REPORT

PRUNES AND LIVER FUNCTION: A CLINICAL TRIAL

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ABSTRACT

Prunes are used by folks as a remedy of various diseases including hepatitis. A clinical trial was designed to see the effects of prunes (*Prunus domestica*) on liver function. 166 healthy volunteers were divided into three groups randomly. Either three (about11.43g) or six (23g approx.) prunes were soaked in a glass of water (250ml) overnight. Each subject from two test groups was asked to drink prune juice & eat whole fruit(single or double dose of prunes) as well, early in the morning, daily for 8 weeks; whereas each subject from control group was given a glass of water to drink. Blood samples were taken at week 0 and week 8 for chemical analysis. There was significant reduction of serum alanine transaminase (p 0.048) and serum alkaline phosphatase (p 0.017) by the lower dose of prunes. There was no change in serum aspartate transaminase and bilirubin. Alteration in liver function by use of prunes may have clinical relevance in appropriate cases and prunes might prove beneficial in hepatic disease.

Keywords: Prunus domestica, Serum Alkaline Phosphatase, Serum Alanine Transaminase, Serum Aspartate Transaminase and Bilirubin.

INTRODUCTION

Plums are widely cultivated for their edible fruit in temperate zones, dried as prunes, juiced, or fermented as a liqueur. Plums may be eaten fresh or preserved in jellies, jams or pickled as umeboshi, a traditional Japanese food with a strong and sour taste (Chiej, 1984). Plums come from different backgrounds: American, European, and Japanese. A variety of *Prunus communis* Huds, *P. institia* is a tree growing on Western Temperate Himalayas. *Prunus domestica* var. is found in Kashmir, Persia and Afghanistan (Nadkarni, 1950). It has been a vital part of alternative medicine e.g. Homeopathy, Hikmat (Awan, 1991; Said, 1996), Ayurvedic (Nadkarni, 1950) and herbal medicine of China and Japan. *Prunus mume* is wormicidal (Rhee *et al*., 1981). Bainiku-ekisu, a concentrate of *Prunus mume* juice, a folk remedy for peptic ulcer, has antibacterial effect on *Helicobacter pylori* infection in human (Nakajima *et al*., 2006). Prunes are regarded useful in cases of torpid and enlarged liver (Awan, 1991) and are effective in liver diseases (Said, 1969).

A diet rich in fruit and vegetables is associated with decreased risk of disease. Free radicals can damage cells, and may play a role in heart disease, cancer and other diseases. Antioxidants are substances that may protect cells against the effects of free radicals. Antioxidants are found in many foods like fruits and vegetables, nuts, grains, and some meats, poultry and fish. Compared with vitamins C and E, dried fruits have superior quality antioxidants with figs and dried plums being the best (Vinson *et al*., 2005). *Prunus domestica* contain relatively high amount of caffeoylquinic acid (CQA) isomers; each CQA isomer in prunes showed high antioxidant activities. Other isolated compounds such as hydroxycinnamic acids, benzoic acids, coumarins, lignans, flavonoid and a novel chromanon showed high ORAC (oxygen radical absorbance capacity) values (Kayano *et al*., 2004a). Dried fruits should be a greater part of the diet as they are dense in phenol antioxidants and nutrients, most notably fiber (Vinson *et al*., 2005). Prunes contain large amounts of phenolic compounds (184 mg/100 g) (Stacewicz *et al*., 2001). Seven phenolic compounds isolated from *Prunus domestica* showed high ORAC are predicted to contribute to antioxidant activity of prunes (Kayano *et al*., 2004b). Total phenolics were also measured; 85 g (½ cup) prunes have a total antioxidant capacity (TAC) of 7,291/serving (Wu *et al*., 2004). In our study, a single dose of 11.43 g (aprox.) of prunes might have 21 mg of phenolic compounds and about 980 of TAC. Present study is conducted in Pakistan to find out whether prunes bring a change in the liver functions in human.

MATERIALS

Plumes (*Prunus domestica*) are dried to prunes as freshly picked plums are first washed and then dried on rice mats,

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Note: This project was approved by the SCM & SIH's (Shifa International Hospital) Ethics Committee. An Urdu written permission was taken from the volunteers after explaining about research and investigations in the local language.

by exposing them to the sunshine. The plums are also left out during the night. At that time dew forms and softens the plums. The next day the sunshine again dries them, and the following night the dew softens them again. This process is repeated for several days. As a result the plums become smaller and many wrinkles appear. At that time the plums are packed in barrels, together with white crude sea salt, and covered by a weight. Through the action of salt and pressure the plums begin to shrink, and their juice starts to collect at the bottom of the barrel. Since the plums have been well - dried, this juice does not cover the plums.

Preparation of Prunes for administration

Prunes are first pitted. Standard weight obtained by weighing 10 prunes. Average weight of one prune equals 3.81g. Single dose consists of 3 prunes equal 11.43g. Packets prepared by the weight of 3 prunes. 1 packet = single dose = 11.43 g, 2 packets =double dose = 22.86 g. The subjects were instructed to soak the contents of the packet in a glass of water (250mL) overnight (7-8 hours). Next morning they were asked to drink the contents of the glass and eat the whole fruit on an empty stomach (Awan, 1991).

METHODS

According to the proposed theory prune juice does not alter liver functions. 166 healthy human volunteers were taken randomly. Each subject was given a complete general physical examination.

Selection procedure of subjects constituted the following data

Inclusion criteria

All adults (above the age of 18 years) coming in out patient department.

Exclusion criteria

Persons with co-morbid factors like diabetes mellitus, malignancy, liver failure, kidney failure, pregnancy and patients taking homeopathic or ayurvedic treatment.

After the selection procedure was complete 166 persons were divided randomly into 3 groups and the dosage per day was: Group A (single dose) = 1 packet of prunes, Group B (Control) = a glass of water and Group C (double dose) = 2 packets. Subjects in Group A and C received prunes according to protocol; those in group B took a glass of water empty stomach in the morning daily for 8 weeks as our experiment suggests that this is the optimum period for a reliable outcome with nutrients.

Blood test

Blood samples were taken on Week Zero and Week 8 for liver function tests (LFTs) i.e. serum alkaline phosphatase (ALP), bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT).These tests were done by enzymatic method. Instruments were BA88 for ALT and Micro lab 200 was used for AST, ALP and bilirubin. Kit by Elitech was used for ALT and AST, Merck for bilirubin and Spin react for ALP.

Statistical methods

Data was entered in SPSS file and analyzed by One-Way ANOVA.

RESULTS

Prunes were given to 166 volunteers (97 males + 69 females) of 43+-10 years of age on week zero. Only 107 who had taken prune juice daily & regularly returned after 8 weeks for blood test (known as compliant volunteers). The non compliant volunteers were 59. On chemical analysis mean of each LFT (ALP, ALT, AST & bilirubin), before and after the administration of prunes/water to all groups, control or those who took either single or double dose of prunes, was within normal limits (tables 1 & 2).

Alkaline phosphatase (ALP)

It was reduced by both single and double dose of prunes on 8 weeks administration that was statistically significant after single dose intake (p 0.017) (table 1).

Alanine transaminase (ALT)

There was significant reduction of ALT by single dose as compared to the control group at 8 weeks administration (p 0.048); but there was no significant reduction by giving double doses.

Aspartate transaminase (AST)

No significant change in both tested and control groups.

Bilirubin

There was no significant difference among all groups both at 0 week and 8 weeks.

DISCUSSION

The most comprehensive Antioxidant Food Database published shows that plant-based foods introduce significantly more antioxidants into human diet than non-plant foods (Carlsen *et al*., 2010). There are some studies on the hepatoprotective effects of various plants and their extracts. *Prunus armeniaca* L. (apricot) fed to Wistar rats decreased oxidative stress and ameliorated histological damage; its dietary intake can reduce the risk of liver steatosis and damage caused by free radicals (Ozturk *et al*., 2009). Chloroform extract of *Prunus africana* (Hook f. Rosaceae) caused the main lesions observed at dose of 1000 mg/kg/d for 2 months were marked centrilobular hepatocellular degeneration and necrosis, rise in blood biochemical parameters namely, ALT, ALP, AST, lactate

Table 1: Comparison of biochemical parameters of groups by One-Way ANOVA

Dependant variable	Group	n	Mean	P
ALP-0 wk	Control	61	201.91+-9.18	Control vs. single = 0.302
	Single	61	185.31+-7.57	Control vs. double = 0.092
	double	43	175.95+-7.51	Single vs. double = 0.728
ALP-8 wk	Control	34	187.02+-11.05	Control vs. single = **0.017**
	Single	37	150.89+-7.65	Control vs. double = 0.725
	double	35	177.00+-8.69	Single vs. double = 0.109
ALT- 0 wk	Control	62	23.20+-1.65	Control vs. single = 0.533
	Single	61	20.62+-1.90	Control vs. double = 0.851
	double	43	21.76+-1.73	Single vs. double = 0.903
ALT-8 wk	Control	35	24.05+-3.61	Control vs. single **=0.048**
	Single	37	15.43+-1.92	Control vs. double = 0.734
	double	35	21.31+-1.78	Single vs. double = 0.237
AST-0 wk	Control	62	27.66+-2.46	Control vs. single = 0.302
	Single	61	23.47+-1.94	Control vs. double = 0.415
	double	43	23.72+-1.33	Single vs. double = 0.997
AST-8 wk	Control	35	30.37+-5.16	Control vs. single = 0.263
	Single	37	22.78+-2.89	Control vs. double = 0.256
	double	35	22.60+-1.44	Single vs. double = 0.999
Bilirubin-0 wk	Control	60	0.59+-0.023	Control vs. single = 0.557
	Single	61	0.56+-0.018	Control vs. double = 0.295
	double	43	0.54+-0.026	Single vs. double = 0.843
Bilirubin-8 wk	Control	34	0.62+-0.023	Control vs. single = 0.989
	Single	37	0.62+-0.022	Control vs. double = 0.248
	double	34	0.57+-0.030	Single vs. double = 0.297

ALP=serum alkaline phosphatase, ALT=alanine transaminase, AST=aspartate transaminase, 0 wk=at zero week, 8 wk= 8 weeks after prune administration. +- = s.e.m. vs. = versus.

Table 2: Normal range reference of biochemical parameters

Variable	Male	Female
Alkaline Phosphatase	Up to 275 mg\dl	
AST	Up to 38 mg\dl	Up to 31 mg\dl
ALT	Up to 40 mg\dl	Up to 32 mg\dl
Bilirubin	Up to 1 mg\dl	

dehydrogenase, creatinekinase and blood urea nitrogen in rats (Gathumbi *et al*., 2002). An aqueous extract of *Prunus africana* administered daily to Sprague Dawley rats caused a moderate rise in blood ALT but it did not cause any significant variations in blood ALP & AST. It was concluded that the extract may contain components that are mildly toxic to the liver and heart of rats after repeated daily oral administrations of 1,000 mg/kg body weight (Gathumbi *et al*., 2000).

In present study, conducted on human volunteers, there was significant reduction of ALT & ALP at lower doses of prunes but no change in AST and bilirubin. Bilirubin is a major physiologic antioxidant cytoprotectant (David *et al.*, 2002). ALT and AST are two of the most reliable markers of hepatocellular injury or necrosis. Their levels can be elevated in a variety of hepatic disorders. Of the two, ALT is thought to be more specific for hepatic injury because it is present mainly in the cytosol of the liver and in low concentrations elsewhere (Giboney, 2005). Many drugs affect the level of ALP in the blood. Higher than normal ALP levels may be due to liver or bone disease (Medline, 2010).

The reduction in ALP & ALT blood levels was at lower doses but not at higher doses. It may be following the theory of increased potency on increased dilution dictated by Hahnemann that the more times the remedy was diluted the more powerful it became; this finding, however, is invalidated by pharmaceutical dose-response studies which show that increasing dosage increases the effect of a drug (whether good or bad) and vice versa (Jackson, 2006). Prunes consist of a lot of antioxidants and many other constituents. This may be an effect of one

of the constituents at lower doses and another constituent might be having a regulatory effect at higher dose that need to be investigated by further studies. Liver functions are not deranged from normal range at all dose levels, therefore prunes can be given safely to patients suffering from hepatitis. It is suggested that prunes might be beneficial for hepatitis due to their antioxidant cytoprotectant role.

CONCLUSION

Prunes significantly reduce serum ALT & ALP levels at lower doses that may have clinical relevance in appropriate cases; as the liver functions were not deranged, prunes can be safely given to patient suffering from liver disease. Prolong administration might prove effective in alleviating liver disease due to their antioxidant properties.

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REFERENCES

Awan HMH (1991). Kitab-al-Mufradat (Khawas-al-Adwiya). Sheikh Ghulam Ali and Sons, (Pvt.) Ltd. Lahore, pp.60-61.

Carlsen MH, Halvorsen BL, Holte K, Bohn SK, Dragland S, Sampson L, Willey C, Senoo H, Umezono Y, Sanada C, Barikmo I, Berhe N, Willett WC, Phillips KM, Jacobs DR Jr. and Blomhoff R (2010). The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. *Nutr J*., **9**: 3.

Chiej R (1984). Encyclopedia of Medicinal Plants. London. MacDonald & Co, (ISBN); 0-(356)-10541-10545.

David E, Barañano, Rao M, Ferris CD and Snyder SH (2002). Biliverdin reductase: A major physiologic cytoprotectant. *Proc Natl Acad Sci*., **99**(25): 16093-16098.

Gathumbi PK, Mwangi JW, Mugera GM and Njiro SM (2002). Toxicity of chloroform extract of *Prunus africana* stem bark in rats: Gross and histological lesions. *Phytotherapy Research*, **16**(3): 244-247.

Gathumbi PK, Mwangi JW, Njiro SM and Mugera GM (2000). Biochemical and hematological changes in rats administered an aqueous extract of *Prunus africana* stem-bark at various dosage levels. *Onderstepoort J. Vet. Res*., **67**(2): 123-128.

Giboney PT (2005). Mildly elevated liver transaminase levels in the asymptomatic patient. *American Family Physicians*, **71**(6): p.15.

Jackson J (2006). Homeopathy. *UK-Skeptics*, http://www.skeptics.org.uk/homeopathy.php.

Kayano S, Kikuzaki H, Yamada NF, Aoki A, Kasamatsu K, Yamasaki Y, Ikami T, Suzuki T, Mitani T and Nakatani N (2004a). Antioxidant properties of prunes (*Prunus domestica* L.) and their constituents. *Biofactors*, **21**(1-4): 309-313.

Kayano S, Kikuzaki H, Ikami T, Suzuki T, Mitani T and Nakatani N (2004b). A new bipyrol and some phenolic constituents in prunes (*Prunus domestica* L.) and their oxygen radical absorbing capacity (ORAC). *Biosci Biotechnol Biochem.*, **68**(4): 942-944.

Medline Plus (2010). Medical Encyclopedia. *American Association for Clinical Chemistry.*

Nadkarni AK (1950). Indian Materia Medica, originally edited by Nadkarni KM revised by Nadkarni AK. 1014-1015.

Nakajima S, Fujita K, Inoue Y, Nishio M, and Seto Y (2006). Effect of the folk remedy, bainiku-ekisu, a concentrate of *Prunus mume* juice, on *Helicobacter pylori* infection in humans. *Helicobacter*, **6**: 589-591.

Ozturk F, Gul M, Ates B, Ozturk IC, Cetin A, Vardi N, Otlu A and Yilmaz I (2009). Protective effect of apricot (*Prunus armeniaca* L.) on hepatic steatosis and damage induced by carbon tetrachloride in Wistar rats. *Br J Nutr*., **102**(12): 1767-1775.

Rhee JK, Woo KJ, Baek BK, and Ahn BJ (1981). Screening of the wormicidal Chinese raw drugs on *Clonorchis sinensis*. *Am. J. Chin. Med*., **9**(4): 277-284.

Said HM (1969). Hamdard Pharmacopoeia of Eastern Medicine. p.170.

Said HM (1996). *The Medicinal Herbal*. Hamdard Foundation Pakistan **1**: 204.

Stacewicz-Sapuntzakis M, Bowen PE, Hussain EA, Damayanti-Wood BI and Farnsworth NR (2001). Chemical composition and potential health effects of prunes: a functional food? *Crit. Rev. Food Sci Nutr*., **41**(4): 251-286.

Vinson JA, Zubik L, Bose P, Samman N and Proch J (2005). Dried fruits: Excellent *in vitro* and *in vivo* antioxidants. *J. Am. Coll. Nutr.*, **24**(1): 44-50.

Wu X, Beecher GR, Holden JM, Haytowitz DB, Gebhardt S E and Prior RL (2004). Lipophilic and hydrophilic antioxidant capacities of common foods in the United States. *Journal of Agricultural and Food Chemistry*, **52**(12): 4026-4037.