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Association between composite dietary antioxidant index and erectile dysfunction: a cross-sectional study from NHANES

Xuexue Hao[1†], Xiangyu Chen[1†], Congzhe Ren[1†], Yang Pan[1], Zhunan Xu[1], Qihua Wang[1] and Xiaoqiang Liu[1*]

Abstract

Background Individual antioxidants may not fully capture the comprehensive antioxidant intake from an individual's diet. This study utilizes the Complex Dietary Antioxidant Index (CDAI) to evaluate the combined effects of various dietary antioxidants in the diet. The goal is to investigate the relationship between CDAI and the incidence of erectile dysfunction (ED), offering insights for dietary guidelines and intervention strategies aimed at mitigating the burden of ED.

Methods This cross-sectional study utilized data from the National Health and Nutrition Examination Survey (NHANES) database in the years 2001–2004. We employed a weighted multivariate logistic regression model to validate the relationship between CDAI and ED. Subgroup analyses were conducted to explore the correlation between CDAI and ED across different subgroups. Additionally, we used propensity score matching (PSM) to adjust for several key confounding variables, enhancing the robustness of the results.

Results In the fully adjusted multivariate logistic regression model for confounding variables, CDAI is negatively correlated with the risk of ED (OR = 0.95, 95% CI: 0.92–0.99, $P = 0.005$). When CDAI is transformed into a categorical variable based on quartiles, Q3 (OR = 0.73, 95% CI: 0.53–0.99, $P = 0.040$) and Q4 (OR = 0.70, 95% CI: 0.51–0.96, $P = 0.026$) show a negative correlation with the risk of ED. Subgroup analysis reveals no significant interaction. After adjusting for major confounding variables through PSM, the association between CDAI and reduced risk of ED remains significant.

Conclusion In our study cohort, there is an association between CDAI and a reduced risk of ED, and further research is needed to validate and refine this conclusion.

Keywords Erectile dysfunction, CDAI, Dietary recall, NHANES, Cross-sectional study

†Xuexue Hao, Xiangyu Chen and Congzhe Ren contributed equally to this work.

*Correspondence:
Xiaoqiang Liu
xiaoqiangliu1@163.com
[1]Department of Urology, Tianjin Medical University General Hospital, 154 Anshan Road, Heping District, Tianjin 300052, China

Introduction

In accordance with the guidelines outlined by the American Urological Association (AUA), erectile dysfunction (ED) is defined as the incapacity to attain or sustain an erection of adequate magnitude to fulfill sexual intercourse, attributed to impairment during the sexual arousal phase [1]. The prevalence of ED is commonly higher among elderly males. Nevertheless, research demonstrates that 25% of men under the age of 40 opt for medical intervention due to ED, and 22.1% exhibit lower scores on the Sexual Health Inventory for Men (SHIM) [2]. This indicates that ED may represent a widespread health issue among the male population. ED is regarded as a harbinger of various diseases, as studies unveil its intimate connection with numerous conditions, including cardiovascular diseases [3], chronic liver disease [4], and cirrhosis [5]. This phenomenon may be ascribed to the shared risk factors, such as smoking, alcohol consumption, obesity, and elevated cholesterol levels [6], with the occurrence of ED happening at an earlier stage. Therefore, as a multifaceted condition influenced by various physiological and lifestyle factors, comprehending the modifiable determinants of ED is crucial for public health.

Oxidative stress is a recognized factor contributing to vascular dysfunction and the pathophysiology of ED, Research indicates that oxidative stress increases the production of reactive oxygen species (ROS), leading to endothelial dysfunction, which reduces the availability of nitric oxide and disrupts vascular homeostasis. This results in decreased blood flow to the tissues and an inability to achieve or maintain an erection, ultimately leading to ED [7]. Dietary antioxidants have been confirmed to play a role in various diseases [8, 9]. The association between specific antioxidants and ED has been subject to research, including the examination of vitamin D [10], zinc [11], and lycopene found in tomatoes [12]. Nevertheless, these singular antioxidants may fall short in capturing the comprehensive antioxidant intake from an individual's diet, given issues related to differences in bioavailability and absorption. Furthermore, an elevated intake of individual antioxidants may potentially transition into pro-oxidants [9, 13], which could have unfavorable implications for health. The Complex Dietary Antioxidant Index (CDAI) serves as a method for gauging the antioxidant capacity of one's diet, Unlike indices such as Total Antioxidant Capacity (TAC), the CDAI is derived from food frequency questionnaires or dietary recalls, accounting for both the types and quantities of antioxidant-rich foods consumed. CDAI emphasizes the relationship between dietary habits and health outcomes, whereas TAC, despite its informative nature, may not fully capture the dietary context and can be influenced by factors beyond food intake, such as individual metabolism and environmental influences [14]. Previous studies have found that higher CDAI scores are associated with a reduced risk of kidney stone formation and that there is a negative correlation between CDAI and related cardiovascular diseases [15, 16]. This index delivers a comprehensive score that encapsulates a spectrum of dietary antioxidants, encompassing vitamin A, C, E, zinc, selenium, and carotenoids [17, 18]. The use of the CDAI offers a more holistic viewpoint in assessing the collective impact of diverse dietary antioxidants within one's diet. Gaining insights into the relationship between the overall antioxidant effects in the diet and erectile function is of paramount importance for devising efficacious intervention strategies and nutritional guidance.

The principal objective of this research is to explore the correlation between the CDAI and the incidence of ED. The intention is to offer insights for dietary guidelines and intervention strategies aimed at mitigating the burden of ED.

Materials and methods

Data source and study population

This cross-sectional study utilized data from the National Health and Nutrition Examination Survey (NHANES) database. The survey is part of a program conducted by the National Center for Health Statistics (NCHS), which is affiliated with the Centers for Disease Control and Prevention (CDC) in the United States. NHANES employs a two-year survey cycle with a complex, multi-stage probability sampling design to select participants from various demographic and socioeconomic groups. The collected data include demographic information, dietary records, physical examinations, laboratory data, and various survey questionnaires. The incorporation of this comprehensive dataset aims to evaluate the health and nutritional status of adults or children.

The participant selection process for the study is illustrated in Fig. 1. The study population consisted of 10,301 adult males who participated in NHANES during the 2001–2004 period. Participants with missing ED data or incomplete dietary information were excluded from the analysis. The final study cohort comprised 3,807 participants, including 1,109 assessed with ED and 2,698 without ED. To better control for confounding factors and derive more robust conclusions, a 1:1 propensity score matching (PSM) was subsequently conducted, and a secondary analysis was performed on the matched 1,808 participants.

Assessment of CDAI

The CDAI is a comprehensive score encompassing various dietary antioxidants, including vitamin A, C, E, carotenoids, selenium, and zinc [17, 19]. The average daily intake data for each dietary antioxidant are derived

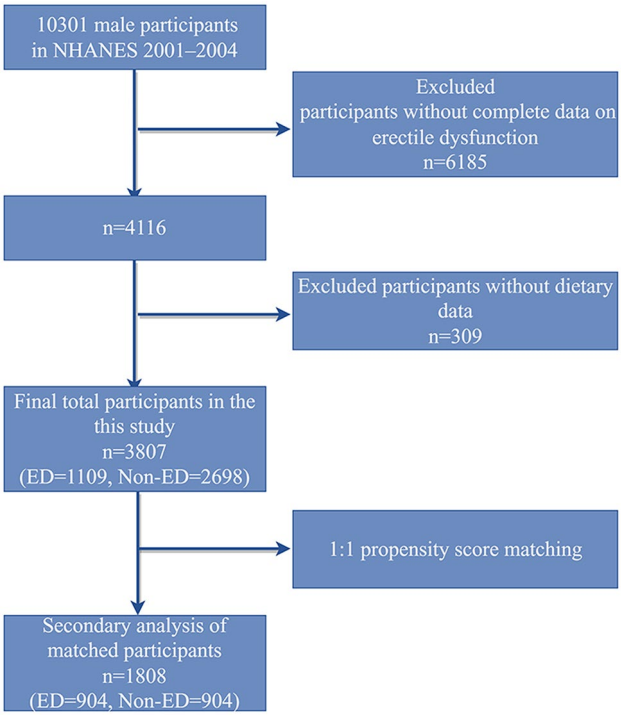

Fig. 1 The flowchart for participant screening in this study

from the dietary interview records of the first and second days in the NHANES database. CDAI is calculated using the measurement method mentioned by Wright et al. [20], which involves subtracting mean intake of the study population from each individual's intake of each dietary antioxidant the and then dividing the result by the population's standard deviation. The sum of these values provides the CDAI, as expressed in the following formula:

$$CDAI = \sum_{i=1}^{n=6} \frac{Individual\ Intake - Mean}{SD}$$

Assessment of ED

We conducted an assessment of ED using NHANES surveys for male participants aged 20 and above. These participants were asked about their capability to achieve and maintain an erection sufficient for satisfactory intercourse. Drawing on recent research [21, 22], responses of "always or almost always able to" or "usually able to" were defined as non-ED participants, whereas responses of "sometimes able to" or "never able to" were categorized as ED participants.

Covariates

In our study, we included various covariates to address potential confounding factors. These encompass age, race, educational level, marital status, economic status, smoking, alcohol consumption, body mass index (BMI), physical activity, hypertension, diabetes, hyperlipidemia, history of cardiovascular disease, history of prostate disease, and overall health status. Based on the smoking and alcohol consumption questionnaires administered to the participants, individuals who have smoked at least 100 cigarettes in their lifetime are defined as smokers, otherwise as non-smokers. Smoking status is further categorized into former smokers and current smokers based on current smoking habits. Participants who have consumed at least 12 alcoholic beverages in their lifetime are defined as drinkers, and daily alcohol consumption is classified as moderate (up to two drinks) or heavy (more than two drinks). Low physical activity is defined as frequent sitting or little movement, moderate physical activity involves regular walking but infrequent heavy lifting, and high physical activity encompasses frequent climbing of stairs or hills and heavy lifting. Participants' blood pressure, measured four times, is averaged, and hypertension is defined as systolic blood pressure ≥ 140mmHg, diastolic blood pressure ≥ 90mmHg, or the use of antihypertensive medication. Diabetes is defined as fasting blood glucose ≥ 126 mg/dL or glycated hemoglobin ≥ 6.5%. High cholesterol is determined by a serum total cholesterol level ≥ 240 mg/dL or the use of cholesterol-lowering medication. Participants with a history of congestive heart failure, coronary artery disease, or angina pectoris are classified as having a history of cardiovascular disease. A history of prostate disease is defined as a previous diagnosis of prostate-related conditions. Health status is self-assessed by participants and categorized as "Good, very good, excellent" or "Fair or poor". Considering the potential for multicollinearity among the covariates, we employed Stata software to assess multicollinearity using the Variance Inflation Factor (VIF). The analysis revealed a mean VIF value of 1.17 for all covariates, with each VIF being less than 2, indicating the absence of multicollinearity among the covariates.

Statistical analysis

This study utilized Stata 17 and SPSS as statistical software. Descriptive statistics were utilized to summarize the demographic characteristics of the study population. Categorical variables were represented using weighted proportions and 95% confidence intervals (95%CI), while continuous variables were presented using weighted means and standard errors (SE). Given the data spanned two survey cycles from 2001 to 2004, MEC weights × 0.5 were applied as the final weights. SPSS was used to conduct Pearson chi-square tests for categorical variables and t-tests for continuous variables to assess group differences. Binary logistic weighted regression analysis was employed to investigate the relationship between CDAI and ED. CDAI, treated as a continuous variable, was categorized based on quartile ranges for analysis. Unadjusted univariate logistic weighted regression analysis was

designated as Model 1. Subsequent multivariate logistic weighted regression analyses included adjustments in Model 2 for age and race and in Model 3 for additional factors, namely education level, marital status, economic status, smoking, alcohol consumption, BMI, physical activity, hypertension, diabetes, hyperlipidemia, history of cardiovascular disease, history of prostate disease, and overall health status. Trend tests were conducted for each model to evaluate the linear trend of the impact of each CDAI interval on the outcome [23].

After conducting multivariate logistic weighted regression analyses for the three models, subgroup analyses were performed for age, race, education level, hypertension, diabetes, hyperlipidemia, and history of cardiovascular disease in Model 3, excluding the grouping variables. The objective of these analyses was to investigate the correlation between CDAI and ED across different subgroups. Interaction tests for CDAI with each subgroup were conducted using SPSS to offer more precise risk estimates for the subgroups in the population [24].

In order to minimize selection bias and alleviate the influence of confounding factors, PSM was employed. PSM is particularly valuable when dealing with datasets containing numerous potential confounding variables [25], Specifically, PSM reduces selection bias by balancing covariates between the groups. Propensity scores were calculated using a logistic regression model that included relevant covariates, and we assessed the balance of covariates in the matched groups to ensure similarity in baseline characteristics. Further analyses were conducted using the matched data. This approach helps ensure that observed differences in outcomes are less likely to be due to confounding variables [26]. We employed PSM to adjust for several key confounding variables, such as age, BMI, hypertension, diabetes, hyperlipidemia, and history of cardiovascular disease. The matching tolerance was set at 0.03. Subsequently, descriptive statistics were performed on the matched population, followed by secondary logistic weighted regression analyses using multiple models.

Results

Characteristics of study participants

The demographic characteristics of study participants, stratified by the definition of ED, are presented in Table 1. All results for demographic characteristics are weighted, and significant inter-group differences were observed ($P<0.05$). A total of 3807 participants were ultimately included in the study, with 1109 classified as ED patients and 2698 as non-ED individuals. The average age of study participants was 45.24 (SE=0.27), with the non-ED group having an average age of 41.32 (SE=0.27), and the ED group having a significantly higher average age of 61.70 (SE=0.56). After categorizing age, the ED group had a significantly higher proportion of participants aged 40 and above compared to the non-ED group (90.75% vs. 53.30%, $P<0.001$). In terms of socio-economic characteristics, the ED group had a higher proportion of individuals with lower educational levels (28.38% vs. 13.52%, $P<0.001$), a higher proportion of individuals who were married or cohabiting with a partner (88.21% vs. 71.1%, $P<0.001$), and a lower proportion of individuals with higher economic status (32.51% vs. 39.85%, $P<0.001$) compared to the non-ED group. In terms of behavioral habits, the ED group had a higher proportion of current or former smokers (69.24% vs. 53.89%, $P<0.001$), fewer alcohol consumers (73.24% vs. 83.4%, $P<0.001$), and a higher proportion of individuals with a BMI of 25 or higher (73.03% vs. 68.71%, $P<0.001$), as well as more individuals with low physical activity (30.71% vs. 20.27%, $P<0.001$). In terms of health, the ED group had a higher prevalence of hypertension, diabetes, cardiovascular diseases, and a history of prostate diseases, with all differences being statistically significant ($P<0.001$).

Association between the CDAI and ED

The weighted multivariate logistic regression models for the relationship between CDAI and ED are presented in Table 2. When CDAI is treated as a continuous variable, it exhibits a negative correlation with ED in all three models, including Model 1 (OR=0.92, 95% CI: 0.89–0.95, $P<0.001$), Model 2 adjusting for age and race (OR=0.93, 95% CI: 0.90–0.96, $P<0.001$), and Model 3 adjusting for all covariates (OR=0.95, 95% CI: 0.91–0.98, $P=0.002$). When CDAI is converted into a categorical variable based on quartile ranges, in Model 1, Q3 (OR=0.64, 95% CI: 0.50–0.82, $P<0.001$) and Q4 (OR=0.52, 95% CI: 0.40–0.68, $P<0.001$) show a negative correlation with ED. In Model 2, adjusting for age and race, CDAI Q3 (OR=0.64, 95% CI: 0.49–0.83, $P=0.001$) and Q4 (OR=0.55, 95% CI: 0.42–0.72, $P<0.001$) exhibit a negative correlation with ED. In Model 3, adjusting for all covariates, Q3 (OR=0.72, 95% CI: 0.53–0.97, $P=0.033$) and Q4 (OR=0.66, 95% CI: 0.48–0.90, $P=0.010$) are also negatively correlated with ED. In all three models, the protective effect against ED becomes more pronounced with increasing CDAI quartile ranges, and this trend is statistically significant ($P<0.001$).

Subgroup analysis

Subgroup analysis results are shown in Fig. 2, indicating that there is no interaction between CDAI and ED across various subgroups. In the population aged 40 and above, CDAI is negatively correlated with ED (OR=0.96, 95% CI: 0.92–0.99, $P=0.018$). Non-Hispanic Black and Mexican American populations show a negative correlation between CDAI and ED (OR=0.89, 95% CI: 0.82–0.96,

Table 1 General characteristics of participants ($N=3807$) stratified by ED or no ED in the NHANES 2001–2004.[a]

Characteristic	Total ($n=3807$)	No ED ($n=2698$)	ED ($n=1109$)	*P*-value
Age (year), mean (SE)	45.24 ± 0.27	41.32 ± 0.27	61.70 ± 0.56	< 0.001
Age (%)				< 0.001
< 40 years	39.37(37.48,41.30)	46.70(44.48,48.94)	9.25(7.22,11.79)	
≥ 40 years	60.63(58.70,62.52)	53.30(51.06,55.52)	90.75(88.21,92.78)	
Race (%)				< 0.001
Non-Hispanic White	74.62(73.13,76.05)	73.99(72.26,75.64)	77.24(74.34,79.9)	
Non-Hispanic Black	9.36(8.63,10.15)	9.65(8.80,10.58)	8.17(6.89,9.66)	
Mexican American	7.57(6.94,8.26)	7.84(7.10,8.64)	6.49(5.38,7.82)	
Hispanic	4.37(3.61,5.28)	4.14(3.31,5.16)	5.33(3.71,7.61)	
Other Race	4.07(3.34,4.95)	4.39(3.53,5.44)	2.77(1.75,4.36)	
Educational level (%)				< 0.001
Below high school	16.43(15.24,17.70)	13.52(12.27,14.88)	28.38(25.37,31.61)	
High school	27.09(25.38,28.87)	28.07(26.09,30.14)	23.07(20.04,26.40)	
Above high school	56.48(54.56,58.37)	58.41(56.21,60.57)	48.55(44.8,52.31)	
Marital status (%)				< 0.001
Living alone	25.43(23.79,27.15)	28.75(26.81,30.77)	11.79(9.47,14.58)	
Married or living with partner	74.45(72.73,76.10)	71.1(69.08,73.05)	88.21(85.42,90.53)	
Not recorded	0.11(0.03,0.47)	0.14(0.04,0.58)	0	
Socioeconomic status (%)				< 0.001
Low	9.85(8.87,10.93)	9.87(8.75,11.11)	9.79(7.94,12.02)	
Moderate	46.78(44.85,48.72)	45.29(43.08,47.52)	52.92(49.15,56.66)	
High	38.41(36.49,40.37)	39.85(37.63,42.10)	32.51(28.93,36.30)	
Not recorded	4.96(4.19,5.85)	5.00(4.12,6.06)	4.78(3.54,6.41)	
Smoking status (%)				< 0.001
Never	43.07(41.15,45.02)	46.11(43.88,48.35)	30.62(27.25,34.21)	
Former	29.53(27.81,31.30)	25.10(23.22,27.09)	47.71(43.99,51.45)	
Current	27.37(25.67,29.13)	28.79(26.82,30.84)	21.53(18.52,24.88)	
Not recorded	0.03(0.01,0.09)	0.01(0.00,0.04)	0.14(0.04,0.46)	
Alcohol intake (%)				< 0.001
Low	7.22(6.28,8.29)	7.27(6.19,8.52)	7.01(5.38,9.08)	
Moderate	34.88(33.04,36.77)	35.03(32.91,37.22)	34.25(30.79,37.88)	
High	46.53(44.60,48.48)	48.37(46.14,50.61)	38.99(35.34,42.76)	
Not recorded	11.37(10.23,12.61)	9.33(8.10,10.71)	19.76(17.08,22.74)	
BMI (%)				< 0.001
< 25 kg/m2	28.98(27.27,30.76)	30.43(28.43,32.51)	23.02(20.12,26.2)	
25–30 kg/m2	40.75(38.85,42.67)	41.20(39.01,43.43)	38.87(35.3,42.56)	
≥ 30 kg/m2	28.81(27.06,30.62)	27.51(25.53,29.58)	34.16(30.59,37.92)	
Not recorded	1.46(1.12,1.91)	0.86(0.55,1.34)	3.96(2.91,5.35)	
Physical activity (%)				< 0.001
Low	22.32(20.74,23.98)	20.27(18.52,22.15)	30.71(27.34,34.30)	
Moderate	46.38(44.45,48.32)	45.32(43.11,47.56)	50.74(46.99,54.48)	
High	31.24(29.45,33.10)	34.37(32.27,36.54)	18.38(15.55,21.58)	
Not recorded	0.06(0.02,0.15)	0.03(0.01,0.12)	0.17(0.05,0.61)	
Hypertension (%)				< 0.001
No	69.25(67.50,70.96)	76.35(74.42,78.17)	40.1(36.39,43.93)	
Yes	30.75(29.04,32.50)	23.65(21.83,25.58)	59.9(56.07,63.61)	
Not recorded				
Diabetes (%)				< 0.001
No	88.87(87.67,89.97)	93.08(91.92,94.08)	71.58(67.98,74.92)	
Yes	10.53(9.46,11.71)	6.36(5.40,7.47)	27.67(24.34,31.26)	
Not recorded	0.60(0.37,0.96)	0.56(0.31,1.01)	0.75(0.38,1.48)	
Hypercholesterolemia (%)				0.013

Table 1 (continued)

Characteristic	Total ($n=3807$)	No ED ($n=2698$)	ED ($n=1109$)	*P*-value
No	81.32(79.74,82.81)	80.80(78.95,82.52)	83.48(80.45,86.12)	
Yes	15.98(14.57,17.50)	16.56(14.93,18.33)	13.60(11.13,16.51)	
Not recorded	2.69(2.17,3.33)	2.64(2.04,3.39)	2.92(2.01,4.24)	
Cardiovascular disease (%)				< 0.001
No	90.39(89.35,91.33)	94.91(93.95,95.73)	71.79(68.47,74.89)	
Yes	9.31(8.38,10.33)	4.93(4.13,5.88)	27.30(24.24,30.59)	
Not recorded	0.30(0.17,0.56)	0.16(0.06,0.44)	0.91(0.44,1.89)	
Prostate disease (%)				< 0.001
No	88.83(87.67,89.89)	93.1(91.89,94.13)	71.31(68.04,74.37)	
Yes	11.01(9.96,12.16)	6.76(5.74,7.95)	28.47(25.41,31.73)	
Not recorded	0.16(0.06,0.42)	0.14(0.04,0.52)	0.23(0.09,0.58)	
Health status (%)				< 0.001
Good, very good, excellent	85.46(84.14,86.68)	89.05(87.66,90.29)	70.71(67.24,73.95)	
Fair or poor	14.47(13.24,15.78)	10.86(9.62,12.24)	29.29(26.05,32.76)	
Not recorded	0.08(0.02,0.36)	0.09(0.02,0.45)	0	
Dietary supplements (%)				< 0.001
No	52.28 (50.33, 54.22)	54.73 (52.48, 56.95)	42.21 (38.56, 45.95)	
Yes	47.68(45.74, 49.63)	45.22 (43.00, 47.47)	57.79 (54.05, 61.44)	
CDAI, mean (SE)	0.25 ± 0.07	0.42 ± 0.08	-0.45 ± 0.12	< 0.001

[a]Categorical variables are presented as weighted percentages with 95% confidence intervals, and continuous variables are reported as weighted means with standard errors

Table 2 The weighted multivariable logistic regression analysis of the relationship between the composite dietary antioxidant index and erectile dysfunction

	ED($n=1109$)	Model 1		Model 2		Model 3	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Continuous	1109	0.92(0.89,0.95)	< 0.001	0.93(0.90,0.96)	< 0.001	0.95(0.91,0.98)	0.002
Quartiles of CDAI							
Q1	340	Reference		Reference		Reference	
Q2	315	0.93(0.73,1.18)	0.545	0.88(0.68,1.14)	0.334	0.99(0.74,1.35)	0.980
Q3	258	0.64(0.50,0.82)	< 0.001	0.64(0.49,0.83)	0.001	0.72(0.53,0.97)	0.033
Q4	196	0.52(0.40,0.68)	< 0.001	0.55(0.42,0.72)	< 0.001	0.66(0.48,0.90)	0.010
P for trend		< 0.001		< 0.001		< 0.001	

Abbreviations CDAI: Composite dietary antioxidant index. Model 1: No covariates were adjusted. Model 2: Age and race were adjusted. Model 3: Based on Model 2, educational level, marital status, socioeconomic status, smoking status, alcohol intake, BMI, physical activity, hypertension, diabetes, hypercholesterolemia, cardiovascular disease, prostate disease, health status, dietary supplements covariates are added

P=0.003; OR=0.90, 95% CI: 0.82–0.98, *P*=0.011). In populations with higher education levels, CDAI is negatively correlated with ED (OR=0.94, 95% CI: 0.89–0.99, *P*=0.015). Among those without hypertension (OR=0.92, 95% CI: 0.87–0.97, *P*=0.001), hyperlipidemia (OR=0.96, 95% CI: 0.93-1.00, *P*=0.03), and cardiovascular disease (OR=0.93, 95% CI: 0.90–0.97, *P*=0.001), CDAI is negatively correlated with ED. In both non-diabetic (OR=0.95, 95% CI: 0.92–0.99, *P*=0.013) and diabetic populations (OR=0.90, 95% CI: 0.83–0.97, *P*=0.008), CDAI is negatively correlated with ED, with the protective effect of CDAI being more significant in the diabetic population.

PSM analysis

After PSM, a total of 1808 participants were included, with 904 in the ED group and 904 in the non-ED group. Descriptive statistics were performed on the matched population, as shown in Table S1. PSM adjusted for several key confounding variables, making the differences in confounding variables between the ED and non-ED groups more significant. Logistic weighted regression analysis was conducted on the included population in the second set of models, and the results are shown in Table 3. When CDAI is treated as a continuous variable, in all three models, CDAI still shows a significant negative correlation with ED (OR=0.93, 95% CI: 0.90–0.97, *P*<0.001; OR=0.93, 95% CI: 0.90–0.97, *P*<0.001; OR=0.95, 95% CI: 0.90–0.98, *P*=0.003). When CDAI is transformed into a categorical variable, in

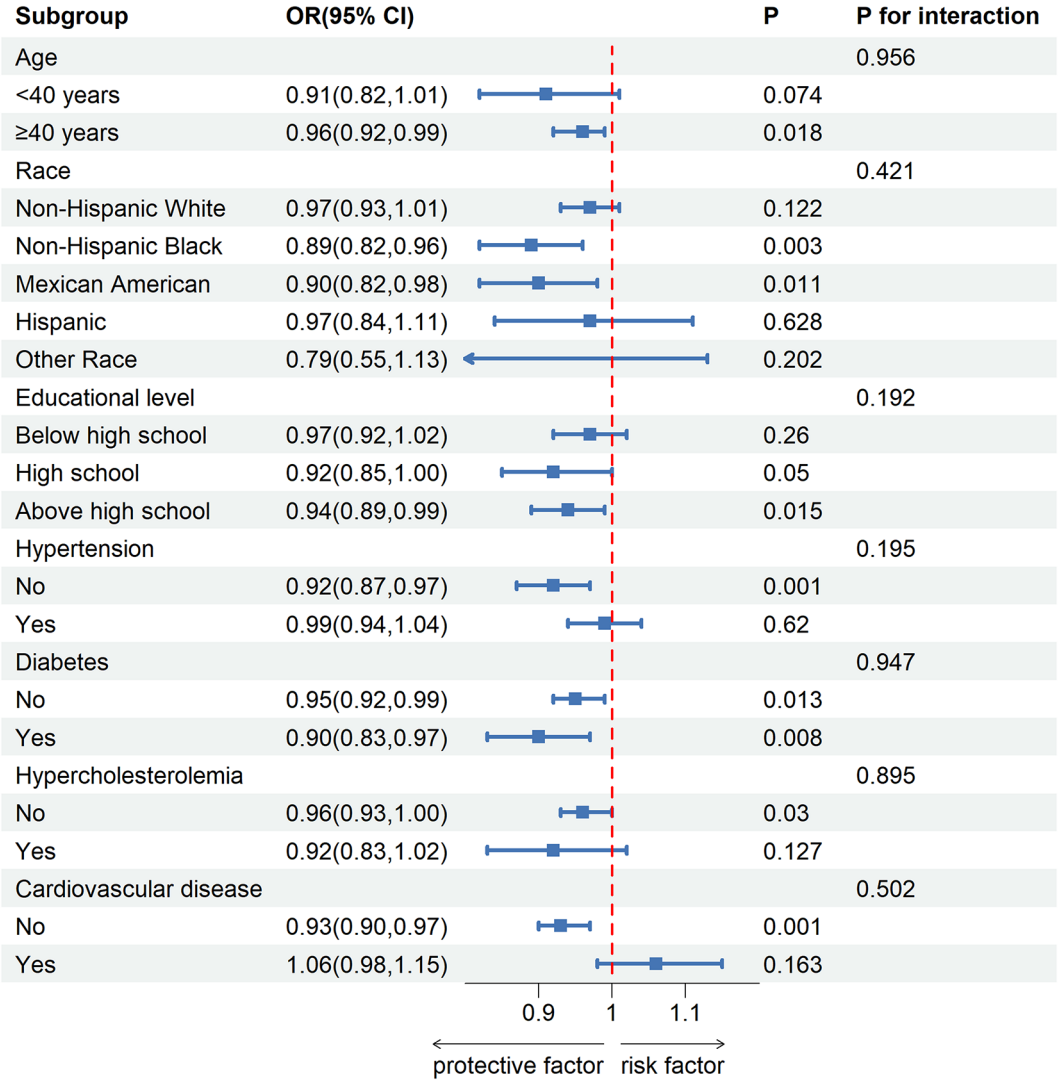

Fig. 2 Subgroup analysis of CDAI and erectile dysfunction. Each group includes adjustment for all covariates except for the grouping factor

Table 3 Weighted multivariable logistic regression analysis of the relationship between the composite dietary antioxidant index and erectile dysfunction after propensity score matching (PSM)

	ED($n=904$)	Model 1		Model 2		Model 3	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Continuous	904	0.93(0.90,0.97)	< 0.001	0.93(0.90,0.97)	< 0.001	0.95(0.90,0.98)	0.003
Quartiles of CDAI							
Q1	274	Reference		Reference		Reference	
Q2	267	1.06(0.77,1.45)	0.738	1.04(0.76,1.44)	0.792	1.03(0.71,1.46)	0.900
Q3	210	0.71(0.51,0.98)	0.037	0.70(0.51,0.98)	0.035	0.71(0.48,1.11)	0.065
Q4	153	0.61(0.43,0.85)	0.004	0.60(0.43,0.85)	0.004	0.66(0.45,0.97)	0.031
P for trend		< 0.001		< 0.001		< 0.001	

Abbreviations CDAI: Composite dietary antioxidant index. Model 1: No covariates were adjusted. Model 2: Age and race were adjusted. Model 3: Based on Model 2, educational level, marital status, socioeconomic status, smoking status, alcohol intake, BMI, physical activity, hypertension, diabetes, hypercholesterolemia, cardiovascular disease, prostate disease, health status, dietary supplements covariates are added

models 1 and 2, CDAI Q3 (OR=0.71, 95% CI: 0.51–0.98, P=0.037; OR=0.70, 95% CI: 0.51–0.98, P=0.035) and Q4 (OR=0.61, 95% CI: 0.43–0.85, P=0.004; OR=0.60, 95% CI: 0.43–0.85, P=0.004) are still negatively correlated with ED, and in model 3, CDAI Q4 (OR=0.66, 95% CI: 0.45–0.97, P=0.031) remains negatively correlated with ED.

Discussion

In this study, we systematically investigated the correlation between CDAI and ED, utilizing data from the NHANES database covering the period 2001–2004. Employing a thoroughly adjusted multivariate logistic regression model, which considered an array of confounding variables, we identified a substantial and negative correlation between CDAI and the risk of developing ED. After categorizing CDAI into quartiles, participants in the Q3 exhibited a 27% reduction in the risk of ED, while those in the Q4 experienced a more pronounced 30% decrease in ED risk. This quartile-based analysis enhances the dose-response nature of the observed association, indicating a consistent correlation between higher composite dietary antioxidant indices and a lowered risk of ED. In subgroup analyses, we explored the distribution of the negative correlation between CDAI and ED risk across different subgroups. Following PSM adjustments, the association between CDAI and reduced ED risk remained statistically significant. This reinforces the robustness of our study findings, suggesting that the observed relationship is less likely to be influenced by confounding factors.

Previous studies have already identified the potential correlation between CDAI and certain diseases. Wang et al.'s research discovered a positive correlation between CDAI and the decreased incidence of chronic kidney disease (CKD) [27]. A prospective cohort study with Singaporean Chinese participants also demonstrated the role of CDAI in lowering the incidence of colorectal cancer in the general population [28]. The intimate relationship between CDAI and cardiovascular diseases has been extensively documented in numerous studies [29, 30]. Antioxidant-rich diets are generally considered beneficial for health [31, 32], a conclusion that aligns with the findings of our study. Animal studies have demonstrated that long-term administration of antioxidants such as resveratrol can reverse ED in mice [33], and certain antioxidant extracts can alleviate ED in rats [34]. Additionally, some human studies have shown that carotenoids and lycopene are associated with a lower risk of ED [12, 35]. While these findings align with our study, it is important to note that these investigations often focus solely on the effects of individual antioxidants in animal models or human studies. The impact of single antioxidants may not comprehensively capture the overall effects of antioxidant-rich diets on ED, and excessive intake of certain individual antioxidants can even be detrimental to health [36]. Some studies suggest that the effects of individual antioxidant treatments on ED may be limited, whereas treatments involving combinations of antioxidant compounds are associated with improvements in ED [37]. Our study addresses this gap by considering the synergistic effects of multiple antioxidants, thereby reducing confounding biases that single antioxidants alone may not adequately explain. This approach enhances the reliability of our findings and provides a clearer understanding of the impact of antioxidant-rich diets on ED.

The onset mechanism of ED is closely associated with oxidative stress [38], Research indicates that dimethyl fumarate enhances erectile function in rats with cavernous nerve injury by activating the Nrf2/HO-1 signaling pathway to suppress oxidative stress [38]. Liraglutide improves ED by modulating oxidative stress through the inhibition of the RhoA/ROCK pathway [39], while apigenin prevents ED by ameliorating endothelial dysfunction and oxidative stress in rats [40]. Previous studies on the mechanisms by which antioxidants improve ED have primarily focused on reducing oxidative stress, which may also be one of the potential mechanisms underlying the association between the CDAI and the reduced risk of ED. CDAI is a comprehensive score derived from vitamin A, C, E, carotenoids, selenium, and zinc. Vitamin A has been identified as playing a pivotal role in reproductive processes [41, 42]. Research indicates that alpha-lipoic acid (ALA) may exert antioxidant effects by regenerating vitamin C and vitamin E, thus potentially preventing ED induced by diabetes [43]. A community cross-sectional study by Fujita et al. observed a correlation between low concentrations of blood alpha-carotene and beta-carotene and severe ED [44]. In animal experiments, zinc has demonstrated the ability to inhibit xanthine oxidase (XO) and uric acid (UA)-driven oxidative stress, leading to an improvement in ED through the upregulation of testosterone via Nrf2-mediated signaling [11]. Nevertheless, further investigations are required to delve into the potential mechanisms of the mixed interactions among these dietary antioxidants in the context of ED.

The present study boasts several strengths. Firstly, NHANES employs a sophisticated sampling design, and the rich sample size, diversity, and representativeness of the data enhance the reliability of the conclusions. We included numerous potential covariates and conducted 1:1 PSM, thereby reinforcing the robustness of the results. Lastly, our study, compared to the focus on individual antioxidants, may better represent the correlation between an antioxidant-rich diet and ED. However, it is crucial to acknowledge certain limitations in our study, including its cross-sectional design, which hinders

the establishment of causal relationships. Secondly, our study findings may not be generalizable to other ethnicities, and future research should be designed to explore these relationships in different racial groups. Additionally, our study incorporated some questionnaire surveys, and when interpreting our results, reliance on self-reported data and the potential presence of unmeasured confounding factors, despite PSM adjustments, should be considered. ED may be influenced by sex steroid hormones; however, due to data limitations, we were unable to include sex steroid hormones in the analysis.

Conclusions

In our study cohort, there is support for the negative correlation between CDAI and the risk of ED. Future investigations, particularly prospective studies and intervention trials, are imperative to elucidate the potential mechanistic role of dietary intervention in mitigating the risk of ED.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20880-4.

Supplementary Material 1

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Author contributions
XH and XC designed the research. XH and CR Collected the article's data and conducted data analysis. YP, ZX and QW has carried out the preliminary drafting of the article. XL participated in the supervision and editing of this study. All authors of this study have contributed to this article and have unanimously agreed to its publication.

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Data availability
All the data involved in our study can be found in the NHANES database (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx), For additional inquiries, please contact the corresponding authors.

Declarations

Ethics approval and consent to participate
All participants provided informed written consent and the study received ethics approval from the NCHS. The present analysis relies on openly accessible data and necessitates no additional ethical endorsement.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, Heidelbaugh J, Khera M, McVary KT, Miner MM, Nelson CJ, Sadeghi-Nejad H, Seftel AD, Shindel AW. Erectile Dysfunction: AUA Guideline. J Urol. 2018;200(3):633–41. https://doi.org/10.1016/j.juro.2018.05.004. eng. Epub 2018/05/11.
2. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, Maggi M, Nelson CJ, Parish S, Salonia A, Tan R, Mulhall JP, Hellstrom WJ. Erectile dysfunction. Nature reviews Disease primers. 2016;2:16003. eng. Epub 2016/05/18. https://doi.org/10.1038/nrdp.2016.3. Cited in: Pubmed; PMID 27188339.
3. Bertini A, Pozzi E, Fallara G, Lanzaro F, Candela L, Costa A, Corsini C, Cilio S, Belladelli F, Capogrosso P, d'Arma A, Montorsi F, Salonia A. The atherosclerotic cardiovascular disease risk score is a reliable tool to identify patients with arteriogenic erectile dysfunction. Andrology. 2023;11(7):1451–9. https://doi.org/10.1111/andr.13437. eng. Epub 2023/04/06.
4. Zang G, Sun X, Sun Y, Zhao Y, Dong Y, Pang K, Cheng P, Wang M, Zheng Y. Chronic liver diseases and erectile dysfunction. Frontiers in public health. 2022;10:1092353. eng. Epub 2023/01/24. https://doi.org/10.3389/fpubh.2022.1092353. Cited in: Pubmed; PMID 36684968.
5. Van Thiel DH. Erectile dysfunction and cirrhosis: prevalence and a potential therapy. Hepatology international. 2023;17(2):277–278. eng. Epub 2023/03/31. https://doi.org/10.1007/s12072-022-10447-z. Cited in: Pubmed; PMID 36995543.
6. Corona G, Cucinotta D, Di Lorenzo G, Ferlin A, Giagulli VA, Gnessi L, Isidori AM, Maiorino MI, Miserendino P, Murrone A, Pivonello R, Rochira V, Sangiorgi GM, Stagno G, Foresta C, Lenzi A, Maggi M, Jannini EA. The Italian society of andrology and sexual medicine (SIAMS), along with ten other Italian Scientific Societies, guidelines on the diagnosis and management of erectile dysfunction. J Endocrinol Investig. 2023;46(6):1241–74. https://doi.org/10.1007/s40618-023-02015-5. eng. Epub 2023/01/26.
7. Kaltsas A, Zikopoulos A, Dimitriadis F, Sheshi D, Politis M, Moustakli E, Symeonidis EN, Chrisofos M, Sofikitis N, Zachariou A. Oxidative stress and Erectile Dysfunction: pathophysiology, impacts, and potential treatments. Curr Issues Mol Biol. 2024;46(8):8807–34. https://doi.org/10.3390/cimb46080521. eng. Epub 2024/08/28.
8. Beetch M, Harandi-Zadeh S, Shen K, Lubecka K, Kitts DD, O'Hagan HM, Stefanska B. Dietary antioxidants remodel DNA methylation patterns in chronic disease. British journal of pharmacology. 2020;177(6):1382–1408. eng. Epub 2019/10/19. https://doi.org/10.1111/bph.14888. Cited in: Pubmed; PMID 31626338.
9. Terao J. Revisiting carotenoids as dietary antioxidants for human health and disease prevention. Food Funct. 2023;14(17):7799–824. https://doi.org/10.1039/d3fo02330c. eng. Epub 2023/08/18.
10. Crafa A, Cannarella R, Barbagallo F, Leanza C, Palazzolo R, Flores HA, La Vignera S, Condorelli RA, Calogero AE. Mechanisms Suggesting a Relationship between Vitamin D and Erectile Dysfunction: An Overview. Biomolecules. 2023;13(6). eng. Epub 2023/06/28. https://doi.org/10.3390/biom13060930. Cited in: Pubmed; PMID 37371510.
11. Besong EE, Akhigbe TM, Ashonibare PJ, Oladipo AA, Obimma JN, Hamed MA, Adeyemi DH, Akhigbe RE. Zinc improves sexual performance and erectile function by preventing penile oxidative injury and upregulating circulating testosterone in lead-exposed rats. Redox report: communications in free radical research. 2023;28(1):2225675. eng. Epub 2023/06/22. https://doi.org/10.1080/13510002.2023.2225675. Cited in: Pubmed; PMID 37345699.
12. Gao Y, Liu C, Lu X, Lu K, Zhang L, Mao W, Pan K, Liang Z, Sun C, Chen M. Lycopene intake and the risk of erectile dysfunction in US adults: NHANES 2001–2004. Andrology. 2024;12(1):45–55. https://doi.org/10.1111/andr.13439. eng. Epub 2023/04/11.
13. Hecht F, Zocchi M, Alimohammadi F, Harris IS. Regulation of antioxidants in cancer. Mol Cell. 2024;84(1):23–33. https://doi.org/10.1016/j.molcel.2023.11.001. eng. Epub 2023/11/30.
14. Pellegrini N, Vitaglione P, Granato D, Fogliano V. Twenty-five years of total antioxidant capacity measurement of foods and biological fluids: merits and limitations. J Sci Food Agric. 2020;100(14):5064–78. https://doi.org/10.1002/jsfa.9550. eng. Epub 2018/12/24.
15. Duan Q, Huang H, Zhang S, Wang Y, Lu D, Wan L, Sun Y, Wu Y. Association between composite dietary antioxidant index and kidney stone prevalence in adults: data from National Health and Nutrition Examination Survey (NHANES, 2007–2018). Frontiers in nutrition. 2024;11:1389714. eng. Epub 2024/06/06. https://doi.org/10.3389/fnut.2024.1389714. Cited in: Pubmed; PMID 38840700.
16. Teng TQ, Liu J, Hu FF, Li QQ, Hu ZZ, Shi Y. Association of composite dietary antioxidant index with prevalence of stroke: insights from

NHANES 1999–2018. Front Immunol. 2024;15. https://doi.org/10.3389/fimmu.2024.1306059. 1306059. eng. Epub 2024/03/25.
17. Wu D, Wang H, Wang W, Qing C, Zhang W, Gao X, Shi Y, Li Y, Zheng Z. Front Nutr. 2023;10. https://doi.org/10.3389/fnut.2023.1147869. 1147869. eng. Epub 2023/04/18. Association between composite dietary antioxidant index and handgrip strength in American adults: Data from National Health and Nutrition Examination Survey (NHANES, 2011–2014.
18. Xu Q, Qian X, Sun F, Liu H, Dou Z, Zhang J. Independent and joint associations of dietary antioxidant intake with risk of post-stroke depression and all-cause mortality. J Affect Disord. 2023;322:84–90. Cited in: Pubmed; PMID 36372128.
19. Zhang J, Lu X, Wu R, Ni H, Xu L, Wu W, Lu C, Feng J, Jin Y. Associations between composite dietary antioxidant index and estimated 10-year atherosclerotic cardiovascular disease risk among U.S. adults. Frontiers in nutrition. 2023;10:1214875. eng. Epub 2023/08/28. https://doi.org/10.3389/fnut.2023.1214875. Cited in: Pubmed; PMID 37637947.
20. Wright ME, Mayne ST, Stolzenberg-Solomon RZ, Li Z, Pietinen P, Taylor PR, Virtamo J, Albanes D. Development of a comprehensive dietary antioxidant index and application to lung cancer risk in a cohort of male smokers. Am J Epidemiol. 2004;160(1):68–76. https://doi.org/10.1093/aje/kwh173. eng. Epub 2004/07/02.
21. Huang L, Liu H, Li L, Wang S, Sun G. Correlation between visceral fat metabolism score and erectile dysfunction: a cross-sectional study from NHANES 2001–2004. Front Endocrinol. 2023;14. https://doi.org/10.3389/fendo.2023.1283545. 1283545. eng. Epub 2023/12/21.
22. Huang Y, Wang Y, Su H, Wang H, Xu H, Xu C, Zhou F, Zhang Y. Association between polyunsaturated fatty acid intake and the prevalence of erectile dysfunction: A cross-sectional analysis of the NHANES 2001–2004. Lipids in health and disease. 2023;22(1):182. eng. Epub 2023/10/26. https://doi.org/10.1186/s12944-023-01950-9. Cited in: Pubmed; PMID 37880723.
23. Yokose C, McCormick N, Lu N, Tanikella S, Lin K, Joshi AD, Raffield LM, Warner E, Merriman T, Hsu J, Saag K, Zhang Y, Choi HK. Trends in Prevalence of Gout Among US Asian Adults, 2011–2018. JAMA network open. 2023;6(4):e239501. eng. Epub 2023/04/21. https://doi.org/10.1001/jamanetworkopen.2023.9501. Cited in: Pubmed; PMID 37083663.
24. Mahemuti N, Jing X, Zhang N, Liu C, Li C, Cui Z, Liu Y, Chen J. Association between Systemic Immunity-Inflammation Index and Hyperlipidemia: A Population-Based Study from the NHANES (2015–2020). Nutrients. 2023;15(5). eng. Epub 2023/03/12. https://doi.org/10.3390/nu15051177. Cited in: Pubmed; PMID 36904176.
25. Arguelles GR, Shin M, Lebrun DG, DeFrancesco CJ, Fabricant PD, Baldwin KD. A systematic review of propensity score matching in the Orthopedic Literature. HSS Journal: Musculoskelet J Hosp Special Surg. 2022;18(4):550–8. https://doi.org/10.1177/15563316221082632. eng. Epub 2022/10/21.
26. Kane LT, Fang T, Galetta MS, Goyal DKC, Nicholson KJ, Kepler CK, Vaccaro AR, Schroeder GD. Propensity score matching: a statistical method. Clin Spine Surg. 2020;33(3):120–2. https://doi.org/10.1097/bsd.0000000000000932. eng. Epub 2020/01/09.
27. Wang M, Huang ZH, Zhu YH, He P, Fan QL. Food Funct. 2023;14(20):9279–86. https://doi.org/10.1039/d3fo01157g. eng. Epub 2023/09/29. Association between the composite dietary antioxidant index and chronic kidney disease: evidence from NHANES 2011–2018.
28. Yu YC, Paragomi P, Wang R, Jin A, Schoen RE, Sheng LT, Pan A, Koh WP, Yuan JM, Luu HN. Composite dietary antioxidant index and the risk of colorectal cancer: findings from the Singapore Chinese Health Study. Int J Cancer. 2022;150(10):1599–608. https://doi.org/10.1002/ijc.33925. eng. Epub 2022/01/11.
29. Wang T, Liu H, Wei X. Association between the composite dietary antioxidant index and stroke: a cross-sectional study. Biological trace element research. 2023 Dec 28. eng. Epub 2023/12/28. https://doi.org/10.1007/s12011-023-04011-5. Cited in: Pubmed; PMID 38153669.
30. Liu C, Lai W, Zhao M, Zhang Y, Hu Y. Association between the Composite Dietary Antioxidant Index and Atherosclerotic Cardiovascular Disease in Postmenopausal Women: A Cross-Sectional Study of NHANES Data, 2013–2018. Antioxidants (Basel, Switzerland). 2023;12(9). eng. Epub 2023/09/28. https://doi.org/10.3390/antiox12091740. Cited in: Pubmed; PMID 37760043.
31. Schneider CD, Bock PM, Becker GF, Moreira JCF, Bello-Klein A, Oliveira AR. Comparison of the effects of two antioxidant diets on oxidative stress markers in triathletes. Biology of sport. 2018;35(2):181–189. eng. Epub 2018/11/21. https://doi.org/10.5114/biolsport.2018.74194. Cited in: Pubmed; PMID 30455547.
32. Hurtado-Barroso S, Martínez-Huélamo M, de Rinaldi JF, Quifer-Rada P, Vallverdú-Queralt A, Pérez-Fernández S, Lamuela-Raventós RM. Acute Effect of a Single Dose of Tomato Sofrito on Plasmatic Inflammatory Biomarkers in Healthy Men. Nutrients. 2019;11(4). eng. Epub 2019/04/18. https://doi.org/10.3390/nu11040851. Cited in: Pubmed; PMID 30991720.
33. Pierre CJ, Azeez TA, Rossetti ML, Gordon BS, La Favor JD. Long-term administration of resveratrol and MitoQ stimulates cavernosum antioxidant gene expression in a mouse castration model of erectile dysfunction. Life sciences. 2022;310:121082. eng. Epub 2022/10/18. https://doi.org/10.1016/j.lfs.2022.121082. Cited in: Pubmed; PMID 36252696.
34. Ademosun AO, Oboh G, Adebayo AA, Olasehinde TA, Fasakin OW. Grapefruit peel extract mitigates paroxetine-induced erectile dysfunction in rats through stimulation of erectile response, antioxidant status, and inhibition of key enzymes related with impaired penile erection. Journal of food biochemistry. 2022;46(11):e14193. eng. Epub 2022/04/24. https://doi.org/10.1111/jfbc.14193. Cited in: Pubmed; PMID 35460094.
35. Wei W, Xu X, Luo Q, Cao L. Associations Between Serum Polar Oxygenated Carotenoids Level and Erectile Dysfunction in Men Older Than 40 Years. American journal of men's health. 2023 Nov-Dec;17(6):15579883231216905. eng. Epub 2023/12/16. https://doi.org/10.1177/15579883231216905. Cited in: Pubmed; PMID 38102781.
36. Kashif M, Yao H, Schmidt S, Chen X, Truong M, Tüksammel E, Liu Y, Bergo MO. ROS-lowering doses of vitamins C and A accelerate malignant melanoma metastasis. Redox Biol. 2023;60. https://doi.org/10.1016/j.redox.2023.102619. 102619. eng. Epub 2023/02/13.
37. Su L, Yang ZT, Qu H, Luo CL, Yuan GX, Wu J, Jiao YZ. Effect of antioxidants supplementation on Erectile Dysfunction: a systematic review and Meta-analysis of Randomized controlled trials. Sex Med Reviews. 2022;10(4):754–63. https://doi.org/10.1016/j.sxmr.2022.01.002. eng. Epub 2022/03/06.
38. Song G, Wang J, Liu J, Ruan Y. Dimethyl fumarate ameliorates erectile dysfunction in bilateral cavernous nerve injury rats by inhibiting oxidative stress and NLRP3 inflammasome-mediated pyroptosis of nerve via activation of Nrf2/HO-1 signaling pathway. Redox Biol. 2023;68:102938. https://doi.org/10.1016/j.redox.2023.102938. eng. Epub 2023/11/07. Cited in: Pubmed; PMID 37931471.
39. Yuan P, Ma D, Gao X, Wang J, Li R, Liu Z, Wang T, Wang S, Liu J, Liu X. Liraglutide Ameliorates Erectile Dysfunction via Regulating Oxidative Stress, the RhoA/ROCK Pathway and Autophagy in Diabetes Mellitus. Frontiers in pharmacology. 2020;11:1257. eng. Epub 2020/09/10. https://doi.org/10.3389/fphar.2020.01257. Cited in: Pubmed; PMID 32903510.
40. de Almeida Feitosa MS, de Almeida A, Dantas SH, de Lourdes AssunçãoAraújo, de Azevedo F, de Souza Júnior JF, Gonçalves TAF, de Lima Silva S, Soares EMC, Alves HF, Lima TT, da Silva Pontes LV, Guerra RR, Araújo IGA, de Medeiros IA. Carvacrol prevents D-(+)-galactose-induced aging-associated erectile dysfunction by improving endothelial dysfunction and oxidative stress in rats. Naunyn-Schmiedeberg's archives of pharmacology. 2024 Jul 5. eng. Epub 2024/07/05. https://doi.org/10.1007/s00210-024-03264-8. Cited in: Pubmed; PMID 38967826.
41. Chen G, Weiskirchen S, Weiskirchen R, Vitamin A. too good to be bad? Frontiers in pharmacology. 2023;14:1186336. eng. Epub 2023/06/07. https://doi.org/10.3389/fphar.2023.1186336. Cited in: Pubmed; PMID 37284305.
42. Vašková J, Klepcová Z, Špaková I, Urdzík P, Štofilová J, Bertková I, Kľoc M, Rabajdová M. The Importance of Natural Antioxidants in Female Reproduction. Antioxidants (Basel, Switzerland). 2023;12(4). eng. Epub 2023/04/28. https://doi.org/10.3390/antiox12040907. Cited in: Pubmed; PMID 37107282.
43. Jeffrey S, Samraj PI, Raj BS. The Role of Alpha-lipoic Acid Supplementation in the Prevention of Diabetes Complications: A Comprehensive Review of Clinical Trials. Current diabetes reviews. 2021;17(9):e011821190404. eng. Epub 2021/01/20. https://doi.org/10.2174/1573399817666210118145550. Cited in: Pubmed; PMID 33461470.
44. Fujita N, Ishida M, Iwane T, Suganuma H, Matsumoto M, Hatakeyama S, Yoneyama T, Hashimoto Y, Mikami T, Itoh K, Ohyama C. Association between Advanced Glycation End-Products, carotenoids, and severe Erectile Dysfunction. World J men's Health. 2023;41(3):701–11. https://doi.org/10.5534/wjmh.220154. eng. Epub 2023/01/18.

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