

## **THE HYPOLIPIDAEMIC EFFECT OF GUM TRAGACANTH IN DIET INDUCED HYPERLIPIDAEMIA IN RATS**

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### **ABSTRACT:**

Previous research indicated that fibre in the diet of men lowers plasma lipid and LDL cholesterol concentration. To further study the lipid lowering effect of fibre, we conducted an animal study using rats with diet induced hyperlipidaemia. Rats were randomly assigned to one of the three experimental diets- Two of the diets contained cholesterol and choice acid to induce hyperlipidaemia, the fibre source in the hyperlipidaemic diet was gum tragacanth (5%). The rats consumed one of the three diets ad libitum for 4 weeks before they were killed. Plasma LDL cholesterol and total cholesterol concentrations were significantly higher in the hyperlipidaemic group than in the non hyperlipidaemic control group. A marked improvement in the plasma LDL cholesterol and total cholesterol concentration was observed in the rats that were fed hyperlipidaemic diet containing gum tragacanth. No significant difference in the plasma triglyceride concentration was detected in the three groups. Plasma HDL concentration was significantly higher in the non-hyperlipidaemic group than in the hyperlipidaemic group. Addition of gum tragacanth to the hyperlipidaemic diet significantly improved the plasma HDL concentration in the hyperlipidaemic rats. These results suggest that fibre from gum tragacanth lowers plasma cholesterol and LDL in hyperlipidaemia. Gum tragacanth could be useful adjunct to the dietary management of hyperlipidaemia.

### **INTRODUCTION**

Speculations on the evolution of human diet together with comparative studies with the diet of other primates suggest that the human gastrointestinal tract and metabolism are adapted to high fibre diets. Epidemiological studies support a negative association between dietary fibre intake and risk of coronary heart disease. Hypercholesterolaemia is one of the major risk factors for ischaemic heart disease and for the development of atherosclerotic plaques. Viscous fibre sources are likely to play a role since they reduce lipid risk factor for coronary heart disease including total and low density lipoproteins, cholesterol and apolipoproteins (Jenkins *et al.*, 1998). Water soluble plant fibres have shown to exert a binding of intestinal cholesterol without being digested or metabolised (Hegele *et al.*, 1993). In addition, in linear regression analyses fibre intake has shown to be inversely associated with fasting glucose (Bakker *et al.*, 1998).

Results from animal and human studies suggest that fat digestion could be reduced or delayed in the presence of fibre rich fractions and that the intestinal absorption of fat and bile salts (Judd and Truswell, 1981) might be impaired. These changes could likely result in some alterations in the post prandial response to a meal as observed in humans (Dubois *et al.*, 1995). Moreover, adults and children with familial hypercholesterolaemia are often resistant to standard dietary management of their hypercholesterolaemia, and the management of hyperlipidaemia in children can involve special problems and considerations (Kwiterovich, 1977). Pharmacological treatment is often necessary in addition to dietary treatment to significantly lower cholesterol and low

density lipoprotein cholesterol (Zavarol *et al.*, 1983). It is therefore appealing to develop food products that contain safe, effective and hopefully, cost effective hypolipidaemic fibres that can be used long term in familial hypercholesterolaenic children and adults as part of their every day diet.

## MATERIALS AND METHODS

Female Wistar rats weighting 120 – 140 g were obtained from H.E.1. Research Institute of Chemistry, Karachi. The animals were housed in the animal house of the Department of Physiology, University of Karachi. The animals were grouped into three, according to the experimental diet: A: Control; B: Hyperlipidaemic; C: Hyperlipidaemic with added gum tragacanth (5%). A basal diet mixture (Table 1) was prepared from which the two experimental diets were derived. Hyperlipidaemic diet was prepared by adding 1% cholesterol and 0.1% cholic acid to the basal diet (Shinnick *et al.*, 1990). To test the effect of gum tragacanth, 5% gum tragacanth was added to the hyperlipidaemic diet. The animals had free access to the experimental diet and water for four weeks. The rats were weighted weekly during the experimental period

### ***Blood and Tissue Collection***

At the end of four weeks, the animals were sacrificed and the blood was collected. Plasma was separated from whole blood within 30 min of collection by centrifugation at 1200 x g for 20 minutes. Body organs including liver, small intestine and caecum were removed immediately, weighed and discarded.

### ***Biochemical Analysis***

Plasma VLDL, LDL and HDL concentration of total cholesterol and total triglyceride and total protein were determined by enzymatic analysis as previously reported (Ney *et al.*, 1987).

### ***Statistical Analysis***

One-way ANOVA was computed using a general linear model with diet as the grouping factor to test against the null hypothesis for each of the response variables. Statistical analysis of body weights for which repeated measures were taken, were computed as two way ANOVA by diet and repeated measure over time.

## RESULT

### ***Body Weights and Organ Weights***

Average body weights over 4 wk period differed significantly among the diet groups (Table 2) and over time as measured during wk 1,2, 3 and 4 (Fig 1). The body weights of animals fed hyperlipidaemic diet containing gum tragacanth showed a stable pattern of weight gain during the 4 week experimental period compared to the animals fed hyperlipidaemic diet only. The animals fed hyperlipidaemic diet containing showed significantly higher body weights ( $P < 0.05$ ) compared to those fed on control (basal) and hyperlipidaemic diets. A significant difference in average body weights after four weeks was observed between all three the groups of animals fed on three different diets (Table 2).

Liver weights and small intestine weights (g wet weight/100 g body weight) differed significantly among the groups (Table 2). Liver weights were significantly higher in animals fed hyperlipidaemic diet with and without fiber compared to the animals fed basal diet. The liver weights were significantly higher in animals fed hyperlipidaemic diet without fibre compared to

those fed hyperlipidaemic diet with fibre. Small intestines and caecum from hyperlipidaemic animals weighed more than those from the control group and weighed slightly less than those from the hyperlipidaemic fibre group (Table 2).

#### ***Plasma Lipids and Lipoprotein Fractions***

Plasma total cholesterol concentrations differed significantly among groups with concentration from the hyperlipidaemic group higher than in the control and hyperlipidaemic + 5% gum tragacanth group (Table 3). No significant difference could be observed in the plasma total triglyceride concentrations among the three diet groups (Table 3). The concentration of VLDL cholesterol was significantly higher in the hyperlipidaemic group than in both the control and hyperlipidaemic + 5% gum tragacanth group. However, the VLDL concentration in the hyperlipidaemic + 5% gum tragacanth group was significantly higher ( $P < 0.05$ ) than the control group. Concentrations of HDL cholesterol also differed significantly among the three diet groups, and was lower in the hyperlipidaemic group to the control and hyperlipidaemic + 5% gum tragacanth group (Table 3). Concentrations of LDL cholesterol also differed significantly among the three diet groups, with the higher concentration in the hyperlipidaemic group than in the control and 5% gum tragacanth group. The LDL cholesterol however, was significantly higher in the 5% gum tragacanth group than the control animals. The total protein concentration was significantly higher in the control diet group compared with the hyperlipidaemic and 5% gum tragacanth group. Among the three groups, the hyperlipidaemic group showed the lowest protein concentration.

## **DISCUSSION**

Cardiovascular disease has a multiple aetiology, as a illustrated by the existence of numerous risk indicators, many of which can be influenced by dietary means. The deleterious effects of saturated animal fat and dietary cholesterol appear to be more important in the aetiology of ischaemic heart diseases (Mann *et al.*, 1997), yet the preventive effect of dietary fibre cannot be ignored. The present study investigated hypocholesterolaemic effects of gum tragacanth in rats with diet induced hyperlipidaemia.

Gum tragacanth is the plant exudate from “*Astragalus gummifera*”, native to Iran, Syria, Turkey and Asia Minor. It is a complex polysaccharide consisting of D-galactose, D-xylose and L-arabinose with cation association. It is probably made up of two major portions, 13-assorin, the larger component comprises 60% of gum and tragacanthin (Klose and Glicksman, 1981).

Hypercholesterolaemia was induced in rats by feeding 1% cholesterol and 0.1% cholic acid in the diet. These amounts were chosen based on the report of Shinnick *et al.*, (1990), which demonstrated hypercholesterolaemia with minimal fatty infiltration. The hyperlipidemic animals had significantly higher body weights compared to the control animals and those fed on 5% gum tragacanth. Diets containing gum tragacanth (5%) did not appear to compromise food intake or growth in hyperlipidemic rats. However, higher small intestine and caecum weights were observed in the rats fed gum tragacanth compared with control and hyperlipidemic rats. Similar findings have been reported by Tinker *et al.* (1994) and Judd and Truswell, (1985) from pectin which is also a water soluble fibre. These results are likely due in part to the soluble fibre feeding. Walter *et al.*, (1986) reported higher concentration of microbes (indicative of increased fermentation) in rats fed a soluble source of fibre (gum arabic) compared with relatively insoluble source of fibre.

Plasma cholesterol and triglyceride concentrations were lower in gum tragacanth fed animals

compared to the hyperlipidemic animals not fed gum tragacanth. These results are in agreement with those from other studies (Judd and Truswell, 1985; Tinker *et al.*, 1994) in which another water soluble fibre pectin was fed to hypercholesterolemic animals. A lower HDL cholesterol has shown to be associated with increased risk of cardiovascular disease in humans (Hegele *et al.*, 1997). In rats, lower HDL concentrations are observed with cholesterol and cholic acid induced hyperlipidemia. Partial improvement in lipoprotein metabolism was seen after feeding gum tragacanth to the hyperlipidaemic rats. An increase in dietary fibre has been associated with favourable alteration in lipid profiles (Benner *et al.*, 1991). The present study shows a significant decrease in the cholesterol VLDL and LDL concentration after addition of gum tragacanth to the hyperlipidaemic diet. Feeding gum tragacanth to hyperlipidaemic rats shows hypocholesterolaemic activity, and probably accounts for the modest reduction in plasma cholesterol concentrations. In this hyperlipidaemic rat model, plasma cholesterol were lower in animals fed gum tragacanth compared with those fed on hyperlipidaemic diet only.

Viscous fibre sources have been shown to reduce lipid risk factors for coronary heart disease including total and low density lipoproteins, cholesterol and apolipoproteins by increasing fecal bile acid losses (Jenkins *et al.*, 1998). In addition soluble fibre may also reduce the rate of nutrient absorption so altering chylomicrons synthesis and reducing postprandial glucose and insulin levels and other risk factors for coronary heart disease (Cherbut *et al.*, 1997; Jenkins *et al.*, 1998; Bakker *et al.*, 1998). Evidence is also now accumulating that a diet rich in fibre may protect against diseases associated with raised clotting factors (Neldman *et al.*, 1997).

Dietary intervention studies and specific dietary trials in the past have demonstrated the feasibility and efficacy of lowering serum cholesterol levels through dietary modification. The physiological effects of dietary fibres in experimental animals and humans are due to their physicochemical properties and these particular properties of gum tragacanth investigated in this study suggest that gum tragacanth would be a suitable ingredient in a healthy diet. Since the response of metabolic variables such as plasma lipoproteins and blood pressure to metabolic diets may be variable (Hegele *et al.*, 1997), the physiological effects of gum tragacanth in humans would require experiments in humans with particular emphasis on the dose related effects of this fibre.

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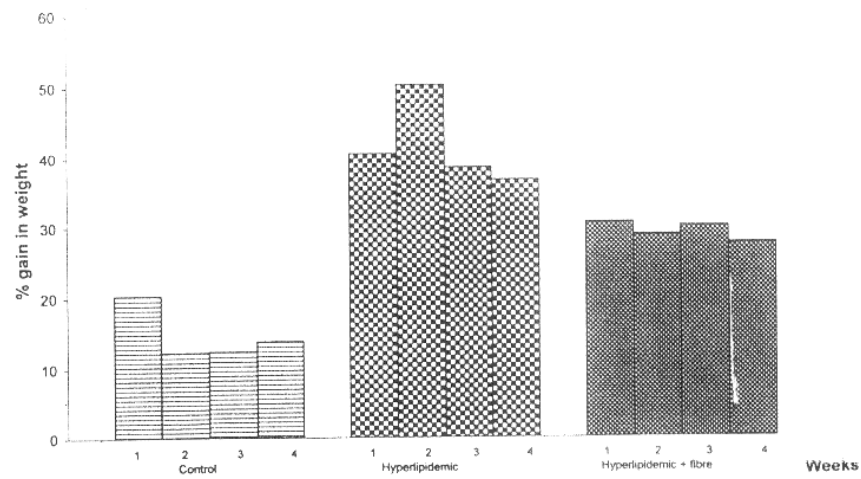


Fig. 1: Weekly weight changes in animals fed on basal, hyperlipidaemic and hyperlipidaemic + fibre diet.

**Table 1**  
Composition of three diets fed to different animal groups

Ingredients	Control (g)	Hyperlipidaemic (g)	Hyperlipidaemic + fibre (g)
<b>(A): Basal Composition</b>			
Wheat flour	500	500	
Corn flour	250	250	
Gram flour	250	250	
Barley flour	250	250	
Wheat fine	250	250	
Corn oil	200 ml	200 ml	
<b>(B): Experimental Hyperlipidaemic</b>			
All the ingredients present in (A)			
Cholesterol		15 g (1.0%)	
Cholic acid		1.5g (0.1%)	
<b>(C): Experimental Hyperlipidaemic +fibre</b>			
All ingredients present in (A) & (B)			
Cholesterol			15 g (1%)
Cholic acid			1.5 g (0.1%)
Gum tragacanth			75g (5%)

**Table 2**  
**Body weights and organ weights in animals fed basal, hyperlipidaemic and hyperlipidaemic + fibre diet**

	Control (n = 10)	Hyperlipidaemic (n = 10)	Hyperlipidaemic + fibre (n = 12)
Body weight (% increase)	42.15***	56.31***	47.18
Liver (g wet weight/100 g body weight)	3.23±0.01***	4.52± 0.04***	3.73± 0.11
Small intestine (g wet weight/100 g body weight)	1.58± 0.008*	1.79± 0.02**	1.95± 0.004
Caecum (g wet weight/100 g body weight)	0.75± 0.001*	0.88± 0.002**	1.07± 0.001

Values are mean ± SEM

n = number of observations, \*p<0.05, \*\* p<0.01, \*\*\* p<0.005

**Table 3**  
**Profile of plasma lipids and proteins in rats fed basal, hyperlipidaemic and hyperlipidaemic + fibre diet**

	Control	Hyperlipidaemic	Hyperlipidaemic + fibre
1.Total Cholesterol (mmol/L)	2.27± 0.12	4.02± 0.14	2.84 ± 0.081
2.Triglycerides (mmol/L)	0.59 ± 0.11 NS	0.63 ± 0.08 NS	0.71 ± 0.107
3. VLDL cholesterol (mmol/L)	0.12 ± 0.002***	2.47± 0.05***	1.344 + 0.004
4. LDL cholestrol (mmol/L)	0.17 ± 0.002***	0.76 ± 0.003***	0.47 + 0.10
5. HDL cholesterol (mmol/L)	1.98 ± 0.004***	0.79 ± 0.002**	0.99 ± 0.025
6. Protein (g/L)	1.33 ± 0.013**	0.62 ± 0.001*	0.80 ± 0.015

Values are means ± SEM

NS Not significant

\* p<0.05, \*\* p<0.01, \*\*\* p<0.005

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