

EFFECT OF AN INFUSION OF *HIBISCUS SABDARIFFA* L. IN HYPERTENSIVE PATIENTS FROM AN URBAN POPULATION: AN IMPORTANT COMORBIDITY BEFORE COVID-19.

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**Abstract**

**Background:** Roselle (*Hibiscus sabdariffa* L.) has traditionally been used in folk medicine to treat hypertension; however, clinical studies are limited to show efficacy as an antihypertensive. Today, hypertension is an important comorbidity in the face of the covid-19 pandemic. The objective of this study was to assess the effect of a commercial *H. sabdariffa* infusion on blood pressure (BP) levels in hypertensive patients through a pilot clinical study.

**Materials and Methods:** Patients with a previous diagnosis of hypertension were chosen, regardless of their BP figures, who frequently came for consultations at a health center. The infusion (10 g/240 mL) was administered orally daily for four weeks in 33 patients, 11 of them presented uncontrolled levels of BP.

**Results:** Statistically significant differences were found in diastolic blood pressure (DBP) values, but not for systolic blood pressure (SBP) (n=33), suggesting that the values could decrease until being significant with a longer supplementation time or higher doses. In uncontrolled patients (n=11), both SBP and DBP showed a significant decrease.

**Conclusion:** The results showed that the use of *H. sabdariffa* in this study could be useful in the management of patients with hypertension. However, future studies should be performed on larger samples so that effectiveness can be fully determined.

**Keywords:** hypertension, roselle, *Hibiscus sabdariffa* L, infusion, blood pressure.

**List of abbreviation:** ANOVA: Analysis of variance; BMI: Body mass index; BP: Blood pressure; °C: degrees Celsius; DBP: Diastolic blood pressure; g: Grams; *H. sabdariffa*: *Hibiscus sabdariffa* L; MAG: Mutual Aid Group; mg: Milligrams; mL: Milliliters; mmHg: Millimeters of mercury; SBP: Systolic blood pressure; WHO: World Health Organization.

**Introduction**

Hypertension is a major public health problem worldwide, being the main risk factor for the development of cardiovascular diseases, which causes 17 million annual deaths worldwide and around 9.4 million suffer complications derived from hypertension (Pan-American Health Organization, n.d.; World Health Organization, 2013), like strokes, coronary artery disease, heart failure, kidney failure and aortic aneurysm (Ahad *et al.*, 2020). Estimates from the World

Health Organization (WHO) show that by 2030, about 23.6 million people will die from cardiovascular related diseases, becoming the leading cause of death worldwide (World Health Organization, 2013). Therefore, hypertension has become a serious problem, whose impact in economic, social and quality of life terms, makes it a priority both nationally and globally. In Mexico, hypertension affects 17.3 million people (Instituto Nacional de Salud Pública, 2016) and more than a billion people worldwide (Ahad *et al.*, 2020). This comorbidity is very important in the negative impact of the pandemic caused by covid-19.

In recent years, there is an approach towards the use of medicinal plants, which in some way have been used to treat diseases since ancient times. Some reports show that about 15 to 20% of the people who take prescription drugs also take herbal remedies, however less than 40% of patients report the use to their doctor, even if they experience side serious effects (Ahad *et al.*, 2020).

*H. sabdariffa* known as “jamaica flower” in Mexico and in other parts of the world as roselle, belongs to the Malvaceae family. It is a plant native to tropical Africa, but is cultivated in different regions of the world like Mexico, Central America and South and Southeast Asia (Da-Costa-Rocha, *et al.*, 2014; Guardiola *et al.*, 2014). The plant and its different parts are used by the industry for the production of different products such as beverages, food products, lotions, dyes, and for medical purposes (Da-Costa-Rocha, *et al.*, 2014; Guardiola *et al.*, 2014; Hernández-Ávila *et al.*, 2016; Ahad *et al.*, 2020), its use has become widespread due to its various applications in traditional medicine as an antimicrobial, antioxidant, anti-inflammatory, hypoglycemic, hypolipidemic as well as antihypertensive agent (Lislivia-Yiang-Nee *et al.*, 2019), especially in countries like United States, Mexico, Iran, India, Taiwan, Greece, and the continent of Africa among others (Guardiola *et al.*, 2014). The hypotensive effects of *H. sabdariffa* have been reported in animal and human studies (Guardiola *et al.*, 2014; Riaz *et al.*, 2018; Al-Anbaki *et al.*, 2019), becoming a safe and effective option to treat hypertension through its diuretic, anti-aldosterone activity and vasodilator effect by inhibiting the angiotensin-converting enzyme attributed to its anthocyanin content (Al-Anbaki *et al.*, 2019).

In this work, we proposed the use of *H. sabdariffa* as an alternative to treat patients with hypertension. Currently, the impact of the covid-19 pandemic has shown that this comorbidity requires an accessible alternative, considering that poverty is becoming more important in terms of morbidity and mortality from covid-19. The objective was to measure its effects on blood pressure, its safety and tolerance, by an oral administration of an *H. sabdariffa* infusion. Using this plant in health could decrease the economic and social costs of managing hypertension and also contribute to the quality of life or delay its complications, which top the list of the death causes and have a high economic cost per capita.

## **Materials and Methods**

### ***H. sabdariffa* infusion preparation**

*H. Sabdariffa* was selected and obtained in a local market of the Tulancingo Valley region (Hidalgo, Mexico), and kept in hermetic bags of low-density polyethylene, impervious to water vapor, later stored in a dry environment at a temperature of  $15\pm 2$  °C. When required, the calyces were cleaned, and the infusion was prepared by mixing 10 g of *H. Sabdariffa* with 240 mL of drinking water and boiling for 5 min. This had to be taken on an empty stomach before breakfast.

### **Study design and intervention**

A quasi-experimental pre-test and post-test pilot study was carried out on the infusion. It included 33 patients with hypertension, 11 of them had uncontrolled BP > 140/90 mmHg at the beginning of the intervention. The patients belonged to a Mutual Aid Group (MAG) of the Rojo Gómez Health Center in Tulancingo de Bravo, Hidalgo. We worked with members of the MAG, since the patients go there regularly for their medical consultation, and weekly sessions of nutrition and physical activity. This reduced the chances that patients could drop out of the study.

### **Participants**

The participants' ages range from 30 to 82 years and they all had a diagnosis of hypertension and were on anti-hypertensive drugs. The participants' selection was determined using the following criteria:

#### **Inclusion criteria:**

- Age  $\geq 20$  years
- Hypertensive patients who attended the Health Center
- Patients with diseases concomitant to hypertension were included.

#### **Exclusion criteria:**

- Patients with complications associated with hypertension
- Pregnant or lactating women
- Patients who reported an adverse reaction to the consumption of *H. sabdariffa*

## Measurement procedure

During the four weeks of the study, the patients continued with their pharmacological treatment (prescribed before the intervention by their responsible doctor) and also took the *H. sabdariffa* extract; the health personnel assigned to the Health Center once a week tested the participants, measuring BP with a sphygmomanometer (Prosphyg 760), body weight with a floor scale (SECA 869) and waist circumference with an ergonomic tape (SECA 201). We trained the personnel and the participants together in the preparation and infusion consumption.

The *H. sabdariffa* calyces were packed in airtight bags and labeled with the days of the week before being given to the participants to have a greater control over their consumption. To verify the infusion consumption, each patient gave the treatment bags weekly to health personnel, both empty and full (in case they had not taken it) to count them, in the same way they were given an "Intake Monitoring Survey of the Infusion and Side Effects", which had to be filled daily by each participant and delivered at the end of the week, so that seven bags of *H. sabdariffa* and a new registration survey could be granted again. Likewise, to have greater accuracy in the infusion preparation, each patient was given a measuring cup of 240 mL and a strainer, to facilitate its consumption. The data were recorded in the clinical record and were subsequently transferred to the Excel® (2016) data sheets.

## Statistical analysis

Results were expressed as mean and standard deviation. For the data analysis, an analysis of variance (ANOVA) of one way and later the Tukey test were applied to determine statistical significance, considering the values of  $p < 0.05$  as acceptable to reject the null hypothesis. The data was analyzed using the SPSS v.20 software, and GraphPad Prism v.7 was used to prepare the graphics.

## Ethical Considerations

All participants voluntarily took part under an informed consent letter, the work was approved by the research and ethics committee of the Hidalgo Health Secretariat (Permit: FSSA2017064), according to the Helsinki declaration.

## Results

Of the 33 patients, 29 were women, representing 87.9% and only 4 patients were men, 12.1%. No one dropped out of the study. The average age was 61.89 years, with the youngest patient being 34 years old and the oldest patient was 82 years. The average evolution time of hypertension was  $6.2 \pm 5.1$  years, and 96.6% of the patients had an additional condition to hypertension. Table 1 shows the concomitant diseases of the participants, which were diagnosed prior to the intervention, as well as the average evolution time.

**Table 1:** Concomitant diseases and evolution time.

<i>Disease</i>	<i>Total</i>	<i>Percentage</i>	<i>Evolution time (years)</i>
<b>Diabetes</b>	15	45.5%	$8.9 \pm 4.8$
<b>Obesity</b>	15	45.5%	$10 \pm 6.9$
<b>Dyslipidemias</b>	30	90.9%	$5 \pm 3$

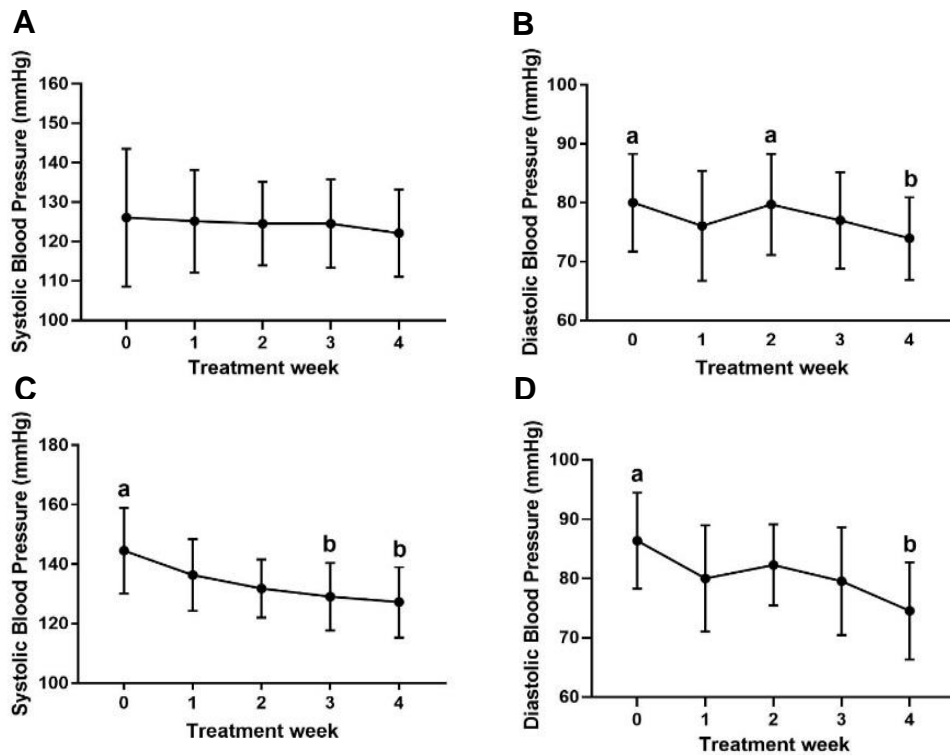
All the participants were taking at least one antihypertensive medication prior to the study, the antihypertensive medications consumed by the patients during the study mentioned are shown in Table 2. These were prescribed prior to the intervention, by their responsible physician at the health Center.

**Table 2:** Medicament consumed during the trial.

<i>Usage</i>	<i>Medicament</i>	<i>Number of patients</i>	<i>Percentage</i>
<b>Antihypertensive</b>	Enalapril	10	30.3%
	Nifedipine	5	15.1%
	Hydrochlorothiazide	5	15.1%
	Captopril	4	12.1%
	Losartan	4	12.1%
	Chlorthalidone	4	12.1%
	Metoprolol	3	9%
	Irbesartan	2	6%
	Telmisartan	1	3%

Figure 1. Shows a decrease in the SBP values ( $126.06 \pm 17.49 / 122.12 \pm 11.11$ ) regarding the baseline measurement of the 33 participants with hypertension (Figure. 1A), showing an average reduction of 3.94 mmHg, however, the decrease

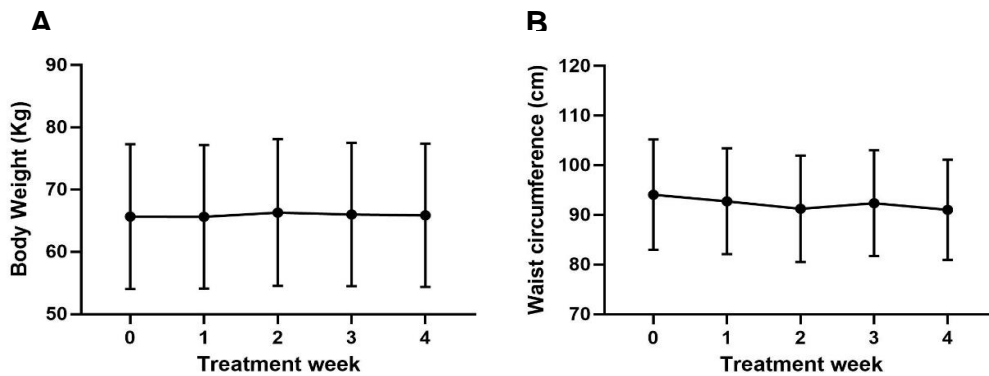
was not significant ( $p=0.7301$ ). In contrast, for DBP, a significant decrease ( $80\pm 8.29/73.94\pm 7.04$ ) ( $p=0.0288$ ) was found at week 4 of supplementation (Figure. 1B), showing a decrease of at least 6.06 mmHg.



**Figure 1:** SBP (A). A decrease in pressure levels was observed throughout the treatment, however, the differences were not significant ( $n=33$ ). DBP (B). Significant differences between weeks of treatment ( $n=33$ ) are described as; a = comparison between day 0 and week 2; with b=week 4; b=ANOVA  $p<0.05$  and Tukey's test. SBP in patients with figures  $>140/90$  mmHg (C). Significant differences between weeks of treatment ( $n=11$ ) are described as; a=between day 0; with b = weeks 3 and 4. ANOVA  $p <0.05$  and Tukey's test. DBP of patients with figures  $>140/90$  mmHg (D). Significant differences between weeks of treatment ( $n=11$ ) are described as; a= comparison between day 0; with b=week 4. ANOVA and Tukey test  $p<0.05$ .

Patients who presented with uncontrolled BP ( $n=11$ ) at the start of the study were analyzed separately. During the *H. sabdariffa* supplementation, they showed a BP reduction ( $144.5\pm 14.5/127.3\pm 11.9$ ) relative to the baseline measurement of SBP, showing significant differences on the third week ( $p=0.0310$ ) and fourth week ( $p=0.0119$ ) of supplementation (Figure. 1C) and an average reduction of 17.3 mmHg. This same trend was observed in DBP, where there was a significant decrease ( $86.4\pm 8.1 / 74.5\pm 8.2$ ) ( $p=0.0056$ ) in DBP levels (Figure. 1D), reducing on average 11.8 mmHg.

Weight measurements remained stable during the study (Figure. 2A), there were no significant differences ( $p=0.9993$ ), waist circumference measurement (Figure. 1B) decreased during the supplementation with *H. sabdariffa*, however, these were not significant ( $p=0.7748$ ).



**Figure 2:** Body weight (A). No decrease in body weight was observed throughout the treatment. Waist circumference (B). A waist circumference decrease was observed throughout the treatment; however, the differences were not significant.

## Discussion

The main thrust of this study was to work with a real and not-so-controlled population, since previous studies excluded patients who were under pharmacological treatment (Herrera-Arellano *et al.*, 2004; Herrera-Arellano *et al.*, 2007; McKay *et al.*, 2009; Mozaffari-Khosravi *et al.*, 2009; Chukwu *et al.*, 2019), or who presented concomitant diseases (Herrera-Arellano *et al.*, 2004; Herrera-Arellano *et al.*, 2007; McKay *et al.*, 2009; Chukwu *et al.*, 2019), in some other studies they included only patients with a recent diagnosis of hypertension (Chukwu *et al.*, 2015) or with specific BP (Herrera-Arellano *et al.*, 2007; McKay *et al.*, 2009; Mozaffari-Khosravi *et al.*, 2009); while we worked with patients with hypertension regardless of the degree, evolution time, drug consumption, or presence of other frequent diseases like diabetes, obesity, or dyslipidemia, which usually accompany this patients. Furthermore, the infusion was made from commercial *H. sabdariffa* calyces obtained in a local market, since it is the plant to which the population has the most access.

In this work, an infusion was prepared with 10 g of *H. sabdariffa* in 240 mL of drinking water and the intake lasted four weeks. When blood pressure figures were analyzed, significant differences were found. SBP figures did not show a reduction that reached any statistical significance, however, a decreasing trend is observed, since they showed the lowest value in the last measurement, suggesting that the values could decrease until they were significant with a longer treatment time. DBP figures also showed their lowest value after 4 weeks of infusion consumption, where a decrease of at least 6.06 mmHg was observed, showing a significant difference.

It should be considered that the baseline average BP was  $126.06 \pm 17.49/80 \pm 8.29$  mmHg, several patients presented values within the normal range even though all patients had a previous diagnosis of hypertension for at least one year that could be attributed to the MAG treatment itself, since they are patients who come to the health units more frequently to receive educational sessions and a more formal follow-up of their condition. It was observed that at baseline SBP levels  $\geq 130$  mmHg, the treatment showed significant reductions in SBP and DBP, while at lower levels, the results obtained did not (Khalesi *et al.*, 2014), therefore an analysis of the patients who presented figures above the control ( $>140/90$ , mmHg) was done, 11 patients were identified who showed a reduction in BP between baseline and four weeks of supplementation, achieving a significant decrease in SBP of 15.5 mmHg, and DBP 11.8 mmHg.

These findings are very similar to the results of Herrera-Arellano *et al.* (2004), where BP were reduced by  $14.5 \pm 11.76/11.18 \pm 6.9$  mmHg in the same time and number of calyces (10 g). Herrera-Arellano *et al.* (2007) obtained an absolute reduction of  $17.14/11.97$  mmHg in four weeks of treatment with 250 mg of anthocyanins. Mozaffari-Khosravi *et al.* (2009) showed a reduction in SBP of 21 mmHg with a similar population, as they administered an infusion twice a day (4 g per day) to patients with type II diabetes mellitus and mild hypertension, according to JNC-VI criteria (SBP  $<160$  mmHg and DBP  $<100$  mmHg), however, for the SBP there were no significant changes. In a study conducted in Nigeria in patients with mild hypertension (SBP 140-159 mmHg or DBP 90-99 mmHg) to moderate (SBP 160-179 mmHg or DBP 100-109 mmHg), a significant reduction of  $17/12.12$  mmHg was recorded after four weeks of treatment with an infusion of *H. sabdariffa* at concentrations of  $150 \text{ mg kg}^{-1}$  once a day, before breakfast (Chukwu *et al.*, 2015).

The possible mechanisms responsible for the antihypertensive effect of *H. sabdariffa* have been mainly attributed to its anthocyanin and proanthocyanidin components, detected in abundance in aqueous extracts of *H. sabdariffa* calyces, highlighting delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside, anthocyanins that have been shown to inhibit the angiotensin-converting enzyme (Herrera-Arellano *et al.*, 2007; McKay *et al.*, 2009; Mozaffari-Khosravi *et al.*, 2009; Ojedaa *et al.*, 2010; Khalesi *et al.*, 2014). It has a vasodilator effect (Sarr *et al.*, 2009), demonstrated in the study by Ajay *et al.* (2007), suggesting a relaxation of the nitric oxide pathway and the inhibition of calcium flow ( $\text{Ca}^{2+}$ ) in vascular smooth muscle cells. Another mechanism for reducing blood pressure is the increase in urinary sodium concentration while maintaining normal potassium levels (Herrera-Arellano *et al.*, 2004; Herrera-Arellano *et al.*, 2007; Ajay *et al.*, 2007; McKay *et al.*, 2009; Mozaffari-Khosravi *et al.*, 2009; Ojedaa *et al.*, 2010; Sarr *et al.*, 2009; Khalesi *et al.*, 2014; Serban *et al.*, 2015).

Results of this research showed that *H. sabdariffa* consumption had no effect on body weight or BMI. Although not all previous studies testing *H. sabdariffa* extracts as an infusion for hypertension control have reported the effects of *H. sabdariffa* on body weight, Mozaffari-Khosravi *et al.* (2009) reported that weight and BMI remain stable throughout treatment. Others like Marhuenda *et al.* (2020), showed a significant reduction in body weight, BMI and central fat, at the end of an 84-day treatment in healthy subjects, which consisted of consuming a capsule that included a mixture of *Lippia citriodora* (325 mg) and *H. sabdariffa* (175 mg) extracts. It should be noted that the results showed a greater reduction in weight in men than in women, perhaps in this research a decrease in body weight would have been observed if a greater number of men had been included, since the majority of patients treated were women (87.9%). Chang *et al.* (2014) demonstrated a significant decrease in BMI, body fat, and waist-to-hip ratio after consumption of a 2-capsule treatment of freeze-dried *H. sabdariffa* (450 mg *H. sabdariffa*+50 mg of starch) three times a day for 12 weeks, this in patients with hepatic steatosis and BMI  $>27$ . Asgary *et al.* (2017) showed that the BMI did not undergo significant changes after four weeks consuming 500 mg daily of *H. sabdariffa* in patients with metabolic syndrome, establishing that the time of treatment is essential to see changes in body weight and BMI, since only after six weeks of consumption significant changes were observed (Chang *et al.*, 2014), which could explain why a significant reduction in waist circumference was not observed either. Another contribution of this research was to determine the therapeutic tolerability of a commercial *H. sabdariffa* infusion, also an accessible and accepted way of consuming the plant. At the same time, it is a study that worked with a population that, together with hypertension, had

some other chronic disease and that consumed drugs to treat them, showing that there is no unfavorable interaction between the infusion of *H. sabdariffa* and the drugs consumed, generating an antecedent for future research.

*H. sabdariffa* could be an alternative in hypertension treatment, since it reduced blood pressure. Currently, the infusion of *H. sabdariffa* could be very useful in the face of the covid-19 pandemic, since arterial hypertension is one of the comorbidities with the greatest negative impact in covid-19 cases and mainly for those people living in poverty and extreme poverty, since its cost is very affordable, it is for food consumption and it is important to continue research on *H. sabdariffa*.

## Conclusion

In this study, we intended to highlight the anti-hypertensive property of *H. sabdariffa*. The results suggest that a higher dose of this infusion or a longer treatment time, the values of the variables will decrease significantly, since the lowest levels of the entire study (except for body weight) were observed in the last month of supplementation, therefore, *H. sabdariffa* could be an alternative in hypertension treatment, since it reduced blood pressure. Future studies will have to be carried out including within the experimental design, positive controls with authorized antihypertensive drugs, including a larger sample size and biochemical indicators, which could provide further information on how *H. sabdariffa* acts and determine the magnitude of its efficacy and activity on BP and body weight.

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**Conflict of Interests.** The authors declare that there is no conflict of interest associated with this study.

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