3

4

Correlation between lycopene intake and blood pressure in healthy adults from Celaya, Mexico

5

6 7 8 9 10

ABSTRACT

Aims: To identify if there is a correlation between lycopene intake and blood pressure levels in healthy adults of Celava.

Study design: Cross-sectional, observational, analytical study.

Place: All students registered at a public university in Celaya, Guanajuato, Mexico.

Methodology: To measure blood pressure, a humeral digital baumanometer with adult bracelet (Rossmax MG150f) was used. The measurement was performed three times with a two-minutes interval and the average systolic and diastolic blood pressure was obtained. The daily intake of lycopene was evaluated with a questionnaire of frequency of consumption of meals. The µg of lycopene were estimated with a software related to frequency of consumption of meals. Descriptive statistics were used for all variables. To identify the correlation and possible linear relationship between lycopene intake and blood pressure, Pearson r was calculated, linear regression equation, t-test, and P-value and Confidence Intervals

Results: We included 446 participants (74.28% women, 25.78% men; between 18-51 years of age). The average systolic blood pressure was 108.30 mmHg, while the average diastolic blood pressure was 71.07 mmHg. The mean daily intake of lycopene was 6477.38 µg. However, there was no correlation or lineal relationship between lycopene intake and the measurement of systolic blood pressure (P=.93) and diastolic blood pressure (P=.5). Conclusion: No correlation was found between daily intake of lycopene and blood pressure (P> .05) in this adult sample from Celaya, Mexico. Studies should be conducted with a different way of determining the intake or level of lycopene in the body.

11 12

Keywords: Lycopene intake, Blood pressure, Adult.

13 14

15

16

17

18

22

23

24 25

1. INTRODUCTION

- The pressure exerted by the blood on the walls of the arteries while the heart pumps blood is known as blood pressure [1]. When there is a chronic elevation of blood pressure (systolic and/or diastolic) above normal values (≥140/90 mmHg) it is considered as high blood pressure or hypertension (HT) [2].
- 19 The cause of HT is mainly associated with the constriction of the arteries; however, it is 20 attributed to various factors and conditions such as genetic factors, metabolic, and mainly 21 lifestyle: sedentary, excess salt intake, alcohol and cigarette consumption, among others [3].
 - However, the most important factors in the development of HT include activation of the sympathetic nervous system, regulation of the renin-angiotensin-aldosterone system and the inflammatory processes at the vascular level. More recent studies also implicate oxidative stress [4].

- Oxidative stress could inactivate nitric oxide, which alters vasodilation, so inhibition of oxidative stress could be an effective method to control blood pressure [5].
- 28 Data from the World Health Organization (WHO), expresses that worldwide, more than one
- 29 in five adults have high blood pressure which causes approximately half of all deaths from
- 30 stroke or heart disease [2].
- In Mexico, the prevalence of hypertension in adults is 25.5%; with higher predominance in
- 32 women (26.1%) than in men (24.9%). Being 4.1 times lower the prevalence in the group of
- 20 to 29 years of age than in the group of 80 or more years of age [6].
- 34 For the treatment of hypertension, although some pharmacological agents are used, an
- 35 alternative and complementary treatment has been suggested for its control, such as
- 36 modifications in lifestyle: physical activity and especially nutritional treatment. A meta-
- 37 analysis indicate that the intake of fruits and vegetables in the diet lowers blood pressure,
- 38 which is often attributed to the role of natural antioxidants, such as lycopene, in improving
- 39 vascular function [7].
- 40 Lycopene (Lycopersicon esculemtum) is a carotenoid, responsible for the characteristic red
- 41 coloration of the tomato. Tomatoes and their products (tomato sauce, juices, among others)
- 42 they are the main source of lycopene, followed by other foods such as watermelon, pink
- 43 guava, papaya and grapefruit [3].
- 44 Due to its chemical structure containing eleven conjugated double bonds, lycopene is a
- 45 powerful antioxidant and a free radical extinguisher; it can reduce oxidative stress and the
- 46 danger of oxidation of cellular components, including lipids, proteins and DNA. Which
- 47 reduces the risk of suffering chronic diseases, such as cardiovascular diseases, cancer and
- 48 osteoporosis [3, 8].
- 49 However, studies investigating the role of lycopene supplements or foods containing
- 50 lycopene and the effects on blood pressure have contradictory results. A meta-analysis that
- 51 included 12 studies in this regard showed that at least four weeks of daily oral supplements
- 52 with tomato extract or tomato juice significantly decreased blood pressure, while others
- 53 showed no obvious relationship or association in the lycopene treatment [8].
- 54 Also, other meta-analysis concluded that lycopene supplementation >12mg/day could
- 55 significantly decrease systolic blood pressure. In addition, more research is needed to
- 56 confirm the suggested beneficial effects on systolic blood pressure and other cardiovascular
- 57 problems [7, 9].
- For this reason, the objective of this study is to identify if there is a correlation between lycopene intake and blood pressure levels in healthy adults from Celaya.

2. METHODOLOGY

62 63

2.1 Study design

64 65

An analytical observational cross-sectional study was designed.

66 67

2.2 Place and Universe of the study

68 69

All students registered at a public university in Celaya, Guanajuato, Mexico.

2.3 Selection of participants

2.3.1 Inclusion criteria

Men or women, 18 years of age or older, registered as students of a public university of Celaya and having agreed to participate voluntarily, signing the informed consent.

2.3.2 Exclusion criteria

People who did not accept to participate.

2.4 Variables

2.4.1 Sociodemographics

Age, discrete quantitative variable; number of years completed from the date of birth; Its scale of measurement is in years and it is summarized with mean and standard deviation.

Weight, continuous quantitative variable; is the body mass expressed in kilograms; it is measured on an altimeter, Medidata® digital, without shoes as with less clothes as possible; Its measurement scale is in kilograms and is summarized with mean and standard deviation. Height, continuous quantitative variable; is the measurement from the feet to the parietal region of the scalp, expressed in meters; it is measured in scale with altimeter, Medidata® digital, without shoes, in erect position and facing forward; Its measurement scale is in meters and it is summarized with mean and standard deviation.

Body mass index, continuous quantitative variable; is the body mass expressed in kg/m²; its measurement scale is low weight (BMI <18.5 kg/m²), normal weight (BMI \geq 18.5 kg/m² to <25 kg/m²), overweight (BMI \geq 25 kg/m² to <30 kg/m²) and obesity (BMI \geq 30 kg/m²); and it is summarized with mean and standard deviation.

Gender, dichotomous categorical variable; they are the phenotypic characteristics that differentiate men from women; Its measurement scale is male or female and is summarized with frequencies and percentages.

Marital status, nominal categorical variable; attribute of the personality that refers to the position a person occupies in relation to the family; necessary budget, together with the political state, to know what is the capacity of a person; his scale of measurement is single, married, divorced, separated, free union; it is summarized with frequencies and percentages. Residence, nominal categorical variable; it is the place of space where a person remains continuously, its scale of measurement is urban, suburban and rural and is summarized with frequencies and percentages.

2.4.2 Independent

Daily mean intake of lycopene; continuous quantitative variable; is a carotenoid, the main pigment responsible for the characteristic red coloration of tomato and some fruits, based on the frequency of food consumption and processed in the SNUT software [10]; Its measurement scale is in µg. It is summarized with mean and standard deviation

2.4.3 Dependent

Systolic blood pressure; continuous quantitative variable; Higher pressure exerted by the blood wave ejected by the ventricular systole against the arterial wall, is measured with humeral digital baumanometer with adult bracelet (Rossmax MG150f), on three occasions with an interval of two minutes and the average systolic blood pressure is obtained, its measurement scale is in mmHg; normotensive to adults with systolic blood pressure <140 mmHg and as hypertensive to adults systolic blood pressure ≥140 mmHg. It is summarized with mean and standard deviation.

Diastolic blood pressure; quantitative variable continues; it is the minimum pressure of blood against the arteries and occurs during diastole. It depends mainly on peripheral vascular resistance. It is measured with humeral digital baumanometer with adult bracelet, on three occasions with an interval of two minutes and the average diastolic pressure is obtained; its measurement scale is in mmHg; normotensive to adults with diastolic blood pressure <90 mmHg and as hypertensive to adults ≥90 mmHg. It is summarized with mean and standard deviation.

2.5 Questionnaires

Two questionnaires were used; one to collect the general data and a questionnaire of frequency of food consumption, SNUT survey [10], validated in Mexican population [11] and use in the National Nutrition and Health Surveys in Mexico [12].

2.6 Procedures

Potential participants were individually explained the objectives of the study and answered the questions they were asked. They were asked to sign the informed consent and the personal data was collected through a general questionnaire. A humeral digital baumanometer with adult bracelet (Rossmax MG150f) was used to measure blood pressure. Firstly, the patient was kept at rest for 10 minutes, the baumanometer was placed in the non-dominant hand, the measurement was made three times with a two-minute interval and the mean systolic and diastolic blood pressure was obtained.

Lycopene intake was assessed by means of a food consumption frequency questionnaire which includes 104 foods. The μg of lycopene were estimated with the software System for the Evaluation of Nutritional Habits and Consumption of Nutrients (SNUT) [10].

2.7 Sample size

Assuming a Pearson's r of 0.7 between lycopene intake and diastolic blood pressure, the minimum number of participants is 11 with 95% accuracy and 80% power. (Epidat, 4.1, 2014, Xunta de Galicia, OPS, Universidad CES).

2.8Statistical analysis

Descriptive statistics was used for all the variables.

To identify the correlation and possible lineal relationship between lycopene intake and blood pressure, we calculated Pearson's r, lineal regression equation, t-test and *P*-value and 95% confidence intervals. To demonstrate the statistical significance of the results, the value of *P* was set at .05.

166 The analysis was p

The analysis was performed in STATA 13.0 (Stata Corp., College Station, TX, USA)

3. RESULTS AND DISCUSSION

The following study was made up of a total of 446 participants. We found predominance of the female gender (74.28%), as well as a higher residence in urban area (78.92%) and single marital status (94.84) as shown in table 1. The study of controlled intervention with healthy volunteers of Thies et al., with 225 participants coincides with ours, having a greater predominance of the female gender [13]. On the other hand, our sample was larger than other research [5, 8, 14, 15].

Table 1. Sociodemographic characteristics of the categorical sample

Variables		n	%
Gender	Female	115	25.78
	Male	331	74.28
Residence	Urban	352	78.92
	Suburban	67	15.02
	Rural	27	6.05
Marital status	Single	423	94.84
	Married	17	3.81
	Divorced	1	0.22
	Separated	1	0.22
	Free Union	4	0.90

 With respect to the quantitative variables, an average of 21 years of age can be observed in table 2. Unlike other studies, such as Thies et al., where he studied adults with an average age of 51 years [13]. Biddle et al., on the other hand, studied elderly adults hospitalized in Central Kentucky with an average age of 65 years [5].

Based on weight and height, the BMI was determined: an average of 24.28 kg/m² was found, so in relation to the classification proposed by WHO, it is classified as normal weight (BMI≥18 to 24.9kg/m²) [16]. While in the study by Thies et al., it was 26.4 kg/m², similar to the study by Ried et al. where the average BMI was 26.9 kg/m². Both classified as overweight [8,13].

Table 2. Sociodemographic characteristics of the quantitative sample

Variables n=446	Range	Mean ± S
Age (years)	17 to 51	21.52 ± 2.99
Weight (kg)	38.7 to 171.2	64.59 ± 15.21
Height (m)	1.17 to 1.98	1.62 ± 0.09

Body mass index (kg/m²)	15.01 to 55.37	24.28 ± 4.48
(kg/iii)		

194 S Standar deviation

 The mean systolic blood pressure was 108.30 mmHg while the mean diastolic blood pressure was 71.07 mmHg, which is classified as low normal.

Blood pressure in other studies was higher; In the study by Thies, et al., It was 130.3/79.13 mmHg [13], while in the study by Ried et al., performed in the Australian population was 133/80 mmHg [8]. The daily intake of lycopene was 6477.38 µg, lower than that proposed in other studies, since it has been determined that the recommended amount of lycopene to achieve an effect in reducing blood pressure is >12mg [5,7,15].

Table 3. Distribution of study variables

Variables n=446	Range	Mean ± S
Systolic blood presure (mmHg)	70 to 140	108.30 ± 11.11
Dyastolic blood presure (mmHg)	50 to 109	71.07 ± 8.51
Daily mean intake of lycopene (μg)	0 to 48.610.6	6477.38 ± 6985.11

S Standar deviation

Figure 1 shows that there is no correlation or linear relationship between lycopene consumption and the measurement of systolic blood pressure (P=.93). However, in some meta-analyzes they analyzed intervention studies with lycopene supplements or tomato-based products, in which the systolic blood pressure was reduced [7, 17]. As in the study by Paran et al. where they intervened with encapsulated tomato extract (15 mg of lycopene) to participants with moderate hypertension. After 6 weeks the results showed a reduction in systolic blood pressure [15]. While the results of Costa-Rodrigues et al., they indicate that the intake of lycopene in tomato products has a greater effect than lycopene supplements [18].

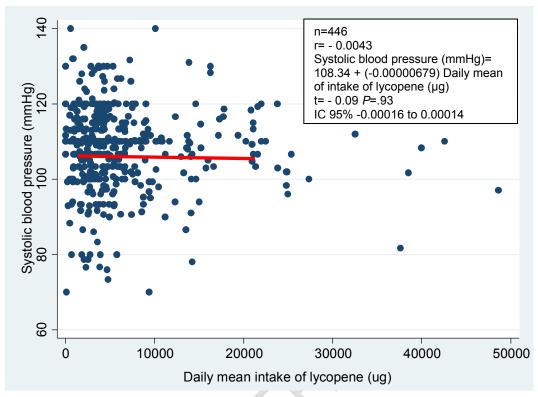


Figure 1 Correlation and lineal regression among intake of lycopene and systolic blood prssure

Figure 2 shows that there is no correlation or linear relationship between lycopene consumption and the measurement of diastolic blood pressure (P=.5). No correlation was found between lycopene consumption and blood pressure, suggesting that a daily intake of tomato-based foods does not lower blood pressure levels. As in a randomized controlled study by Ried et al., no blood pressure lowering effect was found by administering 15 mg of lycopene per day for 12 weeks using a commercially available tomato extract capsule [8]. In another controlled study, 3 dietary intervention groups were carried out, in which group 1 was asked to consume a control diet (low in tomato-based foods), group 2 a diet with a high tomato content and the number 3 a control diet supplemented with lycopene capsules (10 mg/d) for 12 weeks. The results also show no significant change in blood pressure [13].

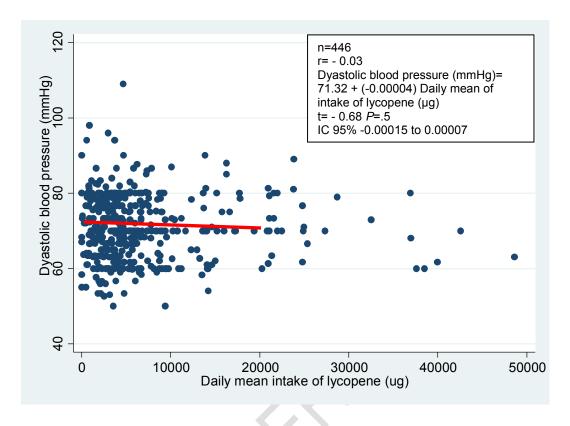


Figure 2 Correlation and lineal regression among intake of lycopene and dyastolic blood pressure

The participation rate of this study was high (94%) and is a strength of the study. There may be a recall bias in the method of evaluating lycopene intake, since the questionnaire is a reminder on average of the last year, In addition, respondents consistently overestimate the food they eat, with more often those who perceive them as "healthy", such as fruits and vegetables [19]; Also, it is a method dependent on the memory and ability of the participants to describe the type and quantity of food consumed [20], for this reason for future research it is recommended that a controlled intervention study be carried out using specific biochemical markers to measure the lycopene intake more precisely. All participants were healthy adults and maybe this reflects no correlation between lycopene intake and levels of blood pressure.

4. CONCLUSION

The results indicate that there is no correlation between daily lycopene consumption and blood pressure (*P*>.05), in this sample of adults from Celaya, Mexico. Studies with different forms should be conducted to determine the intake or level of lycopene in the body.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

CONSENT

260 261

All participants signed informed consent.

262 263

ETHICAL APPROVAL

264 265

The protocol was reviewed and approved by the Research and Bioethics Committees of the Division of Health Sciences and Engineering, Campus Celaya-Salvatierra, University of Guanajuato, Mexico with the registry **CIDCSIC-0911204**.

267268

266

REFERENCES

269 270 271

272

273

- [1] National Heart, Lung and Blood Institute. Presión arterial alta. Available at: https://www.nhlbi.nih.gov/health-topics/espanol/presion-arterial-alta
- [2] Organización Mundial de la Salud. Preguntas y respuestas sobre la hipertensión. 2015. Available at: https://www.who.int/features/qa/82/es/
- 275 [3] Waliszewski KN, Blasco G. Propiedades nutraceúticas del licopeno. Salud Pública 276 México. 2010; 52(3):254-65.
- [4] Montezano AC, Touyz RM. Reactive Oxygen Species, Vascular Noxs, and Hypertension:
 Focus on Translational and Clinical Research. Antioxid Redox Signal. 2014; 20(1):164-82.
 Doi: https://doi.org/10.1016/j.atherosclerosis.2017.01.009
- [5] Biddle MJ, Lennie TA, Bricker GV, Kopec RE, Schwartz SJ, Moser DK. Lycopene Dietary Intervention: A Pilot Study in Patients with Heart Failure. J Cardiovasc Nurs. 2015; 30(3):205-12. Doi: http://doi.org/10.1097/JCN.000000000000108.
- 283 [6] Barquera S, Campos I, Hernández L, Pedroza A, Barrientos T, Romero M, et al. 284 Hipertensión arterial. Encuesta Nacional de Salud y Nutrición a Medio Camino 2016. 2016 285 Available at: https://www.gob.mx/cms/uploads/attachment/file/209093/ENSANUT.pdf
- [7] Li X, Xu J. Lycopene Supplement and Blood Pressure: An Updated Meta-Analysis of Intervention Trials. Nutrients. 2013; 5(9):3696-712. Doi: http://doi.org/10.3390/nu5093696.
- 288 [8] Ried K, Fakler P. Protective effect of lycopene on serum cholesterol and blood pressure: 289 Meta-analyses of intervention trials. Maturitas 2011; 68(4): 299-310. Doi: 290 http://doi.org/10.1016/j.maturitas.2010.11.018
- 291 [9] Siervo M, Lara J, Ogbonmwan I, Mathers JC. Inorganic Nitrate and Beetroot Juice Supplementation Reduces Blood Pressure in Adults: A Systematic Review and Meta-293 Analysis. J Nutr. 2013; 143(6):818-26. Available at: https://academic.oup.com/jn/article/143/6/818/4571708
- [10] Hernandez-Avila JE, Gonzalez-Aviles L, Rosales.Mendoza E, Parra-Cabrera S, Hernandez-Avila M, Romieu I, Willet W, Madrigal H. Sistema de evaluacion de habitos nutricionales y consumo de nutrimentos. Centro de investigacion en salud poblacional. Direccion de informatica. Instituto Nacional de Salud Publica, Mexico, 2003. Available at: http://www.insp.mx/snut2003/index.php)
- [11] Hernandez-Avila M, Romieu I, Parra S, Hernandez Avila J, Madrigal H, Wiliet W. Validity and reproductibility of food frecuency questionnaire to asses dietary intake of women living in Mexico city. Salud Pub Mex. 1998; 39 (40):133-140.
- 303 [12] Gutierrez JP, Rivera J, Shamah T, Oropeza C, Hernendez Avila M. Encuesta Nacional de Nutrición y Salud 2012 [Internet]. 2011. [cited june 22, 2019]. Available at: https://ensanut.insp.mx/informes/ENSANUT2012ResultadosNacionales.pdf
- 306 [13] Thies F, Masson LF, Rudd A, Vaughan N, Tsang C, Brittenden J, et al. Effect of a tomato-rich diet on markers of cardiovascular disease risk in moderately overweight, disease-free, middle-aged adults: a randomized controlled trial. Am J Clin Nutr. 2012 2019]; 95 (5): 1013-22. Doi: https://doi.org/10.3945/ajcn.111.026286

310 [14] Engelhard YN, Gazer B, Paran E. Natural antioxidants from tomato extract reduce blood 311 pressure in patients with grade-1 hypertension: A double-blind, placebo-controlled pilot 312 Heart J. 2006: 151(1): 100.e6-100.e1. 313 https://doi.org/10.1016/j.ahj.2005.05.008 [15] Paran E, Novack V, Engelhard YN, Hazan-Halevy I. The Effects of Natural Antioxidants 314 315 from Tomato Extract in Treated but Uncontrolled Hypertensive Patients. Cardiovasc Drugs Ther. 2009; 23(2): 145-51. Doi: https://doi.org/10.1007/s10557-008-6155-2 316 [16] Organización Mundial de la Salud. 10 datos sobre la obesidad. Available at: 317 318 https://www.who.int/features/factfiles/obesity/facts/es/ [17] Cheng HM, Koutsidis G, Lodge JK, Ashor A, Siervo M, Lara J. Tomato and lycopene 319 320 supplementation and cardiovascular risk factors: A systematic review and meta-analysis. 321 Atherosclerosis. 2017;257:100-8. Doi: https://doi.org/10.1016/j.atherosclerosis.2017.01.009 [18] Costa-Rodrigues J, Pinho O, Monteiro PRR. Can lycopene be considered an effective 322 protection against cardiovascular disease?. Food Chem. 2018; 245: 1148-53. Doi: 323 324 https://doi.org/10.1016/j.foodchem.2017.11.055 325 [19] Perez C, Aranceta J, Salvador G, Varela-Moreiras G. Métodos de Frecuencia de 326 consumo alimentario. Rev Esp Nutr Comunitaria. 2015; 21(1):45-52. Available at: 327 http://www.renc.es/imagenes/auxiliar/files/RENC2015supl1FFQ.pdf 328 [20] Shim J-S, Oh K, Kim HC. Dietary assessment methods in epidemiologic studies. 329 Epidemiol Health.2014; 36:e2014009. Doi: http://doi.org/10.4178/epih/e2014009 330 331 332 333 334 335 336 337 [