

Study of the effect of Gliclazide and Apple Juice on Blood Sugar level in STZ-induced diabetic Male Mice

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ABSTRACT

Increase of blood glucose continuing challenge of public health, and increase of mortality values. Several evidences suggest that antioxidants consumption decreased hyperglycemia. In this study, we compared the effect of apple juice and gliclazide on blood glucose level in STZ-induced diabetic mice. In this study, five male mice groups (n=10 for each group) used. Control group (group 1) received normal saline and four groups received STZ (40 mg/kg). One group received STZ only, and three next group consumed apple juice, gliclazide and apple juice+gliclazide for one month. After one month, glucose concentration was measured. In diabetic group glucose concentration was significantly increased ($p<0.05$) compared with control group. Administration of apple juice, gliclazide and apple juice+gliclazide decreased ($p<0.05$) glucose concentration compared with diabetic group. This effect of apple juice is related to antioxidant effects. However, these properties are needed to be more investigated in human.

Key words: Hyperglycemia, Apple Juice, Gliclazide, Mice.

Introduction

Diabetes is a metabolism disorder that its characteristic is rising blood sugar more than normal range and it happens because of dysfunction of Insulin which regulates blood sugar. According to International federation of Diabetes assessment in year 2003, 194 million diabetic people live in the world and its estimated people live in the world and it's estimated in year 2025 this number achieves 333 million. One out of every 20 people in Iran is diabetic and half of these numbers even don't know about their illness. In every 10 seconds, one person in the world passes a way because of ignorance about Diabetes and ways to control it [16,17]. As regards in our country (Iran) Diabetes and its related diseases are prevalent, researching about it seems to be necessary. Nowadays in addition to treatment with

drugs, fibre supplements and other natural antioxidant compounds are used in this procedure because of having essential elements for diabetic people. It's shown that some fruits and vegetables can stimulate insulin secretion. Researchers have found out that eating fibre supplements in diabetic patients reduces serum cholesterol. So diabetes treatment and finding new ways to prevent and cure it is one of challenges of researchers [16,17]. It is determined that using antioxidants and some foods can reduce incidence of Diabetes in man and laboratory animals [2,4,8,9,15,21,24,31,35,36,37,41, 44,45]. Apple, with scientific name: *Malus Domestica*, is a fruit of a cold region tree from Rosacea family and has different kinds. This aromatic and tasty fruit contains lots of minerals and vitamins like potassium, sodium, calcium, iron, and phosphorus, Vit A, B and C. Apple is a heavenly

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fruit that is used for preventing of diseases it's noteworthy that most of apples vitamins are in the peel or under it, so it's better to eat apple with its peel. Apple is an alkaline fruit and it cleans body and because of having lots of pectin, it sends out extra water from body. A great amount of west people's consumption is allocated to this fruit. The factors that have resulted this are: easy shopping, public availability, different kinds and nurture in different weather conditions [5,7,10,15,18,21,42]. It's shown that about 20-25% of daily need of polyphenols for body and 10-30% of body's fiber necessity in west countries are obviated by apple [6, 7,18,40,49]. Fiber of apple reduces cholesterol value of plasma [16]. Laboratory findings show that about 50% of total apple fiber is pectin. Pectin has the most effect on metabolizer of lipids. Recent researches show that polygalacturonic acid found in pectin has the most influence on decreasing plasma sugar and cholesterol. Apple also contains polyphenols that have anti-oxidant role and influence on metabolism of glucose and lipids [4,6,7,11,12,15, 16,18,21,23,24,28,29,32,34,35,36,37,40,41,42,44, 49]. Researchers also have connected apple's effect on reducing blood sugar and plasma cholesterol and hepatic cholesterol to its anti-oxidant role [9,15,16, 31,34,35,36,37,44]. Therefore the aim of present study was to determine the effect of Gliclazide and Apple Juice on Blood Sugar level in STZ-induced diabetic Male Mice.

Material and method

50 Adult Wistar male albino rats weighing between 150 and 200 g were used for the study. They were kept under standard laboratory conditions and were fed with commercial rat pellets and drinking water ad libitum. The animals were housed in polypropylene cages. Ethical committee in accordance with animal experimentation and care has approved all animal procedures. Animals were divided randomly into five groups, consisting of 10 animals each. The rat dose was calculated on the basis of the surface area ratio.

- Group I Control (Normal saline 10 ml/kg, *p.o*) (n=10)
- Group II Streptozocine (40 mg/kg, *I.p*) (n=10)
- Group III Streptozocine +Apple Juice (10 ml/kg, *orally*) (n=10)
- Group IV Streptozocine +Gliclazide (1 mg/kg, *orally*) (n=10)
- Group V Streptozocine +Apple Juice +Gliclazide (n=10)

All the groups were treated for 30 consecutive days. At the end of this period, animals were kept overnight fasting and were sacrificed. Blood samples

were withdrawn, serum separated and estimated for biochemical parameters. The sugar levels by use of chemical kits were calculated. Values were represented as mean±SEM. Data were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's test using statistical package for social sciences (SPSS) version 10. $P < 0.05$ was considered significant [14,16,17,23].

Results

According to results of this study in group II level of serum glucose shows a significant increase in comparison with control group ($p < 0/05$). In groups of III and IV with administration of Apple Juice and gliclazide respectively shows a significant decrease in comparison with diabetic group ($p < 0/05$). In group IV with administration of Apple Juice and gliclazide with them a significant different with control group were not observed, therefore the administration of gliclazide and Apple Juice with them have strongly anti-diabetic effect in comparison with single administration of them.

Conclusion:

In this study apple reduced serum glucose, compared with diabetic group various researchers have shown its influence on serum glucose in laboratory animals, so that results of this study are consistent with results of that was about rats [35,36]. demonstrated that some natural antioxidant substance of apple called ambiferone and benzopyrone can raise insulin and serum antioxidants and vice versa can reduce glucose and lipid peroxidation index. Also the effect of ambiferone is compared with Glibenclamide and can treat diabetes in animals [36]. In another study on Albino rats, they reported that in addition to these substances, there are phenolic derivatives in apple that these antioxidant compounds have therapeutic effects against neuropathy and nephropathy due to diabetes [35]. In another study, they evaluated these antioxidants role on fatty acids of cell membranes in liver and kidney tissues and suggested that ambiferone can reduce cellular wastage via protective effects on cell membrane fatty acids [37]. reported that apple has variable compounds that have therapeutic effects on cardiovascular diseases, asthma, respiratory disorders, diabetes and cancer. These compounds include hydroxyl cinnamic acid, dihydrocalcones, flavonols, catechins, Oligomericprocianides like triterpenoids and anthocyanins. It's shown that these compounds have antioxidant effects on diabetes in different animals [15]. There have been some studies about effect of apple on blood glucose in mankind. In such a manner that in a study that was performed about women older than 45 years old suffering from

Table 1: Effect of Gliclazide and Apple Juice on Blood Sugar level of experimental diabetic rats (mean±SEM) *(p<0/05) in comparison with control group, # (p<0/05) in comparison with diabetic group.

Group	Control	Diabetic	Apple Juice	Gliclazide	Apple Juice +Gliclazide
Glucose level (mg/dl)	88.42±6.49	*179.22±14.65	*#140.38±7.41	*#124.55±8.66	#103.28±6.51

diabetes type II, reported that there is a relationship between incident of diabetes and serum values of flavonoids, coarsetin, compferrol, myristin, apigenin and luteoline and when there is more of these antioxidants in daily diet (like apple), diabetes type II is less expanded, but they didn't report this relation as a meaningful connection, only represented that there is a role for antioxidants in this process [44]. In a study it was distinguished that eating apple when empty-stomached before breakfast can control blood sugar in diabetic patients that use insulin [22]. Several mechanisms are suggested for anti-diabetic properties of apple. It's shown that 20-25% of daily needs of polyphenols and 10-30% of fiber daily needs is obviated by apple [7,18,40,49]. Fiber of apple has a main role in reducing plasma sugar and cholesterol. Laboratory findings show that about 50% of fiber is pectin. Pectin has the most influence on glucose and lipids metabolism [16,42]. Apple also has polyphenols which have antioxidant virtues and impresses glucose and lipids metabolism [12,15,16,21,24,29,32,34,35,36,37,41,42,44]. Recent researches have shown that polygalacturonic acid found in pectin can reduce plasma cholesterol and sugar the most [41]. Polyphenols of apple have more decrescent power than polyphenols of coitrous fruits, soya and grape extract on plasma sugar, cholesterol and triglycerides. The findings show that most of apple polyphenols is allocated to Quercetin, also phloretin and Isorhamnetin are found in apple too [2,8,21,35,43,44,45]. Researchers connect apples decrescent effect on plasma cholesterol and sugar and liver cholesterol to antioxidant properties of its compounds [9,15,16,31,34,35,36,37,44] lotito and Et. (2006). Suggested that foods having flavonoids can increase total antioxidental capacity of plasma. It's clear that most antioxidant effect is because of polyphenols found in apple [9,25,31]. In addition to previously told elements in apple, there are antioxidant pro cyanidins that can reduce blood sugar and lipid [15,35,36,37,44,48]. According to results of present study Apple Juice causes reduce the blood sugar.

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