"A Single Arm Clinical Trial To Evaluate The Efficacy And Safety Of *Vachadi Yoga* In Management Of Dyslipidemia"

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Abstract: - *Ayurveda* a treasure for humanity. Ancient *Acharya* very smartly bind all knowledge together into texts. There is the solution of every problem in ancient classical texts either related to physical health or mental health. Due to fast forward busy lifestyle people suffering from many lifestyle disorders. These disorders can be easily treated with help of proper ancient regimen, but when condition get worst there are many drugs, or drug formulation or group of drugs which can easily cure the chronic condition. The ancient classical texts like *Sushruta Samhita*, *Astang Hridya*, *Brihatnighantu Ratnakar* and *Nighantu Adarsha* elaborated *Vachadi Gana* very nicely. According to these classical texts the drugs under *Vachadi Gana* having properties like *Tikta-Katu Rasa*, and is capable to treat *Kapha & Vata* related disease condition. Dyslipidemia is a condition in which *Vata* and *Kapha* both are involved. In the present study, we compiled the properties of these drugs and also tried to prove their action on dyslipidemia conceptually and clinically**.** Statistical analysis indicates that the overall effectiveness of the therapy was approximately 41.14 %

Keywords: Dyslipidemia , Ayurveda, Vachadi Gana, MTT assay, Dosha, etc.

INTRODUCTION

In the 21st century, science and technology have brought about rapid advancements in human life, replacing manual labour with mental labour. Man is moving away from nature and up the ladder of success with the aid of science, which has led to the emergence of lifestyle diseases. In response to the mounting challenges of modernization, man has successfully modified his customary behavior in an attempt to maximize his intellectual and physical capabilities in order to derive the highest level of productivity.

Man has also adapted himself to the fast-paced lifestyle by changing his dietary and lifestyle choices to fit the times. As a result, there is a condition of discord between his internal mechanism and the external environment, leading to a plethora of disorders sometimes referred to as lifestyle diseases.

In the contemporary world, Dyslipidemia is one of the most urgent problems. Abnormalities of lipids and lipoproteins are exceeding frequently in the general population. It is one of the known and adjustable risk factor for CHD.[1] Globally, one of the main cause of death is cardiovascular disease (CVD), which includes

illnesses like peripheral artery disease and coronary heart disease. According to estimates provided by the World Health Organization, 17.3 million deaths worldwide in 2008 were attributed to CVD, accounting for 30% of all deaths. Nearly 25 million people are predicted to pass away from CVD by 2030, mainly heart disease and stroke. [2] The Middle East has one of the greatest rates of growth in mortality from CVD worldwide[3]. According to data from 2008, CVD caused 42 and 45% of all fatalities in Saudi Arabia and Lebanon, respectively. However, the accuracy of these numbers is questionable because neither nation maintains a separate illness registration. [3,4]

Lifestyle variables including smoking and a sedentary lifestyle, as well as metabolic disorders like obesity, diabetes, and Dyslipidemia, are well-documented risk factors for cardiovascular disease (CVD). Large-scale randomized studies' meta-analyses have shown that modifying these risk variables lowers the chance of CVD-related morbidity and death, especially when low-density lipoprotein cholesterol (LDL-C) levels are lowered with statins (HMG-CoA reductase inhibitors). [5,6,7,8] Apart from the reduction of elevated low-density lipoprotein cholesterol (LDL-C) levels, there could be significant contributions to the residual risk of CVD from high triglyceride levels and low HDL-C levels. [9,10]

Serum cholesterol levels and early CAD/CVD have been shown to be strongly correlated by epidemiological research.[11] According to data from the ICMR surveillance project, the prevalence of Dyslipidemia (defined as a ratio of total to HDL cholesterol >4.5) was found in 37.5% of persons between the ages of 15 and 64. Among young male industrial workers, the prevalence was considerably higher, at 62%.

Dyslipidemia is defined as elevation of plasma cholesterol, triglycerides, or both, or a low high-density lipoprotein level that contributes to the development of atherosclerosis. The causes can be primary (genetic) or secondary. The diagnosis of Dyslipidemia is made by measuring plasma levels of total cholesterol, triglycerides, and individual lipoproteins. Treatment options include dietary modifications, physical acti8vity, and lipid-lowering medications.

Although there is no *Ayurvedic* name for Dyslipidemia, we can infer that the disease is caused by an increase in *Ama* and *Rasa-raktagata Snehansha* in our bodies. Several *Ayurvedic* herbs, including *Vacha* (Acrous calamus Linn.), *Nagarmotha* (Cyperus rotundus Linn.), *Devdaru* (Cedrus deodara (Roxb.) Loud), *Sunthi* (Zingiber officinale Linn.), *Atish* (Aconitum hetrophyllum Wall. Cat.), etc., are mentioned in our classical texts and can be used as a formulation for managing this kind of condition thanks to their respective properties.

The *Ayurvedic* treatment of Dyslipidemia includes techniques to strengthen *Agni's* ability to break down *Ama*, manage absorption and excretion, and manage the underlying causes. In *Ayurveda*, a number of single herbs as well as combinations of herbs are used to treat *Ama*, *Ras-raktagata Sneha vridhi*, a factor that causes Dyslipidemia and consequently metabolic problems.

The main cause of most ailments, *Ama* and *Rasa-rakta gata Sneha Vridhi,* is believed to be treated by Ayurvedic herbs like *Vacha, Nagarmotha, Devdaru, Sunthi, Atish, and Haritaki*, which have qualities like *Ushna, Tikshna, Katu,* etc. So, these drugs (*Vacha, Nagarmotha, Devdaru, Sunthi, Atish and Haritaki*) were selected for the present study and further to increase the potency of these drugs, the *bhavna* of *lehsun swaras* was given. So, in our present study, we made *Vati Kalpana* with the help of these *Ayurvedic* herbs after giving the *bhavana* of *lehsun swarasa* which enhanced the overall potency of the formulation.

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MATERIALS & METHODS

Material:

Sources of Data:

- **Literacy source**: The literature related to Dyslipidemia and these 7 drugs were explored and discussed from *Ayurvedic* classical text, modern literature, research journals & published articles.

Drugs : Vachadi gana with lahsun swaras bhavna

Table 1: Description Of Drugs Used In Vachadi Yoga

Sr. No.	Constituents	Botanical Name	Family	Part Used	Picture
1	*Vacha*	*Acorus calamus*	*Araceae*	*Kandha*	
2	*Jalad*	*Cyprus rotundus*	*Cyperaceae*	*Kandha*	
3	*Naagar*	*Zingiber officinalis*	*Zingiberacae*	*Kandha*	
4	*Ativisha*	*Aconitum heterophyllum*	*Ranunculacea e*	*Moola*	
5	*Haritaki*	*Terminialia chebula*	*Combritaceae*	*Phala*	

6	*Devdaru*	*Cedrus deodara*	*Pinaceae*	*Kashtha*	
7	*Lahsun*	*Allium sativum Linn.*	*Liliaceae*	*Kanda*	

Safety study of drug: Cytotoxicity of the drug was studied throught MTT assay from progen biology lab, Acme progen Biotech Private Limited Tamil Nadu, India.

Clinical Source: 30 patients were randomly selected from OPD of *Dravyaguna vigyan* department of IAS & R Hospital and college formely known as Shri Krishna Govt. Ayurvedic College and Hospital, Kurukshetra.

Clinical Study- Total 30 patients were enrolled for clinical trial after providing informed consent.

Study Design- Open clinical trial

Sample Size- Maximum 30 patients were selected , and Vachadi Yoga in the form of tablets were given for 60 days.

Study Duration: 60days

Number of visits : 6 visits (1st day, 15th day, 30th day, 45th day, 60th day, 70th day)

Criteria for Selection of Patients- Total 30 patients of either sex of age group 25-50 years were selected randomly for study from OPD of Dravyaguna Department of Shri Krishna Govt. Ayurvedic College and Hospital, Kurukshetra, Haryana after providing informed consent. Total 30 patients were enrolled for the study and all patients had completed the trial.

Ethical Committee Clearance: Institutional Ethical Committee (IEC) approval was taken prior to initiation of research with letter No. IEC Code:SKAU/Acad/2023/8120, Dated on 6/6/2023.

CTRI Registration No.: Study was registered in Clinical Trial Registry of India with No. CTRI/2023/07/055335 (Registered dated on 18/07/2023).

Inclusion Criteria:

Patients who had age between 25– 50 years of either sex,

Were fulfilling the diagnostic criteria (diagnosed with abnormal lipid profile i.e. Total Cholesterol level upto 300mg/dl, LDL level upto200mg/dl, HDL upto 35mg/dl and Triglycerides level upto 500mg/dl)

Were willing to participate in the clinical trial

Exclusion Criteria:

Age below 25 and above 50 years.

Patients who were suffering from type 1 diabetes mellitus and uncontrolled diabetes mellitus or uncontrolled hypertension

Drug induced Dyslipidemia

Patient who had systemic illness like tuberculosis, carcinoma and endocrine disorders or major illness like renal or liver disorder

Patient who had the past history of myocardial infarction & unstable Angina.

Patient who had clinical features of CCF

Patients who had history of untreated thyroid disorder.

Patients on prolonged medication (>6weeks) with corticosteroids, or any other drugs that may have an influence on the outcome of the study.

Patients who were participating in any other clinical trials (since last 6months).

Pregnant females and lactating mothers

Discontinuation criteria:

Any acute or severe illness.

Patientwho were not willing to continue the treatment.

Preparation Of The Trial Drugs: *Vati* of 500 mg were prepared by six drugs mentioned in vachadi gana in equal ratio after giving the *bhavna* of *lehsun swaras* from GMP certified pharmacy named as Chachan Pharmaceuticals, Ellenabad-125102

Pictures showing tablets prepared by Vachadi Yoga

Route of administration and dose: 2 tablets (1000mg) were given orally empty stomach in the morning and before food evening twice in a day.

CRITERIA FOR ASSESSMENT:

Assessment was mainly based on the improvement observed in subjective and objective parameters before and after the treatment.

The *Prakriti, Agnibala, Roga Bala* and *Rogi Bala* was taken into consideration.

Holmes and Rahe stress scale assessment was done in patients at the baseline to assess role of psychological factors in the pathogenesis of Dyslipidemia.

SUBJECTIVE PARAMETERS-

Fatigue, parasthesia, confusion and breathlessness were the cardinal symptoms observed in the patients of Dyslipidemia.

Associated Symptoms- *Kshudrashwasa* (Dyspnoea), *Swedhadhikya* (Excessive sweating), *Trishna* (Increased thirst), *Atinidra* (Increased sleep)

OBJECTIVE PARAMETERS

For the purpose of diagnosing and assessing the patients of Dyslipidemia, the following investigations were performed before and after the completion of trial:

• Complete lipid profile before and after treatment i.e. LDL, HDL, Triglycerides, Total Cholesterol.

• Routine hematological examinations were done to rule out other pathological conditions and assess the efficacy of intervention.

Overall Effect of Therapy: Considering the improvement in symptoms of Dyslipidemia, the subjects were divided into following groups

1. Complete Remission- 100 % relief in symptoms.

2. Marked Improvement- 75 % to < 100 % relief in symptoms.
3. Moderately Improved- 50 % to < 75 % relief in symptoms.
4. Mild Improvement- 25 % to < 50 % relief in symptoms.
5. Unchanged- Below 25 % relief in symptoms.

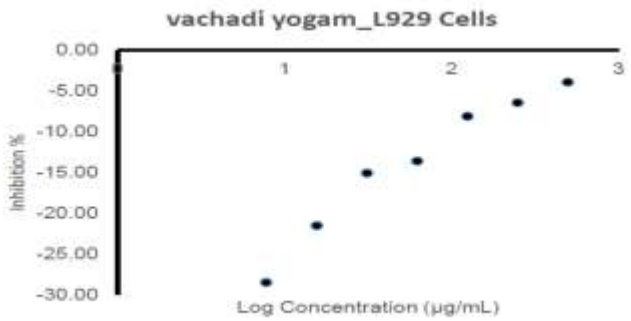
OBSERVATIONS AND RESULTS

RESULTS

Safety study of drug: Cytotoxicity of the drug was studied through MTT assay from progen biology lab, Acme progen Biotech Private Limited Tamil Nadu, India. Which were found non toxic against L929 cell line.

Figure no.1 - below showing results obtained in MTT assay:-

L929 Cell line				
Compound Name	**Conc.µg/ml**	**OD @570nm**	**% inhibition**	**IC50 µg/ml**
Control	0	0.474	0	
Vachadi yoga	7.81	0.629	-28.48	
	15.62	0.576	-21.52	
	31.25	0.546	-15.08	
	62.5	0.539	-13.61	
	125	0.513	-8.12	
	250	0.505	-6.43	
	500	0.493	-3.90	



Clinical results: The following section presents the findings of the study, offering a detailed analysis of the data collected in relation to the research questions/hypothesis.

Wilcoxon Signed Rank test was applied on the Subjective parameters and Paired T-test was applied on the Objective parameters

Table no. 2 -Results obtained by Wilcoxon signed Rank test on subjective criteria:-

Variables	Opts	BEFORE	AFTER	Wilcoxon test	P Value	Result
Breathlessness	No Dyspnoea	0	8	-4.118	<0.001	Highly Significant
	Dyspnoea after moderate works but relieved later and up to tolerance.	11	15			
	Dyspnoea after little works but relieved later and up to tolerance.	9	5			
	Dyspnoea in resting condition	10	2			
Thirst	Normal thirst	0	3	-3.956	<0.001	Highly Significant
	Thirsty but relieved after drinking 1-2 litre of water	5	15			
	Thirsty but not relieved after drinking 1-2 litre of water	11	7			
	Repeated thirst and not relieved at all	14	5			
Fatigue	No fatigue	0	5	-4.725	<0.001	Highly Significant
	Occasional	7	15			
	Present, but not disturbing routine work	9	10			
	Disturbing routine work	14	0			
Sweating	Sweating is never noticeable and never interferes with daily activities	0	5	-3.911	<0.001	Highly Significant
	Sweating is tolerable but sometimes interferes with daily activities	8	13			
	Sweating is barely tolerable and frequently interferes with daily activities	15	10			
	Sweating is intolerable and always interferes with daily activities	7	2			
Increased Sleep	Normal sleep 6-7 hours per day	0	4	-4.490	<0.001	Highly Significant
	Normal sleep 6-7 hours per day	8	22			

	Sleep up to 10 hours per day with Tandra	13	4			
	Sleep more than 10 hours per day with Tandra and klama	9	0			
Confusion	No confusion	1	11	-4.524	<0.001	Highly Significant
	Little confusion when mentally tired	10	15			
	Moderate confusion with routine mental work	14	4			
	Excessive confusion with routine mental work	5	0			
Parasthesia	No any abnormal sensation	2	12	-4.290	<0.001	Highly Significant
	Abnormal sensation lasting for few minutes (2-5 Minutes) to an hour having 1-2 episodes in a week.	12	14			
	Abnormal sensation lasting for few minutes (2-5 Minutes) to an hour having >3 episodes in a week	11	3			
	Abnormal sensation lasting for more than an hour having 1-3 episodes in a week	5	1			

Table no. 3 - Subjective Parameters

Variable	Subjective Parameters	
MEAN	**13.9**	**3.43**
MEAN DIFFERENCE	**10.4**	
CHANGE %	**75.3%**	

Paired T-Test Analysis of objective Parameter :

The paired t-test analysis reveals significant improvements in key health indicators post-intervention:
Serum Cholesterol: Mean score decreased from 234.88 to 220.40, with a significant t-value of 6.907 ($p < 0.001$).
Serum Triglyceride: Mean score decreased from 223.47 to 208.94, with a significant t-value of 7.055 ($p < 0.001$).
LDL: Mean score decreased from 122.81 to 115.52, with a significant t-value of 5.042 ($p < 0.001$).
HDL: Mean score increased from 44.77 to 48.95, with a significant t-value of 5.048 ($p < 0.001$).

Table no. 4 -Total Effect Of Therapy Including Objective And Subjective Criteria :

Sr no	Parameters	% of relief
1.	Subjective	75.3%
2.	Objective parameters	6.98%
Overall effect		41.14%

Table no.5 - Total effect of therapy

Total effect of therapy		
Sr	Improvement	Total relief
1	Good Improvement (75%-100%)	-
2	Moderate improvemnet (51%-75%)	-
3	Mild Improvement (26%-50%)	41.14%
4	No Improvement (0-25%)	

Statistically calculations proves that Overall effect of therapy was 41.14 % while in subjective parameters 75.3 % treatment effect was seen and 6.98% relief in objective parameters. When we see on throw above scale there is totally Mild relief in all the Subjective and objective parameters.

Adverse Drug Reaction:

No adverse drug reactions were reported for the trial drug during the study or follow-up period, given the prescribed dosage and duration.

DISCUSSION: *Dyslipidemia* typically involves *kapha*, *medo* and *pitta dushti*. So, the drug use should have *lekhan, kaphashamak, medonashak* properties. The *pitta* and *rakta* have similar properties thus pacification of pitta dosha and purification of *rakta dhatu* should be done. Drugs with *pitta shamak properties* like *tikta, sothhara, rechana, anulomana* properties should be used. *Kapha* and *medodhatu* are *samandharmi* according to *samanaya vishesh siddhanata* decrease in one lead to decrease in other & vice versa. Pacification of *kapha dosha* is very essential as it plays a major role in the manifestation of disease.In this trial the selected drug for patient was *Vachadi Yoga* which contains *Vacha , Nagarmotha, Devdaru, Sunthi, Atish, Haritaki* in equal parts and to increase the potency of drug, *bhavna* of *Lahsuna swaras* was given. These drugs may be beneficial in breaking down the pathological chain of Dyslipidemia

Figure no.2 - *Probable Mode Of Action Of Drugs -*

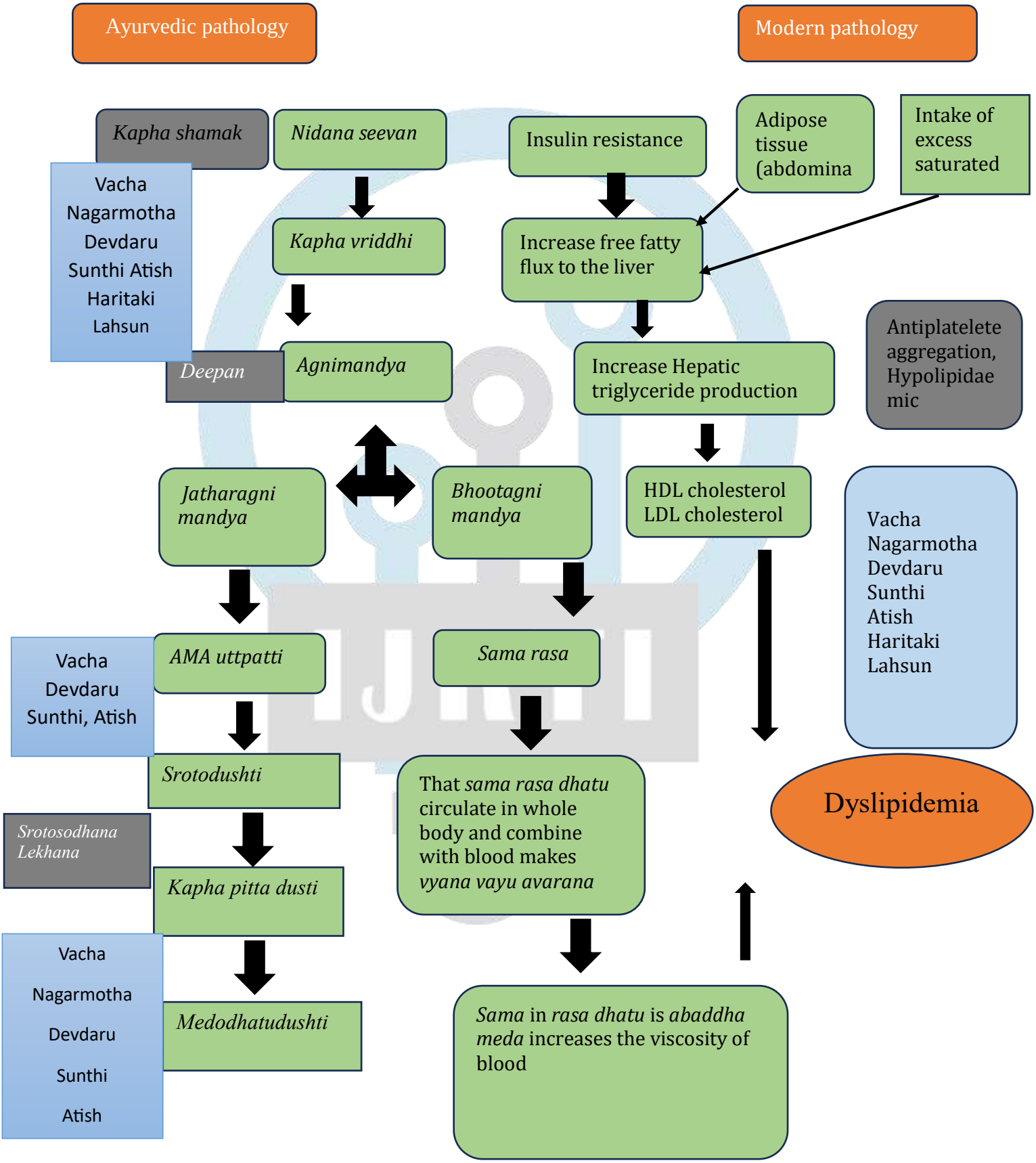


Table no. 6-Mode of action

Sr.No.	Drugs	Mode of Action
1.	*Vacha*	Vacha has properties like *katu, tikta rasa, katu vipaka, ushna veerya* which acts as *deepan, kaphashamak, amapachana, strotoshodhan and lekhana.*
2.	*Haritaki*	Haritaki has shadrasa except lavana has properties like *laghu,ruksha guna,ushna veerya and Madhura vipaka*.It is *tridoshahar* helps in pacifying the vitiated doshas but particularly act on *vata dosha*.It is *deepaniye pachaniya and anulomaka.*
3.	*Shunthi*	Because of *katu rasa and ushna virya*, it efficiently pacifies the vata and kapha doshas by reducing congestion in the *srotas*. It reduces symptoms such *angagaurava, atinidra, utshahani, trishna, and daurbalya* because of its qualities as an *agnideepak, amapachak, ruchikara, triptighana, and vrisya*
4.	*Nagarmotha*	In nature, *Nagarmotha* is *tikta, katu, Kashaya, and kaphapittashamak.* Due to its *agnideepak, pachaka, trsanigrahana, jwaraghana, krimighana, and vishghana* characteristics, it aids in *agni* stimulation, boosts metabolism, and helps avert future *agnimandhya*-related disease.
5.	*Ativisha*	*Ativisha* has properties like *katu, tikta rasa,laghu-ruksha guna,ushna verya and katu vipaka* which acts as *Deepana,pachana,kapha-pittahar,tridoshhar and amahar.*
6.	*Lehsun*	*Lehsun* has properties like *katu and Madhura rasa,guru,snigdha,Tikshna,sara,picchila guna,ushna veerya and katu vipaka* which acts as *vatahar,kaphahar,pachana,amahar and rasayana.*
7.	*Devdaru*	Devdaru has properties like *tikta rasa,laghu, snigdha guna,ushna veerya and katu vipaka,*which acts as *amahar,kaphahar and vatahar*.

Discussion about result in Subjective parameters

The Wilcoxon signed-rank test results across all subjective parameters indicate statistically significant changes. The data presents the analysis of several clinical parameters before and after treatment, focusing on their mean values, mean differences (BT-AT), and statistical significance. The analysis revealed several significant associations between various variables and the outcomes.

The significant reduction in severe dyspnoea indicates that the treatment effectively alleviates breathlessness. (W= -4.118, $p < 0.001$) The reduction in persistent thirst after the intervention suggests that the treatment helps in managing hydration better (W= -3.956, $p < 0.001$). The significant decrease in disturbing fatigue levels post-treatment highlights a substantial improvement in energy levels (W= -4.725, $p < 0.001$). The reduction in intolerable sweating indicates that the treatment alleviates sweating to a degree where it no longer significantly interferes with daily activities (W= -3.911, $p < 0.001$). The significant change in sleep patterns reflects an improvement in sleep quality and duration (W= -4.490, $p < 0.001$). The notable reduction in confusion points to an improvement in cognitive clarity (W= -4.524, $p < 0.001$). The significant improvement in paresthesia indicates that the treatment effectively reduces abnormal sensations (W= -4.290, $p < 0.001$).

Discussion about result of objective Parameters

In paired t-test analysis, most objective parameters show statistically significant changes post intervention. The data presents the statistical analysis of several objective clinical parameters before and after treatment, using metrics such as mean difference, standard deviation, t-value, and P-value to determine the significance of changes. The results demonstrate significant improvements in key measures of Dyslipidemia.

The reduction in serum cholesterol levels from 234.88 mg/dl to 220.40 mg/dl (6.16% decrease) reflecting a significant change with a t-value of 6.907 ($p < 0.001$) suggests that the intervention is effective in lowering total cholesterol.The significant reduction in serum triglycerides from 223.47 mg/dl to 208.94 mg/dl (6.50% decrease) reflecting a significant change with a t-value of 7.055 ($p < 0.001$) reflects positive effects of the intervention on triglyceride levels. LDL levels decreased significantly from 122.81 mg/dl to 115.52 mg/dl (5.94% decrease) reflecting a significant change with a t-value of 5.042 ($p < 0.001$).The increase in HDL from 44.77 mg/dl to 48.95 mg/dl (9.34% improvement) reflecting a significant change with a t-value of 5.048 ($p < 0.001$) is a positive outcome.

Discussion about overall result:

The significant decrease in overall health scores from 625.93 to 593.81 (5.13% reduction) suggests an improvement in overall health status as perceived or measured by the health scores.

CONCLUSION AND RECOMMENDATIONS

- Observing series of patients, Dyslipidemia can be probably co-related with Rasa-rakta gata Sneha vridhi on the basis of etiological basis and clinical manifestations.
- The notion of agnimandhaya, kapha pitta vardhak ahara, obstruction of the srotas, vyan vayu vasyama, and circulation of abadha meda are the aspects that should be brought together in practice to clarify the etiology of dyslipidemia.

- It is possible to associate Rasa-rakta gata Sneha vridhi with Bhedavastha of dyslipidemia. Complications arise if the condition is not appropriately managed. Dyslipidemia complications can result in the development of numerous diseases, including obesity, hypertension, liver, kidney, and coronary artery disease.
- Vachadi yoga shows significant effect in improving the symptoms of patient.Vachadi yoga includes herbs like Vacha ,*ativisha, musta, shunti, haritaki, devdaru* and *lehsun* showed significant effect in lowering the symptoms of patients suffering from dyslipidemia through their properties like deepan, pachan,,ushna,katu tikta ,kashay, amahar, kapha har,pittahar,rasayan etc
- The total effect of therapy was evaluated by taking relief in percentage of each patient.

  ➢ Out of 30 patients, good improvement was seen in 2 patients, moderate improvement was seen in 9 patients and mild improvement was seen in 17 patients and no improvement was seen in 2 patients.

  After the drug intervention for 60 days in patients of Dyslipidemia , the mean difference before and after treatement over subjective symptoms were Breathlessness(47.5%), fatigue(47.8%), confusion(56.6%), parasthesia(53.1%), increased sleep(33.9), thirst(36.2%) and increased sweat(50.8 %)

  Among the objective parameters, , the mean difference before and after treatement were Total cholesterol (6.16%), Serum triglycerides (6.50%), Serum LDL cholesterol (5.94%), Serum HDL cholesterol (9.34%).
- From statistical analysis it can be concluded that patient showed significant improvement in all subjective parameters i.e. Breathlessness, fatigue, confusion, parasthesia, increased sleep, thirst and increased sweat.
- Apart from that, there was also significant improvement in all objective parameters- S. Cholesterol, S. Triglycerides, S. LDL cholesterol after treatment.
- No side effect or complication was observed in patients during and after the course of treatment.
- Large sample studies may be conducted in the future to achieve better drug response and corresponding results, even if the current study was conducted on a small sample.
- This discovery could benefit patients and provide direction for future ayurvedic studies.
- The primary treatment is Nidana-Parivarjana. Therefore, patients should be instructed in suitable pathya-apathya and yoga regimen.
- If ayurvedic hypolipidemic medications are used with certain shodhana methods like vaman, virechana, and lekhan vasti, patients can have a better course of treatment. The patient's disease status may be taken into consideration when making this decision.
- Additional research can be conducted on these patients, with a special emphasis on the primary complications that arise from dyslipidemia.

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