

Moderate red-wine consumption partially prevents body weight gain in rats fed a hyperlipidic diet[☆]

Montserrat Vadillo Bargalló, Anna Ardévol Grau, Juan de Dios Fernández-Larrea, Gerard Pujadas Anguiano, Maria Cinta Bladé Segarra, Maria Josepa Salvadó Rovira, Lluia Arola Ferré, Mayte Blay Olivé*

Department of Biochemistry and Biotechnology, Unitat d'Enologia del Centre de Referència en Tecnologia dels Aliments de la Generalitat de Catalunya, Universitat Rovira i Virgili, 43007 Tarragona, Spain

Received 6 April 2005; received in revised form 3 June 2005; accepted 15 June 2005

Abstract

Red wine is a beverage that can exert a broad spectrum of health-promoting actions both in humans and laboratory animal models if consumed moderately. However, information about its effect on body weight is scarce. We have evaluated the effect of moderate red wine consumption on body weight and energy intake in male Zucker lean rats fed a hypercaloric diet for 8 weeks. For this purpose, we used three 5-animal groups: a high-fat diet group (HFD), a high-fat-diet red-wine-drinking group (HFRWD), and a standard diet group (SD). After 8 weeks, the HFRWD group had a lower body weight gain ($175.66 \pm 2.78\%$ vs $188.22 \pm 4.83\%$; $P < .05$) and lower energy intake (269.45 ± 4.02 KJ/animal.day vs 300.81 ± 4.52 KJ/animal.day; $P < .05$) and had less fat mass at epididymal location respect to the whole body weight (0.014 ± 0.001 vs 0.017 ± 0.001 ; $P < .05$) than the HFD group. However, the red wine didn't modified the feed efficiency 0.012 ± 0.001 g/KJ for HFRWD group versus 0.013 ± 0.001 g/KJ for the HFD one ($P = .080$). These findings, though preliminary, show that moderate red wine intake can prevent the increase of body weight by modulating energy intake in a rat diet-induced model of obesity.

© 2006 Elsevier Inc. All rights reserved.

Keywords: Body weight; Moderate red wine consumption; High-fat diet; Zucker rats; Energy intake

1. Introduction

Red wine is a component of the traditional Mediterranean diet. It is rich in polyphenols and has well-known health-promoting properties if consumed moderately. It has been established that an association exists between moderate red-wine consumption and a lower risk of mortality due to cardiovascular disease in humans who consume diets rich in cholesterol and saturated fat (the “French Paradox”) [1–4]. The relationship between red-wine consumption and body-weight control, however, is

still unclear because human studies on the subject are scarce and sometimes collateral [5]. A recent study in obese humans (The Copenhagen City Heart Study) indicated that prolonged moderate red-wine consumption (but not of other alcoholic beverages) tended to decrease abdominal obesity [6]. However, this effect has not been observed by other authors [7,8].

Rats fed a high-fat diet (HFD) rapidly develop obesity. Moreover, feeding of laboratory rats with HFD in conjunction with sucrose will exert synergistic effects on adiposity and increase total body weight. This diet has proved to be a useful model of the putative effects of Western diet in human obesity [9].

The purpose of this study was to examine the effect of red wine on body weight gain and development of obesity. Specifically, we assess the effect of moderate voluntary red-wine consumption on body weight, ingested energy, epididymal adiposity and feed efficiency in a rat model of diet-induced obesity.

[☆] This work was supported by Grant CO3/08 of the Fondo de Investigaciones Sanitarias (FIS) and AGL2002-00078 ALI from the Ministerio de Ciencia y Tecnología (MCYT) of the Spanish Government. M. Vadillo is the recipient of a fellowship from the Rovira i Virgili University in Tarragona, Spain.

* Corresponding author. Tel.: +34 977 558497; fax: +34 977558232.
E-mail address: mbo@fq.urv.es (M.B. Olivé).

2. Methods

2.1. Animals and diets

Six-week-old male Zucker Fa/? rats were purchased from Charles River Laboratories (Santa Perpètua de la Mogoda, Spain). Animals were bred at the Animal Service of the Rovira i Virgili University under controlled conditions of light (12 h on–12 h off), humidity (50%) and temperature (20–22°C). Prior to the beginning of the experiment, rats were maintained for 1 week in metabolic cages (habituation period). Animal procedures used were approved by the Ethics Committee of the Rovira i Virgili University.

Semipurified diets, in powder format, were supplied by Mas Bové (IRTA, Reus, Spain). The diet formulation conformed to the American National Research Council requirements. The standard diet (SD) contained the following in weight percentage: 60% cornstarch, 18.6% casein, 13% wheat fiber, 4% lard, 1.6% sunflower oil and 3% DL-methionine, vitamins and minerals. The HFD contained 30% sucrose, 17.7% wheat fiber, 18% casein, 30% lard, 1.6% sunflower oil and 3% DL-methionine, vitamins and minerals. See Table 1 for the energy composition of the diets. The diets were isonitrogenous for percent total protein contribution.

2.2. Red wine

The red wine (Appellation Contrôlée Priorat, Scala Dei, Spain) was a young one and contained 13% (v/v) ethanol and 2.09 g/L total polyphenol content expressed as acid gallic units. The total polyphenolic content of the wine was assayed by the Folin-Ciocalteu assay [10]. Briefly, Folin-Ciocalteu reagent was prepared by diluting a stock solution (Panreac, Barcelona, Spain) with distilled water (1:10, v/v). A sample of the wine or gallic acid standards (50 µl) were added to 5 ml of diluted reagent in a test tube followed by 4 ml of Na₂CO₃ (75 g/L). The tubes were stirred and kept at ambient temperature for 2 h. Absorbance at 675 nm was recorded, and wine total polyphenol content was calculated.

2.3. Induction of obesity and wine administration

At 7 weeks of age, the animals weighed 236–264 g and were individually housed in metabolic cages and maintained in them throughout the experimental period. The

animals were randomly assigned to one of dietary treatment groups of five animals each. Group 1 was fed a SD, Group 2 was fed a HFD and Group 3 was fed a high-fat diet and had free access to water and red table wine (HFRWD). Wine was administered in individual drinking troughs and renewed daily. All studies were carried out for 8 weeks after the introduction of the diet. The animals' body weight and food, water and wine consumption were measured daily.

Total energy intake (EI) was calculated in each group considering the energetic density of each diet and that of the red wine (3.2 kJ/ml).

The ratio between grams of body weight gained per energy consumed, termed feed efficiency (FE), was calculated to indicate the amount of body weight gained per kilojoule of energy consumed.

At the completion of the study, the animals were sacrificed, and the epididymal fat pads were excised and weighed.

2.4. Glucose determination

Blood glucose was measured in the tail of the animals by a glucometer after 8 h of fasting (Glucocard, Menarini, Spain).

2.5. Calculations and statistical analysis

Results are expressed as mean±S.E.M. Effects were assessed using ANOVA or Student's *t* test. We used Tukey's test of honestly significant differences to make pairwise comparisons. All calculations were performed using SPSS software.

3. Results

To assess the effect of moderate red-wine consumption on body weight, we worked on an animal model of obesity based on a high-caloric diet. The red-wine group consumed an average of 1.70±0.38 ml/day per animal. The ingestion of red wine was regular in all animals throughout the 8-week experimental period and corresponded to a dose of 3.4±0.79 mg/day per animal of total polyphenols. The mean daily water consumption was similar in the three groups studied (18±1.5, 18.7±1.1 and 17.7±1 ml/day for SD, HFD and HFRWD, respectively). We did not find any differences in liquid consumption (including wine) between groups.

The percentage of final body weight with respect to initial body weight in animals that followed SD, HFD or HFRWD was 160.88±2.83%, 188.22±4.83% and 175.66±2.78%, respectively. All three values were significantly different (*P*<.05) (see Fig. 1A). The ingestion of red wine counteracted part of the increase in body weight induced by a HFD after an 8-week period.

Mean daily EI was different in all three groups. The mean EI of the HFRWD group was smaller (269.45±4.02 kJ/animal per day) than that of the HFD group

Table 1
Energetic value of experimental diets

	SD	HFD
Gross energy content (kJ/g)	14.65	19.84
% Energy as protein	21	16
% Energy as carbohydrate	68	26
% Energy as lipid	11	58

Synthetic diets differed mainly in fat and carbohydrate contributions to the caloric value and were identical in terms of vitamins, minerals and fiber. The SD was low in saturated fat and contained mostly complex carbohydrates (starch). In the HFD, lard was the main source of lipid, and sucrose was the source of carbohydrate.

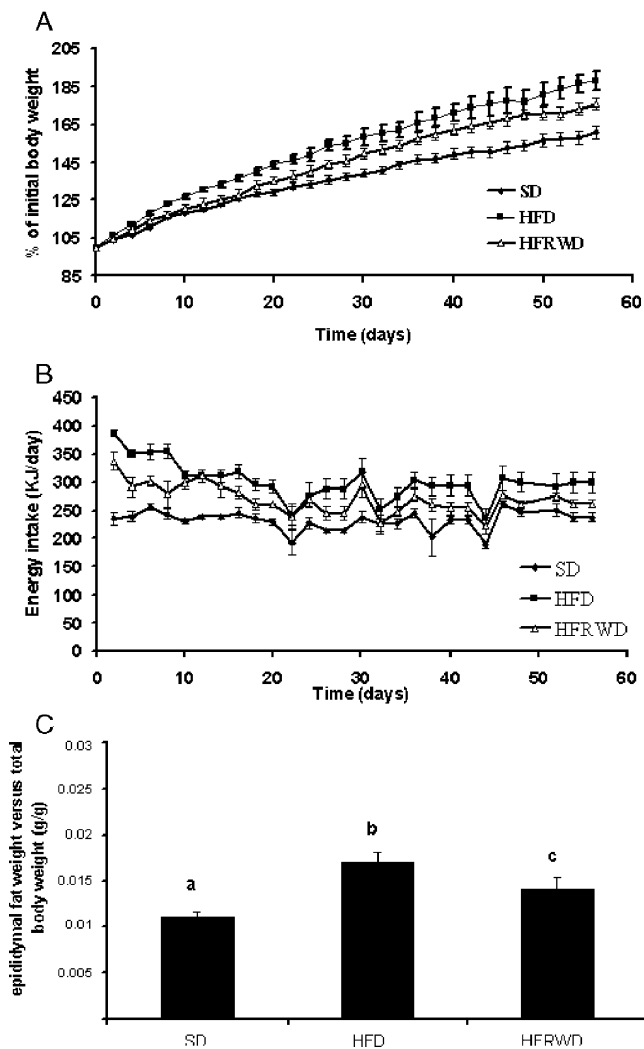


Fig. 1. Body weight and energy intake in rats fed a HFD with or without red-wine consumption or a SD. (A) Body weight changes throughout the experimental period expressed as a percentage of initial weight. (B) Daily energy intake for 8 weeks of treatment of animals fed a SD, HFD or HFRWD. (C) Epididymal fat pad weights vs. total body weight ratio after feeding with SD, HFD or HFRWD. Data are mean \pm S.E.M. ($n=5$). The letters (A–C) indicate statistically significant differences between diets ($P<.05$).

(300.81 ± 4.52 kJ/animal per day) ($P<.05$). As we expected, the SD group ingested less energy (232.32 ± 2.26 kJ/animal per day) than the animals on HFD with or without wine (see Fig. 1B).

In consequence, we found that accrued EI during the experimental period was significantly different between the three groups. For the HFRWD group, this was 14.75 ± 0.64 MJ/animal; for the HFD group, 16.49 ± 0.39 MJ/animal; and for the SD group, 13.068 ± 0.29 MJ/animal ($P<.05$).

Feed efficiency in the HFRWD group was similar to that of the HFD group (0.012 ± 0.001 vs. 0.013 ± 0.001 g/kJ; $P=.080$). However, we found significant differences in FE between the HFD group and the SD

group (0.013 ± 0.001 and 0.011 ± 0.001 g/kJ; $P<.05$). These results indicated that red wine itself did not modify FE, although a HFD did.

The epididymal fat pad weight vs. total body weight of animals was significantly different between the three groups ($P<.05$). It was higher in the HFD group (0.017 ± 0.001) than in the SD group (0.011 ± 0.001) and smaller in the HFRWD group (0.014 ± 0.001) (see Fig. 1C). As shown, changes in body weight are reflected in epididymal fat pad mass.

Blood glucose levels for the SD, HFD and HFRWD groups were 4.07 ± 0.13 , 4.65 ± 0.17 and 4.39 ± 0.21 mM, respectively. No differences were found in blood glucose due to red-wine ingestion. The glucose values were normal.

4. Discussion

In this work, we have reproduced the model for voluntary wine consumption previously assayed in our laboratory in which the red-wine consumption of rats was equivalent to moderate red-wine consumption in humans [11]. We found that moderate red-wine consumption prevents the increase in body weight of rats fed a HFD and that this effect is mainly mediated by a decrease in the energy intake. Thus, red wine counteracts in part the overfeeding induced by the hyperlipidic diet that causes obesity to animals.

Because red wine is a complex mixture of polyphenolics, ethanol and water, we cannot ascertain which specific component of wine is responsible for these effects. It has been shown that ethanol ingestion per se does not modify the amount of ad libitum energy intake in humans in the following meal [12]. On the other hand, some actions of polyphenolics present in red wine on body weight control have been reported in both humans and laboratory animal models. In humans, catechin increases the metabolic rate and fat oxidation levels, and in obese rodents it reduces body weight [13,14]. Epigallocatechin gallate reduces body weight and food intake in laboratory animals, as has been reported by Kao et al. [15]. Tebib et al. [16] showed that a diet supplemented with grape seed tannins induced laboratory rats to gain less weight than was expected. In the work of Tebib et al. [16], the polyphenolic dose was approx. 1 mg/day per animal, which is similar to the dose of 3.4 g/day per animal consumed by the wine-receiving group in the present study.

It is possible that red-wine ingestion could modulate the mechanisms of satiety. The ability of red-wine polyphenolics to interfere with fat absorption has been recently reported in humans [17]. It is possible therefore that there are differing metabolic responses to red-wine ingestion in individuals fed a regular diet and in those receiving a hyperlipidic one because of the supposed delay in fat absorption induced by red wine.

A recent study in humans about the effect of red-wine consumption on ad libitum energy intake shows an enhancement of caloric consumption compared to carbonated soft drink or beer. The absence of a water-drinking group and of free access to water could explain the observed results [18].

On the other hand, an organotoxic effect induced by moderate red-wine consumption on rats has to be discarded, as stated by previous results in Ref. [11]. No alteration in the activities of plasma marker enzymes of tissue damage was found in animals receiving a similar quantity of red wine for 6 months [11].

This study was designed to assess whether moderate wine consumption influences body weight gain in animals that develop obesity. We have shown that red-wine consumption prevents body weight gain in rats fed a hyperlipidic diet by reducing the energy ingested and maintaining the FE. Further studies are needed to ascertain which components of red wine are responsible for this effect and to determine the underlying physiological and metabolic mechanisms involved.

References

- [1] Renaud S, de Lorgeril M. Wine, alcohol, platelets and the French paradox for coronary artery disease. *Lancet* 1992;339:1523–6.
- [2] Saint Leger AS, Cochrane AL, Moore F. Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. *Lancet* 1979;i:1017–20.
- [3] Gronbaek M, Dies A, Sorensen TIA, Becker U, Schohr P, Jensen G. Mortality associated with moderate intakes of wine, beer, or spirits. *BMJ* 1995;310:1165–9.
- [4] Gronbaek M. Factors influencing the relation between alcohol and mortality — with focus on wine. *J Int Med* 2001;250:291–308.
- [5] Cordain L, Melby CL. Alcohol, wine and obesity. *F Bleu OIV* 1998; 49:1–16.
- [6] Vadstrup ES, Petersen L, Sorensen TIA, Gronbaek M. Waist circumference in relation to history of amount and type of alcohol: results from the Copenhagen City Heart Study. *Int J Obes* 2003; 27:238–46.
- [7] Cordain L, Melby CL, Hamamoto AE, et al. Influence of moderate chronic wine consumption on insulin sensitivity and other correlates of syndrome X in moderately obese women. *Metabolism* 2000; 49(11):1473–8.
- [8] Cordain L, Bryan ED, Melby CL, Smith MJ. Influence of moderate daily wine consumption on body weight regulation and metabolism in healthy free-living males. *J Am Coll Nutr* 1997;16:134–9.
- [9] Morris KL, Namey TC, Zemel MB. Effects of dietary carbohydrate on the development of obesity in heterozygous Zucker rats. *J Nutr Biochem* 2003;14:32–9.
- [10] Singleton VL, Rossi JA. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. *Am J Enol Vitic* 1965;4:144–58.
- [11] Arola LI, Roig R, Cascón E, Brunet MJ, Fornós N, Sabaté M, et al. Model for voluntary wine and alcohol consumption in rats. *Physiol Behav* 1997;62(2):353–7.
- [12] Poppitt SD, Eckhart JW, McGonagle J, Murgatroyd PR, Prentice AM. Short-term effects of alcohol consumption on appetite and energy intake. *Physiol Behav* 1996;60(4):1063–70.
- [13] Zheng G, Sayama K, Okubo T, Juneja LR, Oguni I. Anti-obesity effects of three major components of green tea, catechins, caffeine and theanine in mice. *In Vivo* 2004;18(1):55–62.
- [14] Murase T, Nagasawa A, Suzuki J, Hase T, Tokimitsu I. Beneficial effects of tea catechins on diet-induced obesity: stimulation of lipid catabolism in the liver. *Int J Obes* 2002;26(11):1459–64.
- [15] Kao YH, Hiipakka RA, Liao S. Modulation of endocrine systems and food intake by green tea epigallocatechin gallate. *Endocrinology* 2000;141(3):980–7.
- [16] Tebib K, Besançon P, Rouanet J-M. Effects of dietary grape seed tannins on rat cecal fermentation and colonic bacterial enzymes. *Nutr Res* 1996;16:105–10.
- [17] Pal S, Naissides M, Mamo J. Polyphenolics and fat absorption. *Int J Obes* 2004;28:324–6.
- [18] Buemann B, Toubro S, Astrup A. The effect of wine or beer versus a carbonated soft drink, served at a meal, on ad libitum energy intake. *Int J Obes* 2002;26:1367–72.