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Research Article

HYPOLIPIDEMIC ACTIVITY OF FLAVONOIDS FROM BANANA (*MUSA PARADISIACA*) IN RAT FED HIGH FAT DIET

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ABSTRACT

Oral administration of banana (*Musa paradisiaca*) flavonoids have health benefit ie., hypolipidemic effect even in rats fed high fat diet. Banana is the richest source of polyphenolic compounds. Banana is one of the oldest fruits of the world. It is found that the effective dosage of banana flvonoid is 1 mg/ 100 g BW. Concentration of cholesterol, phospholipid, triglycerides,etc. decreased in experimental animals. The activity of enzymes such as HMG CoA reductase, glucose-6 phosphate dehydrogenase etc. were significantly reduced. Significant enhancement was noticed in the activities of LCAT and lipoprotein lipase. The concentration of hepatic and faecal bile acids and faecal neutral sterols were also noticed in the experimental animals, indicating a higher rate of cholesterol degradation. The hypolipidemic activity of flavonoids showed that process of cholesterol degradation exceeds the rate of its synthesis.

Keywords: *Musa paradisiaca*, Flavonoids, High fat diet, Hypolipidemia.

INTRODUCTION

Flavonoids constitute one of the largest groups of naturally occurring phenols. They are widely distributed in higher plants and used as human food. Banana is the richest source of polyphenolic compounds. Banana is one of the oldest fruits of the world. Its names Adam's Fig, Apple of Paradise and the botanical name Musa paradisiacal are suggestive of its antiquity. Banana belongs to the genus Musa of the family Musaceae, which is closely related to the families of the ginger and the ornamental plant Canna. The banana is a valuable food item. The full plant of banana, known as plantain is accorded almost a divine status. No auspicious ritual is complete without banana or its leaves. Banana was supposed to contain all the items necessary for health of the body. Experiments showed that intake of banana helps children to retain many mineral nutrients. Ripe and raw banana have purgative property and hence are useful in children's dietaries, particularly for constipation. It is also useful to combat diarrhoea, dysentery, intestinal lesions etc. The flavonoids found in raw banana are noticeable for its health benefits particularly for their fighting against the dangerous lipids known as cholesterol. Flavonoids have a wide variety of health benefits as reported by Anila & Vijayalakshmi, (2002). The same result was also reported by Koshy & Vijayalakshmi, (2001) based on their studies from *Cocos nucifera, Myristica fragrance, and Grcinia cambogia.*

It is estimated that nearly half of all deaths in the world are due to heart related diseases and cholesterol is the culprit. The most widely recognized biological activity of cholesterol is that of a nutritional agent capable of inducing atheromas of the aorta and other arteries and hypercholesterimias. (Lewis *et al*., 1999) reported that natural flavonoid present in unripe banana has many health promoting effects. (Gomathy *et al*., 1989) reported the hypolipidemic effect of banana plantain stem juice. The present study highlights hypolipidemic effect of banana flavonoids in rats fed high fat diet.

MATERIALS AND METHODS

Male albino rats (Sprague-Dawley strain weighing 100-125 g) were grouped into 3 with six rats. Group I was treated as control. Rats of II and III were given flavonoids at doses 0.5 and 1 mg/100 g BW/day respectively by gastric intubation. Crude flavonoids were collected from mature

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unripe banana by standard laboratory procedures of (Markham, 1982). Rats were fed high fat diet.

Composition of high fat diet (g/100 g diet)

Dextrose-62, Casein -16, Coconut oil -15, Salt mixture -4 Vitamin mixture – 1 Cholsterol -2.

Composition of Salt mixture (g/Kg)

Sodium chloride -105, Potassium chloride -120, Potassium dihydrogen sulphate- 310, Calsium phosphate -149, Calcium carbonate -210, Ferrous phosphate -14.7, Manganese sulphate - 0.20, Potassium aluminium sulphate - 0.09, Copper sulphate – 0.39, Sodium fluoride -0.57, Potassium iodide - 0.05, Magnesium sulphate - 90, Zinc chloride -15, Cobalt chloride -0.15

Composition of vitamin mixture

Retenyl palmitate -1000 IU, Ergocalciferol -150 IU, α-tocopherol -12 mg, Menadione -0.3 mg, Thiamine -1.0 mg, Riboflavin -1.0 mg, Pyridoxine - 0.6 mg, Niacin -10 mg, Calcium panthothenate - 5 mg, Inositol - 20.0 mg, Choline chloride -300 mg, Folic acid -0.4 mg, Vitamin B12 -3µg, P-aminobenzoic acid -5 m, Biotin -20 mg, Made up to 1 g with dextrose.

The rats were housed in polypropylene cages and were given water ad-libitum. The duration of the experiment was 90 days. At the end of this period, the rats were deprived of food overnight, stunned by a blow at the back of the neck and killed by decapitation. Blood and tissues were removed and collected in ice cold container for various estimation.

The protocol used for various estimations are as follows. HMG CoA reductase activity by Rao & Ramakrishnan, (1975), Malic enzyme by Lengyel *et al*. (1960), Glucose-6 phosphate dehydrogenase by Morse & Horecker, (1968), lipoprotein lipase by Llobera *et al*., (1979), Plasma LCAT and hepatic and faecal bile acids and neutral sterols by Lewis *et al.*, (1999), protein in the enzyme by Lowry *et al*., (1951). Statistical analysis was performed using ANOVA. Differences between treatment means were determined and the significance was accepted at $p < .05$ (Snedecor & Cochran, 1967).

RESULTS AND DISCUSSION

Diet consumption and weight gain were almost similar in all the 3 groups. The concentration of various biochemicals showed significant change in the experimental animals than the control group. The concentration of cholesterol decreased significantly in the serum, liver, kidney, and heart of experimental animals. But in the aorta there was no significant reduction (Table 1). Phospholipids levels were decreased in the liver, kidney and heart of flavonoid treated animals when compared to control group. Aorta did not show any significant change (Table 2). The concentration of free fattyacid was decreased significantly in the serum, kidney, and heart of experimental animals (Table 3). Triglycerides were decreased in the serum and liver of flavonoids treated group than the control group (Table 4). Bile acids levels were enhanced significantly in the experimental animals than the control group (Table 5). HDL cholesterol concentration was increased whereas VLDL+ LDL cholesterol fractions were decreased in the serum of experimental animals (Table 6). There was an increase in the activity of HMG CoA in the liver and intestine of experimental animals than the control animals (Table 7). Glucose-6-phosphate dehydrogenase activity was decreased significantly in the III group and no significant change was observed in the II group than the control group. Malate dehydrogenase activity showed significant decrease in all the experimental animals than control group (Table 8). The activity of lipoprotein lipase showed significant increase in both experimental groups than the control group (Table 9). The activity of plasma LCAT was also enhanced significantly in the experimental animals than the control group (Table 9). Studies of flavonoids from *Solanum melongena* also showed similar results (Sudheesh *et al*., 1997).

The association between hyperlipidemia and the increased incidence of atherosclerosis has been repeatedly demonstrated in numerous epidemiologic studies among different population groups in many parts of the world. Our data suggests that flavonoids from raw banana elicit significant hypolipidemic activity in experimental animals. It is found that the tissue cholesterol deposits were effectively lowered in many groups, but blood cholesterol level was appreciably reduced only in group III. To explain this particular effect, the drug lipoprotein interaction hypothesis could be of value. It is known than modified circulating LDL affect the regulation of cholesterol synthesis by the cells and the also that HDL are involved in the cholesterol excretion of cells. Moreover, it is known that some drugs which seem to be less active on the blood lipid levels have a more important effect on the tissue lipid deposits. In cholesterol fed rats significant reduction of cholesterol was observed in the serum and tissues except in the aorta. Animals received 1 mg flavonoid showed marked decrease in the levels of phospholipids, triglycerides and freefattyacids in serum and liver irrespective of the nature of diet (low fat or high fat) they consumed. However HMG CoA activity was found to be elevated in the liver of these rats. The increase denotes that some other mechanism is responsible for hypocholesterolemic activity in these animals. Further analysis on the results pointed out that LCAT activity was enhanced significantly in normal and cholesterol fed rats. This accounts for the removal of cholesterol esters from the extrahepatic tissues through circulating serum lipoproteins. Concentration of HDL cholesterol was increased significantly in the serum of rats received flavonoid and cholesterol containing diet. Lipoprotein lipase activity was highly stimulated in the heart and adipose of normal and cholesterol fed rats received 0.5 and 1.0 mg flavonoid. The higher acivity of enzymes indicate that hypotriglyceridemia prevalent in the serum and liver of group III rats. The lipogenic enzyme Glucose-6 phosphate dehydrogenase and malate dehydrogenase were significantly declined in the liver of

group III rats on administration of flavonoids when compared to their controls. The concentration of bile acids in the liver and faeces of rats fed 0.5 and 1.0 mg flavonoid in both the experiments showed highly significant increase (Valsa *et al.*, 1998). Similar results were obtained in the case of neutral sterols also. The elevated levels of bile acids and faecal neutral sterols suggest there is an increased turnover of cholesterol into bile acid and neutral sterols. Though there is an increase in the rate of synthesis of cholesterol in the liver, the process of degradation exceeds the rate of synthesis. It may also be noted that the bile acids and neutral sterols can bind to the flavonoids present in the lumen of the intestine and are no longer available for reabsorption and transportation to the liver by the hepatic portal system the mechanism behind the hypolipidemic activity of flavonoids may be summarized as follows. Though there is an increase in the rate of synthesis of cholesterol, hypocholesterolemia ia manifested in rats administered flavonoid by virtue of increased degradation and elimination of cholesterol in to the bile acid and neutral sterols. The non availability of cholesterol and the bile acids for reabsorption is also an important reason for inducing hypocholesterolemia.

Table 1. Concentration of cholesterol in rats fed cholesterol containing high fat diet (Values expressed as mg/100 ml serum; mg/100g wet tissues).

Groups	Doses (mg/100g BW/day)	Serum	Liver	Kidney	Heart	Aorta
I	-	173.75±4.34	2102.13±52.55	533.71±13.34	305.68±7.64	390.15±9.75
II	0.5	169.25±3.72	1923.37±42.31[b]	496.63±10.92	276.73±6.08[b]	376.70±8.28
III	1.0	148.34±2.96[a]	1763.21±35.26[a]	468.74±9.37[a]	264.88±5.29[a]	364.97±7.29

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 2. Concentration of phospholipids in rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Liver	Kidney	Heart	Aorta
I	-	4015.76±100.39	2360.01±59.00	1880.83±47.02	1790.00±44.75
II	0.5	3667.21±80.67[b]	2026.55±44.58[a]	1626.70±35.78[a]	1745.30±38.39
III	1.0	3324.99±66.49[a]	1824.78±36.49[a]	1530.69±30.61[a]	1700.22± 34.00

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 3. Concentration of free fattyacids in rats fed cholesterol containing high fat diet. (Values expressed as mg/100 ml serum; mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Serum	Liver	Kidney	Heart	Aorta
I	-	142.78±3.56	667.15±16.67	465.72±11.64	180.34±4.5	86.16±2.15
II	0.5	130.13±2.86[b]	603.22±13.27[b]	432.48±9.51	162.21±3.56[b]	80.03±1.76
III	1.0	126.54±2.53[b]	596.37±11.92[b]	416.66±8.33[b]	148.70±2.97[a]	72.11± 1.44[a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 4. Concentration of triglycerides in rats fed cholesterol containing high fat diet. (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Serum	Liver
I	-	22.17±0.55	724.33±18.10
II	0.5	18.31±0.4[a]	656.57±14.44[b]
III	1.0	15.24±0.3[a]	637.69±12.75[a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 5. Concentration of bile acids and faecal neutral sterols of rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Liver	Faeces	Faecal neutral sterols
I	-	49.6±0.99	60.16±1.20	75.34±1.5
II	0.5	58.17±1.27[a]	84.10±1.85[a]	88.26±1.94 [a]
III	1.0	64.13±1.60[a]	102.37±2.55[a]	101.75± 2.54 [a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 6. Concentration of cholesterol in lipoprotein fraction in serum of rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue)

Groups	Doses (mg/100 g BW/day)	LDL+VLDL	HDL	Total cholesterol
I	-	70.69±1.76	42.32±0.84	113.01±2.82
II	0.5	64.32±1.41[b]	49.76±1.09[a]	114.08±2.5
III	1.0	51.48±1.02[a]	54.31±1.35[a]	105.79± 2.11

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 7. Activity of HMG CoA in liver and intestine of rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Liver	Intestine
I	-	3.96±0.09	2.2±0.05
II	0.5	3.61±0.07[b]	1.97±0.04[a]
III	1.0	3.54±0.07[a]	1.90±0.03[a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01, b= P<0.05.

Table 8. Activity of lipogenic enzymes in the liver of rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Lipogenic enzymes units/g protein	
		Glucose-6 phosphate dehydrogenase*	Malate dehydrogenase**
I	-	133.21±3.33	1169.7±29.24
II	0.5	126.10±2.77	975.0±21.45[a]
III	1.0	117.65±2.35[a]	834.14±16.68[a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01.
*One unit is defined as that amount of the enzyme that causes an increase of 1.0 in optical density/mt/g protein.
** One unit is defined as that amount of the enzyme that causes an increase of 1.0 in optical density/mt/g protein.

Table 9. Activities of lipoprotein lipase in the heart and adipose and that of plasma LCAT in rats fed cholesterol containing high fat diet (Values expressed as mg/100g wet tissue).

Groups	Doses (mg/100 g BW/day)	Lipoprotein lipase µ moles of glycerolliberated /hr/g protein		Plasma LCAT
		Heart	Adipose	
I	-	24.65±0.49	120.74±2.41	24.44±0.48
II	0.5	33.1±0.72[a]	150.0±3.3[a]	31.65±0.69[a]
III	1.0	42.23±1.05[a]	172.99±4.32[a]	43.38±1.08 [a]

Average of the values of 6 rats in each group ± SE. Groups II and III are compared with group I. a=P<0.01.

The binding capacity of polyphenols with cholesterol and bile acids is an important phenomena and from provide evidence for the significant increase of faecal excretion of cholesterol when crude catechin mixtures or epigallocatechingallate was added to a cholesterol containing diet. The enhance activity of LCAT, the enzyme involved in the transport of cholesterol from the tissues to the liver for its catabolism and the interaction of this enzyme with HDL which enhances the cholesterol ester content of this lipoprotein which is present significantly higher amounts in the experimental rats also accounts for the hypocholesterolemia. HDL is a protein rich particle secreted from the liver and once in the circulation, it has the ability to acquire and exchange cholesterol from other circulating lipoprotein particles and can directly take up cholesterol from arterial intima. Its plasma concentration is universally related to the risk of heart diseases. On the contrary plasma concentration of cholesterol in LDL is directly related to the risk of heart diseases. Thus, high plasma concentration of LDL cholesterol confers a relatively high risk of coronary heart diseases, whereas the reverse is true for high concentration of HDL cholesterol. Flavonoids isolated from raw banana thus act as an effective hypolipidemic agent, both in normal as well as high fat fed rats.

CONCLUSION

Banana is one of the staple foods widely used by people all over the world. It has the both nutritive as well as medicinal value. The medicinal value of this is due to the presence of flavonoids. Consumption of banana provides health benefit even in people who are having high cholesterol level in their blood. Our experiment proved that banana flavonoids maintain the blood as well as tissue cholesterol by promoting the activity of enzymes involved in the lowering of the various fractions of cholesterol.

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