Original article:

Possible role of grape fruit in controlling hyperglycemia and associated complications: Better glycemic control in healthy subjects through fruits fibers as compared to fruit juices

*Somia Gul[*1], Humera Khatoon[2], Nameera Ahmed[3], Haneen Rashid[4], Agha Zeeshan Mirza[5]*

Abstract:

Background*:** Diabetes is regarded as a chronic disorder, which is globally spreading at an alarming rate and individuals are being pushed down by the burden of diabetes. Different measures and control programs have been conducted for awareness of this disaster endocrine disease as its associated complications. ***Objective: Current study has been conducted to evaluate the hypothesis that whole fruits provide better glycemic control than fruit juices. ***Materials & Methods:*** The study includes two groups of healthy volunteers, one group was on whole fruits while another group was supplied with fruit juices of same fruits and fasting blood sugar and random blood sugar were monitored. ***Results:*** Results revealed that whole grapefruit and orange fruit play effective role in maintaining random blood sugar levels in comparison to juices. Further suggested that dietary fibers are not only effective in regulating blood sugar, but also influence on blood pressure and pulse rate. ***Conclusion*:** Based on above findings, it has been concluded that type 2 diabetes patients can achieve better glycemic control by dietary fibers rather than juices, and it may be helpful in controlling diabetes related complication such as high blood pressure.

Keyword: Type 2 diabetes mellitus (T2DM); fruit fibers; fruit juice; healthy life style.

Bangladesh Journal of Medical Science Vol. 19 No. 03 July'20. Page : 480-485
DOI: https://doi.org/10.3329/bjms.v19i3.45866

Introduction

Type 2 diabetes mellitus (T2DM), non-insulin dependent diabetes mellitus, is the most rapidly growing disease, estimated to affect 439 million adults by 2030. The rate is faster in developing countries than developed countries[1] which in turn results in higher healthcare expenditure[2]. Thus it becomes a priority to identify different measures and control programs should be arranged to prevent the disease. Dietary factors contribute to T2DM and promote early diabetes in healthy individuals and increased mortality and morbidity in type 2 diabetic patients. Delayed development and prevention of T2DM was shown to be effective by lifestyle intervention which involved dietary modification[3, 4]. The WHO has recommended the public for consuming more fruit and vegetables per day to minimize the risk of dietary factors and reduce the incidence of T2DM[5]. In previous studies, it is found that increased daily intake of fruits than juices could significantly reduce the risk of developing T2DM[6, 7, 8]. Recent studies show a relationship between the intake of fruit and vegetables and the risk of T2DM[9, 10, 11]. Many plant based drugs are also in use along with the synthetic drugs for treatment of T2DM[12]. In addition, a study showed the dose–response relations and indicate that relatively high fruit intake may still decrease the risk of T2DM[13]. Fruits and vegetables have many beneficial nutrients and phytochemicals that are thought to protect against hypertension, obesity and other diseases[14, 15, 16] and diabetes[17- 20, 8]. However, epidemiologic data on fruits and vegetables intake and its relationship with type 2 diabetes are very limited[21].

1. Somia Gul, Faculty of Pharmacy,Jinnah Uni. for Women, Karachi, Pakistan.
2. Humera Khatoon, Faculty of Pharmacy,Jinnah Uni. for Women, Karachi, Pakistan.
3. Nameera Ahmed, Faculty of Pharmacy,Jinnah Uni. for Women, Karachi, Pakistan.
4. Haneen Rashid, Faculty of Pharmacy,Jinnah Uni. for Women, Karachi, Pakistan.
   Agha Zeeshan Mirza, Science and Technology Unit, Umm Al-Qura University, Mecca, Saudi Arabia

Correspondence to: Dr. Somia Gul, Associate Professor/ Ex-Chairperson, Faculty of Pharmacy, Jinnah University for Women, Karachi. drsomi1983@yahoo.com, SomiaGul@juw.edu.pk

Multiple biological mechanisms are likely to be accountable for the favorable effects of fruits and vegetables on diabetes risk. High fiber content with low glycemic load may be one of the reason or rich amounts of plant proteins, antioxidants, vitamins, magnesium, potassium, and other individual phyto-chemicals may be useful in reducing risk of T2DM[22]. The role of fruit juices could be important and has not been well studied yet. It is found that although fruit juices may have antioxidant activity but they lack fiber, are less satiating, and tend to have high sugar content[23]. **Several other studies also emphasized that u**tilization of fruits as compare to juices are associated with a lower risk of diabetes, especially among women[24, 25, 26]. A meta-analysis showed that fruit juice has a borderline significant effect on reducing diastolic blood pressure, but had no effect on systolic blood pressure[27, 28].

So, the current study has been yet another attempt to evaluate the hypothesis that whole fruits provide better glycemic control than fruit juices.

Methodology

Selection of study subjects

To evaluate the hypothesis that fruits provide better glycemic control than fruit juice, we performed experiment on healthy subjects (with sample size N= 60) by dividing it into two groups. One group (n= 30) was treated with whole fruits while another group (n= 30) was served with fruit juice. Each group was further divided into three sub groups with respect to specific whole fruits and their respective fruit juices.

Fruit selection, administration and dosing schedule

The study was conducted on three types of fruits and their respective juices i.e. Apple, Grapefruit and Orange. All apples were green in color. The weight of an apple was about 120-130 g. The frequency of apple fruit consumption was one whole fruit once a day after fasting blood sugar (FBS). One glass of green apple juice was equal to 250 mL which consume approximately 4 apples in each glass. The frequency of apple juice consumption was 250 mL once a day after FBS.

All grapefruit were yellow in color. The weight of each grapefruit was about 290-300 g. The frequency of fruit consumption was one whole fruit once a day after FBS. One glass of grapefruit juice is equal to 250 mL which consume approximately 2 grapefruits in each glass. The frequency of grapefruit juice consumption was 250 mL once a day after FBS.

Medium sized oranges were used during the study. All were orange in color. The weight of an orange was about 165-170 g. The frequency of orange fruit consumption was one whole fruit once a day after FBS. One glass of an orange juice is equal to 250 mL which consume approximately 4 oranges in each glass. The frequency of orange juice consumption was 250 mL once a day after FBS. All the juices were in pure condition .They weren't diluted by water.

Study protocol

All the study subjects were kept on 12-hours fasting one day before the study was started. On next day morning FBS of all the study participants was monitored. The participants were then administered with whole fruit or fruit juice as per their assigned group. After two hours of administration, postprandial blood sugar levels were monitored. The study subjects were also monitored for any change in systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse rate before and after treatment with fruits and fruit juices. The duration of our experiment was about 2 months and there was no follow–up period.

Statistical Analysis

Data was analyzed by two-way ANOVA using SPSS version 20.0 for windows followed by Scheffe for post-hoc analysis. The results were presented as mean±S.D, n=10, $p \leq 0.05$ were considered to be statistically significant.

Ethical clearance: All procedures performed in the study involving human participants were in accordance with Helsinki declaration (1964)[29] and study was approved by the institution's ethical committee.

Results

Data analyzed by two-way ANOVA (df= 5, 54) showed significant effect of treatments and time intervals ($F=5.50$, $p<0.001$) on blood sugar levels. However, there is non-significant difference on systolic blood pressure ($F=0.990$), diastolic blood pressure ($F= 2.01$) and pulse rate ($F=1.10$) before and after treatments.

Post–hoc analysis done by Scheffe test revealed highly significant effect ($p<0.01$) on 2-hrs postprandial blood sugar levels when whole grapefruit treated group compared with grapefruit juice group (Table 1). However, there was no significant change in 2-hrs postprandial blood sugar levels when whole apple fruit and whole orange fruit treated groups were

Table 1: Effect of Treatment on Blood Sugar Levels, Blood Pressure and Pulse Rate

		Treated Groups	Blood Sugar (mg/dl)		SBP (mm Hg)		DBP (mm Hg)		Pulse	
			Fasting	2-hrs postprandial	Before Tx	After Tx	Before Tx	After Tx	Before Tx	After Tx
Group 1 (n=30)	Sub-group1 (n=10)	Whole Apple fruit	104.7±6.1	99.4±6.9	99.1±13.1	100.4±6.2	72.6±11.3	74.2±7.3	79.9±14.5	81.2±9.2
	Sub-group 2 (n=10)	Whole Grapefruit	102.4±5.4	97.6±5.9**	102.5±16.4	107.2±24.0	68.2±11.6	71.0±6.3	78.3±10.5	72.6±6.6
	Sub-group 3 (n=10)	Whole Orange fruit	101.6±2.0	99.0±4.8	106.0±11.8	102.0±9.8	75.7±7.8	74.5±8.1	81.9±11.3	82.4±10.0
Group 2 (n=30)	Sub-group 1 (n=10)	Apple Juice	101.9±4.6	106.4±7.7	106.6±11.8	99.9±14.5	75.3±10.4	68.2±9.4	77.7±15.7	80.0±8.9
	Sub-group 2 (n=10)	Grapefruit Juice	100.2±5.1	107.6±12.3	103.5±9.9	103.8±6.3	75.2±8.6	72.5±7.2	76.1±7.9	76.4±6.1
	Sub-group 3 (n=10)	Orange Juice	98.10±5.3	103.6±7.8	105.8±9.7	106.0±12.4	72.1±7.9	75.4±6.9	80.5±11.2	81.5±12.0

Values are mean±SD, n=10. Significant difference by Scheffe test.
** p≤0.01when whole Grapefruit compared with grapefruit juice following Two-way ANOVA.

compared with their respective juices treated groups. Post–hoc analysis showed that after treatment with fruit fibers and fruit juices no significant change in systolic blood pressure, diastolic blood pressure and pulse rate in whole apple fruit, whole grapefruit and whole orange fruit treated groups was observed when compared with apple juice, grapefruit juice and orange juice treated groups respectively (Table 1).

Results also showed significant decrease ($p<0.05$) in 2-hrs postprandial blood sugar levels when fasting blood sugar level of whole apple fruit and whole grapefruit treated groups were compared with 2-hrs postprandial blood sugar levels of similar groups (Graph 1). However, no significant change in 2-hrs postprandial blood sugar levels was observed when compared with fasting blood sugar level in whole orange fruit treated group (Graph 1).

Results also showed non-significant change in systolic blood pressure when after treatment SBP was compared with SBP measured before treatment within the similar treatment groups (Graph 2). However, significant decrease ($p<0.05$) in diastolic blood pressure was observed in apple juice treated group when after treatment DBP was compared with DBP measured before treatment within the similar treatment group (Graph 3).

Post–hoc analysis showed significant decrease ($p<0.05$) in pulse rate in whole grapefruit treatment group when after treatment pulse rate was compared with pulse rate measured before treatment within the similar treatment group (Graph 4).

Discussion

Fruits and vegetables are enriched with vitamins and minerals and also good source of dietary fibers, carbohydrate and resistant starch, all of which are required by the body to stay healthy[30]. Fibers help our body in maintaining blood sugar level by delaying gastric emptying and thus reducing the rate of absorption of macronutrients into blood[31]. Literature search showed that dietary fibers obtained from fruits and vegetable have found to be more effective in reducing the risk of developing type 2 diabetes mellitus[6-11].

The results of current study revealed that whole grapefruit is very effective in maintaining 2-hrs postprandial blood sugar levels in comparison to juices (Table 1). This effect was due to delayed absorption of carbohydrate by resistant fibers[31] (Martin and Andreas 2008). These findings are in accordance with the previous study, which reported that rats fed on high resistant starch diet showed slow glucose absorption and relatively low insulinemia[32]. In contrast, intake of fruit juices results rapid rise in blood sugar in comparison to insulin release, as reflected in the results of our present study (Graph 1).

It is noticeable that dietary fibers are not only helpful in regulating blood sugar, but also showed change (insignificant) in systolic blood pressure (Graph 2). Decrease in pulse rate in whole grapefruit treated group was although significant (Graph 4), but it is within normal physiological range[33]. Thus, from the results of our study it has been concluded that dietary fibers, specifically obtained from whole grapefruit, could help in maintaining blood sugar levels towards

normal. Regular intake of fruit fibers also could be beneficial in controlling tachycardia and maintaining heart rate towards normal in patients with diabetes.

High serum cholesterol is the major risk factor for cardiovascular events especially in those with disturbed glycemic control[34]. Recently, Khatoon and Najam reported highly significant reduction in cholesterol level when diabetic rats were treated with cornstarch diet along with acarbose[33]. Nephropathy is another complication associated with uncontrolled high blood sugar levels[35]. Some other recent studies reported beneficial effect of resistant starch diet in diabetic rats as indicated by reduction in serum electrolytes Blood Nitrogen Urea (BUN) and serum creatinine[36] and are associated with less risk of drug-induced nephropathy in the treatment of T2DM[37].

Thus, from the results of above findings it has been suggested that concurrent administration of dietary fibers in patients with T2DM is not only required to maintain euglycemia, but also needed to lower the risk of diabetes related complications including high blood pressure, hypercholesterolemia and diabetic nephropathy[4]. In future, further studies are required to determine whether dietary fiber may be able to aid in the control of normal blood glucose levels in subjects with established T2DM.

Conclusion

Based on above findings, it has been concluded that dietary fiber intake is effective in lowering the risk of diabetes in subjects with risk of having diabetes in their later age because of presence of positive family history, high blood pressure, hypercholesterolemia and other risk factors. Patients with T2DM could be maintained on dietary fibers not only for better glycemic control, but also for controlling diabetes related complication such as high blood pressure. This study could further be extended to assess the effects of dietary fibers (especially obtained from grapefruit) in controlling other diabetes related complications.

Conflict of interest: None declared.

Contribution of Authors:

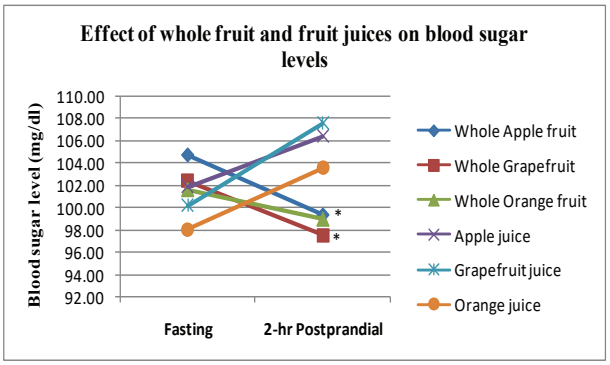
Conception and design: Somia Gul, Nameera Ahmad and Haneen Rashid

Analysis and interpretation of the data: Somia Gul, Humera Khatoon

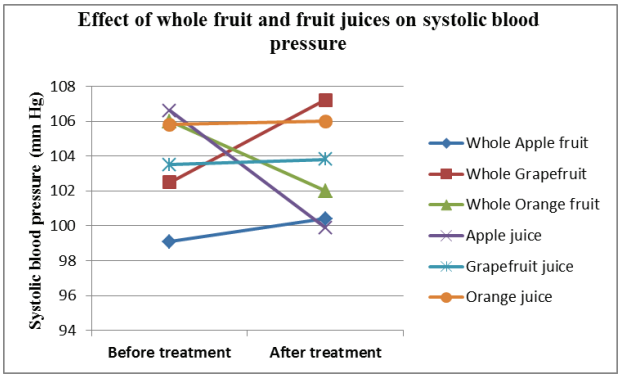
Drafting of the article: Somia Gul, Nameera Ahmad and Haneen Rashid, Agha Zeeshan Mirza

Final approval of the article: Somia Gul

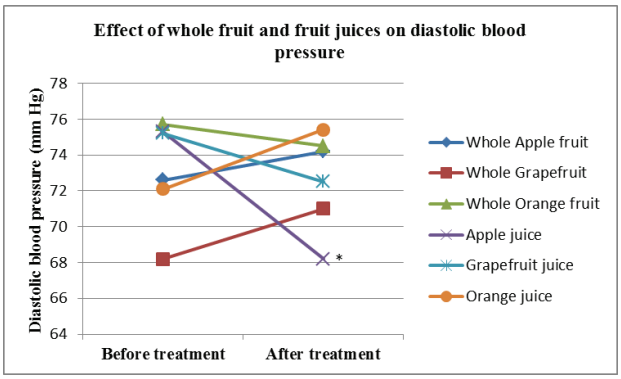
Collection and assembly of Data: Nameera Ahmad and Haneen Rashid



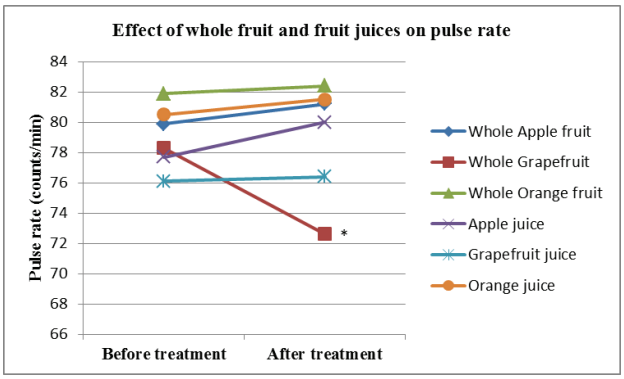
Graph: 1. Values are mean±SD, n=10. Significant difference by Scheffe test.
* $p \leq 0.05$ when 2-hr postprandial blood sugar level compared with fasting blood sugar levels within the similar groups following Two-way ANOVA.



Graph: 2. Values are mean±SD, n=10. Significant difference by Scheffe test. Non-significant difference when after treatment SBP compared with SBP measured before treatment within the similar groups following Two-way ANOVA. SBP; systolic blood pressure.



Graph: 3. Values are mean±SD, n=10. Significant difference by Scheffe test. p≤0.05* when after treatment DBP compared with DBP measured before treatment within the similar group following Two-way ANOVA. DBP; diastolic blood pressure.



Graph: 4. Values are mean±SD, n=10. Significant difference by Scheffe test. p≤0.05* when after treatment pulse rate compared with pulse rate measured before treatment within the similar group following Two-way ANOVA.

References:

1. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin.Pract 2010; 87:4–14.
2. Jonsson B. Revealing the cost of type II diabetes in Europe, Diabetologia 2002; 45:S5–12.
3. Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* 2007; **334**:299.
4. Somia Gul, Nathasha Jawed and Lailoona Jaweed, Pre Diabetes: An alarming and frightening situation about life time syndrome (Diabetes), *Bangladesh Journal of Medical Science* 2016; **15**(4).
5. World Health Organization/UN Food and Agriculture Organization. Diet, nutrition and the prevention of chronic diseases: Report of a Joint FAO/WHO Expert Consultation. Geneva: World Health Org., 2003. (Tech. Rep. Ser., no. 916).
6. Cooper AJ, Sharp SJ, Lentjes MA, et al. A prospective study of the association between quantity and variety of fruit and vegetable intake and incident type 2 diabetes. *Diabetes* Care 2012; **35**:1293–300.
7. Hamer M, Chida Y. Intake of fruit, vegetables, and antioxidants and risk of type 2 diabetes: systematic review and meta-analysis. *J Hypertens* 2007; **25**:2361–9.
8. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. *BMJ.* 2010; **341**: c4229. doi: 10.1136/bmj.c4229.
9. Kurotani K, Nanri A, Goto A, et al. Vegetable and fruit intake and risk of type 2 diabetes: Japan Public Health Center-based Prospective Study. *Br J Nutr* 2013; **109**:709–17.
10. Cooper AJ, Forouhi NG, Ye Z, et al. Fruit and vegetable intake and type 2 diabetes: EPIC-InterAct prospective study and meta-analysis. *Eur J Clin Nutr* 2012; **66:**1082–92.
11. Muraki I, Imamura F, Manson JE, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *BMJ* 2013; **347:**f5001.
12. Arayne M. S., Sultana N., Mirza A. Z., Zuberi M. H. and Siddiqui F. A., *In vitro* hypoglycemic activity of methanolic extract of some indigenous plants, *Pak. J. Pharm. Sci*., 2007, **20**(4), 261-268.
13. Min Li, Yingli Fan, Xiaowei Zhang, Wenshang Hou,

Zhenyu Tang, Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies, *BMJ Open* 2014**; l4** (11).

14. Liu S, Manson JE: Dietary carbohydrates, physical inactivity, obesity, and the "metabolic syndrome" as predictors of coronary heart disease. *CurrOpin Lipidol*; 2001, **12**:395–404, .
15. He K, Hu FB, Colditz GA, Manson JE, Willett WC, LiuS, Changes in intake of fruits and vegetables in relation to risk of obesity and weight gain among middle-aged women, Int. J Obes Relat Metab Disord. 2004; 28(12):1569-74.
16. Joshipura KJ, Ascherio A, Manson JE, Stampfer MJ, Rimm EB, Speizer FE, Hennekens CH, Spiegelman D, Willett WC., Fruit and vegetable intake in relation to risk of ischemic stroke, *JAMA.* 1999; **282**(13):1233-9.
17. Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE: Diet and risk of clinical diabetes in women. *Am J Clin Nutr*., 1992, **55**:1018–1023.
18. Feskens EJ, Virtanen SM, Rasanen L, Tuomilehto J, Stengard J, Pekkanen J, Nissinen A, Kromhout D: Dietary factors determining diabetes and impaired glucose tolerance: a 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care,* 1995, **18**:1104–1112.
19. Ford ES, Mokdad AH: Fruit and vegetable consumption and diabetes mellitus incidence among U.S. adults. *Prev Med*., 2001, **32**:33–39.
20. Hung HC, Joshipura KJ, Jiang R, Hu FB, Hunter D, Smith-Warner SA, Colditz GA, Rosner B, Spiegelman D, Willett WC., Fruit and vegetable intake and risk of major chronic disease, *J Natl Cancer Inst.* 2004; **96**(21):1577-84.
21. Simin Liu, Mary Serdula, Sok-Ja Janket, Nancy R. Cook, Howard D. Sesso, Walter C. Willett, Jo Ann E. Manson and Julie E. Buring, A prospective study of fruit and vegetable intake and the risk of Type 2 diabetes in women. *Diabetes Care*, 2004, **27** (12), 2993-299.
22. Bazzano LA, Serdula MK, Liu S: Dietary intake of fruits and vegetables and risk of cardiovascular disease. *Curr Atheroscler Rep.2003, **5**:492–499.*
23. Kris-Etherton PM, Hecker KD, Bonanome A, Coval SM, Binkoski AE, Hilpert KF, Griel AE, Etherton TD. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. *Am J Med*. 2002; 113 Supp l9B:71S-88S.
24. Lydia A. Bazzano, Tricia Y. Li, Kamudi J. Joshipura and Frank B. Hu, Intake of fruit, vegetables, and fruit juices and risk of diabetes in women, *Diabetes Care*. 2008; 31(7): 1311–1317.
25. Eshak ES, Iso H, Mizoue T, Inoue M, Noda M, Tsugane S., Soft drink, 100% fruit juice, and vegetable juice intakes and risk of diabetes mellitus. *Clin.Nutr*. 2013; **32**(2):300-8. doi: 10.1016/j.clnu.2012.08.003. Epub 2012.
26. Wang B, Liu K, Mi M, Wang J. Effect of fruit juice on glucose control and insulin sensitivity in adults: a meta-analysis of 12 randomized controlled trials, *PLoS One.* 2014; **9**(4):e95323.
27. Liu K, Xing A, Chen K, Wang B, Zhou R, Chen S, Xu H, Mi M., Effect of fruit juice on cholesterol and blood pressure in adults: a meta-analysis of 19 randomized controlled trials. *PLoS One,* 2013, **8**(4):e61420. doi: 10.1371/journal.pone.0061420.
28. Al-Mahmood, A., Afrin, S., & Hoque, N. Metabolic Syndrome and Insulin resistance: Etiopathegenesis and influencing factors. *Bangladesh Journal of Medical Biochemistry*, 2013**: *4***(2), 26-31. https://doi.org/10.3329/bjmb.v4i2.13773
29. Robert V Carlson, Kenneth M Boyd and David J Webb, The revision of the Declaration of Helsinki: past, present and future. *Br J Clin Pharmacol.* 2004; **57**(6): 695–713.
30. Joanne L. Slavin. Carbohydrates, Dietary Fiber, and Resistant Starch in White Vegetables: Links to Health Outcomes, *Adv. Nutr*., 2013, **4**: 351S-355S.
31. Martin O. Weickert and Andreas F. H. Pfeiffer, Metabolic effects of dietary fiber consumption and prevention of diabetes, *J. Nutr*., 2008, **138** (3) 439-442.
32. Khatoon Humera and Najam Rahila, Study on efficacy of Acarbose (with and without Cornstarch Diet) in comparison with rosiglitazone in diabetic rats, *International Research Journal of Pharmacy*, 2013; **4** (02):067-070.
33. Hall, Arthur C. Guyton, John E. (2005). Text book of medical physiology (11thed.) Philadelphia: W.B. Saunders. Pp.166-122.
34. Turner R C, Millns H, Neil H A W, Stratton I M, Manley S E, Matthews D R, Holman R R., Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom prospective diabetes study (UKPDS: 23).*BMJ* 1998; **316.**7134.823.
35. Ritz E and Orth S R. Nephropathy in patients with Type 2 Diabetes Mellitus, *N Engl J Med*. 1999; **341**:1127-1133.
36. Khatoon Humera and Najam Rahila, Effects of rosiglitazone and acarbose (with and without Cornstarch Diet) on serum electrolytes in diabetic rats, *J App Pharm* Sci. 2012; **2**(9): 050-053.
37. Khatoon Humera, Najam Rahila and Bushra Riaz, Effects of acarbose (with and without corn starch diet) and rosiglitazone on kidney functions in alloxan-induced diabetic rats, *World J Pharm Sci*, 2014; **2**(7): 595-692.