Int J Diabetes & Metab (2011) 19:1-9

Red wine alters the glucose-insulin relationship when consumed alone after a meal

Anna Kokavec and Mark A. Halloran
School of Psychological Science, La Trobe University, Bendigo, Australia

Abstract
The aim of this study was to assess the effect of a small-moderate dose of red wine on the level of serum insulin and plasma glucose before and after a meal. A total of 18 non-diabetic males aged between 19-22 years participated in the current investigation. In the fasting trial participants underwent a 6 hour fast before consuming 4 standard units of red wine (40g alcohol) or the equivalent amount of placebo over a period of 135-min. Food was then presented alone for 45-min. Alternatively, in the feeding trial food was consumed for 45-min prior to participants ingesting 4 standard units of red wine (40g alcohol) or the equivalent amount of placebo over a 135-min period. The serum insulin and plasma glucose level was assessed at regular 45-min intervals across the four 180-min experimental periods. The results showed a significant alcohol-induced decrease in postprandial glucose and no significant change in serum insulin concentration when red wine is consumed alone following a meal. Alternatively, the ingestion of red wine alone prior to food promoted a significant reduction in serum insulin concentration despite preprandial glucose remaining unchanged. It was concluded that red wine may promote an alteration in the feedback mechanism by which plasma glucose controls the insulin rate, which under specific conditions could potentially provide some health benefits to diabetic individuals.

Keywords: *alcohol, insulin, feeding, wine, glucose, fasting*

Introduction

Early studies aimed at investigating fasting insulin-glucose relationships have suggested the existence of a "feedback" mechanism by which the synthesis of insulin is regulated by the plasma glucose level.[1] In non-diabetic individuals a meal high in carbohydrate causes a sudden increase in postprandial glucose, which stimulates insulin release by the β-cells in the pancreas.[2] Following food intake, plasma insulin usually remains elevated until the blood glucose level begins to drop and often a decrease in insulin secretion does not occur until several hours later.[3]

Alcohol can artificially lower the plasma glucose level without the mediation of insulin when consumed prior to food,[1] due to the ability of alcohol to inhibit gluconeogenesis.[4] Clinical "Alcohol Hypoglycaemia" characterized by an abnormally low blood glucose and impairment in ketogenesis was reported in a large number of patients at least four decades ago.[5] The degree of hypoglycaemia was noted to be variable and significantly related to the period of food deprivation at the time alcohol is consumed.[6] Thus, suggesting the possibility that alcohol if consumed under certain conditions may promote some impairment to the usual glucose-insulin feedback relationship.

Red wine contains resveratrol, a potent anti-oxidant with known hypoglycaemic and hypolipidemic properties.[7] Data obtained from animal studies using diabetic rats has shown that resveratrol treatment can simultaneously promote a significant decrease in plasma glucose and a significant increase in plasma insulin.[8] Moreover, the added observation that a small-moderate dose of red wine may improve insulin sensitivity[9] has led researchers to suggest that red wine ingestion may provide some health benefits to type 2 diabetic patients.

In fasted individuals a moderate-large amount of alcohol does not stimulate insulin secretion,[10] with a lower rate[11] and/or no change[12] in the level of fasting insulin being observed following moderate alcohol intake. However, the consumption of a small-moderate amount of alcohol after a high carbohydrate meal can significantly lower the level of plasma insulin with a non-significant trend for a lowering of postprandial glucose also being observed.[13] Alternatively, when alcohol ingestion precedes food intake the consumed alcohol can potentiate the insulin stimulating properties of glucose and promote a rapid release of insulin.[14] Thus, consuming alcohol before, after, or with food could be an important factor that if not controlled for could likely contribute to variability in the insulin data.

The consumption of a small-moderate amount of red wine is

Received on: 28/12/2009
Accepted on: 11/02/2011

Correspondence to: Dr. Anna Kokavec, School of Psychological Science, La Trobe University, Bendigo, Australia, Email: A.Kokavec@latrobe.edu.au

often promoted as being beneficial to cardiac health.[15, 16,17] Red wine has been shown to have a positive effect on lipid production and may protect against the development of metabolic syndrome and its associated cardio-metabolic derangements.[18] Of concern is that there is an absence of ecologically valid data relating to the effect of commercially available red wine on serum insulin and plasma glucose under variable nutritional conditions. Any dysregulation in the glucose-insulin feedback mechanism could negatively alter the availability of energy for cells so it is vital that the exact effect of consuming commercially available alcohol on glucose production and utilization is understood before any amount of alcohol is promoted as being beneficial to health.

The aim of this study is to clarify the effects of a small-moderate amount of commercially available red wine on the glucose-insulin feedback relationship when red wine is ingested alone before and after a high carbohydrate meal.

Methods

Participants

A total of 18 non-diabetic adult males aged between 18 to 22 years participated in this investigation. Participants were excluded if they reported: a history of psychiatric illness; any neurological conditions; any major physical compliant; a history of drug use; taken any prescription medication within the last seven days, or; satisfied the DSM-IV-TR criteria for alcohol abuse and/ or dependence (American Psychiatric Association, 2000).

Participants were all white Caucasians of Australian or European descent, and no participant was obese. All participants fitted the profile of 'social' drinkers consuming an average of 10.3 standard units (SD = 7.21 U) of alcohol (i.e. each containing 10g/alcohol), on an average of 8.8 days (SD = 4.9 U) per month.

Subject participation was obtained by informed consent. Approval for the study was granted by the La Trobe University Human Ethics Committee, who determined that the procedures were consistent with the ethical guidelines for human research set by the National Health and Medical Research Council of Australia.

Measures and Equipment

Serum insulin was assessed utilising Cobas Elecsys 2010® radioimmunoassay (Roche Diagnostics, Indianapolis, IN, USA). The analytical sensitivity (lower detection limit) of this assay is 0.20 μU/ml, and the intraassay coefficient of variation was 4.9% at 6.85 μU/ml, 3.7% at 16.7 μU/ml, and 3.4% at 55.1 μU/ml. Staff at Analytic Reference Laboratories (St Kilda Road, Melbourne, Australia), who were blind to the experimental procedure, performed all biochemical analyses. Plasma glucose was monitored using a Caresens® (i-SENS Inc, Korea) blood glucose monitoring system. The functional sensitivity of this assay has a lower detection limit of 0.50 IU/ml. Semi-quantitative urinalysis was performed using Labstix™ (Bayer Australia Limited) to measure ketones (sensitivity was 0.5-1.0 mmol/L acetoacetic acid). Blood alcohol readings (BAL) were performed using a Lion alcometer™ (Lion laboratories Limited, Cardiff. UK). The alcohol used in both alcohol trials was Penfold's Rawson's Retreat 2007 cabernet sauvignon red wine containing 14% alcohol (Penfolds wines, Magill, South Australia). Edenvale de-alcoholised red wine containing < .5% alcohol (JMB Beverages Pty Ltd, Hornsby, New South Wales) was used as a placebo.

Procedure

The alcohol/placebo feeding and alcohol/placebo fasting trials were held on separate occasions with at least a three-week interval between trials. Blood alcohol readings taken prior to the commencement of all trials showed a zero blood alcohol level (BAL) in all participants. Participation in all trials was preceded by a six hour fast, which commenced at 1100 h (Eastern Standard Time) and testing for all trials began at 1700h. In order to minimize discomfort to participants a catheter was fitted to facilitate repeated blood sampling.

Fasting trial

Upon arrival participants were asked to provide a 50ml urine sample for urinalysis prior to having 10ml of blood drawn from the left forearm for assessment of plasma glucose and serum insulin. Following the blood taking procedure participants slowly ingested a total of four standard units of red wine (40g alcohol) or the equivalent volume of placebo over a 135-min period. Blood sampling for the assessment of plasma glucose and serum insulin, measurement of BAL, and urinalysis was performed regularly at 45-min intervals between 1700h and 1915h. Food and a non-alcoholic beverage in the form of a large non-vegetarian pizza and at least 200ml Cola soft drink was provided at 1915 h and readings for all parameters were taken once participants had finished eating at 2000 h. Wine and placebo ingestion was monitored to ensure that the rate of consumption was the same for all participants during the study. At the completion of the alcohol trial all participants reported moderate intoxication. No subject experienced gastrointestinal or other distress during the course of the study.

Feeding trial

Food and a non-alcoholic beverage in the form of a large non-vegetarian pizza and at least 200ml Cola soft drink was consumed by participants between 1700 h and 1745 h. Participants provided a 50ml urine sample for urinalysis prior to having 10ml of blood withdrawn from their left forearm for the assessment of serum insulin and plasma glucose upon arrival and following food intake. All participants were then required to slowly ingest four standard units of red wine (40g alcohol) or the equivalent volume of placebo over a 135-min period. Wine and placebo ingestion was monitored to ensure that the rate of consumption was the same for all participants during the 135-min experimental period. Blood sampling for the assessment of serum insulin and plasma glucose, and urinalysis was performed at regular 45-min intervals between 1700 h and 2000 h. At the completion of the

alcohol trial all participants reported mild feelings of intoxication. No subject experienced gastrointestinal or other distress during the course of the study.

Data Analysis

A 2 x 4 mixed design Analysis of Variance (ANOVA) with Trial (feeding, fasting) as the 'between subjects' factor and Time (Baseline, 45-min, 90-min, 135-min) as the 'within subjects' factor was used to compare the effect of red wine and placebo on plasma glucose and serum insulin concentration under feeding and fasting conditions. A 2 x 2 mixed design ANOVA with Trial (feeding, fasting) as the 'between subjects' factor and Time (135-min, Food) as the 'within subjects' factor was used to compare the effect of consuming red wine and placebo prior to food on plasma glucose and serum insulin concentration. Results were classed as significant if the calculated probability was less than .05.

Results

Ketones were detected by urinalysis in all the participants prior to participation in the fasting and feeding trials, which confirmed that all participants had complied with the fasting conditions.

Fasting Trial

The consumption of four standard units (40 g alcohol) of red wine under fasting conditions resulted in ketone production ceasing in 50% of participants at 90-min and all but one participant at 135-min. The average effect of consuming red wine prior to food on the level of plasma glucose and serum insulin is graphically presented in Figures 1A and 1B, respectively.

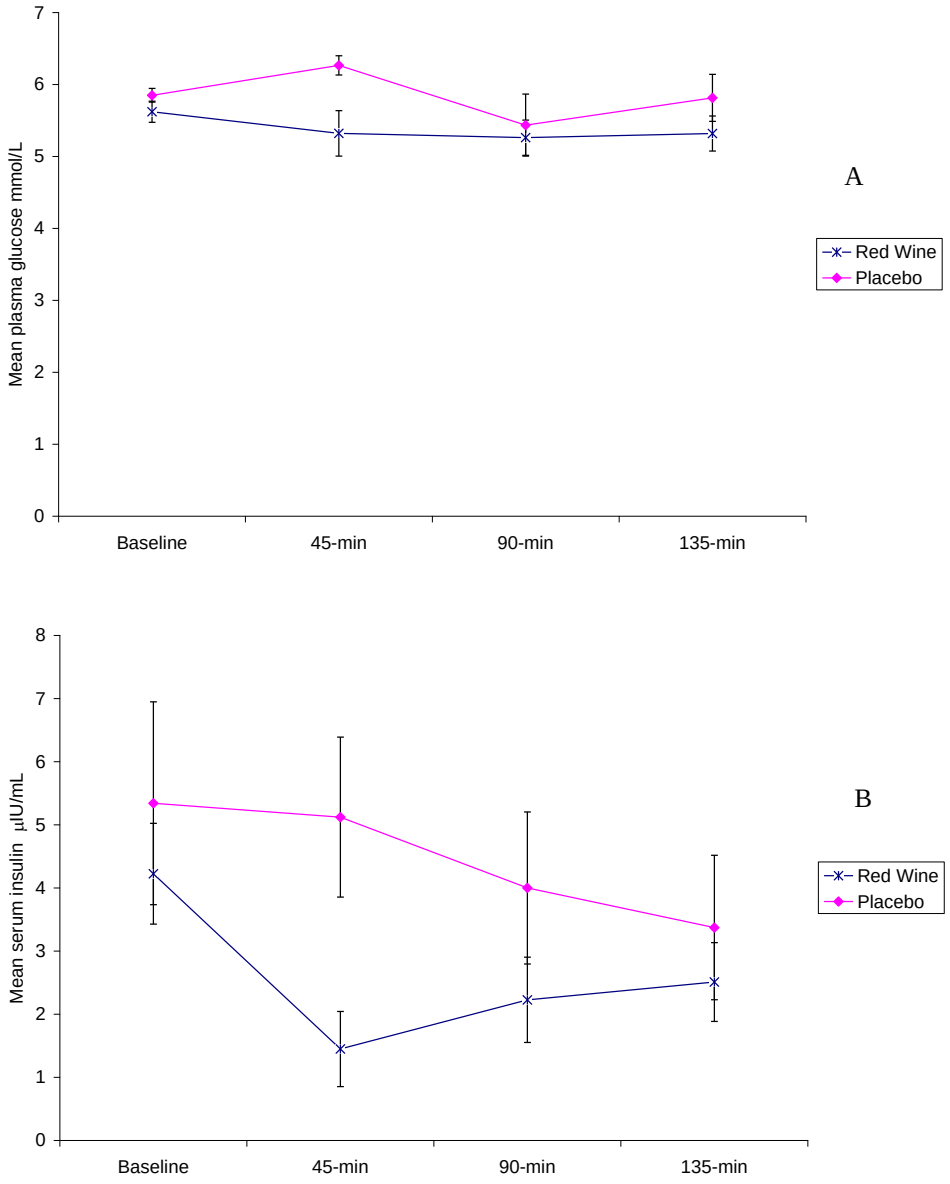


Figure 1: Mean plasma glucose (A) and mean serum insulin (B) concentration at Baseline and during consumption of red wine containing 40g alcohol or placebo (45-135min). Data are presented as the mean ± *SEM*. *N* = 18.

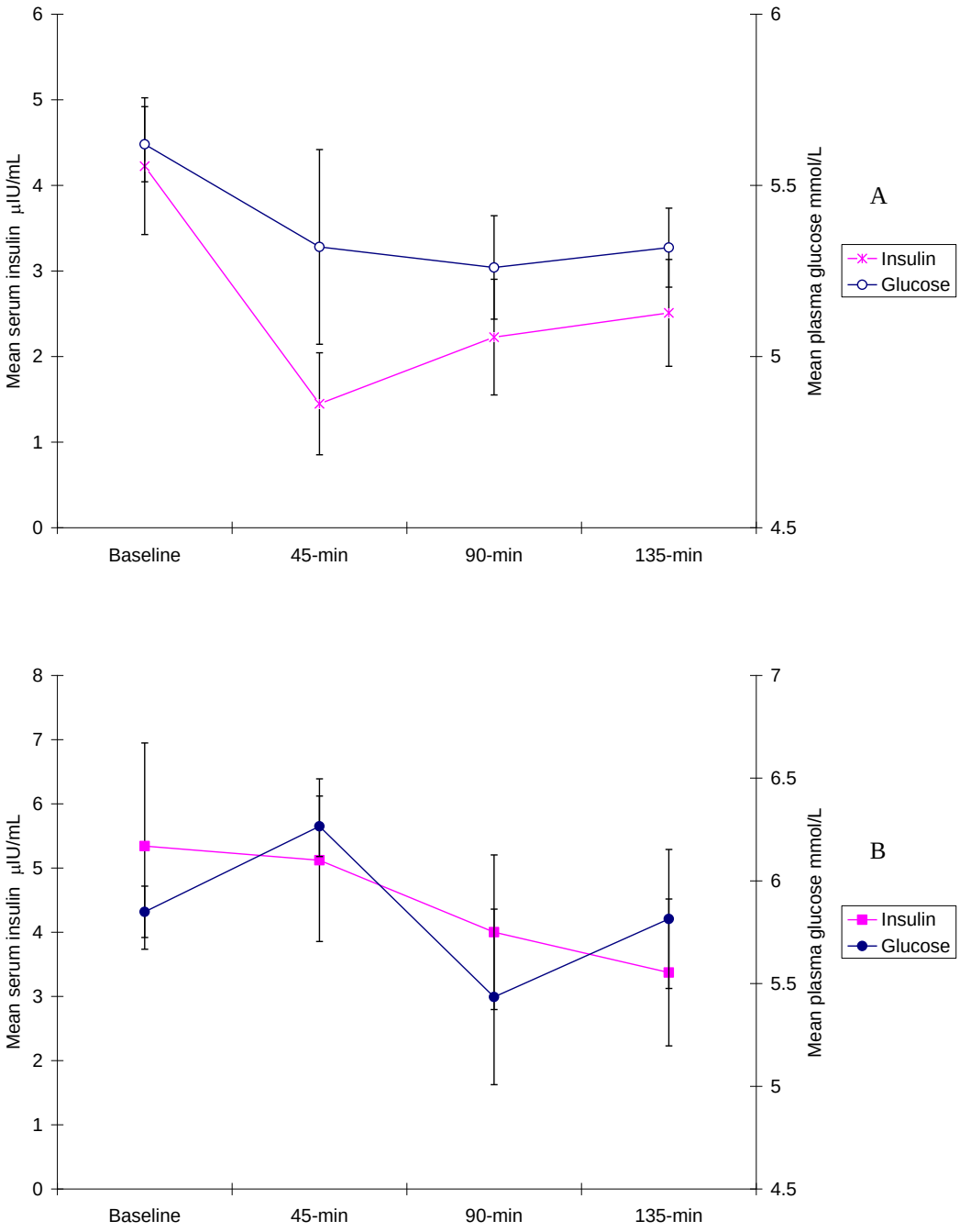


Figure 2: Mean insulin-glucose relationship during consumption of red wine containing 40g alcohol (A) or placebo (B) at Baseline and under fasting conditions (45-135 min). Data are presented as the mean ± *SEM*. *N* = 18.

The 2 x 4 mixed design ANOVA analysis revealed a non-significant main effect for Time (F (3, 45) = 1.89, P = .145), non-significant main effect for Trial (F (1, 15) = 2.71, P = .12), and non-significant Time x Trial interaction (F (3, 45) = 1.47, P = .236) when plasma glucose was compared in the two fasting trials. Alternatively, a significant main effect for Time (F (3, 48) = 4.76, P < .01) and significant Time x Trial interaction (F (3, 48) = 2.68, P = .05) was noted in serum insulin concentration. The Trial main effect was not significant (F (1, 16) = 2.30, P = .15). Post hoc analysis revealed the level of serum insulin in the alcohol trial was significantly lower at 45-min. The average effect of consuming red wine prior to food on the glucose-insulin feedback relationship is graphically presented in Figures 2A and 2B, respectively.

Feeding Trial

Food consumption in the feeding trial inhibited ketone production in all participants confirming that participants were not fasted prior to alcohol being consumed. However, ketones were detected in the urine of 50% participants at 90-min in the alcohol trial (only). The mean plasma glucose and serum insulin level measured in the feeding trials is graphically presented in Figures 3A and 3B, respectively.

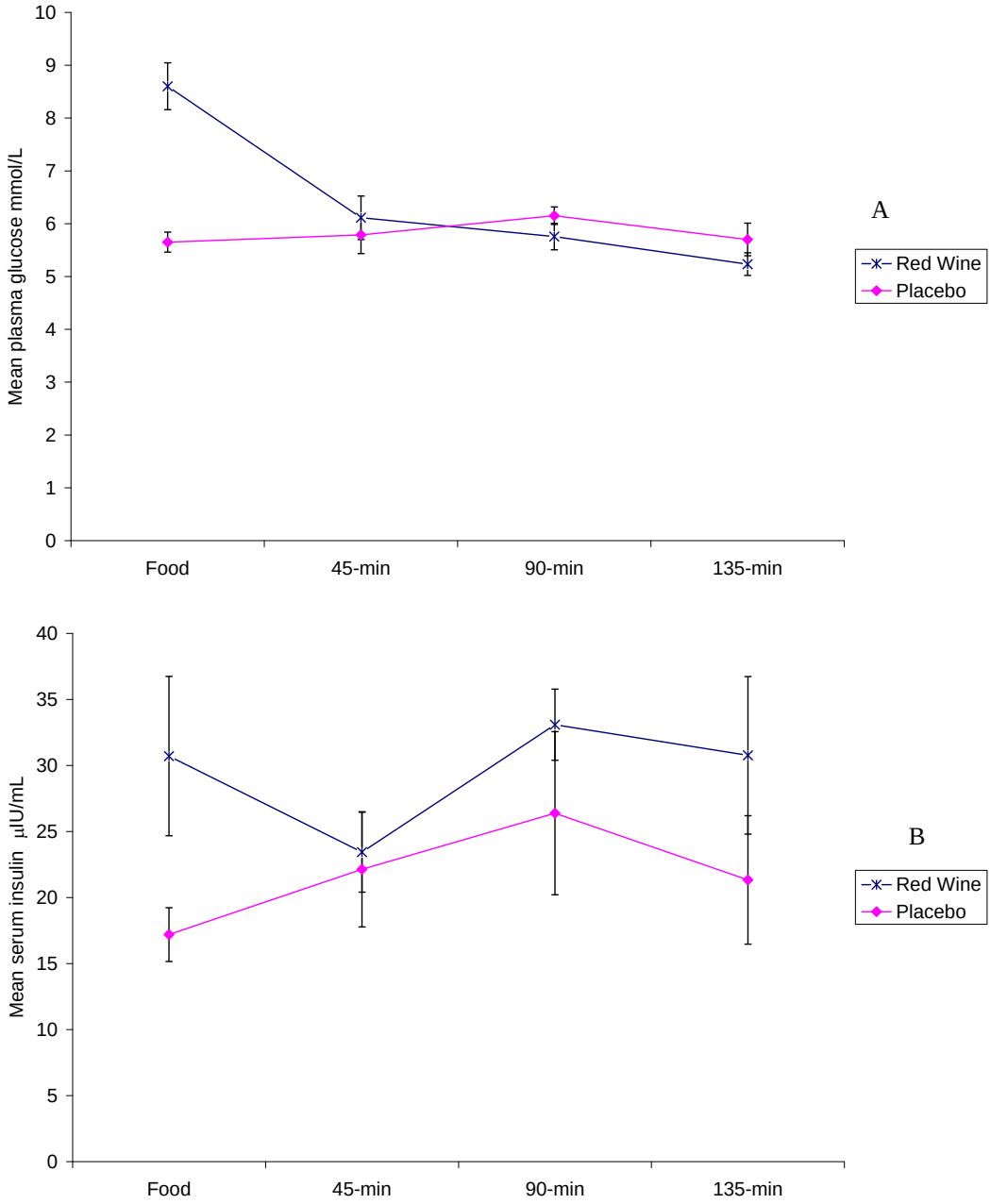


Figure 3: Mean insulin-glucose relationship at Baseline and after Food and during consumption of red wine containing 40g alcohol (A) placebo (B). Data are presented as the mean ± SEM. N = 18.

The 2 x 4 mixed design ANOVA analysis revealed a significant main effect for Time (F (3, 48) = 20.69, P < .001) and non-significant main effect for Trial (F (1, 16) = 2.70, P = .12) for plasma glucose. However, this was modified by a significant Time x Trial interaction (F (3, 48) = 26.75, P < .001). Post hoc analysis revealed the level of plasma glucose in the alcohol trial was significantly lower at 45-min. Alternatively, when serum insulin was compared in the two feeding trials the main effect for Trial (F (1, 16) = 4.27, P = .06), main effect for Time (F (3, 48) = .91, P = .44), and Time x Trial interaction (F (3, 48) = .64, P = .59), were all non-significant. The average effect of consuming red wine after food on the glucose-insulin relationship is graphically presented in Figures 4A and 4B, respectively.

Red Wine Prior to Food

The average effect of consuming red wine containing 40g alcohol prior to food on the level of plasma glucose and serum insulin is graphically presented in Figures 5A and 5B, respectively.

The 2 x 2 mixed design ANOVA produced a significant main effect for Time (F (1, 15) = 41.58, P < .001) and significant Time x Trial interaction (F (1, 15) = 6.20,

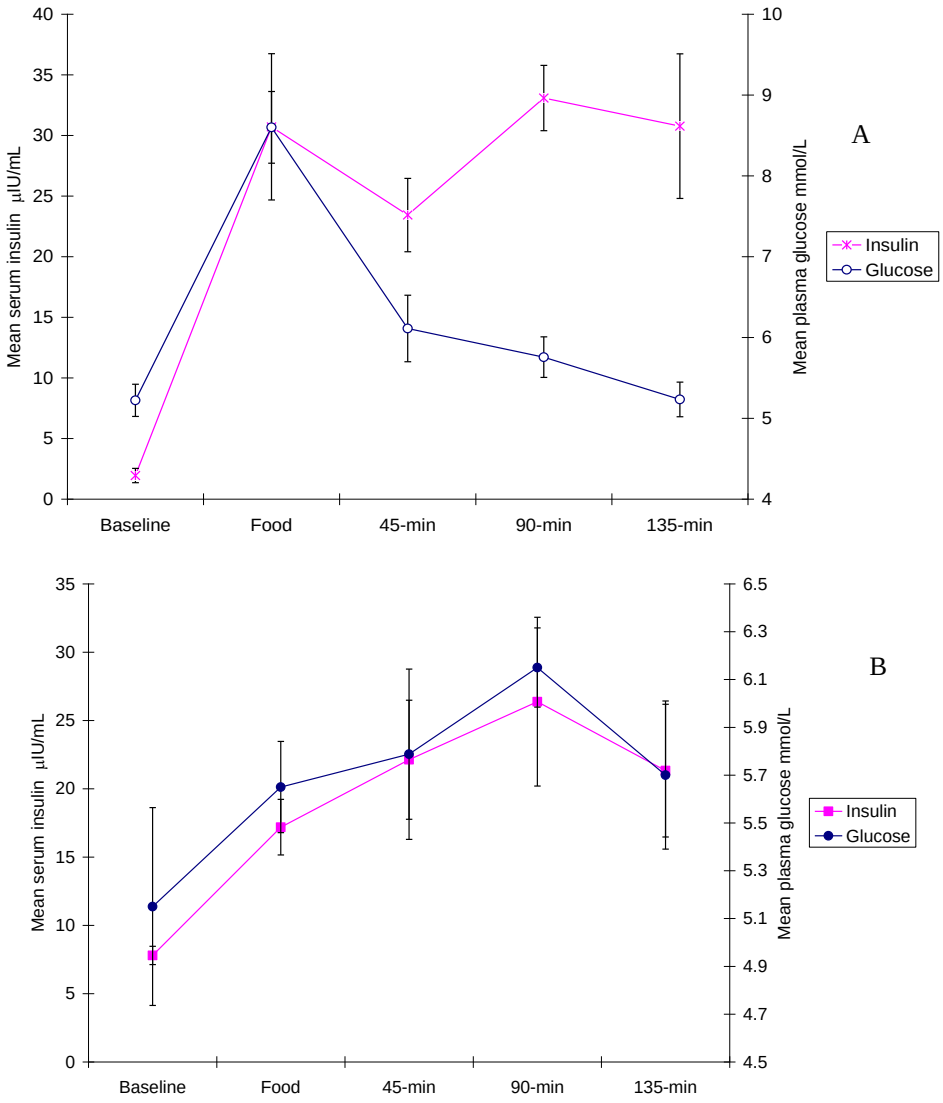
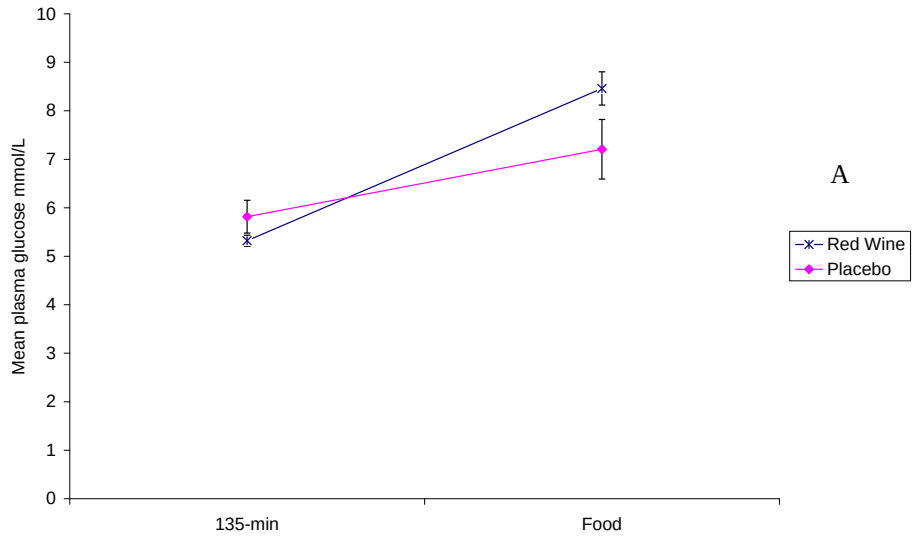


Figure 4: Mean insulin-glucose relationship at Baseline and after Food and during consumption of red wine containing 40g alcohol (A) placebo (B). Data are presented as the mean ± SEM. N = 18.



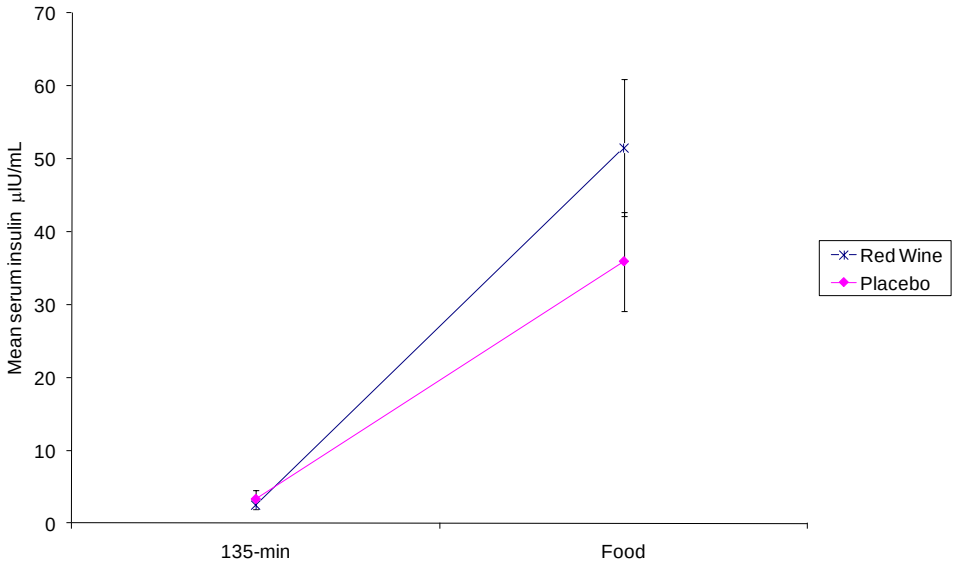


Figure 5: Mean plasma glucose (A) and mean serum insulin (B) concentration after consumption of red wine containing 40g alcohol or placebo (135min) and after Food. Data are presented as the mean ± *SEM*. *N* = 18.

P = .03) for plasma glucose. However, the Trial main effect was not significant (*F* (1, 15) = .77, *P* = .40). Post-hoc analysis revealed the level of plasma glucose was higher after food in the alcohol trial. Similarly, a significant main effect for Time (*F* (1, 16) = 47.96, *P* < .001) and non-significant main effect for Trial (*F* (1, 16) = 1.35, *P* = .26) was noted for serum insulin. However, the Time x Trial interaction was not significant (*F* (1, 16) = 1.95, *P* = .18), suggesting the significant food-induced elevation in serum insulin in the two fasting trials was the same.

Discussion

The results showed that the consumption of red wine prior to food can result in a significant decrease in the level of serum insulin despite preprandial glucose concentration remaining unchanged. However, when food is consumed after ingestion of four standard units of red wine (i.e. 40g alcohol) the consumed alcohol can increase postprandial glucose while the level of serum insulin is similar to that noted with a placebo. Alternatively, the consumption of four standard units of red wine after food does not significantly alter the level of serum insulin despite a significant alcohol-induced lowering of postprandial glucose.

Early work suggests that alcohol can artificially lower the plasma glucose level without the mediation of insulin when consumed prior to food.[1] It is well accepted that alcohol can inhibit gluconeogenesis,[4] and promote the development of clinical Alcohol Hypoglycaemia[5] with the degree of hypoglycaemia significantly related to the nutritional status of the individual when alcohol is consumed.[6,19] However, we did not observe any significant alcohol-induced alteration in preprandial glucose concentration following a six hour fast. Thus, consuming red wine under fasting conditions does not appear to impair glucose production.

The results of the present study support the suggestion that in fasted individuals a moderate-large amount of alcohol does not stimulate insulin secretion [10] and may even lower the rate of insulin synthesis.[11] Furthermore, the fasting serum insulin data provides some support, albeit small, for the suggestion that ingestion of alcohol prior to food may promote symptoms of frank clinical diabetes due to alcohol-induced impairment in insulin secretion.[20] However, while a significant lowering of serum insulin was noted in the fasting trial this appeared to be transient with the level of serum insulin gradually increasing after more than three standard units of red wine (> 30g alcohol) had been consumed by fasted participants.

Food intake by increasing the level of plasma glucose concentration,[2] usually promotes a gradual increase in insulin release until the level of postprandial glucose begins to drop several hours later.[3] We have previously reported that the consumption of white wine alone after a meal can promote a significant decrease in the level of serum insulin.[13] However, the serum insulin data obtained in the feeding trail appears to be at odds with this claim despite both studies being conducted under similar experimental conditions. Thus, the effect of consuming red and white wine alone after a meal on serum insulin concentration is not the same and the data may be highlight that only the ingestion of red wine after food may impair the glucose-insulin feedback mechanism.

The significant alcohol-induced alteration in plasma glucose noted in the red wine feeding trial may have occurred due to red wine (unlike white wine) containing resveratrol, a potent anti-oxidant, with known hypoglycaemic properties.[7] As already mentioned, resveratrol treatment can promote a significant decrease in blood glucose while at the same time promoting a significant increase in plasma insulin.[8] Animal data has suggested that red wine may have a positive effect on lipid production and may protect against the development of metabolic syndrome and its associated cardio-metabolic derangements.[18] However, further

investigation is required before the exact mechanism responsible for the significant alcohol-induced decrease in postprandial glucose that has been reported here can be identified.

The finding that postprandial glucose is significantly decreased if red wine is consumed after a high carbohydrate meal could imply that ingesting red wine may encourage the development of a hypoglycaemic condition. Moreover, if we consider these glucose findings together with the urinalysis data from the red wine trial it would not be unreasonable to suggest that insulin sensitivity remains unaltered (or even increases) during red wine consumption. Urinalysis only detected ketone bodies in the urine of participants who had consumed red wine with ketones present in 67% of participants after < 30 g alcohol and in all but one participant after 40 g alcohol. Therefore, the level of insulin did not appear to be elevated due to the development of an insulin-resistant state. Experimental animal research has suggested that a small-moderate dose of red wine may improve insulin sensitivity[9] and the results of this study are to some extent consistent with these findings. Thus, this study could add further support for the suggestion that small-moderate red wine ingestion may provide some health benefits to diabetics.

Pizza was the food consumed by participants in this study due to previous work demonstrating that ingestion of pizza can result in a significant elevation in plasma glucose over the course of 4-9 h.[21] However, inspection of the raw plasma glucose data in the feeding trial revealed an alcohol-induced trend for a gradual reduction in plasma glucose concentration after the pizza meal. Moreover, the significant alcohol-induced decrease in postprandial glucose noted with red wine in the feeding trial is consistent with the non-significant trend for an alcohol-induced lowering of postprandial glucose reported for white wine under similar experimental conditions.[13] Thus, the results here suggest that ingesting red wine alone after a meal may alter glucose production.

When alcohol ingestion precedes food intake the consumed alcohol can potentiate the insulin stimulating properties of glucose and promote a rapid release of insulin.[14] However, while food intake significantly increased the level of serum insulin in the fasting trial, the ingestion of red wine prior to food did not appear to potentiate the insulin stimulating properties of glucose despite a significant alcohol-induced increase in plasma glucose production when compared to placebo being recorded.

A significant alcohol-induced decrease in the level of fasting serum insulin was noted after ingestion of less than 15g alcohol and the data here does not allow for the identification of the mechanism responsible for the alcohol-induced decrease in serum insulin under fasting conditions. However, by way of explanation we would like to suggest that the data could be implying that it is only when red wine is consumed alone prior to food that a thiamine deficient state occurs. It is well accepted that when alcohol enters the body the ability of cells to maintain the store of thiamine is severely compromised due to alcohol-induced impairment in thiamine absorption.[22] A major consequence of thiamine deficiency is an irregularity in glucose metabolism,[23] which could impair the biosynthesis of insulin.[24] However, more research is required before this can be determined.

The role of histamine in the brain is to enhance the supply of glucose to cells when the organism is presented with a metabolic challenge.[25] Activation of hypothalamic histamine in response to glucoprivation may modulate homeostatic control of energy supply in the brain by activating glycogenolysis during energy depletion. Thus, histamine in response to an energy deficit may play an essential role in glucose utilization through glycogenolytic processes in the hypothalamus.[26]The consumption of red wine can promote histamine release and the increase in histamine synthesis is not a general alcohol-induced effect, but specific to red wine alone.[27] The red wine consumed in this study was relatively immature by red wine standards, being only bottled in 2007. Wines that have been cellared for short periods contain a higher histamine concentration[28] as the histamine found in red wine is produced at the beginning of the aging process.[29] Therefore, it is could be that the histamine content in the red wine consumed during this study was fairly high, which may have promoted glycogenolysis in the hypothalamus. This could have resulted in sufficient energy being produced to meet the needs of the brain leading to a decrease in ketone production and increase in serum insulin in most (but not all) participants. Therefore, the consumption of a small-moderate amount of red wine prior to a meal, unlike white wine,[12] might not create a metabolic challenge for cells located in the CNS.

The results of this study have demonstrated that the prior nutritional status of the individual can significantly influence the effect of red wine on glucose production and utilization. The consumption of a small-moderate amount of red wine alone prior to a meal can significantly decrease serum insulin concentration despite the level of preprandial glucose remaining unchanged. Alternatively, consuming red wine following a meal can significantly decrease the level of postprandial glucose independent of any significant alteration in serum insulin concentration. These findings could suggest that red wine may promote an alteration in the feedback mechanism by which plasma glucose controls the insulin rate. A lowering of plasma glucose in conjunction with a sustained increase in serum insulin may have potential health benefits to some diabetic individuals. However, any alteration in the glucose-insulin feedback relationship is likely to have some influence on cellular energy utilization, which over time could potentially be detrimental to the health of non-diabetic individuals.

References

1. Turner RC, Oakley NW, Nabarro JDN. Changes in plasma insulin during ethanol-induced hypoglycemia. Metabolism 1973; 22: 111-121.
2. Kaplan LA, Pesce AJ. Clinical Chemistry. Theory, Analysis, Correlation. St.Louis: Mosby; 1996.
3. Berg, JM, Tymoczko JL, Stryer, L. Biochemistry. New York: WH Freeman and Company; 2007.

4. Freinkel N, Singer DL, Arky RA, Bleicher SJ, Anderson JB, Silbert CK. Alcohol hypoglycemia: I Carbohydrate metabolism of patients with clinical alcohol hypoglycemia and the experimental reproduction of the syndrome with pure ethanol. J Clin Invest 1963; 42: 1112-1133.
5. Steer P, Marnell R, Werk EE Jr. Clinical alcohol hypoglycaemia and isolated adrenocorticotrophic hormone deficiency. Ann Intern Med 1969; 71: 343-348.
6. Freinkel N, Arky, RA. Effects of alcohol carbohydrate metabolism in man. Psychosomatic Med 1966; 28: 551-563.
7. Su HC, Hung LM, Chen JK. Resveratrol, a red wine antioxidant, possesses an insulin-like effect in streptozotocin-induced diabetic rats. Am J Physiol Endocrinol Metab 2006; 290: 1339-1346.
8. Palsamy P, Subramanian S. Resveratrol, a natural phytoalexin, normalizes hyperglycemia in streptozotocin-nicotinamide induced experimental diabetic rats. Biomed Pharmacother 2008; 62: 598-605.
9. Napoli R, Cozzolino D, Guardasole V, Angelini V, Zarra E, Matarazzo M, Cittadini A, Sacca L, Torella R. Red wine consumption improves insulin resistance but not endothelial function in type 2 diabetic patients. Metabolism 2005; 54: 306-313.
10. Joffe BI, Seftel HC, Van As M. Hormonal responses in ethanol-induced hypoglycaemia. J Stud Alcohol 1975; 36: 550-554.
11. Lazarus R, Sparrow D, Weiss ST. Alcohol intake and insulin levels. The normative aging study. Am J Epidemiol 1997; 145: 909-916.
12. Kokavec A, Crowe SF. Effect of moderate white wine consumption on serum IgA and plasma insulin under fasting conditions. Ann Nutr Metab 2006; 50: 407-412.
13. Kokavec A, Crowe SF. Effect of consuming white wine alone after a meal on plasma insulin and plasma glucose. Alcohol Clin Exp Res 2003; 27: 1718-1723.
14. O'Keefe SJ, Marks V. Lunchtime gin and tonic, a cause of reactive hypoglycaemia. Lancet 1977; 1: 1286-1288.
15. Andersen UO, Jensen G. Decreasing blood pressure: 15 year follow-up in the Copenhagen city longitudinal heart study. Blood Pressure 2004; 13: 176-182.
16. Szmitko, PE, Verma S. Red wine and your heart. Circulation 2005; 111: 10-11.
17. Zern TL, Fernandez ML. Cardioprotective effects of dietary polyphenols. J Nutr 2005; 135: 2291-2294.
18. Liu L, Wang Y, Lam KS, Xu A. Moderate wine consumption in the prevention of metabolic syndrome and its related medical complications. Endocr Metab Immune Disord Drug Targets 2008; 8: 89-98.
19. Freinkel N, Arky RA, Singer DL, Cohen AK, Bleicher SJ, Anderson JB, Silbert CK, Foster AE. Alcohol hypoglycemia. IV: Current concepts of its pathogenesis. Diabetes 1965; 14: 350-361.
20. Yoshitsugu M, Sekiya Y, Ihori M. A chronic alcoholic patient with the development of frank diabetes after heavy drinking and perfect improvement following abstinence from alcohol. Arukoru Kenkyuto Yakubutsu Ison 1992; 27: 276-283.
21. Ahern JA, Gatcomb PM, Held NA, Petit WA, Tamborlane WV. Exaggerated hyperglycemia after a pizza meal in well-controlled diabetes. Diabetes Care 1993; 16: 578-580.
22. Thomson AD, Baker H, Leevy CM. Patterns of 35S-thiamine hydrochloride absorption in the malnourished alcoholic patient. J Lab Clin Med 1970; 76: 34-45.
23. Hakim AM, Carpenter S, Pappius HM. Metabolic and histological reversibility of thiamine deficiency. J Cerebr Blood Flow Metab 1983; 3: 468-477.
24. Rathanaswami P, Sundaresan R. Effects of thiamine deficiency on the biosynthesis of insulin in rats. Biochem Int 1991; 24: 1057-1062.
25. Thomas J, Linssen M, van der Vusse GJ, Hirsch B, Rosen P, Kammermeier H, Fischer Y. Acute stimulation glucose transport by histamine in cardiac microvascular endothelial cells. Biochim Biophys Acta 1995; 1268: 88-96.
26. Sakata T, Tamari Y, Kang M, Yoshimatsu H. 2-deoxy-D-glucose suppresses food intake through activation of the hypothalamus histamine in rats. Am J Physiol 1994; 267: 616-618.
27. Intorre L, Bertini S, Luchetti E, Mengozzi G, Crema F, Soldani G. The effect of ethanol, beer, and wine on histamine release from the dog stomach. Alcohol 1996; 13: 547-551.
28. Landete JM, Ferrer S, Polo L, Pardo I. Biogenic amines in wines from three Spanish regions. J Agri Food Chem 2005; 23: 1119-1124.
29. Jiménez Moreno N, Torrea Goñi D, Ancín Azpilicueta C. Changes in amine concentration during aging of red wine in oak barrels. J Agri Food Chem 2003; 10: 5732-5737.