

## ORIGINAL ARTICLE

# UNRIPE GRAPE JUICE (VERJUICE) AS A LIPID-LOWERING AGENT: FACT OR FICTION

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**Background and Objective** – It is generally believed in our community that unripe grape juice (verjuice) has a lipid-lowering effect. There is no published data on the lipid-lowering effect of verjuice, so this study sought to test this hypothesis.

**Methods** – In a prospective crossover study, 97 persons with primary hyperlipidemia were enrolled. Group A ( $n = 47$ ) received 80 mL verjuice daily at lunchtime for the first two months of the study and group B ( $n = 50$ ) received the same amount for the last two months of the study. The total duration of the study was four months. The serum lipid profiles were measured at the beginning and two and four months after starting the trial. Results were analyzed by paired-samples *t*-test.

**Results** – The mean  $\pm$  standard deviation levels of triglyceride, total cholesterol, low-density (LDL) and high-density (HDL) lipoprotein cholesterol were measured. The *p* value for all pairs was more than 0.05, indicating that verjuice has no lipid-lowering effect.

**Conclusion** – Our study revealed that unripe grape juice has no lipid-lowering effect, but its antioxidant effect on LDL cholesterol should be studied.

**Keywords** hyperlipidemia LDL cholesterol triglycerides unripe grape juice

### Introduction

The impetus to intervene in lipoprotein abnormalities comes from animal models, case-control clinical and prospective epidemiologic studies that demonstrated an association between levels of the various blood lipids, including triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), and coronary heart disease. Regardless of age and sex, hyperlipidemia is a risk factor for coronary heart disease. Based on human observational evidence, there is little doubt that elevated cholesterol levels increase the risk of coronary heart disease.<sup>1, 2</sup> Observational studies indicate a 20–30% increase in the risk of coronary heart disease for each 10% increase in serum

cholesterol level.<sup>3,4</sup> For some individuals, dietary and lifestyle modification may be all that is needed to prevent coronary heart disease; for others, dietary and lifestyle modification provides the base to which drug therapy should be added to minimize the risk of coronary heart disease.<sup>5</sup>

For many years, it has been a general belief in our society that consumption of some kinds of herbal drugs, fruit juices and vegetables such as red yeast rice, garlic and Soya protein exerts a lipid-lowering effect.<sup>6</sup> This survey evaluated the lipid-lowering effect of unripe grape juice (verjuice) in humans.

### Patients and Methods

This study was conducted at the Nemazee Hospital, Shiraz. From April 1, 2000, to December 10, 2001, individuals with primary hyperlipidemia who were not taking any drugs were randomly divided into two groups. The study duration was

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**Table 1.** Mean levels of TG, TC by groups.

	LDL-C			HDL-C		
	A	B	p Value	A	B	p Value
Start	272 ± 146	278 ± 147	0.83	230 ± 40	222 ± 40	0.32
2 <sup>nd</sup> month	246 ± 112	275 ± 173	0.42	224 ± 36	212 ± 44	0.24
4 <sup>th</sup> month	254 ± 150	226 ± 122	0.30	218 ± 32	219 ± 31	0.87

Group A used verjuice during the first 2 months of the study and group B during the second 2 months of the study. TG = triglyceride, TC = total cholesterol.

four months for each person. Group A received 80 mL of verjuice with their lunch everyday during the first two months and group B received the same during the last two-month of the study .

During the study a visiting dietician maintained all subjects on diet control.

At three time intervals, the start of the study and after two months and four months of the study, 10 mL of blood was taken in the morning from each individual after 12 hours of fasting. The serum levels of TG, TC and HDL-C were measured and LDL-C levels were calculated by applying the Friedewald formula<sup>7</sup>: LDL-C = TC - (HDL-C + TG/5). All measurements were made under standard conditions by one technician. The mean levels of TG, TC, LDL-C and HDL-C in each group at the three time points were analyzed using the paired-samples *t*-test (SPSS version 9.01).

## Results

Of the 160 persons enrolled in the study, 63 were excluded from the study because of headache, epigastric pain and low compliance. After randomization, 47 persons were enrolled in group A and 50 in group B. There was no statistically significant difference between the TG, TC, LDL-C and HDL-C levels in the two groups at the start of the study ( $p > 0.05$ , power = 80%), after two months ( $p = 0.4, 0.24, 0.13$  and  $0.44$ , respectively, power = 80%) and after four months ( $p = 0.3, 0.87, 0.51$  and  $0.45$ , respectively, power = 80%) (Tables 1 and 2).

In group A, the only statistically significant pair (by paired Student's *t*-test) was the mean TC, which decreased from  $230 \pm 40$  mg/dL at

the start of the study to  $218 \pm 32$  mg/dL at the end of the study ( $p = 0.04$ ) (Table 1). In group B, the only statistically significant pair (by paired student's *t*-test) was the mean TG, which decreased from  $278 \pm 148$  mg/dL at the start of the study to  $226 \pm 122$  mg/dL at the end of the study ( $p = 0.007$ ) (Table 1).

## Discussion

Based on the results of this study (95% confidence interval and 80% power), verjuice has neither significant lowering effects on serum levels of TG, TC and LDL-C, nor incremental effects on HDL-C. Two statistically significant parameters (decreases in serum TC in group A and serum TG in group B) can be explained by the effect of diet, not verjuice.

In our center, the only previous study on the lipid-lowering effect of verjuice (1985, unpublished data) concluded that verjuice significantly lowered serum TC levels but had no statistically significant lowering effect on serum TG levels. A major drawback of that study was that the variables in the experimental group were not compared with those in the control group. A MEDLINE search revealed no study on the lipid-lowering effect of verjuice, and few studies show the effect of grape juice on hyperlipidemia. Ingestion of red grape juice concentrate results in increased antioxidant capacity and protection of LDL from oxidation, and thus nonalcoholic red grape extract may have a similar beneficial effect to red wine.<sup>8, 9</sup> Vinson et al showed that grape juice was equivalent to red wine with respect to lowering the risk of heart disease in a hamster model.<sup>10</sup>

**Table 2.** Mean levels of LDL-C and HDL-C by groups.

	LDL-C			HDL-C		
	A	B	p Value	A	B	p Value
Start	148 ± 35	140 ± 31	0.11	40 ± 12	38 ± 10	0.36
2 <sup>nd</sup> month	146 ± 39	132 ± 30	0.13	38 ± 10	38 ± 11	0.92
4 <sup>th</sup> month	146 ± 29	141 ± 27	0.50	39 ± 4	39 ± 7	0.45

Group A used verjuice during the first 2 months of the study and group B during the second 2 months of the study. LDL-C = low-density lipoprotein cholesterol. HDL-C = high-density lipoprotein cholesterol.

## Verjuice as a Lipid Lowering Agent

On the other hand, Goldberg et al showed that the favorable effect of red wine in modulating plasma lipid and lipoprotein concentration couldn't be reproduced by grape juice.<sup>11</sup> Miyagi et al found that the *in vitro* antioxidant effect of red wine as well as grape juice on LDL was closely associated with an abundance of flavonoids.<sup>12</sup> *In vivo* antioxidant activity was demonstrated in humans after ingesting red wine but not grape juice, suggesting that flavonoids in red wine can be absorbed from the intestine more efficiently than those in grape juice. Constant reported that grape juice has about half the amount of flavonoids by volume as red wine.<sup>13</sup>

Luz et al found that red wine and a non-alcoholic red wine concentrate inhibited atherosclerosis without affecting lipids in a rabbit model.<sup>14</sup> In our study, quantitative lipid levels did not improve after ingestion of verjuice, but the antioxidant effect of verjuice should be studied because grape juice and verjuice are very similar in structure and both have a flavonoid component, which may have an antioxidant effect on LDL.

In conclusion, our study revealed that unripe grape juice has no lipid-lowering effect, but its antioxidant effect on LDL should be further studied.

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