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Role of Ashvattha Patra (Leaf of *Ficus religiosa* Linn.) in the Secondary Prevention of Dyslipidemia

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Abstract

Introduction: Dyslipidemia is a group of disorders of lipoprotein metabolism, which includes over production or deficiency of lipoproteins or both. In developed countries, most of dyslipidemias are hyperlipidemias; that is, an elevation of lipids in the blood, which is an important risk factor for coronary heart disease and stroke. The prevalence of dyslipidemia is very high in India, which calls for urgent lifestyle intervention strategies to prevent and manage this important cardiovascular risk factor. **Aim:** The aim of the study was to assess the effect of *Ashvattha Patra* in dyslipidemia. **Materials and Methods:** A total number of 41 patients were included in the study and were randomly divided into two groups. Patients of Group A were treated with 100 ml of *Ashvattha Patra Kwath* (decoction) and Group B patients were provided 100 ml lukewarm water as placebo for 45 days. The outcome of clinical treatment was analyzed statistically using paired, unpaired *t*-test on GraphPad-Instat software Version 3.06. **Results:** Significant improvements were seen in total cholesterol, serum triglyceride level, and serum very low-density lipoprotein level not significant result recorded in serum low-density lipoproteins level. **Conclusion:** Decoction of leaves of *Ficus religiosa* was able to work on lipid and lipoprotein significantly.

Keywords: *Ashvattha Patra*, Dyslipidemia, *Ficus religiosa Linn.*, Lipid profile

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Introduction

Cardiovascular disease (CVD) is the single largest cause of death in developed countries and is among the leading causes of death and disability in the developing nations. CVDs contributed 28.1% (95% Uncertainty Interval 26.5–29.1) of the total deaths and 14.1% (12.9–15.3) of the total disability-adjusted life years in India in 2016.[1] Dyslipidemia considered as one of the important risk factor for the development of coronary heart disease (CHD) and stroke.[2]

Dyslipidemia is not directly correlated with any disease, which is describe in Ayurvedic classics but derangement of Agni and hypo-functioning of the Medodhatvagni, leads to quantitatively excessive homologous *Poshaka Medodhatu* or *Asthayi Medodhatu* (comprising different categories of lipoproteins) in circulation, this particular stage could be correlated with dyslipidemia.

Ficus religiosa (L.), commonly known as *Pipal* (*Ashvattha*), is the richest source of polyphenol compounds, flavonoids. These compound having a strong antioxidant property to prevent various oxidative stress-related diseases such as atherosclerosis, diabetes, and dyslipidemia.

Aim and Objective

Aim

The aim of the study was to assess the effects of *Ashvattha Patra* in dyslipidemia.

Objective

The objectives are as follows:

1. To assess the effect of Ashvattha Patra in serum low-density lipoproteins (LDL) level, serum triglyceride level, serum total cholesterol level
2. To assess the effect of Ashvattha Patra in serum high-density lipoprotein (HDL) Level.

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Materials and Methods

Randomly 100 undiagnosed dyslipidemia patients were screened and tested for dyslipidemia from out patient department (OPD) of Department of Swasthavritta, Kayachikitsa and Panchkarma of Pt. Khushilal Sharma Government (Autonomous) Ayurveda College and Hospital, Bhopal, (Madhya Pradesh) and got 41 patients as a Dyslipidemic patient.

Drug

Fresh leaf of *Ashvattha (F. religiosa L.)* regularly collected from tree which is situated near the Pt. K. L. Sharma Ayurvedic Institute Bhopal and fresh decoction was prepared daily in the department of Swasthavritta.

Preparation of drug

Ashvattha Patra Kwath (Decoction of leaf of *F. religiosa*) was prepared as per Ayurvedic classical preparation method of decoction described in *Sarandhar Samhita*. For this, the fresh

collected leafs of *Ashvattha Patra* [Image 1] were washed, chopped [Image 2] and grinded and made fine Paste [Image 3]. Then this fine paste along with 16 times of water (from the weight of leafs) was boiled on medium flame till remain to one forth [Image 4]. Then, the lukewarm decoction was filtered with the help of strainer [Image 5]. This isolated decoction was used as research drug.

Dietetic Regimen

All the patients were advised to avoid oily food preparations, tin packed food, butter, cheese, burger, pizza, fast food as well as junk food during study period. Also patients were advised to take food on time.

Method

Selection of patients

100 patients were screened for study those were attended OPD for miner ailment; from the OPD of Department of Swasthavritta, Kayachikitsa and Panchkarma of Pt. Khushilal Sharma Government (Autonomous) Ayurveda College and Hospital, Bhopal (M.P) and tested for lipid profiles. In which, 41 patients found lipid abnormalities. These all patients were selected for study with purposive sampling method. 20 patients assigned in Group "A" and 21 patients assigned in Group "B" after signed the informed consent form.

Image 3: Fine paste

Image 1: Ashvattha leaves

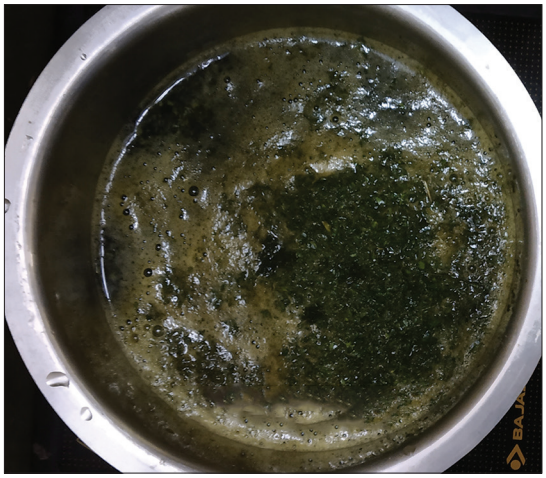

Image 4: Boiling till remain one forth

Image 2: Chopped leaves

Image 5: Prepared decoction

Ethical Clearance

The study was cleared by the Institutional Ethics Committee dated on May 27, 2017, and synopsis submitted to MPMSU University with Ref. No/Student Section/2017/1287/Bhopal Dated: November 21, 2017, written informed consent was obtained from patients before inclusion in the study.

Criteria for Diagnosis

Patients were diagnosed on the basis of the lipid profile. Patients in which lipid profile showing one or more of the criteria given below were considered as dyslipidemic patients as recommended by National Cholesterol Education Program (NCEP). NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).[3]

Serum total cholesterol >200 mg/dL
Serum triglycerides >150 mg/dL
Serum HDL <40 mg/dL and >60 mg/dL
Serum LDL >100 mg/dL
Serum very low-density lipoprotein (VLDL) >30 mg/dL.

Inclusion Criteria

The following criteria were included in the study:

- Patients those were fulfilling the diagnostic criteria
- Patient's age between ≥25 and ≤60 years
- Body mass index (BMI) ≥18 or ≤35
- Submitting an informed consent form.
- Either sex.

Exclusion Criteria

The following criteria were excluded from the study:

- Patient's age below 25 and above 60 years
- BMI <18 and >35
- Patients having history of serious systemic disorders such as myocardial infarction, cardiac failure, tuberculosis, severe renal disease, severe liver disease, malignancy, AIIDS, hepatitis-B, schizophrenia and depression, and untreated thyroid disorders
- Patients those are on or had been on hypolipidemic drugs
- Type I Diabetes Mellitus, and poorly controlled type-II DM
- Dyslipidemia due to use of drugs, that is, glucocorticoids and oral contraceptive pills
- Pregnant women and lactating mothers
- Patient using oral contraceptives therapy.

Study Design

In this study, 41 dyslipidemia patients randomly assigned in to two groups (experimental and control group), namely, 20 patients in Group "A" and 21 in Group "B": Group A (Experimental Group) was treated with 100 ml of *Ashvattha Patra Kwath* in two divided dose at morning and evening. Moreover, Group B (Control group) patients were provided 100 ml lukewarm water morning and evening as placebo. Total duration of study was 45 days. Out of 41 patients, 38 patients were completed study while, 20 patient of Group A and 18 patients of Group B, total three patients withdraw the study from Group B in between the study due to their personal reason. The outcome of clinical treatment was analyzed on the basis of improvement in lipid profile parameter as per ATP III Guide line. A pro forma was specially designed encompassing all the aspects of the disease for collection of data.

Investigations

Biochemical examination

- Complete blood count (CBC)
- Complete lipid profile
- Fasting blood sugar.

CBC, fasting blood sugar was conducted before the study and complete lipid profile was conducted before and after the study.

Physical Examination

- Blood pressure
- Pulse rate
- Height
- Weight
- BMI.

Criteria for assessment

The assessment of the treatment was based on objective parameters.

Objective assessment

Objective assessment was done on the following basis.

1. Biochemical test: Complete lipid profile, including serum cholesterol, serum triglycerides, serum HDL-cholesterol, serum LDL-cholesterol, and serum VLDL-cholesterol were done before and after the completion of the treatment
2. BMI was assessed before and after the completion of the treatment.

Statistical Analysis

The information regarding age, sex, religion, socioeconomic status, and occupation of the patients was recorded in numbers then calculated in percentage. Various observations were made and the results obtained were analyzed statistically using paired *t*-test and unpaired *t*-test on GraphPad-Instat software Version 3.06. The scoring of assessment was analyzed statistically in terms of mean values of before treatment, mean value of after treatment, standard deviation, and Standard error. The obtained results were interpreted on the bases of *P*-value as blow-

Not significant (NS) - $P > 0.05$,
Significant (S) – $P \leq 0.05$,
Highly significant (HS) – $P \leq 0.01$ and
Extremely significant (ES)- $P \leq 001$.

Observations and Results

Out of 41 patients, 38 patients were completed study while three patients from Group B were withdrawn in between study due to their personal reason. Hence, result was analyzed in 38 patients and observation was made on total 41 patients. In the present study, patients were selected between the age of 25 and 60 years and maximum number of patients 41.67% found in 31–40 year of age group. Other observations are as following.

Observations

Out of All patients, 65.85% were male, 90.2% patients were belong to Hindu religion, 51.21% patients were graduate and postgraduate, 53.66% patients were service class persons, 87.80% patients were married, 63.41% patients were belong to upper middle class, 31.7% patients were tobacco addicted, 65.85% patients were reported vegetarian, 73.17% patients were having *Madhyama kostha,*85% patients were having *Madhya Saar* and 73% patients *Madhya Samhanan* and 73% patients were having *Madhyam Praman*, and 60% patients were having Agni disturbance in these 60%, 26.83%, and 26.83% subjects were reported *Mandagni* and *Tikshani,* respectively. About 63% patients were having *Madhyam Abhyavaran Shakti* and 68% patients were having *Madhyam Jaran Shakti*, 61% patients were taking *Madhura* Rasa dominant *Ahara*, 83% were taking *Snigdha Guna* Ahar, 58.5% were taking *Guru Ahar*, and 48.8% were taking *Sheet Guna* predominant Aahar. As it is consider that *Guru*, *Snigdha*, *Sheeta Guna* help to increase the *Kapha Dosha* and *Sapta Dhatu* including *Meda Dhatu* as causative factor for development of Dyslipidemia.[4] About 68.2% were doing *Vismashana* (taking food in improper time and improper quantity), 39.02% patients were habitual to do *Adhyashana* (taking food again while last meal has not digested properly), 26.83% patients were habitual to do *Samshana* (combined intake of wholesome and unwholesome food), and 51% patients found in normal BMI limit. About 39% patients in pre obesity range and only 10% patients were reported in obesity Class I. About 75.6% patients were insufficiently active.

In this study, 58.5% patients were having Type "A" behavior pattern and 41.5% patients were having Type "B" behavior pattern. Various researchers were identified Type A behavior pattern as an important risk factor for CHD.[5]

In the present study, only 4.8% patients were reported low HDL cholesterol level, 36.6% patients were having high LDL cholesterol level, 83% patients were having high VLDL cholesterol level, and 22% patients were having high total cholesterol while in 83% patients serum triglyceride were found in above the normal limit.

Results

The effect of the therapy in all variables of lipid profile was found different with each other.

Effects of the therapy in Group A

Table 1 shows, In Group A initial mean score of total cholesterol was 178.23 mg/dl and it reduced to 150.19 mg/dl after treatment which was extremely significant statistically ($P < 0.0001$), triglycerides were 210.38 mg/dl and it reduced to 141.30 after treatment which was extremely significant statistically with $P < 0.001$, LDL was 86.8 mg/dl and it reduced to 73.76 mg/dl after treatment which was significant statistically with $P < 0.05$, VLDL was 42.44 mg/dl and it reduced to 28.75 mg/dl after treatment which was highly significant statistically with $P < 0.005$, HDL was 48.50 mg/dl and it reduced to 46.60 mg/dl after treatment which was not significant statistically with $P > 0.05$, total cholesterol/HDL cholesterol was 3.72 and it reduced to 3.21 after treatment which was extremely significant statistically with $P < 0.005$, FR SCORE was 4.15 before treatment and it reduced to 2.05 after treatment which was extremely significant statistically with $P < 0.0001$, and BMI was 26.08 and it reduced to 25.28 after treatment which was extremely significant statistically with $P < 0.0001$.

Effects of the therapy in Group B

Table 2 shows, in Group B initial mean score of total cholesterol was 182.51 mg/dl and it increase to 186.66 mg/dl after treatment which was not significant statistically with $P > 0.05$. Initial mean score of triglycerides was 206.69 mg/dl and it increase 231.27 mg/dl after treatment which was not significant statistically with negative mean difference ($P > 0.05$). Initial mean score of LDL was 92.58 mg/dl before treatment and it reduced to 90.23 mg/dl after treatment which was not significant statistically with $P > 0.05$. Initial mean score of VLDL was 41.30 mg/dl before treatment and 46.23 mg/dl after treatment which was not significant statistically with negative mean difference ($P > 0.05$), HDL was 49.48 mg/dl and it reduced to 48.61 mg/dl after treatment which was not significant statistically with $P > 0.05$, total cholesterol/HDL was 3.66 before treatment and 3.76 after treatment which was not significant statistically with $P > 0.05$, FR SCORE was 2.05 and 1.77 after treatment which was not significant statistically with $P > 0.05$, mean score of BMI was 25.89 and it reduced to 25.57 after treatment which was significant statistically with $P < 0.05$.

Comparative Effects (Between Group A and B) of the therapy on lipid profile

Table 3 shows, the mean difference on serum cholesterol, S TG, S LDL, S VLDL, S HDL, total cholesterol (TC)/HDL, FR SCORE, and BMI in Group A was reported 28.03, 69.08, 13.04, 13.693 1.190, 0.510, 0.51, and 0.80, respectively, while, in Group B it were reported as −4.14, −24.57, 2.35, −4.9, 0.87, −0.099, 0.278, and 0.32, respectively. In inter group comparison of both groups statistically highly significant result found in serum cholesterol level ($P = 0.0039$) and serum TG level ($P = 0.0020$). Extremely significant result found in VLDL with $P = 0.0001$, statistically not significant in LDL ($P = 0.3810$), statistically not significant in HDL ($P = 0.8524$), statistically significant ($P = 0.0106$) in TC/HDL and FR SCORE and highly significant result found in BMI with ($P = 0.0023$) thus result indicating that Group "A" (*Ashvattha patra kwath*) patients got better improvement in serum cholesterol, S TG, S VLDL, TC/HDL, FR SCORE, and BMI in comparison to relief in Group "B" patients.

Discussion

The prevalence of dyslipidemia in India found very high, which demands urgent lifestyle intervention policies to prevent and manage this essential cardiovascular risk factor. The Indian Council of Medical Research–India Diabetes Phase I study was conducted in a representative population of three states of India (Tamil Nadu, Maharashtra, and Jharkhand) and one Union Territory (Chandigarh), 213 million people were covered in the study. Study reported that in the urban residents had the highest prevalence of lipid abnormalities compared to rural residents and found 13.9% had high cholesterol range, 29.5% had high triglyceride range, 72.3% had low HDL-cholesterol range, 11.8% had high LDL-Cholesterol range levels, and 79% had any one of the lipid abnormalities.[6] Previously some preclinical study shows beneficial effect of leaf of *F. religiosa* in hyperlipidemia.[7-9] Hamed in 2011 found hypolipidemic and antioxidant properties of *F. religiosa* Linn in high-fat-diet-induced hypercholesterolemia rats.[10] *F. religiosa also* belongs to

Table 1: Effect of the Therapy on lipid profile in Group 'A'

Parameter (mg/dl)	*Mean score*		*Mean*	*SD*		*t-value*	*P-value*	*Significance*
	BT	*AT*	*difference*	*BT*	*AT*			
Serum cholesterol	178.23	150.19	28.03	31.31	12.84	4.785	0.0001	ES
Serum triglyceride	210.38	141.30	69.08	95.61	43.18	3.99	0.0008	ES
Serum LDL	86.80	73.76	13.04	26.90	12.81	2.13	0.0465	S
Serum VLDL	42.45	28.75	13.69	19.28	8.14	3.82	0.0012	HS
Serum HDL	48.50	46.60	1.19	4.60	4.74	1.55	0.1366	NS
TC/HDL	3.72	3.21	0.51	1.25	0.44	2.38	0.0277	ES
FR Score	4.15	2.05	2.1	6.01	6.38	5.48	<0.0001	ES
BMI	26.08	25.28	0.80	3.81	3.57	5.53	<0.0001	ES

BT: Before treatment, AT: After treatment, SD: Standard deviation, LDL: low-density lipoproteins, HDL: High-density lipoproteins, VLDL: Very low-density lipoproteins, TC: Total cholesterol, BMI: Body mass index

Table 2: Effect of the therapy on lipid profile in Group 'B'

Parameter(mg/dl)	*Mean score*		*Mean*	*SD*		*t-value*	*P-value*	*Significance*
	BT	*AT*	*difference*	*BT*	*AT*			
Serum cholesterol	182.51	186.66	−4.14	39.42	33.38	0.4676	0.646	NS
S TG	206.69	231.27	−24.57	71.73	80.42	1.08	0.292	NS
S LDL	92.58	90.23	2.35	45.78	38.47	0.21	0.829	NS
S VLDL	41.30	46.23	−4.93	14.33	16.15	1.08	0.291	NS
S HDL	49.48	48.61	O.87	3.61	3.92	0.75	0.462	NS
TC/HDL	3.66	3.76	−0.099	0.85	0.68	0.60	0.553	NS
FR SCORE	2.05	1.77	0.27	6.30	6.34	0.35	0.728	NS
BMI	25.89	25.57	0.32	3.27	3.13	2.66	0.016	S

BT: Before treatment, AT: After treatment, SD: Standard deviation, LDL: low-density lipoproteins, HDL: High-density lipoproteins, VLDL: Very low-density lipoproteins, TC: Total cholesterol, BMI: Body mass index

Table 3: Comparative Effects (Between Group A and B) of the therapy on lipid profile (Unpaired T test)

Parameter (mg/dl)	*MD*		*SD*		*P-value*	*t-value*	*Significance*
	Group A	*Group B*	*Group A*	*Group B*			
Serum cholesterol	28.03	−4.14	26.202	37.60	0.0039	3.08	HS
S TG	69.08	−24.57	77.45	96.01	0.0020	3.32	HS
S LDL	13.04	2.35	27.39	45.60	0.3810	0.88	NS
S VLDL	13.69	−4.93	16.02	19.23	0.0001	24.40	ES
S HDL	1.19	O.87	5.46	4.92	0.8524	0.18	NS
TC/HDL	0.51	−0.099	0.95	0.69	0.0106	2.69	S
FR SCORE	2.1	0.27	1.71	3.34	0.0385	0.03	S
BMI	0.80	0.32	0.64	0.51	0.0023	3.28	HS

MD: Mean difference, SD: Standard deviation, LDL: low-density lipoproteins, HDL: High-density lipoproteins, VLDL: Very low-density lipoproteins, TC: Total cholesterol, BMI: Body mass index

Rasayana drugs in *ayurveda*.[11] *Rasayana* drugs work as rejuvenators, immunomodulators and reduces oxidative stress in the body.[12] Free radicals generated during oxidative stress causes various diseases. It reduces oxidative stress also due to *Rasayan* activity.[13]

Probable mode of action of *Ashvattha Patra Kwath* in Dyslipidemia

Biologically active phytochemicals of *F. religiosa L.* leaves are campesterol, stigmasterol, isofucosterol, α-amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, glycine, threonine, alanine, proline, tryptophan, tyrosine, methionine, valine, isoleucine, leucine, nonacosane, n-hentricontanen, hexa-cosanol, and n-octacosan.[14-17] In these phytochemicals, Campesterol is a phytosterol whose chemical structure is resemble to cholesterol[18] Campesterol, compete cholesterol absorption from intestine and reduce exogenous production of serum cholesterol.[19] That helps to lower plasma cholesterol concentrations.[20] Stigmasterol is an unsaturated phytosterol[21] which has potential to reduce LDL cholesterol. Consumption of 2 g/day of plant sterols is associated with a lessening in blood LDL cholesterol of 8–10%[22] Just like that Pratima Tripathi *et al*. in 2012 the studies of "Role of l-Arginine on Dyslipidemic Conditions of Acute Myocardial Infarction Patients" and found that l-arginine supplementation lead to a significant reduction in the total serum cholesterol levels.[23] Itoh *et al*. (2009). found in his study that Lupeol decreases triglyceride and cholesterol synthesis in human hepatoma cells.[24] Zhou *et al*. in 2018 found Serine prevents high-fat diet-induced oxidative stress.[25] Jiang *et al*. in 2017 found Threonine supplementation improves lipid metabolism in Pekin ducks.[26] All these results obtained from various studies clearly indicated that leaf of *F. religiosa* has significant role in the management of dyslipidemia.

According to *Bhava Prakasha Nighantu,*[27] *Ashvattha* is *Ruksha* (dry), and *Kashaya* (astringent) in Properties, according to *Madan Pal Niganthu*[28] *-Ashvattha* pacifying *pitta-kapha dosha*, and purifying *rakta* (blood) also. As *Ruksha Guna* (dry property) is having *Vayu* and *Agni Mahabhuta*[29] in Dominance so has absorption (*Shoshana*)[30] and *kapha* pacifying (*Kaphahar*)[29] Property. Thus, by this mechanism decoction of *Ashvattha Patra* definitely was reducing *Kapha Dosha* which was considered as

main aggravated *dosha* in the development of Dyslipidemia. Also by astringent property of *Ashvattha*, this decoction was might helping in reduction of circulating unconsolidated *Meda dhatu* in blood, that is, *Abaddha Meda*, due to its inherent dry and absorbing properties.[31]

Conclusion

Dyslipidemia is identified as an important risk factor for the development of cardio vascular diseases. Due to its Chemical composition and *Ruksha* and *Kashya* property, leaves of *F. religiosa* had been acts on lipids and lipoproteins significantly. Thus, decoction of leaves of *F. religiosa* could be used as to potentially manage dyslipidemia as well as to reduce risk factor of cardio vascular diseases.

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