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# Moderate alcohol intake is associated with decreased risk of insulin resistance among individuals with vitamin D insufficiency

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**Abstract**

**Objective:** To determine whether moderate alcohol intake modifies the association between low vitamin D levels and insulin resistance (IR), we hypothesized that moderate alcohol intake would have a modifying effect on IR in people with low vitamin D levels.

**Methods:** This was a cross-sectional analysis of subjects ≥20 y old without a history of diabetes, coronary heart disease, or stroke in the National Health and Nutrition Examination Survey 2001–2004. Main outcome was IR status measured by homeostasis model assessment for IR (HOMA-IR; ≥ 2.6) and fasting insulin (>12.2 μU/mL) in moderate drinkers compared with non-drinkers by vitamin D levels (deficient ≤20 ng/mL, insufficient 21–32 ng/mL, normal >32 ng/mL).

**Results:** Two thousand seven hundred twenty-one subjects met the inclusion criteria, representing a weighted total of >138 million people. Of these, 34% were vitamin D deficient and 47% insufficient. In adjusted analysis, compared with moderate drinkers with normal vitamin D levels, non-drinkers had no increased risk of IR by HOMA-IR levels (odds ratio [OR] 1.18, 95% confidence interval [CI] 0.61–2.30). Vitamin D–deficient individuals had a higher risk of IR regardless of alcohol consumption (moderate drinkers OR 2.12, 95% CI 1.41–3.19; non-drinkers OR 2.22, 95% CI 1.29–3.83). However, in those with insufficient vitamin D levels, moderate alcohol intake had a modifying effect on the odds of IR, with no difference seen in moderate drinkers (OR 1.29, 95% CI 0.92–1.80) and an increased risk found in non-drinkers (OR 1.82, 95% CI 1.07–3.11). Similar results were seen with fasting insulin.

**Conclusion:** Moderate alcohol consumption appears to have a modifying effect on the risk of IR in individuals with insufficient levels of vitamin D. 

*Keywords:* Alcohol intake; Insulin resistance; Vitamin D; Diabetes; National Health and Nutrition Examination Survey

## Introduction

Insulin resistance (IR) is a marker of early cardiovascular disease (CVD) and relates to impairment of physiologic response of tissues to insulin, leading to disruption of various metabolic processes. Patients with IR are more likely to progress to various CVDs including hypertension and type 2 diabetes [1,2].

Cardiovascular disease and glucose metabolism are also related to vitamin D insufficiency. Fasting serum glucose has been found to be significantly higher in subjects with 25-hydroxyvitamin D levels <80 nmol/L compared with subjects with levels >80 nmol/L [3]. A similar result was found in a study of elderly patients with insufficient vitamin D status [4]. Subjects in the lowest tertile of 25-hydroxyvitamin D had a significantly higher blood glucose increase and a higher blood insulin increase after an oral glucose load compared with subjects in the highest tertile [4]. Analyzing the Third National Health and Nutrition Examination Survey (NHANES III), Scragg et al. [5] found an inverse association of 25-hydroxyvitamin D with fasting glucose in non-Hispanic whites and Mexican Americans, but not in non-Hispanic blacks. The homeostasis model assessment of IR (HOMA-IR) was inversely associated with 25-hydroxyvitamin D in Mexican Americans, but not in non-Hispanic whites ($P = 0.058$) or non-Hispanic blacks ($P = 0.93$).

In terms of alcohol consumption, many epidemiologic studies have found that moderate alcohol intake decreases

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coronary heart disease risk and cardiovascular mortality [6–9]. This has been observed in those at high risk for coronary heart disease and those at lowest risk [10,11]. In the Physicians Health Study, there was a decrease in total and cardiovascular mortality risk in hypertensive men who drank alcohol compared with rare or non-drinkers [12]. King et al. [13] recently showed that middle-aged people free of CVD who started drinking in midlife had lower rates of CVD morbidity in just 4 y.

Research for more than a decade has shown that moderate alcohol consumption has a favorable affect on insulin sensitivity and is protective against IR in various populations. The Bruneck study of 820 healthy men and women 40–79 y of age in Italy showed that low to moderate amounts of alcohol were associated with improved insulin sensitivity as measured by fasting insulin and HOMA [14]. Further, favorable effects have been demonstrated in postmenopausal women [15], overweight women in the Nurses' Health Study II [16], in young adults [17], and in the nationally representative NHANES III [18].

It is unknown whether alcohol intake can offset the detrimental effects of low serum vitamin D levels on IR. The purpose of this study is to determine whether moderate alcohol intake is associated with lower IR in individuals with low vitamin D levels.

## Materials and methods

### *Survey description*

We analyzed data from the 2001–2004 NHANES. The NHANES 2001–2004 is a product of the National Center for Health Statistics that consists of detailed household interviews and physical and laboratory examinations. It is a continuous annual survey consisting of participants from a nationally representative sample of non-institutionalized residents of the United States. Certain groups such as African Americans, Mexican Americans, and older people are oversampled to ensure adequate numbers for subgroup analyses. Samples are weighted so they are representative of the U.S. population. Sampling weights were calculated by taking into account unequal probabilities of selection due to sample design and oversampling and then matched to known population control totals to be representative of the U.S. population. Descriptions of the NHANES design and sampling methods are available from the National Center for Health Statistics [19,20].

### *Subsample population*

The subpopulation analyzed included adult men and women $\geq$20 y of age in NHANES 2001–2004. Participants with fasting insulin and fasting glucose levels were selected. Because we were interested in looking at IR as a prediabetic state and as a risk factor for later disease, we excluded any patients with a history of diabetes because they are known to already have IR. Diabetes was operationalized by patients' self-report of having ever been told by a doctor they have diabetes or are currently taking medications for diabetes. We also excluded participants with a history of heart attack, a history of stroke, and excessive alcohol drinkers. Excessive alcohol drinking was defined as more than two drinks per day for men and more than one drink per day for women. A drink was defined as 12 oz of beer, a 4-oz glass of wine, or 1 oz of liquor.

Insulin resistance was defined by the established marker of a fasting insulin level $>$12.2 mU/L, which was established by correlation with the glycemic/euglycemic clamp method [21], considered the gold standard for determining IR. We also used the HOMA-IR. HOMA-IR is calculated by multiplying fasting serum insulin (milliunits per liter) and fasting plasma glucose (milligrams per deciliter) divided by 405 [22]. Standardized cutoff values for HOMA-IR have been determined at the 75th percentile in only one study [23]. However, this level of $\geq$2.6 corresponds to a fasting insulin level representative of IR established by the glycemic/euglycemic clamp method. We also used ''score 2B'' by McAuley et al. [21] to characterize the insulin sensitivity index as a categorical variable using fasting insulin and fasting triacylglycerol levels. A score 2B $>$1 corresponded to a 73% chance of IR.

### *Vitamin D*

The Diasorin (Stillwater, MN, USA) 25-hydroxyvitamin D assay consists of a two-step procedure. The first step involves extraction of 25-hydroxyvitamin D and other hydroxylated metabolites from serum with acetonitrile. After extraction, the treated sample is assayed by using an equilibrium radioimmunoassay procedure. The radioimmunoassay method is based on an antibody with specificity to 25-hydroxyvitamin D. Vitamin D deficiency was characterized as $<$20 ng/mL [24], insufficiency as 20–32 ng/mL [25], and normal as $>$32 ng/mL.

### *Alcohol consumption*

Participants were also classified as non-drinkers or moderate drinkers within vitamin D categories. Moderate drinking was defined as no more than two drinks per day for men and no more than one drink per day for women. A drink was defined as 355 mL of beer, a 118-mL glass of wine, or 30 mL of liquor.

### *Covariates*

Several potential confounding variables were assessed. The covariates included were age, gender, race/ethnicity, smoking status, body mass index (BMI), and physical activity. For race/ethnicity, participants were categorized into non-Hispanic white, non-Hispanic black, and Hispanic plus other race including multiracial based on patient self-report. Smoking status was categorized as current smoker or not.

Regular physical activity was defined as moderate or vigorous activity in the previous 30 d versus sedentary based on participant self-report. Age in years and BMI in kilograms per meter squared were each categorized for univariate analysis and included as continuous variables in regression modeling. BMI was calculated in NHANES from the measured weight and height of the participant.

*Data analysis*

Descriptive statistics and logistic regression modeling of the sample population were conducted using SUDAAN 9.0.1 (Research Triangle, NC, USA) to account for the complex sampling methods of the NHANES data. Weighted population estimates are given for covariates and vitamin D/alcohol consumption categories. Multivariable logistic regression models predicting odds of IR, as defined by HOMA-IR and fasting insulin, were also performed controlling for gender, race/ethnicity, smoking status, and physical activity as categorical variables and age and BMI as continuous variables. Results for all regression models are presented as odds ratios (OR) with 95% confidence intervals (CI), with vitamin D >32 ng/mL and moderate alcohol drinking as the referent category.

## Results

Characteristics of the sample are presented in Table 1. There were 2721 individuals (unweighted) in the sample representing >138 million people in the United States. Of those, 18.7% had normal vitamin D levels, 47.3% insufficient levels, and 34% deficient levels.

In unadjusted analysis, a higher percentage of individuals with low vitamin D levels had IR by HOMA-IR (Table 2) and fasting insulin (Table 3) measurements compared with those with normal vitamin D levels. For example, 48.9% of non-drinkers and 43.7% of moderate drinkers with vitamin D levels ≤20 mg/mL (deficient category) had elevated HOMA-IR levels compared with 27.9% of non-drinkers and 21.2% of moderate drinkers with normal vitamin D levels (Table 2; $P < 0.01$), with those with insufficient levels of vitamin D (>20–32 ng/mL) falling in between. Similar results were shown with fasting insulin (Table 3).

In adjusted analysis assessing the impact of moderate alcohol consumption on IR markers in individuals in the three vitamin D categories, we found that those with deficient vitamin D levels had higher odds of IR by HOMA-IR regardless of alcohol consumption, with non-drinkers having an OR of 2.22 (95% CI 1.29–3.83) and moderate drinkers an OR of 2.12 (95% CI 1.41–3.19) compared with the referent group of moderate alcohol intake and normal vitamin D levels (Table 4). Similarly there was no difference by alcohol consumption for risk of IR for those with normal vitamin D levels (non-drinkers OR 1.18, 95% CI 0.61–2.30).

In the vitamin D insufficient group (>20–32 ng/mL), however, moderate alcohol consumption had a modifying effect. Non-drinkers had a higher odds of IR by HOMA-IR (OR 1.82, 95% CI 1.07–3.11), whereas the odds of IR in moderate drinkers was statically no different than the referent group (OR 1.29, 95% CI 0.92–1.80). Similar results were seen for moderate drinkers with insufficient vitamin D levels for fasting insulin in adjusted analysis (Table 5). The score 2B insulin sensitivity index [21] (using insulin and triacylglycerols) showed the same trend as HOMA-IR and fasting

Table 1
Demographics of sample

| | |
|---|---|
| Unweighted (*n*) | 2721 |
| Weighted (*n*) | 138 020 372 |
| Age (%) | |
| 20–39 y | 45.95 |
| 40–64 y | 42.57 |
| ≥ 65 y | 11.48 |
| Gender (%) | |
| Male | 48.96 |
| Female | 51.04 |
| Race/ethnicity (%) | |
| Non-Hispanic white | 74.31 |
| Non-Hispanic black | 10.05 |
| Hispanic and other race | 15.64 |
| Smoking (%) | |
| Non-smoker | 77.34 |
| Current smoker | 22.66 |
| Body mass index (%) | |
| < 25 kg/m$^2$ | 35.17 |
| 25–29.9 kg/m$^2$ | 35.69 |
| ≥ 30 kg/m$^2$ | 29.14 |
| Physical activity (%) | |
| None | 31.65 |
| Moderate | 30.40 |
| Vigorous | 37.95 |
| Vitamin D and alcohol consumption (%) | |
| Vitamin D ≤20 ng/mL | |
| Non-drinker | 9.73 |
| Moderate drinker | 24.27 |
| Vitamin D >20–32 ng/mL | |
| Non-drinker | 11.28 |
| Moderate drinker | 36.00 |
| Vitamin D >32 ng/mL | |
| Non-drinker | 3.56 |
| Moderate drinker | 15.16 |

Table 2
Relation of elevated HOMA to vitamin D and alcohol consumption

| | Total weighted (*n*) | HOMA ≥2.6 (%) | *P* |
|---|---|---|---|
| Vitamin D ≤20 ng/mL | | | |
| Non-drinker | 13 427 870 | 48.88 | <0.01 |
| Moderate drinker | 33 494 259 | 43.69 | |
| Vitamin D >20–32 ng/mL | | | |
| Non-drinker | 15 566 032 | 37.69 | |
| Moderate drinker | 49 693 155 | 30.42 | |
| Vitamin D >32 ng/mL | | | |
| Non-drinker | 4 916 213 | 27.88* | |
| Moderate drinker | 20 922 842 | 21.20 | |

HOMA, homeostasis model assessment
* Unreliable estimate (unweighted $n < 30$).

Table 3
Relation of elevated insulin to vitamin D and alcohol consumption

| | Total weighted (*n*) | Insulin >12.2 μU/mL (%) | *P* |
|---|---|---|---|
| Vitamin D ≤20 ng/mL | | | |
| Non-drinker | 13 427 870 | 42.61 | <0.01 |
| Moderate drinker | 33 494 259 | 38.09 | |
| Vitamin D >20–32 ng/mL | | | |
| Non-drinker | 15 566 032 | 31.08 | |
| Moderate drinker | 49 693 155 | 22.18 | |
| Vitamin D >32 ng/mL | | | |
| Non-drinker | 4 916 213 | 22.12* | |
| Moderate drinker | 20 922 842 | 15.26 | |

* Unreliable estimate (unweighted $n < 30$).

insulin. Non-drinkers in the vitamin insufficient group (>20–32 ng/mL) had an OR of 2.22 (95% CI 1.00–4.91), whereas moderate drinkers were not significantly different from the referent group (OR 1.23, 95% CI 0.65–2.31).

## Discussion

In this cross-sectional study, we demonstrated that moderate alcohol intake is associated with improved insulin sensitivity in people with vitamin D insufficiency but not in people with vitamin D deficiency or normal vitamin D levels. There were no differences by gender, and the effects were independent of age, race/ethnicity, smoking status, BMI, and physical activity.

Previous research has shown that low vitamin D levels increase the risk of IR and diabetes. The biochemical processes underlying this are complex. Studies have shown that vitamin D has an effect on β-cells and insulin production [26], including a positive correlation between serum vitamin D levels and insulin sensitivity [26,27]. In Chiu et al. [26], vitamin D levels <20 ng/mL showed a higher risk of IR and other components of metabolic syndrome. Further, favorable effects of moderate alcohol consumption on IR and markers of glucose metabolism have been demonstrated in postmenopausal women [15], overweight women in the Nurses' Health Study II [16], ing young adults [17], and in the nationally representative NHANES III [18]. In addition, one study showed that diabetics given muscadine grape wine compared with those given muscadine juice had better glycemic control after 28 days [28].

Table 4
Logistic regression describing relation of elevated HOMA (≥2.6) to vitamin D and alcohol consumption*

| | Odds Ratio | 95% CI |
|---|---|---|
| Vitamin D ≤20 ng/mL | | |
| Non-drinker | 2.22 | 1.29–3.83 |
| Moderate drinker | 2.12 | 1.41–3.19 |
| Vitamin D >20–32 ng/mL | | |
| Non-drinker | 1.82 | 1.07–3.11 |
| Moderate drinker | 1.29 | 0.92–1.80 |
| Vitamin D >32 ng/mL | | |
| Non-drinker | 1.18 | 0.61–2.30 |
| Moderate drinker | 1.00 | — |

CI, confidence interval; HOMA, homeostasis model assessment

* Adjusted for age, gender, race/ethnicity, smoking status, body mass index, and physical activity.

Table 5
Logistic regression describing relation of elevated insulin (>12.2 μU/mL) to vitamin D and alcohol consumption*

| | Odds Ratio | 95% CI |
|---|---|---|
| Vitamin D ≤20 ng/mL | | |
| Non-drinker | 2.44 | 1.15–5.19 |
| Moderate drinker | 2.44 | 1.43–4.14 |
| Vitamin D >20–32 ng/mL | | |
| Non-drinker | 1.99 | 1.02–3.90 |
| Moderate drinker | 1.21 | 0.71–2.07 |
| Vitamin D >32 ng/mL | | |
| Non-drinker | 1.37 | 0.71–2.64 |
| Moderate drinker | 1.00 | — |

CI, confidence interval

* Adjusted for age, gender, race/ethnicity, smoking status, body mass index, and physical activity.

Interestingly, studies on the effects of vitamin D supplementation (with calcium) on blood glucose and development of diabetes have not shown as favorable results [29,30]. It is low serum vitamin D levels and not vitamin D supplementation that has been linked to various outcomes including higher mortality [31]. For this reason we chose to focus on serum vitamin D levels.

One possible explanations for the findings observed in this study is that, in the deficient range of serum vitamin D, β-cell dysfunction and decrease in insulin sensitivity are profound enough that the beneficial effects of alcohol on insulin profiles are biochemically overwhelmed. Conversely, in the context of normal vitamin D levels, no further effect of alcohol may be seen because insulin sensitivity is maximized. Only the intermediate state, when vitamin D is insufficient but still present, are the β-cells and insulin sensitivity machinery in a ''vulnerable'' condition to be stimulated by moderate alcohol consumption. Evidence from animal studies point in this direction, demonstrating that vitamin D deficiency impairs insulin secretion [32,33]. Further, in vivo animal studies have shown improved glucose clearance and insulin secretion with restored vitamin D levels [34,35] and improved conversion of proinsulin to insulin [36].

Limitations include the cross-sectional design of the study, which only allows for establishment of associations. Further studies will need to be performed longitudinally to establish if alcohol can slow or prevent the development of IR in those with vitamin D insufficiency. Alcohol consumption was measured by self-report. However, this is the method necessarily used in most studies of alcohol use. The alcohol cutoff levels used in this study are based on recommended daily intake amounts for men and women. Vitamin D levels are not fully established, and there is no consensus on the level of serum vitamin D that denotes insufficiency or deficiency. We used cutoff levels of vitamin D that have been commonly used in other studies [24,25].

It has been shown from the NHANES III cohort that serum vitamin D levels vary depending on time of year measured [37]. Within the publicly available dataset used for this study (2001–2004), information regarding time of year and latitude was not available from the data. Overall, we feel this would not change our finding that non-drinkers with insufficient vitamin D levels have higher odds of IR. We acknowledge that we did not use the gold standard euglycemic clamp method for determining IR. This is a time-consuming and invasive test and is not routinely performed in the NHANES examinations. Fasting insulin and HOMA-IR as markers of IR correlate well with the clamp method [21,23]. Variability may exist between these measurements and the gold standard, but we found similar results using three different measurements of IR and thus feel confident in our findings.

## Conclusion

Moderate alcohol moderates the association between vitamin D and insulin sensitivity when individuals are vitamin D insufficient, but not when vitamin D levels are normal or deficient. Future prospective studies will be able to confirm the association and provide insight into the complex interaction between vitamin D and insulin sensitivity.

## References

[1] Facchini FS, Hua N, Abbasi F, Reaven GM. Insulin resistance as a predictor of age-related diseases. J Clin Endocrinol Metab 2001;86:3574–8.
[2] Wilson WF, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005;112:S3066–72.
[3] Need AG, O'Loughlin PD, Horowitz M, Nordin BEC. Relationship between fasting serum glucose, age, body mass index and serum 25 hydroxyvitamin D in postmenopausal women. Clin Endocrinol 200;62:738–41.
[4] Baynes KC, Boucher BJ, Feskens EJ, Kromhout D. Vitamin D, glucose tolerance and insulinaemia in elderly men. Diabetologia 1997;40:344–7.
[5] Scragg R, Sowers MF, Colin B. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care 2004;27:2813–8.
[6] Fuchs FD, Chambless LE, Folsom AR, Eigenbrodt ML, Duncan BB, Gilbert A, Szklo M. Association between alcoholic beverage consumption and incidence of coronary heart disease in whites and blacks: the Atherosclerosis Risk in Communities Study. Am J Epidemiol 2004;160:466–74.
[7] Camargo CA Jr, Stampfer MJ, Glynn RJ, Grodstein F, Gaziano JM, Manson JE, et al. Moderate alcohol consumption and risk for angina pectoris or myocardial infarction in U.S. male physicians. Ann Intern Med 1997;126:372–5.
[8] Rehm JT, Bondy SJ, Sempos CT, Vuong CV. Alcohol consumption and coronary heart disease morbidity and mortality. Am J Epidemiol 1997;146:495–501.
[9] Tolstrup J, Jensen MK, Tjonneland A, Overad K, Mukamul KJ, Gronback M. Prospective study of alcohol drinking patterns and coronary heart disease in women and men. BMJ 2006;332:1244–8.
[10] Femia R, Natali A, L'Abbate A, Ferrannini E. Coronary atherosclerosis and alcohol consumption: angiographic and mortality data. Arterioscler Thromb Vasc Biol 2006;26:1607–12.
[11] Mukamul KJ, Chiuve SE, Rimm EB. Alcohol consumption and risk for coronary heart disease in men with healthy lifestyles. Arch Intern Med 2006;166:2145–50.
[12] Malinski MK, Sesso HD, Lopez-Jimenez F, Burning GE, Gaziano JM. Alcohol consumption and cardiovascular disease mortality in hypertensive men. Arch Intern Med 2004;164:623–8.
[13] King DE, Mainous AG III, Geesey ME. Adopting moderate alcohol consumption in middle age: subsequent cardiovascular events. Am J Med 2008;121:201–6.
[14] Kiechl S, Willeit J, Poewe W, Egger G, Oberhollenzer F, Muggeo M, Bonora E. Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck Study). BMJ 1996;313:1040–4.
[15] Davies MJ, Baer DJ, Judd JT, Brown ED, Campbell WS, Taylor PR. Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women. JAMA 2002;287:2559–62.
[16] Kroenke CH, Chu NF, Rifai N, Spiegelman D, Hankinson SE, Manson JE, Rimm EB. A Cross sectional study of alcohol consumption patterns and biologic markers of glycemic control among 459 women. Diabetes Care 2003;26:1971–8.
[17] Flanagan DE, Moore VM, Godsland IF, Cockington RA, Robinson JS, Phillips DI. Alcohol consumption and insulin resistance in young adults. Eur J Clin Invest 2000;30:297–301.
[18] Freiberg MS, Cabral HJ, Heeren TC, Vasan RS, Ellison RC. Alcohol consumption and the prevalence of the metabolic syndrome in the U.S. A cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey. Diabetes Care 2004;27:2954–9.
[19] National Center for Health Statistics. NHANES 1999–2000 data files. Available at: http://www.cdc.gov/nchs/about/major/nhanes/currentnhanes.htm. Accessed May 13, 2009.
[20] National Center for Health Statistics. Analytic guidelines. June 2004. Available at: http://www.cdc.gov/nchs/data/nhanes/nhanes_general_guidelines_june_04.pdf. Accessed May 13, 2009.
[21] McAuley KA, Williams SM, Mann JI, Walker RJ, Lewis-Barned NJ, Temple LA, Duncan AW. Diagnosing insulin resistance in the general population. Diabetes Care 2001;24:460–4.
[22] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin. Diabetologia 1985;28:412–9.
[23] Ascaso JF, Pardo S, Real JT, Lorente RI, Priego A, Carmena R. Diagnosing insulin resistance by simple quantitative methods in subjects with normal glucose metabolism. Diabetes Care 2003;26:3320–5.
[24] Levis S, Gomez A, Jiminez C, Veras L, Ma F, Lai B, et al. Vitamin D deficiency and seasonal variation in an adult South Florida population. J Clin Endocrinol Metab 2005;90:1557–62.
[25] Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: Implications for establishing a new effective dietary intake recommendation for vitamin D. J Nutr 2005;135:317–22.
[26] Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr 2004;79:820–5.
[27] Lind L, Heanni A, Lithell H, Hvarfner A, Seorensen OH, Ljunghall S. Vitamin D is related to blood pressure and other cardiovascular risk factors in middle-aged men. Am J Hypertens 1995;8:894–901.
[28] Banini AE, Boyd LC, Allen JC, Allen HG, Sauls DL. Muscadine grape products intake, diet and blood constituents of non-diabetic and type 2 diabetic subjects. Nutrition 2006;22:1137–45.
[29] Pittas AG, Harris SS, Stark PC, Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. Diabetes Care 2007;30:980–6.
[30] De Boer IH, Tinker LF, Connelly S, Curb D, Howard BV, Kestenbaum B, et al. Calcium plus vitamin D supplementation and the risk of incident diabetes in the Women's Health Initiative. Diabetes Care 2008;31:701–7.
[31] Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med 2008;168:1629–37.

[32] Chertow BS, Sivitz WI, Baranetsky NG, Clark SA, Waite A, DeLuca HF. Cellular mechanisms of insulin release: the effects of vitamin D deficiency and repletion on rat insulin secretion. Endocrinology 1983;113:1511–8.

[33] Norman AW, Frankel JB, Heldt AM, Grodsky GM. Vitamin D deficiency inhibits pancreatic secretion of insulin. Science 1980; 209:823–5.

[34] Cade C, Norman AW. Vitamin D3 improves impaired glucose tolerance and insulin secretion in the vitamin D deficient rat in vivo. Endocrinology 1986;119:84–90.

[35] Ayesha I, Bala TS, Reddy CV, Raghjuramulu N. Vitamin D deficiency reduces insulin secretion and turnover in rats. Diabetes Nutr Metab 2001;14:78–84.

[36] Bourlon PM, Faure-Dussert A, Billaudel B. The de novo synthesis of numerous proteins is decreased during vitamin D3 deficiency and is gradually restored by 1,25-dihydroxyvitamin D3 repletion in the islets of Langerhans of rats. J Endocrinol 1999;162:101–9.

[37] Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. Bone 2002;30:771–7.