IMPACT OF LONG TERM CYCLAMATE AND SACCHARIN CONSUMPTION ON BIOCHEMICAL PARAMETERS IN HEALTHY INDIVIDUALS AND TYPE 2 DIABETES MELLITUS PATIENTS

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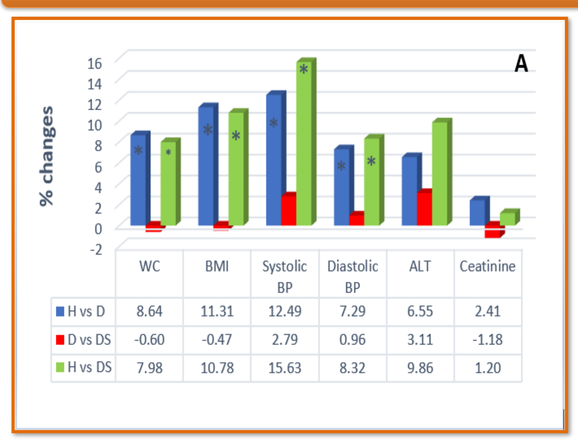
Introduction:
Previous studies conducted on saccharin and cyclamate were either limited to experimental animals or lacking evaluation of their long term consumption effects in humans. With increased consumer interest in reducing sugar intake, food products made with sweeteners rather than sugar have become more common. Obese and diabetic patients, in addition to individuals concerned about their diet, are more likely to use sugar-free and low-calorie products to reduce calorie consumption and control blood glucose levels. Several low-calorie synthetic sweeteners have recently emerged in the pharmaceutical and food industries, but their health risks due to their side effects restrict their use. Several previous studies have shown that the use of artificial sweeteners can be hazardous to human health.

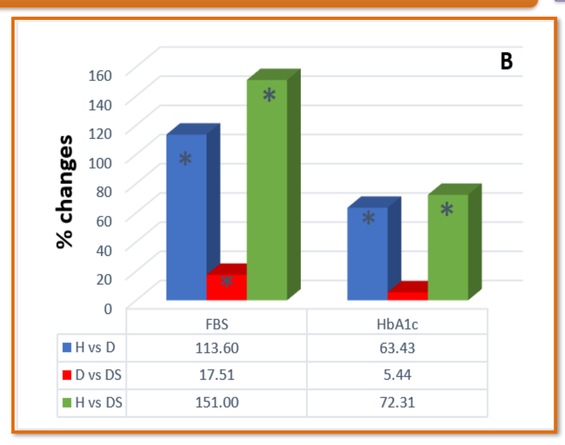
Objectives:
The current study evaluated the effect of chronic consumption of tablets containing a mixture of saccharin and cyclamate on biochemical parameters in healthy individuals and patients with type 2 diabetes mellitus.

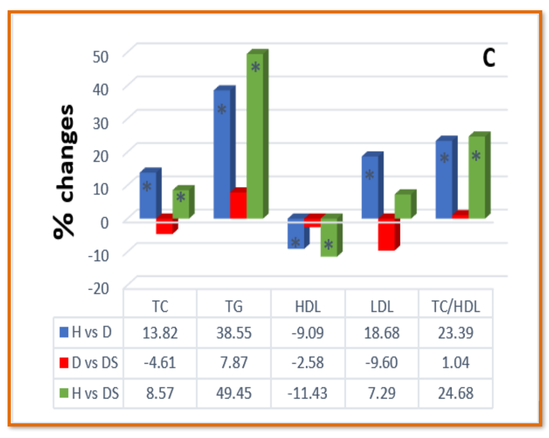
Statistical analysis:
Statistical Package for Social Science (SPSS) software version (23.0) was used to analyze all the data. Data is expressed as mean ± Standard Deviation (SD). P value <0.05 was considered as statistically significant for all analyses. One-way ANOVA was used to compare mean values between the groups. Independent t-test was used to compare the percent of changes occurred between the sweetener consumers group versus non-consumers. Pearson's correlation coefficients were used to evaluate the associations between biochemical parameters in diabetic patients and increasing amounts of sweetener consumption.

Subjects and Methods:
This cross-sectional study was carried out between July 2015 to October 2016 at the Diabetic Center in Duhok, Kurdistan Regional Government - Iraq. Healthy participants were classified into 2 groups based on whether they consumed sweeteners or not. Similar classification was done to the diabetic patients. The volunteers were also classified according to the amount of sweetener consumed per day (<5, 5-10, and >10 tablets) and according to the duration of sweetener consumption (<5, 5-10 and >10 years). The Diabetic groups included 181 type 2 diabetic patients of which 88 consumed sweeteners and 93 who did not consume sweeteners. The groups of healthy people included 107 individuals of which 14 consumed sweetener and 93 did not consume sweeteners. Venous blood samples were treated with EDTA for the estimation of HbA1c, while serum was used for measuring all other parameters. The categories of parameters measured were antioxidant parameters - serum catalase activity and serum peroxynitrite, as well as, pro-oxidant parameters - serum ceruloplasmin (CP) and the oxidation product - malondialdehyde (MDA). In addition, glycated haemoglobin (HbA1c), fasting serum glucose (FSG), serum creatinine, alanine transaminase activity (ALT) and lipid profile were also evaluated.

Results:







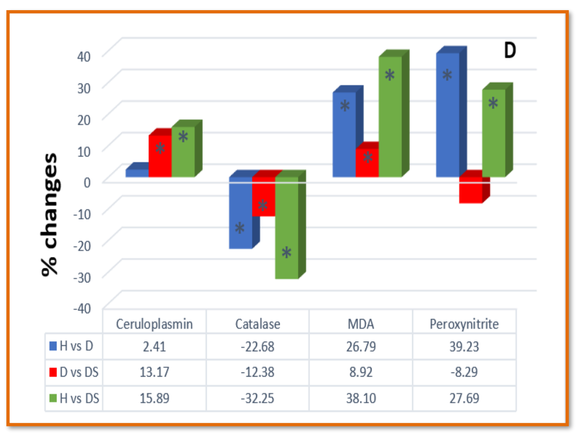
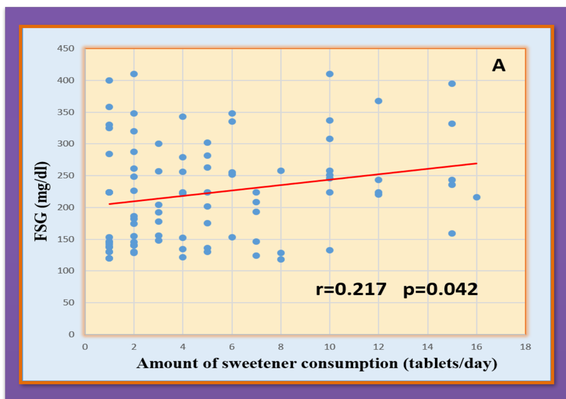
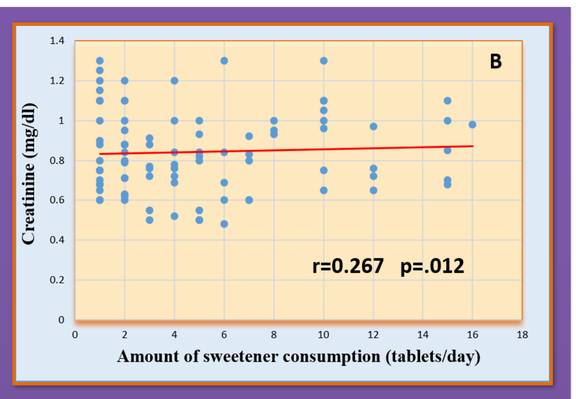
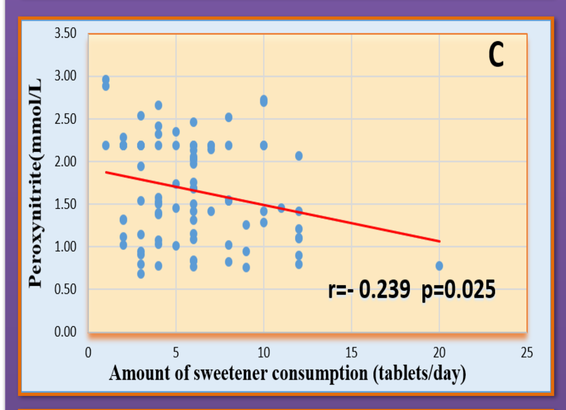
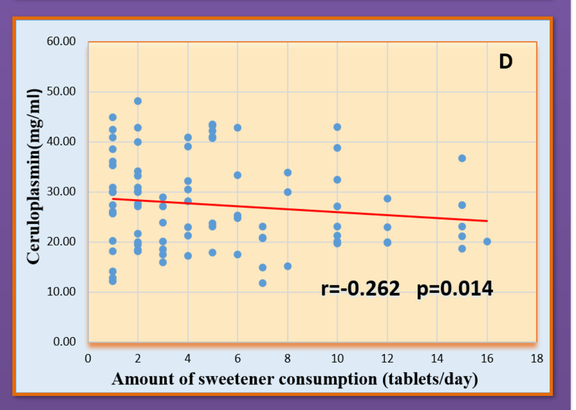


Figure 1 - Percentage of change in (A) WC, BMI, Blood pressure, ALT activity and creatinine level, (B) FSG and HbA1C, (C) Lipid profile parameters and (D) Oxidative stress parameters among healthy individuals (H), diabetic (D) and diabetic using sweetener (DS). *P<0.05 (independent t-test).









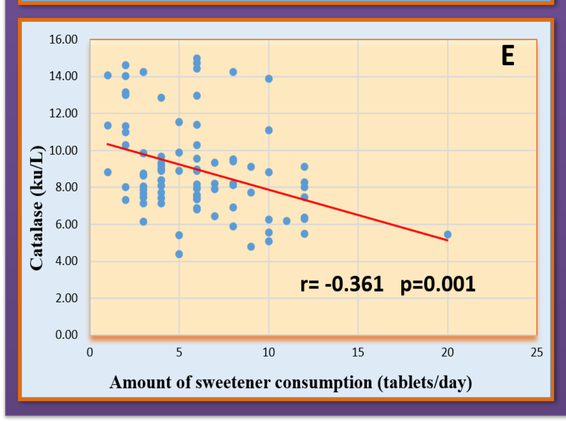
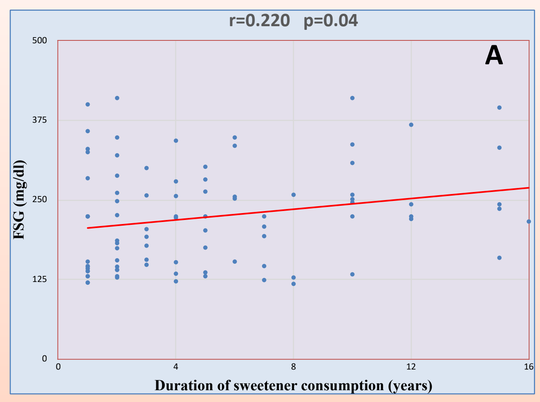


Figure 2- Correlation between sweetener consumption and (A) FBS, (B) Serum Creatinine, (C) Serum Peroxynitrite, (D) serum Ceruloplasmin and (E) Serum Catalase activity in diabetic patients.



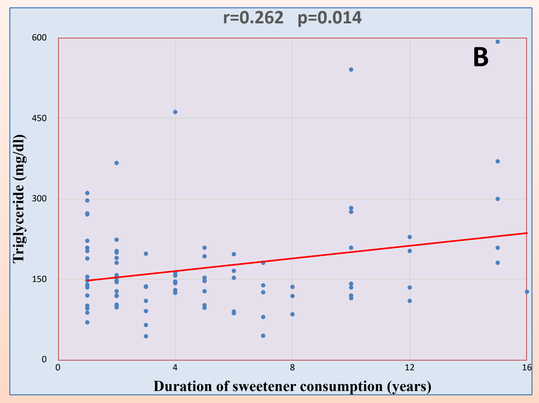


Figure 3- Correlation between the duration of daily sweetener consumption and levels of (A) Serum TG and (B) FSG in diabetic patients.

Table 1- Percentage of change in healthy groups for demographic and biochemical parameters

Variables	H vs HS	P* Value
WC (Cm)	2.45	NS
BMI (Kg/m²)	2.14	NS
SBP (mm Hg)	2.11	0.022
DBP (mm Hg)	1.50	NS
FSG (mg/dl)	2.02	NS
HbA1c (%)	11.16	NS
ALT (U/L)	18.54	NS
Creatinine (mg/dl)	7.23	NS
TC (mg/dl)	8.28	NS
TG (mg/dl)	16.74	0.006
HDL (mg/dl)	-7.13	NS
LDL (mg/dl)	13.39	0.034
TC/HDL	13.11	NS
Ceruloplasmin (mg/ml)	-32.97	0.002
Catalase (kU/L)	-37.38	0.015
MDA (nmol/ml)	52.38	<0.001
Peroxynitrite (mmol/L)	-10.00	NS

Conclusion:
Consumption of the saccharin and cyclamate tablets mixture affected biochemical parameters related to metabolic function in a time and dose dependent manner and appear to increase oxidative stress in healthy and diabetic type 2 patients. The present results add further evidence of an atherosclerotic effect caused by artificial sweeteners in healthy individuals and diabetic patients. Furthermore, the artificial sweetener mixture showed harmful effects on kidney and liver functions. The amount of sweetener taken was positively associated with FSG and creatinine, while being negatively associated with catalase, peroxynitrite and ceruloplasmin. The period of consumption was positively associated with FSG and TG levels in diabetic patients. The present results indicate that saccharin and cyclamate mixtures cannot be considered as healthy sugar substitutes and their use should not be recommended.

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