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Effect of different galactomannans on absorption of cholesterol in rabbits

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Abstract

Objective: The aim of the present investigation was to study the effect of different galactomannans on cholesterol absorption in rabbits. Materials and methods: Guar, fenugreek and locust bean galactomannans of # 200 having different galactose: mannose ratios of 1:2, 1:1 and 1:4 respectively and 1%w/v aqueous dispersion of these galactomannans having viscosities of 3215 ± 280 cps, 1050 ± 80 cps and 600 ± 52 cps respectively were selected for the present study. Antihyperlipidemic activity of galactomannans was studied using cholesterol loaded rabbit model. Cholesterol was administered by gastric gavage in a daily dose of 500mg/kg bodyweight, for induction of hyperlipidemia. The different galactomannans were administered in a daily dose of 250 mg/kg body weight. The study was carried out for a period of 18 days. Blood specimens were collected before commencement of study, on day 9 and on the last day. The total lipid profile in serum was determined using auto-analyzer. Results: All the three galactomannans under study showed significant antihyperlipidemic activity ($p<0.05$) in comparison to the control group. Guar and fenugreek galactomannans had statistically ($p<0.05$) a similar effect. Locust bean galactomannan had significantly ($p<0.05$) a lower activity in comparison to the other two galactomannans. The effects of galactomannans so observed can be explained and correlated with their galactose: mannose ratios i.e. galactomannans with a high galactose: mannose ratio like fenugreek and guar have a better effect in comparison to a galactomannan with low galactose: mannose ratio like locust bean. Conclusion: It is concluded that different galactomannans having different galactose: mannose ratios affect the absorption of cholesterol to different extent.

Key words: galactomannans, galactose: mannose ratio, antihyperlipidemic activity.

1. Introduction

Atherosclerosis, a disease of modern day civilization, results due to deposition of cholesterol crystals in arteries, impeding the flow of blood [1, 2]. Different mechanisms appear to underlie the varying levels of blood cholesterol in normal population. Use of soluble dietary fibre, like galactomannans, is a safe and natural way of lowering blood cholesterol and reducing the

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possibility of developing atherosclerotic plaque [3-8]. It is desired that an ideal hypo-cholesterolimic agent should lower not only the low-density lipid levels but should also maintain the high-density lipid levels constant.

Galactomannans are found as reserve food material in the endosperms of leguminous plant seeds. These are referred to as galactomannans, because they consist of β-(1-4)- mannose backbone having single α-(1-6)-galactose side chains. The various seed galactomannans differ from each other in galactose: mannose ratios, molecular weight, fine structure regarding the distribution of galactose side groups on the main chain [9,11]. In the present study the effect of different galactomannans affecting the absorption of cholesterol was studied.

2. Materials and methods

2.1 Samples of galactomannans

Guar, fenugreek and locust bean galactomannans were selected for this study, which have a galactose: mannose ratio of 1:2, 1:1 and 1:4 respectively. The viscosities of 1% w/v aqueous dispersions of these galactomannans are 3215 ± 280 cps, 1050±80 cps and 600±52 cps respectively. Galactomannans of mesh size 200 were employed for the study.

2.2 Chemicals

Cholesterol (Benzo Chem, Bombay)

2.3 Preparation of dispersions of galactomannans and cholesterol

A 3.8%w/v aqueous dispersions of the three galactomannans were prepared using mechanical stirrer at 1500±200 rpm. Warm water was used for preparing the dispersion of locust bean galactomannan; while the other galactomannans are dispersible in cold water. A 50%w/v dispersion of cholesterol was prepared in *vanaspati* with the aid of little heat. The prepared dispersion was than allowed to come to room temperature.

2.4 Antihyperlipidemic activity

Rabbits of either sex weighing 1.75 - 1.9 kg were fasted for 18 h prior to commencement of study. Thereafter, they had free access to food and water. Animals were divided into four groups with five animals in each group.

The method selected for producing hyperlipidemia was cholesterol feeding by gastric intubation [12-15]. All the four animal groups were administered cholesterol (500 mg/kg body weight daily) for 18 days. The first group was fed cholesterol alone. The second group received aqueous dispersion of guar galactomannan, (250 mg/kg body weight) in addition to cholesterol dispersion (500 mg/kg body weight daily). The animals in third and fourth groups received aqueous dispersions of fenugreek and locust bean galactomannans respectively (250 mg/kg body weight) in addition to cholesterol (500 mg/kg body weight daily).

2.5 Collection of blood samples

Blood samples were collected on day 1 i.e. just prior to feeding of cholesterol and galactomannan dispersions; then on day 9 and on day 18. About 1ml blood was collected from the rabbits' marginal ear veins using needle of gauge 22 in graduated centrifuge tubes by 'milking' i.e. dropwise collection of blood through a needle pierced in the vein.

The collected blood was left for an hour and allowed to clot. Then it was centrifuged for 20 min. The separated serum, about 0.5 ml, was transferred to a sample vial using pasture pipette. The serum so obtained was analyzed for total lipid profile using AMES SEAC CH – 100 autoanlyzer.

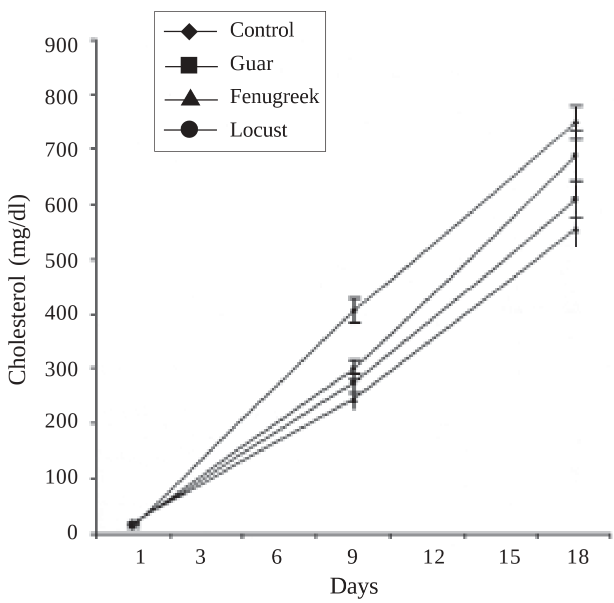
2.6 Statistical analysis

The results of total lipid profile of the four animal groups were reported as mean ± S.D. Using the software 'Analysis ToolPak', the data was tested

Table 1.
Total lipid profile of different animal groups as on day 18.

Parameter→ Group ↓	Cholesterol	High Density Lipids	Low Density Lipids	Very Low Density Lipids	Triglyceride	LDL/HDL ratio
Control	748 ± 31	88 ± 16	548 ± 4	111 ± 11	557 ± 44	6.2
GG	603 ± 35*[a]	103 ± 18	449 ± 10	51 ± 7	253 ± 35	4.3
FG	550 ± 32*[a]	100 ± 21	412 ± 8	38 ± 3	189 ± 14	4.1
LBG	681 ± 46*[b]	98 ± 14	511 ± 26	72 ± 6	360 ± 30	5.2

All values in mg/dl. The data indicates mean ± S.D. n = 05.
Data analyzed using ANOVA followed by Dunnett's Test and Studentized range test.
*$p<0.05$ significant activity in comparison to control. (Dunnett's Test)
[a] $p<0.05$ significantly similar activities of GG and FGM. (Studentized range test)
[b] $p<0.05$ significantly different activity of LBG from GG and FGM. (Studentized range test)
GG = guar galactomannan; FG = fenugreek galactomannan; LBG = locust bean galactomannan.



Graph is plotted using mean ± S.D. n = 05.

Fig. 1.
Effect of various galactomannans on reducing cholesterol absorption in rabbits.

for statistical significance using one way Analysis of Variance (ANOVA) followed by Dunnett's test and Studentized range test for multiple comparisons between the treated groups and control and among the three galactomannan groups respectively. The activity was considered significant at $p<0.05$ in all cases.

3. Results and discussion

Based on the results depicted in Table 1 and Fig. 1, it is observed that the three galactomannans have a significant activity to reduce the absorption of cholesterol on oral feeding. The activities of guar and fenugreek galactomannans are statistically similar, while locust bean galactomannan has a lower activity. The similar effect of fenugreek and guar galactomannans can be attributed to their higher galactose: mannose ratio in comparison to that of locust bean galactomannan having a lower galactose: mannose ratio.

One of the important parameters considered for evaluation of antihyperlipidemic agents is their ability to affect the ratio between low-density and high-density lipids or LDL / HDL ratio. Normally, the ratio should be between 3 to 4. From the results (Table 1), it is seen that fenugreek galactomannan is the most effective galactomannan in keeping the ratio down, to about 4.

Galactomannans are not absorbed through the gut, wherein they possibly act by forming hydrogen bonds with cholesterol and interfering with its adsorption. They also possibly bind with bile salts and interfere with their prime functions of emulsification and solubilization of cholesterol. Interaction with bile salts would also affect enterohepatic cycling of the bile salts, since the complexed bile cannot be reabsorbed and would be excreted out through the feaces. As a result LDL from the lipid pool of the body would be mobilized for synthesis of bile salts to make-up for their loss.

The better activity of fenugreek and guar galactomannans can also be explained on the basis that a galactomannan having a high galactose: mannose ratio offers more sites for hydrogen bond formation with cholesterol and bile salts resulting in their reduced absorption.

4. Conclusion

Different galactomannans reduce the absorption of cholesterol to different extents. A galactomannan with a higher galactose: mannose ratio has a higher activity than a galactomannan with a lower galactose: mannose ratio.

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References

1. Guyton AC. (1991) Textbook of Medical Physiology, 8th Edn. Prism Books Pvt. Ltd.: Bangalore; 728.

2. Scwertz CJ, Valente AJ, Sprague EA, Kelly JL, Nerem RM. (1991) *Clin. Cardiol.* 14:1-16.

3. Lansky PS. (1993) *Acta Horticulture.* 332: 131-136.

4. Jenkins DJA. (1976) *Am. J. Clin. Nutri.* 16: 32-34.

5. Trowell H. (1972) *Am. J. Clin. Nutr.* 25: 926-932.

6. Jenkins DJA. (1979) *Lancet.* 2: 1287-1290.

7. Ebling P, Hannel YJ, Aro A, Helve E, Sinisalo M, Koivisto VA. (1988) *Am. J. Clin. Nutr.* 48: 98-103.

8. Fuessssl HS, Williams G, Adrian TE, Bloom SR. (1987) *Diabetic Med.* 4: 463-8.

9. Chudzikowski RJ. (1971) *J. Soc. Cosmet. Chem.* 22: 43-60.

10. Whistler RL. (1973) *Industrial Gums*, 2nd Edn., Academic Press: New York; 1-806.

11. Nagori BP. (1994) Synthetic studies and pharmacological screening of galactomannan derivatives in sustained release of drugs, Ph. D. dissertation, Department of Chemistry, JNVU: Jodhpur.

12. Laurence DR, Laurence AL. (1964) *Evaluation of Drug Activities: Pharmacometrics,* Vol. II, Academic press: London; 875-890.

13. Vogel HG, Vogel WH. (1996) *Drug Discovery and Evaluation:* Pharmacological Assays, Springer: Germany; 598-617.

14. Lambert GF. (1958) *Proc.Soc. Exp. Biol. Med.* 97: 544-49.

15. Mittal SR, Mathur AK, Tandon R. (1990) *Int. J. Card.* 27: 275-276.