Effects of Red Wine, Tannic Acid, or Ethanol on Glucose Tolerance in Non–Insulin-Dependent Diabetic Patients and on Starch Digestibility In Vitro

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This study examines the effect of moderate intake of red wine, tannic acid, or ethanol during a meal in type 2 diabetic patients and the influence of tannic acid on the digestibility of starch by α-amylase. Thirty non–insulin-dependent diabetes mellitus (NIDDM) patients aged 53 ± 6 years were studied (in vivo study) 10 of whom received red wine (200 mL), 10 tannic acid (150 mg), and 10 ethanol (16 g) with their midday meal (600 calories, 65 g carbohydrate, 20 g lipid, and 34 g protein). All patients were tested on two occasions (water or placebo *v* wine, alcohol, or tannic acid). The influence of tannic acid (0.25, 0.5, and 1 mg) on the digestibility of starch (100 mg) by α-amylase (100 U) was tested in vitro by sequential incubation at 37°C (in vitro study). The maximum glucose excursion after lunch was 2.6 ± 0.8 mmol/L at 90 minutes (T90) for water and 1.8 ± 0.9 mmol/L at T90 for red wine taken with the meal. The values at T60 and T90 were significant ($P < .01$). Comparable results were obtained with tannic acid alone (nonalcoholic component of wine): the maximum glucose excursion after lunch was 2.76 ± 0.9 mmol/L at T120 for placebo and 1.97 ± 0.9 mmol/L at T90 for tannic acid ($P < .01$); no difference in glucose and insulin excursion was observed between water and ethanol. No interaction between tannic acid and starch was observed in the in vitro experiments, although after preincubation of α-amylase with tannic acid, digestion was slowed in a dose-dependent manner (6.1 ± 1.1 minutes for 0.25 mg tannic acid and 13.1 ± 1.59 minutes for 1 mg tannic acid). Drinking red wine with a meal did not increase blood glucose in NIDDM patients, and led to a slight decrease in some instances. The effect appeared to be mediated by the nonalcoholic compounds in wine such as tannic acid. Ethanol itself had no effect on plasma glucose or insulin levels.

ALCOHOL CONSUMPTION plays an important role in many societies and constitutes a normal part of meals in many countries. It accounts for 4% to 6% of the total energy intake in most Western countries,[1-3] which has implications for the management of patients with diabetes mellitus. It is widely recognized that excessive or long-term intake of large amounts of alcohol has adverse effects (weight gain, hypertriacylglycerolemia, and hepatic cirrhosis). In France, most alcohol is consumed in the form of red wine taken regularly with meals.

The effects of ethanol on carbohydrate metabolism are complex. When administered to individuals whose glycogen stores have been depleted by fasting, ethanol can lead to severe hypoglycemia, primarily by reducing hepatic glucose production via inhibition of gluconeogenesis.[4,5] However, the effects of ethanol in fed individuals are less well understood. Ethanol has been associated with reduced,[6] improved,[7,8] or unchanged[9,10] glucose tolerance. In diabetic patients, alcohol can have both hypoglycemic and hyperglycemic effects. Ethanol enhances glucose-stimulated insulin secretion in healthy individuals and patients with type 2 diabetes[10,11] and reduces gluconeogenesis in the liver.[5,12] On the other hand, alcohol causes peripheral insulin resistance by reducing both glucose oxidation and storage.[13,14] In diabetic patients, hypoglycemic effects[15,16] or no effect on blood glucose[17] have been reported after consumption of alcohol. It should be noted that with binge drinking, dietary adherence is generally poor and it is often unclear whether the hypoglycemia is due to skipping meals or to the direct effect of alcohol.

Investigations on the effects of ethanol on glucose tolerance and insulin secretion have produced conflicting results. In most studies, large quantities of ethanol were administered and the effects on the tolerance to glucose ingested in the morning after an overnight fast were assessed. This is not readily comparable to the normal modes of ingestion of alcoholic beverages, which are themselves complex mixtures of ethanol with other substances such as tannic acid and procianidol. It is thus possible that red wine may have different effects versus the equivalent quantity of pure ethanol. Among the various constituents of red wine, one class represented by phenolic compounds including tannic acid and procianidol has been singled out. Procianidols are widely distributed in plant foods and beverages such as red wine. In the grape, some are free in the cell-soluble fraction, although the majority are bound to the cell wall. Benzoic acid and flavone form the basic structures of tannic acid, which can be divided into different groups including flavones, flavonoids, and anthocyanidins.[18,19] The combination of these molecules constitute the tannins that characterize the various types of wine. They are known to impair protein digestibility due to their ability to bind and precipitate proteins[20-22] and to reduce the activity of digestive enzymes.[23] The inhibition of digestive enzymes affects the digestibility and absorption of dietary constituents such as starch[24,25] and lipids.[26,27]

In view of the clinical and social implications of "normal" ingestion of alcoholic beverages, we investigated the acute effects of red wine, tannic acid, or ethanol on the postprandial excursion in blood glucose levels in type 2 diabetic patients. In a controlled design, we examined the effect of moderate intake of red wine, tannic acid, or ethanol during the midday meal. The effect of tannic acid on α-amylase activity was also measured in vitro.

SUBJECTS AND METHODS

In Vivo Study

Patients. Thirty men with non–insulin-dependent diabetes mellitus (NIDDM) participated in the study. The patients were aged 53 ± 6 years (range, 42 to 63); the body mass index was 27 ± 2 kg/m^2 (range, 24 to 31), and the duration of diabetes was 10 ± 5 years. Patients continued

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taking their usual treatment: three were treated by diet alone, five with biguanides and diet, four with sulfamides and diet, and the other 18 with diet, sulfamides, and biguanides. None of the patients received insulin, and all medication was taken normally, including the day of the study.

The patients were split into three groups of 10: red wine group, tannic acid group, and ethanol group. All participants had evidence of endogenous insulin production with postprandial serum C-peptide levels higher than 2.4 ng/mL. None of the participants had a history of liver disease or alcohol abuse. The patients were in fairly good diabetic control as indicated by a hemoglobin A_{1c} level of 7.9% ± 0.50% (range, 7.2% to 9.1%; reference range, 4% to 6%). None of the patients had any significant chronic microvascular complications (except background retinopathy) were receiving treatment apart from diabetes therapy.

All patients provided informed consent after the nature, purpose, and potential risks of the study were explained. The study procedure was approved by the Ethics Committee of our institution.

Study design. The study was performed in the metabolic ward of our hospital, and the patients reclined in bed throughout the test. The test started at 12:30 PM, but every patient received an identical typical French breakfast at 7:30 AM (70 g bread, 20 g butter, 120 mL milk, and coffee).

Procedure 1: red wine group. Ten patients were tested twice in random order with or without red wine during a test meal eaten in 20 minutes. A minimum of 2 days were allowed between the wine and control tests (water), which were performed under identical conditions. The patients reclined in bed throughout the test, and the same meal was served at 12:30 PM (100 g tomatoes, 80 g beef, 120 g pasta, 100 g green beans, 20 g cheese, 150 g orange, 50 g bread, 5 g sunflower oil, and 5 g butter, totaling 600 calories with 65 g carbohydrate, 20 g lipid, and 34 g protein). Two glasses (200 mL) of wine or water were given during the meal. Red wine was obtained from the Institut National de Recherche Agronomique (INRA), and the water was mineral water.

A catheter for blood sampling was placed in a peripheral vein and kept patent by a slow infusion of normal saline. A heated blanket (55°C) was used for blood arterialization, and blood samples for determination of plasma glucose and insulin were taken 15 minutes before the start of the meal (time = 0 minutes [T0]), 15 minutes after, and at 30-minute intervals over the subsequent 5 hours.

Procedure 2: tannic acid group. Ten other patients were tested twice in random order with or without 150 mg tannic acid or placebo. Tannic acid was obtained from the Centre d'Expérimentation Pharmaceutique (Léognan, France) and was prepared in a 150-mg capsule at our hospital dispensary. The dose of 150 mg was chosen to approximate that supplied by two glasses of INRA red wine as recommended by the Oenologic Institut that usually controls wine tannic acid composition with the Bate-Smith reaction (tannic transformation into cyanidine).[28] An identical procedure to that already described was used: two glasses of water were consumed for both tests, and the capsules were taken during the middle of the meal.

Procedure 3: ethanol group. The last 10 patients were also tested twice in random order with or without ethanol (16 g; equivalent to the ethanol content of 200 mL INRA red wine) diluted in 200 mL water. The patients received a meal and procedure identical to that described in procedure 1.

Analytical procedure. Plasma glucose was determined by a glucose oxidase method using an automated procedure.[29] The serum insulin level was measured by radioimmunoassay (Pharmacia, Uppsala, Sweden).

Results are expressed as the mean ± SD and were subjected to ANOVA. Blood glucose and serum insulin responses are expressed as increments above the fasting levels.

In Vitro Study

The digestibility of starch by α-amylase in the presence or absence of tannin was tested. We also examined the capacity for cross-linking between tannin and starch or α-amylase.

Materials. α-Amylase (REF A0521, 790 U/mg) was purchased from Sigma Laboratories (Paris, France). Tannin was obtained from the Centre d'Expérimentation Pharmaceutique, and cornstarch was obtained from the INRA.

Procedure. α-Amylase was constituted at a concentration of 100 U/mL in saline, starch at 500 mg in 100 mL physiological saline, and tannin at 250 mg/L, pH 6.9. Two sets of experiments were performed (10 replicates per experiment).

In the first set (starch-tannin interaction), starch was preincubated with tannin and then α-amylase was added. Starch (100 mg, 20 mL of the solution) was incubated for 5 minutes at 37°C with 0.25, 0.5, or 1 mg tannin, and then 100 U α-amylase (1 mL of the solution) was added. Three minutes later, starch degradation was evaluated by testing with iodine every minute until total degradation.[30]

In the second set (amylase-tannin interaction), α-amylase was preincubated with tannin and then starch was added. α-Amylase 100 U was incubated with 0.25, 0.50, or 1 mg tannin for 5 minutes at 37°C and then 100 mg starch was added. Starch degradation was evaluated 3 minutes later and then every minute until total degradation.

RESULTS

In Vivo Study

All patients adhered well to the schedule and consumed the entire meal. There were no significant differences in fasting serum levels of glucose or insulin, and no ethanol was detectable in the fasting blood samples. No adverse effects were observed during water, wine, ethanol, or tannic acid tests, and meal tolerance was comparable in all patients. None experienced nausea or vomiting, and there were no reports of flushing during the study.

Procedure 1: wine versus water test. The maximum glucose excursion after the start of the meal was 2.6 ± 0.8 mmol/L at T90 for water and 1.8 ± 0.9 mmol/L at T90 for red wine. Red wine taken during the meal reduced the blood glucose excursion (Fig 1). The differences were statistically significant at T60 and T90 ($P < .01$). No differences were observed for insulin levels between the two tests at any time (Fig 2).

Procedure 2: tannic acid versus placebo test. The maximum glucose excursion was 2.76 ± 0.9 mmol/L at T120 with placebo and 1.97 ± 0.9 mmol/L at T90 with tannic acid (Fig 3). The difference was statistically significant ($P < .01$). No differences were observed for insulin levels between the tannic acid and placebo tests (Fig 4).

Procedure 3: meal taken with or without 24 g ethanol. No difference was observed in the blood glucose excursion or plasma insulin level between the meals with and without ethanol (Table 1).

In Vitro Study: Starch Digestibility

Incubation of tannin with starch before the action of α-amylase had no influence on the digestibility of starch at the concentrations of tannin tested. However, when tannin was incubated with α-amylase before the action on starch, the starch took longer to be completely digested (+6.1 ± 1.1 minute at 0.25 mg, +10.1 ± 1.1 minute at 0.5 mg, and +13.1 ± 1.59

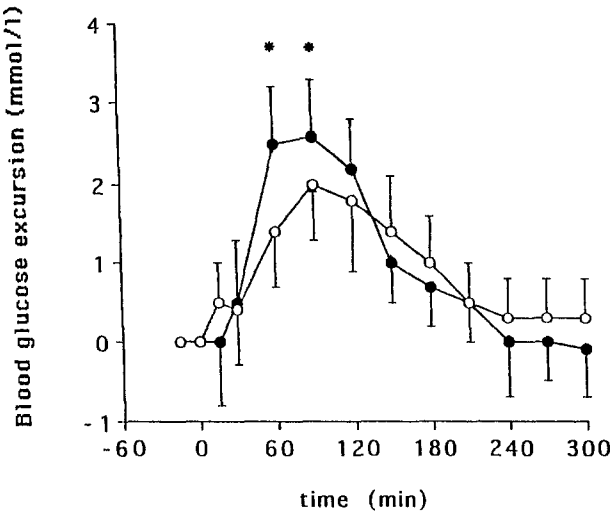

Fig 1. Glucose excursion after lunch with water intake (●) or red wine intake (○). *$P < .01$.

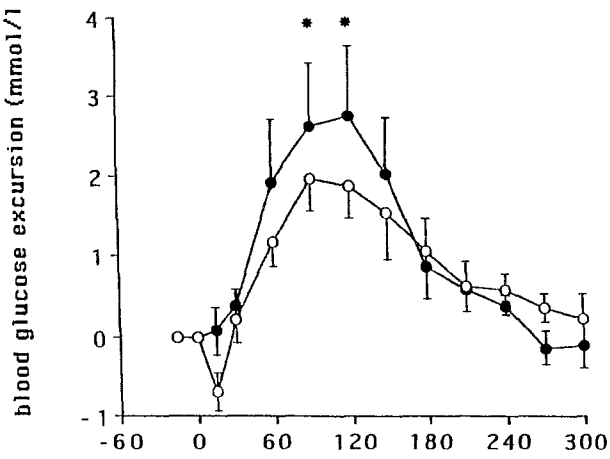

Fig 3. Glucose excursion after lunch with placebo intake (●) or 150 mg tannic acid intake (○). *$P < .01$.

minute at 1 mg tannin). Tannin was thus assumed to interact with α-amylase.

DISCUSSION

Alcohol has been found to induce hypoglycemia in normal and insulin-dependent diabetic patients,[31,32] which is attributed to an inhibition of gluconeogenesis in the liver.[13] This effect is more pronounced when the liver is glycogen-depleted.[31] But in short-term studies, moderate doses have been found either to reduce slightly[7,17] or not to affect[33] the blood glucose response in NIDDM patients. Unequivocal dietary advice therefore cannot be given to such patients. Furthermore, the addition of alcohol to beverages[34] appears to have a different effect versus alcohol taken in the form of wine.[35] It should be kept in mind that drinking red wine is part of the way of life in France, and so needs to be taken into account in dietary recommendations.

The present study was designed to compare the effect of red wine, water, and tannic acid (a nonalcoholic component of red wine) on the postprandial glycemic excursion. The patients received identical food in the different tests, although the total energy load was increased by the added wine or ethanol (120 calories). The amount and quality of food were equivalent to a normal meal, and a realistic amount of wine (200 mL) or ethanol equivalent was supplied.

We found that red wine taken during the meal induced a smaller increase in blood glucose versus the same meal accompanied by an equivalent amount of water, with no statistically significant effect on plasma insulin levels. Comparable results were obtained after prandial consumption of 150 mg tannic acid, one of the nonalcoholic constituents of wine, while ethanol (alcoholic compound) was without effect on the plasma levels of glucose or insulin.

The in vitro study showed no interaction of tannic acid with starch but an interaction of α-amylase activity after preincuba-

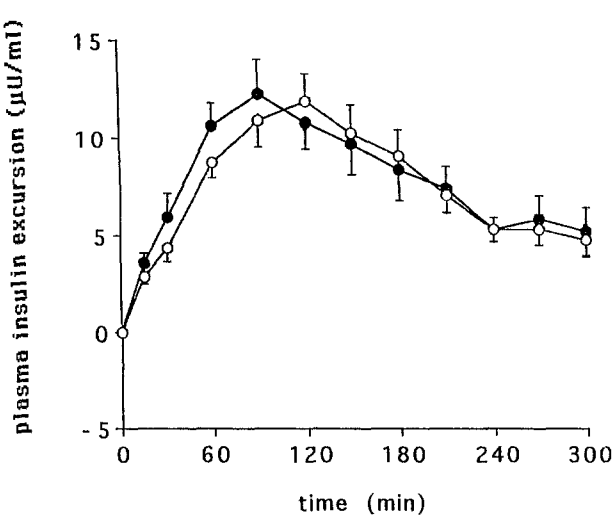

Fig 2. Plasma insulin excursion after lunch with water intake (●) or red wine intake (○).

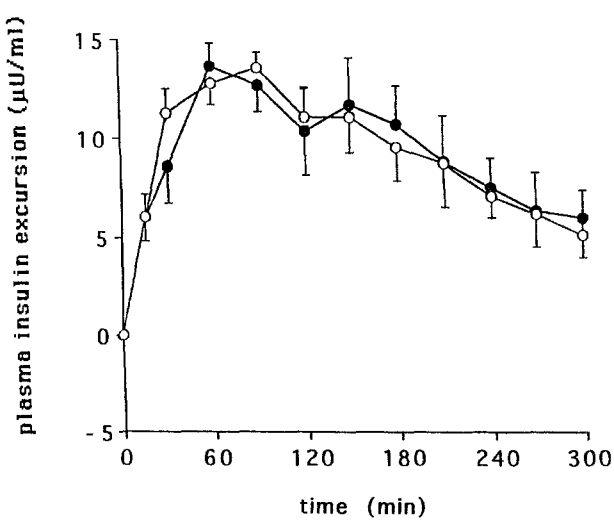

Fig 4. Plasma insulin excursion after lunch with placebo intake (●) or 150 mg tannic acid intake (○).

Table 1. Blood Glucose (mmol/L) and Plasma Insulin (μU/mL) Excursion During a Meal With and Without Ethanol

Parameter	T0	T30	T60	T90	T120	T150	T180	T240	T300
Glucose excursion									
Water	0	1.5 ± 0.4	2.6 ± 0.4	2.7 ± 0.6	2.2 ± 0.5	1.3 ± 0.3	0.9 ± 0.4	0.3 ± 0.3	0.2 ± 0.3
Ethanol	0	1.3 ± 0.3	2.4 ± 0.4	2.8 ± 0.5	2.4 ± 0.6	1.4 ± 0.3	1 ± 0.3	0.2 ± 0.2	0.1 ± 0.3
Insulin excursion									
Water	0	5.9 ± 1.3	10.6 ± 1.2	12.2 ± 1.8	10.8 ± 1.3	9.8 ± 1.6	8.4 ± 1.6	5.3 ± 0.8	5.2 ± 1.3
Ethanol	0	6 ± 1.2	8.6 ± 1.9	12.7 ± 1.3	10.4 ± 2.2	10.7 ± 2	8.9 ± 2.3	6.4 ± 1.9	6 ± 1.4

tion of the enzyme with a tannic mixture. This effect may have been due to degradation or inhibition of the enzyme. It is possible that we used rather high concentrations of tannic acid in the in vitro study, as the intraluminal concentrations are not known in man. However, the concentrations we used were in line with those used in the food industry. The starch did not appear to bind with tannic acid during the in vitro study, but perhaps this is due to the very short incubation (5 minutes).

Many studies have demonstrated the hypoglycemic effect of alcohol intake, but in all cases, the subjects were in the postabsorptive state and large amounts of alcohol were ingested (1 g/kg[32] or 0.75 g/kg intravenously over 30 minutes[14]). Some investigators have suggested an alcohol-augmented, glucose-induced secretion of insulin,[10] although the consensus view is an inhibition of hepatic glucose output.[5,12]

We did not observe any difference for the increase in insulin secretion after ingestion of 200 mL red wine or 16 g ethanol with the meal, although Christiansen et al[34] demonstrated that the addition of 0.25 or 54 mL alcohol/L to 500 mL nonalcoholic beer led to a dose-dependent stimulation of insulin secretion in NIDDM patients.

In our study, a lower postprandial increase in blood glucose was observed after red wine intake, but it should be noted that our patients were not fasted and the amount of alcohol ingested (200 mL red wine = 16 g alcohol) was low. A direct alcohol effect was considered unlikely, and 16 g ethanol was without effect. Interestingly, we found that one of the nonalcoholic constituents of red wine had a comparable effect to that observed with red wine. It was thus thought that the glycemic effect may have been due to the tannic acid fraction of the wine. Tannic acids are plant derivatives, and their effects may be akin to those of fiber.[36] Fibers are known to affect glucose tolerance and interact with digestive enzymes. Our in vitro results indicated an interaction with α-amylase, which has been found by other investigators.[37] Phenolic constituents and tannins (polyphenols) are known to impair the utilization of proteins in animal and human diets, due to their ability to bind with and precipitate protein. Tannins also inhibit digestive enzymes such as trypsin and α-amylase.[23] Deshpande and Salunkhe[37] showed that tannic acid and catechin interact with various starches and increase their resistance to the action of α-amylase.

A normal intake of red wine during a meal is unlikely to induce a bout of hypoglycemia, as the glycemic effect of red wine appears to depend on tannic acid and not on alcohol, and tannic acids are not known to be insulin secretagogues. The difference observed had no clinical significance, and there does not appear to be any scientific justification for avoiding red wine taken in moderation with meals.

The nonalcoholic components of red wine may have other effects. Whitehead et al[38] have shown that ingestion of 300 mL red wine led to an 18% increase in the serum antioxidant capacity after 1 hour, whereas white wine, which has a lower content of nonalcoholic compounds, led to only a 4% increase. Frankel et al[39] showed that the phenolic substances in Californian red wine protected low-density lipoprotein from peroxidation.

In the long term, the energy content of wine must be taken into account and the potential effects on body weight, especially in overweight and obese NIDDM patients, should not be overlooked.

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REFERENCES

1. Bebb HT, Houser HB, Witschi JC, et al: Calorie and nutrient contribution of alcoholic beverages to the usual diets of 155 adults. Am J Clin Nutr 24:1042-1052, 1971

2. Block G, Dresser CM, Haretmann AM, et al: Nutrient sources in the American diet: Quantitative data from the NHANES II Survey. II. Macronutrients and fats. Am J Epidemiol 122:27-40, 1985

3. Thomson M, Fulton M, Elton RA, et al: Alcohol consumption and nutrient intake in middle-aged Scottish men. Am J Clin Nutr 47:139-145, 1988

4. Freinkel N, Singer DL, Arky RA, et al: Alcohol hypoglycemia. I. Carbohydrate metabolism of patients with clinical alcohol hypoglycemia and the experimental reproduction of the syndrome with pure ethanol. J Clin Invest 42:1112-1133, 1963

5. Madison LL, Lochner A, Wulff J: Ethanol-induced hypoglycemia. II. Mechanism of suppression of hepatic gluconeogenesis. Diabetes 16:252-258, 1967

6. Dornhorst A, Ouyang A: Effect of alcohol on glucose tolerance Lancet 2:957-959, 1971

7. McMonagle J, Felig P: Effects of ethanol ingestion on glucose tolerance and insulin secretion in normal and diabetic subjects. Metabolism 24:625-632, 1975

8. Metz R, Berger SQ, Mako M: Potentiation of the plasma insulin response to glucose by prior administration of alcohol. Diabetes 18:517-522, 1969

9. Walsh CH, O'Sullivan DJ: Effect of moderate alcohol intake on control of diabetes. Diabetes 23:440-442, 1974

10. Nikkila EA, Taskinen MR: Ethanol-induced alterations of glucose tolerance, postglucose hypoglycemia and insulin secretion in normal, obese, and diabetic subjects. Diabetes 24:933-943, 1975

11. Metz R, Berger S, Nako M: Potentiation of the plasma insulin response to glucose by prior administration of alcohol. Diabetes 18:517-522, 1868

12. Puhakainen I, Koivisto VA, Yki-Järvinen H: No reduction in total hepatic glucose output by inhibition of gluconeogenesis with ethanol in NIDDM patients. Diabetes 40:1319-1327, 1991

13. Yki-Järvinen H, Koivisto VA, Ylikahri R, et al: Acute effects of

ethanol and acetate on glucose kinetics in normal subjects. Am J Physiol 254:E175-E180, 1988

14. Shelmet JJ, Reichard GA, Skutches CL, et al: Ethanol causes acute inhibition of carbohydrate, fat and protein oxidation and insulin resistance. J Clin Invest 81:1137-1145, 1988

15. Lange J, Arends J, Willms B: Alcohol-induced hypoglycemia: Social drinking after supper increases risk for hypoglycemia next morning. Diabetologia 29:563A, 1986 (abstr)

16. Arky RA, Veverbrantd E, Abramson EA: Irreversible hypoglycemia: A complication of alcohol and insulin. JAMA 206:575-578, 1968

17. Gin H, Morlat P, Ragnaud JM, et al: Short-term effect of red wine (consumed during meals) on insulin requirement and glucose tolerance in diabetic patients. Diabetes Care 5:546-548, 1992

18. Singleton VL: Naturally occurring food toxicants: Phenolic substances of plant origin common in foods. Adv Food Res 27:149-242, 1981

19. Harborne JB: General procedures and measurement of total phenolics, in Harborne JB (ed); Methods in Plant Biochemistry, vol 1. Plant Phenolics. London, UK, Academic, 1972, pp 1-28

20. Eggum BO, Pedersen B, Jacobsen I: The influence of dietary tea, coffee and cocoa on protein and energy utilization of soya-bean meal and barley in rats. Br J Nutr 50:197-205, 1983

21. Aw TL, Swanson BG: Influence of tannin on *Phaseolus vulgaris* protein digestibility and quality. J Food Sci 50.67-71, 1985

22. Oh HI, Hoff JE, Haff LA: Immobilized condensed tannins and their interaction with proteins. J Food Sci 50:1652-1654, 1985

23. Tamir M, Alumot E: Inhibition of digestive enzymes by condensed tannins from green and ripe carobs. J Sci Food Agric 20:199-202, 1969

24. Thompson LU, Yoon JH: Starch digestibility as affected by polyphenols and phytic acid. J Food Sci 49 1228-1229, 1984

25. Björck IM, Nyman ME: In vitro effects of phytic acid and polyphenols on starch digestion and fiber degradation. J Food Sci 52.1588-1594, 1987

26. Nyman ME, Björck IM: In vivo effects of phytic acid and polyphenols on the bioavailability of polysaccharides and other nutrients. J Food Sci 54:1332-1335, 1989

27. Bravo L, Abia R, Martin A, et al: Degradation of polyphenols (catechin and tannic acid) in the rat intestinal tract. Effect on colonic fermentation and faecal output. Br J Nutr 71:933-946, 1994

28. Ribereau-Gayon J, Peynaud E, Sudraud P: Sciences et techniques du vin. Paris, France, Dunod, 1975

29. Bergmeyer HV: Methods of Enzymatic Analysis. New York, NY, Academic, 1974

30. Lecoq R: Manuel d'analyses médicales. Paris, France, Doin, 1967

31. Freinkel N, et al: Alcohol hypoglycemia. IV. Current concepts of pathogenesis. Diabetes 4:350-361, 1971

32. Connor H, Marks V: Alcohol and diabetes. Diabet Med 2:413-416, 1985

33. Walsh CH, O'Sullivan DJ: Effects of moderate alcohol intake on control of diabetes. Diabetes 23:440-442, 1974

34. Christiansen C, et al: Acute effects of graded alcohol intake on glucose and insulin levels in non insulin-dependent diabetic subjects. Eur J Clin Nutr 47:648-652, 1993

35. Koivisto A, et al: Alcohol with a meal has no adverse effects on postprandial glucose homeostasis in diabetic patients. Diabetes Care 16:1612-1614, 1993

36. O'Dea K: Factors influencing carbohydrate digestion: Acute and long-term consequences. Diabetes Nutr Metab 3:251-258, 1990

37. Deshpande SS, Salunkhe DK: Interactions of tannic acid and catechin with legume starches. J Food Sci 4:2080-2082, 1982

38. Whitehead P, Robinson D, Allaway S, et al: Effect of red wine ingestion on the antioxidant capacity of serum. Clin Chem 41:32-35, 1995

39. Frankel EN, Kanmer J, German JB, et al: Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. Lancet 341.454-457, 1993