

Hypoglycemic and Hypolipidemic Effects of Grapefruit Juice in Diabetic Rats

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Abstract:

The goal of this study was to investigate the hypoglycemic effect and the hypolipidemic changes following the ingestion of an extract of grapefruit juice, which was fed intra-esophageally, to healthy and alloxan-induced diabetic male rats.

Treatment of diabetic animals with the grapefruit juice extract resulted in a significant decrease in the serum glucose and cholesterol level. The percentages of decrease are 67.5% for serum glucose level and 30.8% for serum cholesterol level, after ingestion of 0.5 ml twice a day for 12 days. And the percentages of decrease

Keywords: Grapefruit juice (*citrus paradisi*) • diabetes • rats

Introduction:

The fruit has only become popular from the late 19th century; before that it was only grown as an ornamental plant. Grapefruit juice (*citrus paradisi*); is a member of the *Rutaceae* family and its juice and pulps parts have showed hypoglycemic and hypolipidemic effects in both normoglycemic and alloxan-induced hyperglycemic rats[1], [2]. Grapefruit is an excellent source of vitamin C. It is also a good source of dietary fiber, vitamin A, potassium, folate, and vitamin B5. Grapefruit also contains phytochemicals including limonoids and lycopene[3].

The pulp of the fruit may be yellow, pinkish, or reddish. It can be more or less sharp-tasting, acidic, sweet, and fragrant. Grapefruit forms a core part of the "grapefruit diet", the theory being that the fruit's low glycemic index is able to help the body's metabolism burn fat [4].

Another theory is that the fruit's low glycemic index is able to help the body's metabolism burn fat [1] so people have been attracted to grapefruit because of its cholesterol-lowering abilities. Another relation between grapefruit and Cholesterol Control show that grapefruits are especially high in pectin, a soluble fiber that helps lower blood cholesterol [5], [6].

A 2004 study led by Dr. Ken Fujioka at the Nutrition and Metabolic Research Center at Scripps Clinic found in a 12-week pilot study that on average, participants who ate half a grapefruit with each meal lost 3.6 pounds and those who drank a serving of grapefruit juice three times a day lost 3.3 pounds. Additionally, many patients in the study lost more than 10 pounds [4].

The nutrition values of juice extracted from the grapefruit fruit are [7]:

Calories (kcal)	12	Fiber	0 g
Energy (kj)	50	Sugars	2.8 g
Fats	0 g	Cholesterol	10 mg
Carbohydrates	2.8 g	Sodium	0.3 mg
Protein	0.2 g	Alcohol	0 g

Other benefits of grape fruit are high in vitamin C and potassium, a good source of folate, iron, calcium, and other minerals. Pink and red varieties are high in beta

are 70.6% for serum glucose level and 38.4% for serum cholesterol level, after ingestion of 1ml twice a day for 12 days.

This study suggest that grapefruit juice extract play a good rule in controlling the levels of glucose and cholesterol in experimental animals and can be applied clinically on patients with diabetes and lower cholesterol level.

Although the aqueous extract of grapefruit juice (*citrus paradisi*) has strong hypoglycemic and hypolipidemic properties in experimental animals.

carotene, a precursor of vitamin A, high in fiber, low in calories and they contain protective plant chemicals include phenolic acid, limonoids, terpenes, monoterpenes, and bioflavonoids that protect against cancer and heart disease.

The major bioflavonoid in grapefruit is Naringin (4', 5, 7-trihydroxyflavanone-7-rhamnoglucoside) [8], [9], and gives grapefruit juice its bitter taste. Naringin exerts a variety of pharmacological effects such as antioxidant activity, blood lipid-lowering [10], anticarcinogenic activity [9], and inhibition of selected cytochrome P450 enzymes including CYP3A4 and CYP1A2, which may result in several drug interactions in-vitro[6], [11].

The medicinal Value of grapefruit are stimulates the appetite and used for its digestive, stomachic, antiseptic, tonic, and diuretic qualities [7].

Recent studies indicate that grapefruits contain substances that are useful in preventing several diseases. Pink and red grapefruits are high in lycopene [9], [11] an antioxidant that appears to lower the risk of prostate cancer [12].

Other Uses of grapefruit showed some people with rheumatoid arthritis [13] and other inflammatory disorders find that eating grapefruit daily seems to alleviate their symptoms. This is thought to presence of chemicals that block Prostaglandins, substances which cause inflammation.

Some side effects noticed: people who are allergic to citrus fruits are likely to react to grapefruits, too. The sensitivity may be to the fruit itself or to oil in the peel. Grapefruit has serious interactions with many commonly prescribed medications by inhibiting a special enzyme in the intestines that is responsible for the natural breakdown and absorption of many medications. When the action of this enzyme is blocked, the blood levels of these medications increase, which can lead to toxic side effects from the medications [13].

Grapefruit juice research has suggested that flavonoids and/or furanocoumarin compounds are the substances

that act to block the enzyme in the intestines that normally metabolizes many drugs [11].

Materials and Methods:

Reagents:

Reagents used in this study included alloxan monohydrate (BDH limited Poole, UK) and the enzymatic kit for glucose determination (INVITRO DIAGNOSTIKUM, Bio com, Germany) and (BIOLABO SA., Maizy, France) for cholesterol determination. All other reagents were of analytical grade and obtained through other commercial sources.

Preparation of grapefruit juice extract :

The Juice of *grapefruit* (2Kg, grapefruit obtained from Mosul Area) was dried by lyophilizer. Approximately 100 g of gummy substance was obtained. The gummy substance was dissolved in distilled water at a concentration of 1 g/mL. This preparation which is referred to as the aqueous extract and corresponds to 20 g of the original fruits per mL is employed as the hypoglycemic and hypolipidemic agent throughout this study.

Animal experiments:

Six groups of adult male rats (5 rats per group) with a weight ranging from 200 to 250 g were used as experimental animals. Each group was separately housed in a cage and fed rat chow diets which are prepared according to NAC/NRC.

Four groups of the rats were injected intraperitoneally with alloxan (80 mg/kg body weight [14], [15]) after fasting for 24 hours; the alloxan dose was prepared

directly by dissolving it in 0.5 ml of normal saline (0.9% NaCl). The animals were fed with 5% glucose solution with their drinking water, two hours after injection [16], [17].

Two weeks prior to the initiation of treatments. After obtaining blood from the eyes using heparinized tubes, serum glucose and cholesterol of all groups was measured prior to the beginning of the aqueous-extract treatment [18].

Results:

Normoglycemic group (normal control rats) followed only the normal feeding protocol, group A, serum glucose level reached 4.6 mM. Two weeks after alloxan treatment, the serum glucose level of normoglycemic animals (normal experimental rats, group B) received 1 mL of the aqueous extract twice a day for a period of 12 days reached 3.8 mM. Two weeks after alloxan treatment, the serum glucose level of the control diabetic rats reached 12.6 mM. (experimental diabetic rats with normal feeding, group C) and reached 22.7 mM. (experimental diabetic rats with sweet feeding, group D). Other group E received 0.5 mL of the aqueous extract twice a day, and group F received 1 mL of the aqueous extract twice a day for a period of 12 days, the serum glucose level reached 4.1 and 3.7 mM respectively.

The effects of the aqueous extract of grapefruit juice (*citrus paradisi*) on serum glucose and cholesterol levels of normoglycemic and alloxan-induced diabetic rats are shown in Table 1.

Table(1): Effects of aqueous extract of grapefruit juice (*citrus paradisi*) on serum glucose and cholesterol levels of alloxan -induced hyperglycemic rats, (normal range of glucose level 3.6 - 6.1 mM).

Experimental groups	Serum glucose (mmole/L) in the 12 th day	Serum cholesterol (mmole/L) in the 12 th day
Normoglycemic control A	4.6	1.95
Normoglycemic experimental B (1mL X 2)	3.8	1.8
Diabetic control C (with normal food)	12.6	2.6
Diabetic control D (with sweet food)	22.7	3.2
Diabetic experimental E (0.5ml X 2)	4.1	1.8
Diabetic experimental F (1ml X 2)	3.7	1.6

Discussion:

Intra-esophageal feeding of 2×1 gm of the extract of Grapefruit juice decreased serum glucose level of the alloxan-induced diabetic rats within 24 h and with the continual feeding of 2 × 1 g of the extract per day, the blood glucose level of the diabetic rats decreased about 70.6% and the blood cholesterol level of the diabetic rats decreased about 38.4% after 12 days and remained in the normal range thereafter. Several flavonoids and terpenoids have been demonstrated to be present in grapefruit juice. It is, therefore, possible to conclude that the hypoglycemic effects of grapefruit juice may be due to its content of flavonoids and/or terpenoids. The relation between grapefruit and Cholesterol Control show that grapefruits are especially high in pectin as indicated by Cerda J.J. et al [5] , a soluble fiber that helps lower blood cholesterol and another theory is that the fruit's low glycemic index is able to help the body's metabolism burn fat [4]. Also from health magazine said Researchers

have a hunch that grapefruit reduces insulin levels and so may encourage weight loss [19].

Intra-esophageal administration of 0.5 g of the extract for 12 days had a significant effect on serum glucose level of the normoglycemic animals, the blood glucose level of the diabetic rats decreased about 67.5% and the blood cholesterol level of the diabetic rats decreased about 30.8% after 12 days and remained in the normal range thereafter.

In conclusion, we should emphasize that although the extract of grapefruit juice has potent hypoglycemic and hypolipidemic effects in experimental animals, it is strongly recommended that its use will be with warning due to its inhibition of a special enzyme in the intestines that is responsible for the natural breakdown and absorption of many medications [20]. When the action of this enzyme is blocked, the blood levels of these medications increase, which can lead to toxic side effects from the medications [11].

References:

1. Javascript; A.G.(2002). Grapefruit, J. Altern Complement Med 8; 333-40.
2. Free encyclopedia, Grapefruit (2002). (<http://en.wikipedia.org/wiki/Grapefruit>).
3. Mateljan, G. (2006). The worlds healthiest foods- Grapefruit. (<http://www.whfoods.com/genpage.php?tname=foodspice&dbid25#healthbenefits>).
4. Free encyclopedia, Grapefruit (2006). (http://en.wikipedia.org/wiki/Grapefruit_diet).
5. Cerda J.J., Robbins F.L., Burgin C.W., Baumgartner T.G. and Rice R.W. (1988). The effects of grapefruit pectin on patients at risk for coronary heart disease without altering diet or lifestyle. Clin. Cardiol., 11; 589-94.
6. Free encyclopedia, Naringin (2005). (<http://en.wikipedia.org/wiki/Naringin>, html).
7. Herbal Medicine, Grapefruit (2000). (http://www.holistic-online.com/Herbal-Med/_Herbs/h_grapefruit.htm).
8. Giovannucci E., Rimm E.B., Liu Y., Stampfer M.J. and Willett W.C. (2002). A Prospective study of tomato products, Lycopene, and prostate cancer risk. J. Natl. cancer. Inst, 94; 391-8.
9. Armando C., Maythe S. and Beatriz N. P. (1998). Antioxidant activity of grapefruit seed extract on vegetable oils. Journal of the Science of Food and Agriculture ,77; 463-7.
10. Gorinstein S, Caspi A, Libman I, Lerner HT, Huang D, Leontowicz H, Leontowicz M, Tashma Z, Katrich E, Feng S. and Trakhtenberg S. (2006). Red Grapefruit Positively Influences Serum Triglyceride Level in Patients Suffering from Coronary Atherosclerosis: Studies in Vitro and in Humans. J Agric Food Chem. Mar 8; 54(5):1887-1892. , PMID: 16506849.
11. Gao K, Henning SM, Niu Y, Youssefian AA, Seeram NP, Xu A. and Heber D. (2006). The citrus flavonoid naringenin stimulates DNA repair in prostate cancer cells. J Nutr Biochem. Feb; 17(2):89-95.
12. Web site, FILE: Shari Henson et al, 2005, Prostate Cancer, February 15.
13. Don Brown N.D., Steven F. and Lori G. (2002). Grapefruit and drugs interaction, J. Alternm Complement Med, 8(4):521.
14. Aguilar F. J., Romas R.R., Saenz J.L. and Garcia F.A. (2002). Investigation of the hypoglycemic effects of extracts of four Mexican Medicinal Plants in Normal and alloxan-diabetic mice. Phytotherapy Research, 16; 383 -6.
15. Galicia E. H., Contreras A.A., Santamaria L.A., Romas R.R. and Aguilar F. J. (2002). Studies on hypoglycemic Activity of Mexican Medicinal Plants. Proc. West Pharmacol. Soc., 45; 118-24.
16. Ayoub R.S., Yousif W.H. and Aziz B.N. (2000). Serum glucose, cholesterol and total lipid levels and tissue lipid peroxidation in alloxan diabetic rats treated with aqueous extract of Nigella sativa seeds. Iraqi J. Vet.Sci., 1; 44-48.
17. Aguilar F. J., Galicia E. H. and Sepulveda A. E. C.(2002). Evaluation of the hypoglycemic effect of cacurbita ficifolia (Cucurbitaceae) in different experimental model . Journal of Ethnopharmacology, 82;185-9.
18. Aguilar F. J., Estrada M.J., Chilpa R.R. and Romas R.R. (2000). Hypoglycemic effect of extracts and fractions from Psacalium decomposition in healthy and alloxan-diabetic mice. Journal of Ethnopharmacology, 72; 21-7.
19. Health magazine (2006). (http://diets.aol.com/a-z/grapefruit_diet_main).
20. Bakalar, N.(2006). Experts Reveal the Secret Powers of Grapefruit Juice - New York Times. Published: March 21, Article.

تأثير عصير الكريب فروت على تخفيض مستوى السكر والكوليسترول في الجرذان المصابة بالسكري

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المخلص:

الهدف من هذه الدراسة هو بحث خفض مستوى السكر والكوليسترول للمستخلص المائي لعصير الكريب فروت المعطى عن طريق المريء لذكر الجرذان السليمة والمصابة بداء السكر المستحدث بالالوكسان. اظهرت النتائج ان المستخلص المائي للعصير احدث انخفاضا معنويا في مستوى السكر والكوليسترول في الجرذان المصابة بالسكري المستحدث وكانت نسبة الانخفاض 67.5% لمستوى الكلوكوز و 30.8% لمستوى

الكوليسترول عند اعطائها جرعة 0.5 ml مرتين يوميا ولمدة 12 يوم. وكانت نسبة الانخفاض 70.6% لمستوى الكلوكوز و 38.4% لمستوى الكوليسترول عند إعطائها جرعة 1 ml مرتين يوميا ولمدة 12 يوم. نستنتج من هذه الدراسة ان عصير الكريب فروت له دور مهم في السيطرة على مستوى السكر والكوليسترول في حيوانات التجارب ويمكن تطبيقه على الاشخاص المصابين بداء السكر وارتفاع الكوليسترول.