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RESEARCH ARTICLE

Hypolipidemic Effect of Hyppophae ramnoids L. (sea buckthorn) Fruit Juice in Experimentally Induced Hypercholestermic Rabbits

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Abstract

Background and purpose of the study
The goal was to evaluate the Efficacy of the Ayurvedic herbal Hyppophae ramnoid L. (Sea buckthorn) fruit Juice on Triglycerides, Total cholesterol, Low density lipoprotein, atherogenic index, High density lipoprotein and high sensitivity total cholesterol reactive protein (hs CRP) Has Studied on Hyperlipidemic Cholesterol Rabbits.

Methods
In experimental groups four groups of rabbits (each group 6) were subjected to different treatments for 8 weeks .control group, CHOL group (1%w/w Cholestrol for 8 weeks), R group (1% W/W Cholesterol and Sea buckthorn fruit Juice. For 8 weeks) A group (1% W/W Cholestrol and atorvastatin for 8 weeks) and the Biochemical parameters has studied

Results
The results showed significant increases In TG, TC, LDL, AL and has CRP In hypercholestermic rabbits which was significantly reduced in sea buckthorn ® fruit Juice treated hypercholesterolemic rabbits. The data showed that the sea buckthorn ® fruit Juice has significantly reduced the cholesterol parameters of LDL, TG, TC, AL and hs CRP and significantly increased the HDL Levels.

Conclusions
This suggests that sea buckthorn ® might act through multiple mechanisms. Thus protective role of Hyppophae ramnoids in reducing complications of Atherosclerosis could be due to its lipid lowering, anti inflammatory, anti oxidant properties and may be effects on atherosclerotic vessels in high cholesterol diet-fed rabbits [8].

Introduction

Several studies shown that the increased risk of CHD and atherosclerosis is associated with high serum concentration of TC, TG and LDL and increased level of inflammation factor CRP and level of HDL.The high mortality of atherosclerosis[12], the wide spread suffering, and the huge economic impact demand integrated medical approaches and therapies. To reflect that demand, the Hyppophae ramnoids L. Family of Elaeagnaceae is an ancient plant available mainly in Europe, spain, asia to japan, origin of the plant is Nepal and Himalayas [1, 2], it has been used as a Folk medicine in that particular area for the treatment of increased serum cholesterol, Triglycerides, Atherosclerosis, Anti oxidant, anti-tumor other Forms of CVD by the tribal people. The Sea buckthorn ® fruit contains a numbers of Anti-oxidants, B-carotene, *flavanoids. Vitamins,oleic ,omega acid essential minerals [7, 16] in* natural form, which may play a vital role in the treatment and also prevention of Atherosclerotic blockage in the blood vessels and in particularly coronary and cerebral blood vessels [1, 2]. In order to decrease the cost and side-effects we have studied the hypolipodemic effect of that Himalayan Ayurvedic herb Hyppophae ramnoids fruit Juice in

experimentally induced Hypercholestermic Rabbit model.

MATERIALS AND METHODS

Herb authentication tests were done at the National Institute of Science Communication and Information Resources, New Delhi (NISCAIR / RHM / F-3/Conslt /06/690/07).

Drug and Dosage: Sea buckthorn fruit juice 1 ml/kg/day ® were administered using an oral infant feeding tube inserted through a wooden oral gag. Atorvastatin [8] (5mg/kg/d) was administered as a suspension, prepared with 0.5% carboxymethyl cellulose (CMC).

Animals: One – month-old New Zealand white rabbits (1-1.5g) of either sex were selected for this study and used with the approval of the Institutional Animal Ethics Committee. They were housed in a well-ventilated animal unit with normal daylight (12-h light / dark cycle, lights on at 07:00). The animals were fed with a standard (Amrit Laboratory Feed Pvt. Ltd., India) rabbit chow diet and water adlibitum. The animals were divided into four groups (n=6), and the following treatments were given simultaneously to each group for 8 weeks [11].

Experimental groups the control group received the standard chow diet and water. In the treatment groups, the CHOL group was fed a f-enriched (1% w/w cholesterol +10% v/w groundnut oil)[3,4] fatty diet, the R group (1% w/w cholesterol + 10% v/w groundnut oil) diet plus test drug , and the A group was fed a f-enriched (1% w/w cholesterol+10 % v/w groundnut oil) diet plus the standard drug (atorvastation 5 mg/kg/d)[5].

Estimation of Biochemical Parameters.

After the experimental regimen, the animals were subjected to overnight fasting, although water was provided adlibitum. Two –milliliter blood samples were drawn using a marginal ear vein puncture and centrifuged (10 g, 1000 rpm) the serum has collected and used

For measuring the Biochemical parameters [4] it has determined using the following kits. LDL cholesterol, TC, TG, and HDL cholesterol kits were procured from Qualigens Diagnostics [15], and the hc CRP kit was A Spinreact from ARK Diagnostics. [15, 6] Heparin sodium (Beparin) was procured from Biological E.Limited, India. The cholesterol powder was procured from SD Fine-Chem Limited, India.

Statistical Analysis Data are presented as mean ± S.D. of 6 animals. Statistical evaluation was done using one-way analysis of variance (ANOVA) with SPSS version 11.5. For comparison between the groups, the significance level was fixed at P<0.001.

RESULTS

BIOCHEMICAL PARAMETERS

Changes in serum total cholesterol (TC)

Over 8 weeks of study period, serum TC was significantly (P<O.001) high in group CHOL, group R and group A, when compared to group control (1905 ± 95.7, 609.45 ± 17.5, 5 71.75 ±4.2 vs 64.83 ± 1.67), In group A, serum TC was significantly (P<0.001) low compared to group CHOL (609.45± 17.5, 571.42 ± 4.2, VS 1905 ± 95.7) There was no significant difference in serum TC between group HR and group A as described in Figure -1

FIGURE 1(Effect of drugs on TC (mg/dl) at the 8th Week) R = sea buckthorn

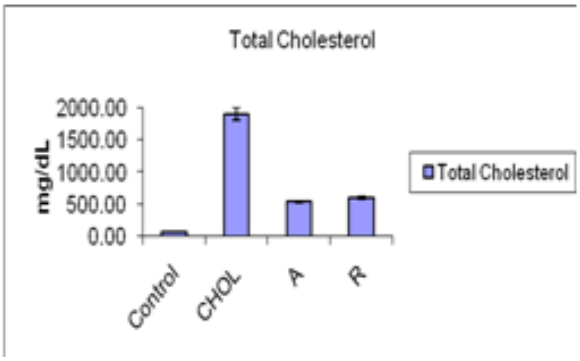


FIGURE 2(Effect of drugs on TG (mg/dl) at the 8th Week) R = sea buckthorn

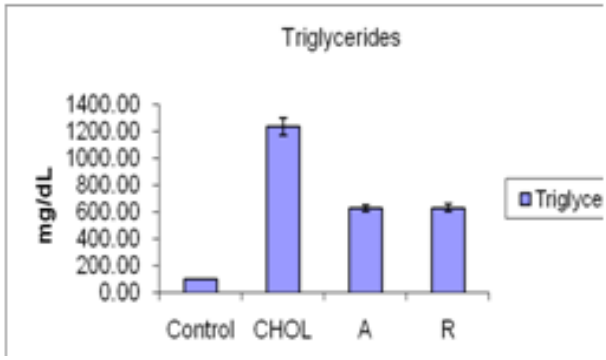


FIGURE 3 (Effect of drugs on HDL-C (mg/dl) at the 8thWeek) R = sea buckthorn.

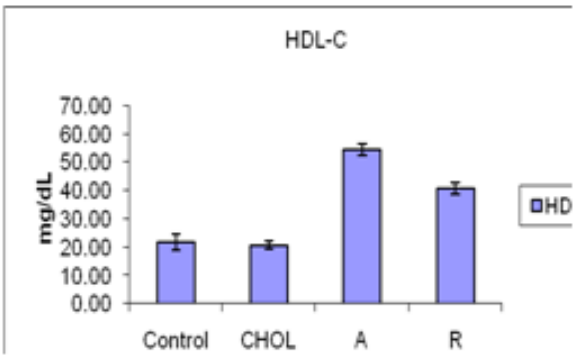


FIGURE 4 (Effect of drugs on LDL-C (mg/dl) at the 8thWeek) R = sea buckthorn

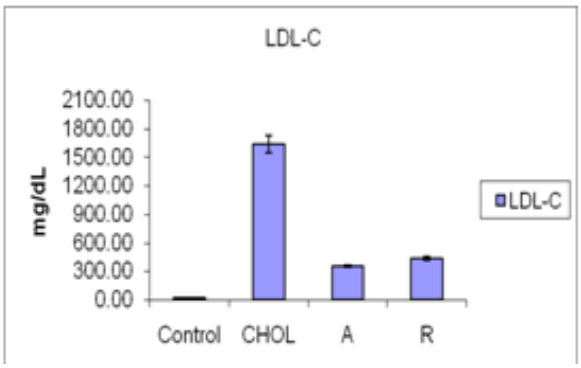


FIGURE 5(Effect of drugs on AI (mg/dl) at the 8thWeek) R = sea buckthorn

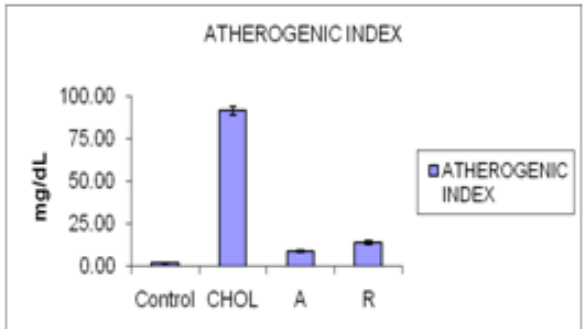
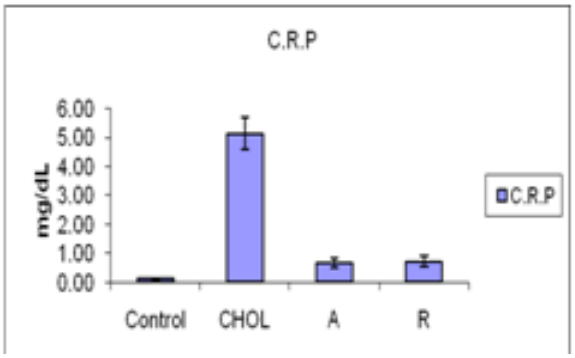


FIGURE 6(Effect of drugs on CRP (mg/dl) at the 8thWeek) R = sea buckthorn



Changes in serum Triglycerides (TG)

Over 8 weeks of study Period, serum TG was significantly (P<0.001) high in group CHOL, group R and group A, when compared to group chol (634.18 ± 24.49, 405±0.93 VS 1240.17 ± 65). In group R and groupA, serum TG was significantly (P<0.001) low compared to group control (20.71 ± 1.31, 54.37 ±1.97 VS 21.89±2.77). There was no significant difference in serum TG between group HR and groupA as described in Figure -2.

Changes in serum HDL-Cholestrol (HDL-C)

Over 8 week of study period, serum HDL-C was lower in group CHOL (NS) and was significantly (P<0.001) higher in group R and groupA, when compared to group control (20.7 ± 1.31, 40.85 ± 2.03, 13.49 ±0.06VS 21.89 ± 2.77). In group R and group A serum HDL-C was significantly (P<0.001) high when compared to group CHOL (54.37 ± 1.97, 75.22 ± 1.45 VS 20.71 ± 1.31), There was no significant difference in serum HDL – C between group R and group A as described in Figure-3.

Changes in serum LDL-Cholestrol (LDL-C)

Over 8 weeks of study period, serum LDL-C was significantly (P<0.001) high in group CHOL, group R and group A, when compared to group control (357.39 ± 10.46, 300.24±8.23, VS 22.33 ± 2.8). In group R and group A, serum LDL-C was significantly (P<0.001) low compared to group CHOL (22.37± 2.8, 357.39±10.46 VS 1637.83 ± 92.8) There was no significant difference in serum LDL-C between group R and group A, as described in figure -4.

Changes in Atherogenic index (A1)

Over 8 weeks of study period, atherogenic index was high in group CHOL (P<0.001), group (NS) and group A (P=0.007), when compared to group control (91.55 ± 2.67, 14.19 ± 1.12, 5.27± 0.7 VS 2.07 ± 0.27) in group HR and group A, atherogenic index was significantly (P< 0.001) 1ow compared to group CHOL (14.19 ± 1.12, 5.27 ± 0.7 VS 91.55 ± 2.67). There was no significant difference in figure -5

Changes in serum C – reactive protein (CRP)

Over 8 weeks of study period, serum CRP was significantly (P<0.001) high in group CHOL, group R and groupA, when compared to group control (3.14 ± 0.55, 0.72 ± 0.19, 0.05 ± 0.04VS 0.11 ± 0.032). In group R and group A, serum CRP was significantly (P<0.001) cow compared to group

CHOL (0.72 ± 0.19, 0.05± 0.04 VS 3.14 ± 0.55). There was no significant difference in serum CRP between group HR and group A as described in Figure -6.

DISCUSSION

Despite several animal models used in Atherosclerosis. Cholesterol – Fed rabbits often used as a model to reflect human condition in this model high fat diet is used to produce hyper lipidemic and it is important because a purely non dietary method of induction does not produce the desired lesion consistently and a hyper lipedemic state analogous to that humans can be created.

Mice and rats are lacking the receptor for monocyte chemolactic protein-1 (MCP-1) / CCR 2 (it is foremost ever contributed to atherosclerosis)[4,5].

CRP is prodigiously expressed in humans and rabbits but is minimally induced by inflammatory stimuli in mice, where as in rats, it is constituently expressed at high level, with only a several Fold increase after stimulation. [12]. in the present study, rabbits were fed 1% (W/W cholesterol enriched diet mixed with 10% (V/W) groundnut oil for 8 weeks. Several studies shown that increased risk of CHD and atherosclerosis is associated with high serum concentration of TC, LDL, TG and Low concentration of HDL.when compare with control group there was ~30 times increase in the total cholesterol (TC) level which was accompanied by ~74 times increase in serum LDL-C and ~12 times increase in serum TG levels with almost same serum high density lipoprotein (HDL-C) levels in cholesterol fed animal group (CHOL). Cholestrol feeding in rabbits has shown high hyperlipedemic condition. The serum TC might also be contributed by fatty acids present in the vehicle (groundnut oil)

Atherogenic index was increased up to~ 45 times, the atherogenic index are widely regarded as powerful predictors of CHD risk changes in there indict in the present study indicate pronounced increase in bad cholesterol i.e., serum LDL-C levels. In addition when compare with control group serum C-RP levels were increased ~46 times in cholesterol fed animal group which indicates a high inflammatory response in CHOL group. The present study has showed the R fruit Juice
(1ml/kg/day) reduces the in serum TC, serum TG, serum LDL-C and significant increase in serum HDL-C level has been observed. Sea buckthorn L has also reduced the high fat diet induced rise in atherogenic indices Value. Similar changes were also observed C atorvastatin (5 mg /Kg/ days) treatment. In addition Rhododendnon arboreum Sm reduced serum C-reactive protein level significantly, which was a similar change observed with atorvastatin, previous studies shown that importance of Hyppophae ramnoides L. fruit Juice and anti inflammatory activity, sea buckthorn oils anti inflammatory activity .

Hyppophae ramnoides L. Fruit Juice might be attributed to the number of chemical ingredients, which were previously shown to have such an effect e.g. flavanoids, iso flavones reduce arterial stiffness, flavanoids have been shown to act as metal chealaters free radical scavengers[16] and chain breaking anti – oxidants, Polyphenols inhibit LDL-C oxidation, which is a protecting activity of polyphenoles from atherogenesis (Anderson KJ et.al, 2001). Several studies shown that CHD protective activity of Hyppophae ramnoids L. fruit juice is associates with its anti oxidation activity. Previous reports showed that essential fatty acids plays important role in lowering plasma cholesterol and triglycerides in humans.

This suggests that Hyppophae ramnoides L. might act through multiple mechanisms. Thus protective role of HR in reducing complications of Atherosclerosis could be due to its lipid lowering, anti inflammatory and anti oxidant properties and may be effects on atherosclerotic vessels in high cholesterol diet-fed rabbits [8].

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References

1, Orient Longman.Indian medicinal plants Vol.2, published by, orient Longman, Limited 160, Annasalai, Chennai.

2. Red berries, future dietary supplement, European journal of clinical Nutrition (2003) 57. 37-42

3. Hironobu Mitari, Misatotakimoto, Tsutomu Bandoh, Massaki Kimura.
Increases of vascular endothelin – converting enzyme activity and endothelin -1, level on atherosclerotic lesions in hyperlipidemic rabbits. European Journal of pharmacology 2000; 387, 3,313-319.

4. Alandaughery, Guistav schonfeid, Burton E.Jobel and Louis G. Lange. Metabolism of very low density lipoproteins after cessation of cholesterol feeding in rabbits. Journal of clinical invest. 1986; volume 77, 1108-1115.

5. Nalini M, Rajamannan, Malayannan Subramaniam, Margaret Springett; Thomasc, sebo, Marek Niekrasz, et.al, Atorvastatin inhibits hypercholesterolemia - induced cellular proliferation and rabbit aortic valve circulation 2002; 105: 2660

6. Kinosian B, Glick H, Presis L, Puder KL., Cholestrol and Coronary heart disease: Predicting risks in men by changes in levels and ratios, J investing Med.1995; 43(5): 443-50.

7. Indian Medicinal plants kirtikar & Basu vol-11 Page No.1459-1461

8. Hironobumitani, Kensuke Egashira, Massaki Kimora., HMG-COA reductase inhibitor, Fluvastatin, has cholesterol lowering independent "direct" effects on atheroselerotic vessels in high cholesterol diet – Fed rabbits Pharmacologicol research. 2003; 48(5); 417-427

9. Terrance D.Barrett, James K. Hennan,et.al., C-reactive protein-Associated increase in myocardial intract size after ischemia Repurfusion JPET 2002;;vol.303,(3)1007-1013,

10. Naoumova RP, Tosil, pater D, Neuwirth c, Horswell SD, Mara is AD, Van Heyningen C, Soutar AK. Severe hypercholesterolemia in four British Families with the D 374y Mutation in the pcsk 9 gene: Long –term Follow-Up and treatment response. Arterioscler Thromb Vasc Bio1. 2005; 25 (12) 2654-60.

11. Gerhord Vosel, H.Wolfgansh Vogel. Drug Discovery and Evaluation 1996; 598-603.

12. Goodmen and Gilmen are the Pharmacologies, basis of therapeutics 9th edition.

13. Anti-inflammatory activity of flowers of rhododendron arboreum (smith) in rat's find paw oedema by various physiological agents, Indian Journal of Pharmacology 1998; Vol. 20, 2-4, P86-89

14. Trinder P, Determination of blood glucose using 4- amino phenazone as oxygen acceptor Jclin path 1969; March 22(2): 246.

15. MC Gowan, M.W, Artiss JD, Sinand Berg Dr, Zakb, A., peroxidese Couple method for the colorimetric determination of serum triglycerides .clin chem.1983; 23, 530

16. Muldoon MF, Kritchevsky SB.flavonoids and heart disease Br. Med J. 1996; 312: 458-9.

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