.389
SEM	0.2837	0.2132	0.07927	0.2837	0.3107	0.3107
Lower 99% CI	7.973	8.77	10.03	7.973	8.001	8.001
Upper 99% CI	9.597	9.99	10.49	9.597	9.779	9.779
ANOVA summary	F=17.51, F ² =0.4795, p<0.0001; HS			F=3.015, R ² =0.137, p=0.0609; NS		

Bonferroni's multiple comparison test

Parameter	Mensosan				Placebo			
	Mean Diff.	t value	p value	99% CI of Diff.	Mean Diff.	t value	p value	99% CI of Diff.
Baseline vs. 1 month	-0.595	2.372	p<0.05	-1.343 to 0.1525	-0.105	2.127	p>0.05	-0.2521 to 0.04215
Baseline vs. 3 months	-1.475	5.881	p<0.001	-2.223 to -0.7275	-0.105	2.127	p>0.05	-0.2521 to -0.04215

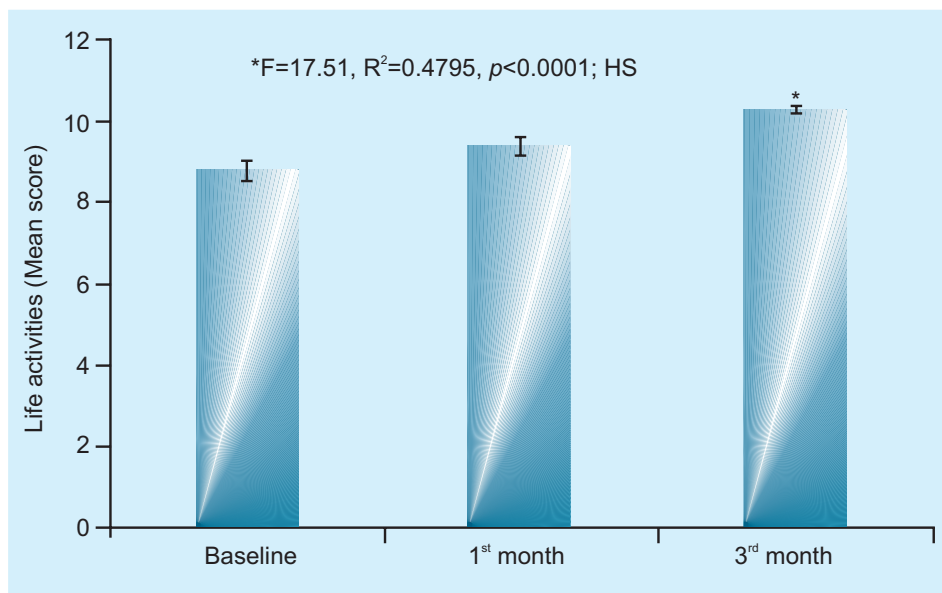


Figure 7: Improvement in the mean score for "Life activities" with Menosan treatment

directly related to the loss of endogenous estrogen protection. The oxidative modification of LDL-C is a prerequisite for the uptake of LDL-C by macrophages in the arterial wall (an initial step in the formation of atheroma), and incorporating antioxidants into LDL-C particles, may be a possible strategy for preventing lipoprotein oxidation. Dietary phytoestrogens has been found to be antiatherogenic, and the proposed mechanisms for the hypocholesterolemic effect of phytoestrogens are: the up-regulation of LDL-C receptors

and/or the inhibition of endogenous cholesterol synthesis.⁴⁵⁻⁴⁷ Phytoestrogens stimulate the clearance of cholesterol, probably by up-regulating LDL receptors and thereby increasing LDL-C receptor activity.⁴⁸ Lignans also affect cholesterol homeostasis, as they inhibit the activity of cholesterol-7-alpha hydroxylase, the rate-limiting enzyme in the formation of primary bile acids from cholesterol.⁴⁹

Mensosan is also a good source of calcium because it contains Kukkutandatvak bhasma, which is a rich source of natural organic calcium,

resulting in healthy bone formation and improvement in body mass density, which helps prevent PMO.

CONCLUSION

Ovarian senescence is accompanied by physical changes and psychological changes, and life stressors, surgical menopause and poor health exacerbate these menopausal symptoms. Recent studies have cast doubt on the cardioprotective effects of HRT, as the combination of HRT have been shown to lead to increased risks of CADs, CVAs, pulmonary embolism, in addition to increased risks of vaginal bleeding and breast cancer. These short- and long-term adverse events have given fillip to clinically effective and much safer alternative approaches, and phytoestrogens are currently heralded as the potential therapy for estrogen-dependent diseases. Menosan is a polyherbal formulation, and is a rich source of phytoestrogens. This study was planned to evaluate the efficacy and safety of Menosan in postmenopausal syndrome, with special reference to the improvement in the QOL.

This study observed highly significant improvement in the "Physical health", "Psychological health", and "Social relationships" domains in the Menosan group, as compared to the placebo group, at the end of the study

period. Also, there were no clinically significant changes in the hematological and biochemical parameters and there were no clinically significant adverse reactions, which is reflected in the excellent patient compliance. These effects might be due to the phytoestrogens and calcium present in the Menosan. Therefore, it may be concluded that Menosan is clinically effective and safe in the management of postmenopausal syndrome, for improving QOL.

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