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Presentation of the Content

In the first chapter we present, *Generalized Super-Twisting Control for an Insulin Infusion System for Patients with Type 1 Diabetes* by GUERRERO, Jesús, FRAUSTO-SAAVEDRA, Bryan, CHIMAL-CRUZ, Martín Alberto and ORTIZ-SANTOS, Salvador, with adscription in the Tecnológico Nacional de México/ ITS Abasolo, Universidad Politécnica de Guanajuato and Universidad Autónoma de Querétaro, as the following article we present, *Degradation of AMARANTH with TiO_2 Synthesised by Sol-Gel Process* by MONCADA-SÁNCHEZ, Cristina, SALAZAR-HERNÁNDEZ, Mercedes, BALTAZAR-VERA, Juan Carlos and CAUDILLO-GONZÁLEZ, Martín, with adscription in the Universidad de Guanajuato, as the following article we present, *Hand orthosis design for the rehabilitation of people with rheumatoid arthritis* by LÓPEZ, Pedro, RAMIREZ, Mayra, GONZÁLEZ, Lizbeth and PADRÓN, Jonathan, with adscription in the Universidad Politécnica del Bicentenario, as the following article we present, *Antimicrobial effect of Eysenhardtia polystachya homemade extracts on bacteria causing urinary tract infections* by PÉREZ-GARCÍA, Luis Antonio, PÉREZ-ROCHA, Briseida, MACÍAS-PÉREZ, José Roberto and ALVARADO-SÁNCHEZ, Brenda, with adscription in the Universidad Autónoma de San Luis Potosí.

Content

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Generalized Super-Twisting Control for an Insulin Infusion System for Patients with Type 1 Diabetes

Control Super-Twisting Generalizado para un Sistema de Infusión de Insulina para Pacientes con Diabetes Tipo 1

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Abstract

Type-1 diabetes is the number 1 disease in the world. When a person becomes ill, the patient's pancreas is no longer able to generate insulin to lower blood glucose levels when food is eaten. An alternative way to treat patients with diabetes is automatic insulin infusion systems. In this article, a control based on higher order sliding modes for the control of blood glucose is designed. The proposed controller is based on the Generalized Super-Twisting algorithm, which offers convergence in finite time, and is robust against external disturbances and parametric uncertainties. Also, the stability of the proposed controller is tested using Lyapunov arguments. Finally, the control performance is compared against other proposed methodologies. Those controllers were proven under several scenarios through computer simulations in MATLAB.

Diabetes, Sliding Mode Control, Stability, Robust

Resumen

La diabetes es la enfermedad número 1 en el mundo. Cuando una persona enferma, el páncreas del paciente ya no es capaz de generar insulina para reducir los niveles de glucosa en la sangre cuando un alimento es ingerido. Una alternativa para tratar a los pacientes con diabetes, son los sistemas de infusión de insulina automática. En este artículo se diseña un control basado en modos deslizantes de orden superior para el control de la glucosa en la sangre. El control diseñado se basa en el algoritmo Super-Twisting Generalizado, el cual ofrece convergencia en tiempo finito, es robusto ante perturbaciones externas e incertidumbres paramétricas. También, se prueba la estabilidad del controlador propuesto mediante argumentos de Lyapunov. Finalmente, se compara el desempeño del control contra otros propuestos en la literatura mediante simulaciones por computadora, bajo diversos escenarios.

Diabetes, Control por Modos Deslizantes, Estabilidad, Robusto

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Introduction

Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels. Diabetes is one of the leading causes of blindness, kidney failure, heart attacks, strokes, and lower-limb amputation. In 2021, according to the World Health Organization (WHO), an estimated 422 million people worldwide will have diabetes. However, its consequences can be avoided or delayed by adopting proper diets, physical activity, medication, and so on. The automatic glucose regulation system belongs to treatments based on medication. This system requires a robust control to regulate the glucose concentration to a basal state.

For this purpose, the minimum Bergman model is used, this represents the glucose dynamics and insulin kinematics [1], which is represented in three nonlinear differential equations [2]; this is also the most famous and widely used model in clinical assessments [3]. The first challenges to regulate blood glucose levels require precise measurements and specific assessment protocols that allow mitigate the adverse effects in treatments based on insulin application. In practice, measurement methods are used at the Point of Care (POC) with capillary or arterial blood. These analyzers can be based of gases, plasma, or serum of venous or arterial blood that are measured in the laboratory in an invasive way [4]. In the last years, there have been advances towards the development of nano biosensors or apt sensors [5] using various non-invasive nanomaterials for continuous glucose monitoring, especially optical biosensors [6], [7].

These tools have not been efficient by themselves. These devices require theoretical techniques to achieve accurate measurements in glucose prediction, such as Luenberger observer for state estimation [8], deep learning algorithms [9], incremental learning algorithms [10], machine learning [11], artificial neural networks [12], construction of prediction models [13], and so on. Classical or artificial intelligence predictors require models with Gaussian processes; however, this requirement cannot always be satisfied because unmeasurable disturbances and noise may not satisfy the mentioned distribution.

Consequently, a robust controller is proposed, the Generalized Super Twisting Algorithm (GSTA) [14], which is robust towards parameter uncertainties in the model and external disturbances. The GSTA is an extended version of the Super-Twisting Algorithm (STA) which has been applied successfully in several cases (see [15]-[19]).

For design purposes of the GSTA, this algorithm only requires knowledge of the external disturbance upper bound. This control method makes it possible to reduce blood glucose levels in the patients that are in situations of hyperglycemia. This process is made through an infusion pump that provides in real-time a variable insulin rate, and the controller can adjust the insulin concentration according to the readings of a continuous sensor.

The rest of the paper is organized as follows: The mathematical model that describes the glucose concentration dynamics in a human being is described in Section 2. In section 3, a glucose controller design based on a high order sliding modes control is shown. Additionally, the stability proof of the proposed controller is given. In Section 4, several computer simulations were carried out to test the proposed algorithm's robustness and effectiveness. Also, the behavior of the closed-loop control under different scenarios is analyzed. Finally, a concise conclusion about the article is offered in Section 5.

Mathematical Description

The mathematical model that describes the dynamic response of glucose concentration to an insulin injection of a patient with type 1 diabetes is known as the minimum Bergman model, which is described below:

$$\begin{aligned} \dot{x}_{b1}(t) &= -\big(p_1 + x_{b2}\,(t)\big)x_{b1}\,(t) + \\ & p_1\, G_{bl} + D(t) \\ \dot{x}_{b2}(t) &= -p_2 x_{b2}(t) + p_3(x_{b3}(t - I_{bl}) \\ \dot{x}_{b3}(t) &= -n(x_{b3}(t) - I_{bl}) + u(t) \end{aligned} \qquad (1)$$

Where $x_{b1}(t)$ is the concentration of glucose in the blood plasma [mg/dl], $x_{b2}(t)$ is the concentration of insulin in the remote compartment [1/min], $x_{b3}(t)$ represents the concentration of insulin in plasma at time t [μU/ml], G_{bl} is the basal glucose level [mg/dl], I_{bl} is the basal insulin level [μU/ml], p_1 is the insulin-independent rate constant of glucose uptake in muscles a liver [l/min]. The rate for decrease in tissue glucose uptake ability is defined by p_2 en [1/min]. p_3 represents the insulin-dependent increase in glucose uptake ability in tissue per unit of insulin concentration above the basal level [(μ/ml) min^{-2}]. The parameter n is the first-order decay rate for insulin in blood [1/min].

From the study [20], it can be concluded that the value of p_1 is drastically reduced and approaches to zero for patients with diabetes. Note that the parameters shown in Table I have been calculated for an average person. However, it is necessary to mention that these parameters are not constant and vary from person to person, which makes the control design even more complex. Finally, from Eq. (2), the term $D(t)$ represents the rate at which glucose is absorbed into the blood by the intestine after food has been consumed. In patients with diabetes, glucose uptake is considered an external disturbance to the system's dynamics (2). This disturbance can be modeled as an exponential function as follows [20]:

$$D(t) = A_B e^{B_B t} \tag{2}$$

Where t is the time [min] and $A_B, B_B \in R^+$. The unit of D is in [mg/dl/min].

Finally, from model (1), the function *u(t)* represents the control signal, which is the function that will modify the system dynamics to regulate the glucose concentration in the diabetic patient's blood plasma.

Generalized Super-Twisting Control Design

The control objective is to regulate the blood's glucose concentration at the basal state value. Then, the error variable is defined as:

$$e(t) = x_{b1}(t) - G_{bl} \tag{3}$$

Where G_{bl} is the blood's glucose concentration in the basal state (desired value), and $x_{b1}(t)$ is the current patient blood's glucose concentration measured by the sensor. Moreover, the parameters shown in model (1) are not exactly known and vary from patient to patient. Also, the external disturbance is not completely known. For these reasons, the controller should be robust towards parameter uncertainties and external disturbances. At the same time, the controller requires fast convergence in finite time. Taking into consideration all the listed requirements, we will design a controller based on the high order sliding modes technique.

Considering the output $y = x_{b1}(t)$, we can observe that its relative degree is 3. Roughly speaking, the relative degree is the number of consecutive derivatives of the output until the signal control appears explicitly. In this particular case, the input signal comes out at the third derivative with respect the time of x_{b1}, this yields to:

$$\dddot{x}_{b1} = \varphi - p_3 x_{b1} u \tag{4}$$

Where φ is defined as:

$$\begin{aligned}\varphi = {} & [-p_1({p_1}^2 + 3p_3 I_{bl}) - \\ & p_3 I_{bl}(p_2 + n) - p_3\gamma[x_{b1} - h] + \\ & t]x_{b1} + [-{p_1}^2(1 + G_{bl}) + \\ & p_1 p_2(2G_{bl} - 1) + 2D(p_1 + p_2)]x_{b2} + \\ & [-2p_3(p_1 + D)]x_{b3} + [-(p_1 + p_2)^2 - \\ & 3p_3 I_{bl}]x_{1b}x_{b2} + [p_3(3p_1 + p_2 + \\ & n)]x_{b1}x_{b3} + [-3(p_1 + p_2)]x_{b1}{x_{b2}}^2 + \\ & (p_1 G_b + D){x_{b2}}^2 + 3p_3 x_{b1}x_{b2}x_{b3} - \\ & x_{b1}{x_{b2}}^3 + \ddot{D} + (p_1 G_{bl} + D)({p_1}^2 + \\ & 2p_3 I_{bl}) - p_3 x_{b1} u(t)\end{aligned} \tag{5}$$

The parameter φ will be relevant because, based on [21], it is part of the controller and is the term known as equivalent control. However, it is necessary to establish two critical implications: (1) φ depends on the dynamical model, which means that is crucial to know the exact value of the dynamical model's parameters, which is impossible to determine precisely in practice. (2) φ contains the disturbance D and its dynamics, which implies that is necessary to precisely known the disturbance D. In real terms, this is impossible. For these reasons, the parameter to determine φ, will be broken down into two terms, the nominal $\hat{\varphi}$, and the error term $\tilde{\varphi}$, as follows:

$$\varphi = \hat{\varphi} + \tilde{\varphi} \tag{6}$$

Where $\hat{\varphi}$ is the term that contains dynamical model nominal parameters and does not include the external disturbance. On the other hand, the term $\tilde{\varphi}$ encloses all the unknown terms and its dynamics. Substituting (6) in (4), yields to:

$$\ddot{x}_{b1} = \hat{\varphi} - p_3 x_{b1} u + \tilde{\varphi} \tag{7}$$

Based on the relative degree of the output, we choose the sliding surface as in [21], which is defined as:

$$\sigma(e) = \ddot{e} + \alpha_2 \dot{e} + \alpha_1 e \tag{8}$$

Where α_1 and α_2 are design positive constants.

Remark 1: The constants α_i are used to modify the convergence rate to the sliding surface.

Assumption 1: The external disturbance and its dynamics are considered bounded as follows:

$$\begin{aligned} \|D(t)\| &\leq \delta_1 \\ \|\dot{D}(t)\| &\leq \delta_2 \end{aligned} \tag{9}$$

The main result of this manuscript is summarized in the following theorem.

Theorem 1. Consider the dynamical model of the blood's glucose concentration of the diabetes type 1 patient given by Eq. (1), assume that the external disturbance *D(t)* is bounded, and it satisfies the Assumption 1. Then, for every initial condition $\sigma(0)$, the sliding surface $\sigma = 0$ will be reached in finite time by the following Generalized Super-Twisting Controller:

$$u(t) = \frac{1}{p_3 x_{b1}} (\hat{\varphi} + \alpha_2 \ddot{e}_r + \alpha_1 \dot{e}_r - u_{ST}) \tag{10}$$

Where the GSTA is represented by u_{ST}, and is defined as:

$$\begin{aligned} u_{ST} &= -k_1 \phi_1(\sigma) + \lambda \\ \dot{\lambda} &= -k_2 \phi_2(\sigma) \end{aligned} \tag{11}$$

Where the functions $\phi_i(\sigma)$ have the following structure:

$$\begin{aligned} \phi_1(\sigma) &= |\sigma|^{\frac{1}{2}} sgn(\sigma) + \sigma \\ \phi_2(\sigma) &= \frac{1}{2} sgn(\sigma) + \frac{3}{2} |\sigma|^{\frac{1}{2}} sgn(\sigma) + \sigma \end{aligned} \tag{12}$$

The feedback controller gains are k_1 and k_2.

Finally, when the sliding mode is reached ($\sigma = 0$), this means that the error converges to zero, and $x_{b1} \rightarrow G_b$ in finite time.

Proof: Consider the dynamic system (1) and the sliding surface (8). Computing the time derivative of σ, we have:

$$\dot{\sigma} = -k_1 \phi_1(\sigma) - k_2 \int_0^t \phi_2(\sigma) + d(t) \tag{13}$$

Where *d(t)* encloses the system unknown dynamics and the external disturbances.
Let us define:

$$\begin{aligned} s_1 &= \sigma \\ s_2 &= -k_2 \int_0^t \phi_2(\sigma) + d(t) \\ \dot{d}(t) &= \beta(t) \end{aligned} \tag{14}$$

Then, the sliding surface dynamics can be rewritten as:

$$\begin{aligned} \dot{s}_1 &= -k_1 \phi_1 + s_2 \\ \dot{s}_2 &= -k_2 \phi_2 + \rho(t) \end{aligned} \tag{15}$$

Defining the vector $z = [\phi_1, s_2]^T$ and $\rho = \frac{\beta(t)}{\phi_1'}$. Next, the sliding Surface dynamics can be expressed as:

$$\dot{z} = \phi_1'(Az + B\rho) \tag{16}$$

Where *A* and *B* are matrices defined as:

$$A = \begin{bmatrix} -k_1 & 0 \\ -k_2 & 0 \end{bmatrix} \quad \text{y} \quad B = \begin{bmatrix} 0 \\ 1 \end{bmatrix} \tag{17}$$

Considering the following Lyapunov function:

$$V = z^T P z \tag{18}$$

Where P is a positive definite matrix which satisfies the Lyapunov's equation:

$$A^T P + PA = -Q \tag{19}$$

Where Q is a positive definite matrix. Based on results shown in [22], we assume that the disturbance satisfies the sector condition:

$$d = -\rho^2(\rho, z) + L^2 z^T C^T C z \geq 0 \tag{20}$$

Note that the upper and lower bounds of the sector are symmetric. Moreover, we choose $C = [1\ 0]$. For control design purpose, the matrix A can be rewritten as:

$$A = A_0 - K_0 C_0 \tag{21}$$

Where

$$A_0 = \begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix}, K_0 = \begin{bmatrix} k_1 \\ k_2 \end{bmatrix}, C_0 = [1\ 0] \tag{22}$$

Computing the derivative of the Lyapunov function along the system trajectories, yields to:
$\dot{V} = 2z^T P \dot{z}$

$$\dot{V} = -\phi_1' \begin{bmatrix} z \\ \rho \end{bmatrix}^T \begin{bmatrix} A^T P + PA & PB \\ B^T P & 0 \end{bmatrix} \begin{bmatrix} z \\ \rho \end{bmatrix} \tag{23}$$

$$\leq -\phi_1' \left\{ \begin{bmatrix} z \\ \rho \end{bmatrix}^T \begin{bmatrix} A^T P + PA & PB \\ B^T P & 0 \end{bmatrix} \begin{bmatrix} z \\ \rho \end{bmatrix} + d \right\}$$

After some manipulations and considering the sector conditions, we obtain the following:

$$\dot{V} \leq -\phi_1' \left\{ \begin{bmatrix} z \\ \rho \end{bmatrix}^T W(K_0, P|\overline{\alpha}, L) \begin{bmatrix} z \\ \rho \end{bmatrix} - \overline{\alpha} z^T P z \right\} \tag{24}$$

Where

$$W(K_0, P|\overline{\alpha}, L) = \begin{bmatrix} W_{11} & W_{12} \\ W_{21} & W_{22} \end{bmatrix} \tag{25}$$

Each matrix element is described below:

$$W_{11} = A_0^T P + PA_0 + L^2 C^T C - C_0^T K_0^T P - PK_0 C_0 + \overline{\alpha} P$$

$$W_{12} = PB$$

$$W_{21} = B^T P$$

$$W_{22} = -1 \tag{26}$$

Choosing $K_0 > 0$ and the matrix $P > 0$,there exists a constant $\overline{\alpha} > 0$, such that $W(K_0, P|\overline{\alpha}, L)$ will be negative semidefinite. Therefore, the time derivative of V is expressed as:

$$\dot{V} \leq -\frac{\overline{\alpha}\, \lambda_{min}^{0.5}(P)}{2} V^{0.5} - \overline{\alpha} V \tag{27}$$

Therefore, it can be concluded that the time derivative of V will be negative definite if the gains k_1 and k_2 are selected large enough so that the matrix W will be negative semi-definite. If this condition is fulfilled, the states z will converge to zero, so the sliding surface will go to the origin, which implies that the errors tend to zero and, finally, the state x_{b1} will converge to the basal state in finite time.

Remark 2: In the proposed control law given by Eq. (10), the term that multiplies the control $\frac{1}{p_3 x_{b1}}$, depends on the state x_{b1}. However, this value is well defined and belongs to a neighborhood $p_3 x_{b1} \in [1.2 \times 10^{-4},\ 3 \times 10^{-2}]$.

Simulation Results

Several computer simulations were carried out to test the proposed controller effectiveness and robustness towards parametric uncertainties and external disturbances. The proposed controller was simulated with the MATLAB 2017a software, and the ODE45 solver with the variable step was used.

For the simulation, it is considered that the reference glucose level is $G_{bl} = 80$ [mg/dl]. The patient has hyperglycemia, so the initial condition was at 220 [mg/dl]. The control objective is that the sensor measurement tends to the baseline blood glucose state $G_{bl} = 80$ [mg/dl]. Three scenarios were tested to evaluate the performance of the control:

1. **Nominal Scenario**: The patient is hyperglycemic; insulin is infused to reach a basal state. Disturbances are not considered in this case.
2. **Scenario with external disturbance**: It is simulated that the patient consumes food, affecting the system's dynamics. The disturbance acts at minute 600.
3. **Scenario with parametric uncertainty**: In this simulation, the controller is tested with a different patient, for which the system parameters change. The two previous cases are considered. That is, the nominal case and disturbances are tested. Table I shows the patient parameters used in the simulation.

1. Nominal Scenario

Figure 1 shows the controller performance under nominal conditions. In this case, the patient's glucose measurement is 220 mg/dl, and drops to the nominal reference level (dashed black line) of 80 mg/dl. A comparison of the proposed controller (green line) is made against the method proposed in [21] (pink line), and both controllers converge to the reference practically at the same time.

2. Robustness Towards External Disturbances Scenario

Figure 1 compares the proposed controller (red line) and Ahmad's (namely STA) method (blue line) [21]. In this scenario, the patient is hyperglycemia, and the controller acts by infusing insulin until the glucose is regulated in its basal state. Then, at minute 600, a food intake disturbance is introduced, and the patient's glucose goes lift again. The controller acts in regulation and causes the glucose to drop to the nominal value. From the graph, the disturbance affects the performance of the STA controller. In contrast, the GSTA controller converges to the nominal glucose value faster than the STA, demonstrating the effectiveness of the proposed methodology.

3. Robustness Towards Parametric Uncertainties Scenario

In this scenario, both controllers are simulated for a second patient. Therefore, the dynamical system parameters have changed. As seen in Figure 2, patient 2 starts with hyperglycemia with$x_{b1} = 220$ [mg/dl].

From the graph for a nominal scenario, both controllers converge to the reference practically simultaneously. For a second test, it is considered that the patient has eaten food and that this produces a disturbance of blood glucose, as observed at minute 600. After the disturbance, it is observed that the performance of the proposed controller in this item is higher than the nominal STA since it converges to the reference value in a shorter time. In contrast, the STA converges to a neighborhood of the nominal value.

Conclusions

In this article, a sliding mode controller based on the Generalized Super-Twisting Algorithm was designed for an insulin infusion system for patients with type 1 diabetes. The dynamic model of a patient with diabetes was shown. Afterward, a controller robust to external disturbances and parametric uncertainties based on sliding modes was designed. Using Lyapunov's theory, the stability of the developed control was demonstrated. Finally, its superior performance in rejecting disturbances was demonstrated through computer simulations compared to another similar methodology.

	Patient 1	Patient 2
p_2	0.02	0.0072
p_3	5.3×10^{-6}	2.15×10^{-6}
n	0.3	0.2465

Table 1 Parameters used in the simulation of the closed loop control

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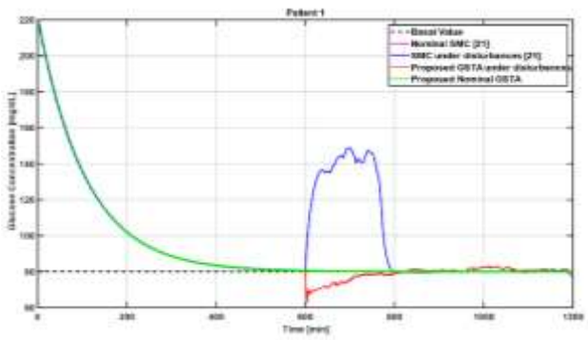

Figure 1. Performance of the proposed controller (GSTA) against the STA [21] for patient 1 for the nominal and disturbed case.

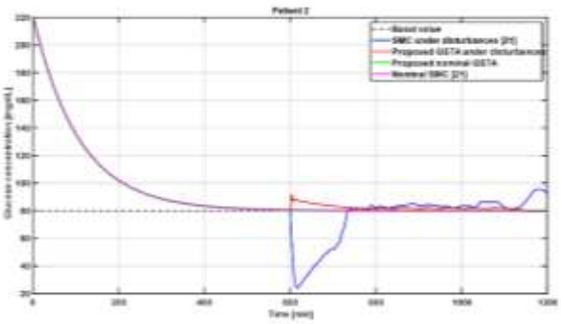

Figure 2 Performance of the proposed controller (GSTA) against the STA [21] for patient 2 for the nominal and disturbed case.

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Degradation of AMARANTH with TiO_2 Synthesised by Sol-Gel Process

Degradación de AMARANTH con TiO_2 Sintetizada Mediante Proceso Sol-Gel

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Abstract

The photo-degradation of persistent contaminants in aqueous systems such as drugs, pesticides or dyes has been proposed as an alternative for the remediation of aqueous systems. TiO_2 is one of the main photocatalysts that have been used for these purposes, it has two phases with photocatalytic properties, anatase and rutile, the latter being the one with the lowest conduction band 3.0 eV. The present work shows the synthesis of TiO_2 by sol gel process, observing that the rutile phase is favored with heat treatment at temperatures above 600ºC, the comparative study of the degradation kinetics of AMARANTH with synthesized TiO_2 and commercial TiO_2 was evaluated, observing a rate constant of 1.38 and 0.345 $Lmol^{-1}min^{-1}$ for commercial and synthetic TiO_2, respectively.

Photo-degradation, TiO_2, AMARANTH

Resumen

La foto-degradación de contaminantes persistentes en sistemas acuosos tales como fármacos, pesticidas o colorantes se ha planteado como una alternativa para la remediación de sistemas acuosos. La TiO_2 es uno de los principales foto-catalizadores que se han empleado para estos propósitos, esta presenta dos fases con propiedades fotocatalíticas, anatasa y rutilo, siendo esta última la que presenta la menor banda de conducción 3.0 eV. El presente trabajo muestra la síntesis de TiO_2 mediante proceso sol gel, observándose que la fase de rutilo se favorece con el tratamiento térmico a temperaturas superiores a los 600ºC, se evaluó el estudio comparativo de la cinética de degradación del colorante AMARANTH con la TiO_2 sintetizada y la TiO_2 comercial tratadas a 600ºC, mostraron una constante de velocidad de 1.38 y 0.345 $Lmol^{-1}min^{-1}$ para la TiO_2 comercial y la sintética respectivamente.

Foto-degradación, TiO_2, AMARANTH

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Introducción

Nowadays, nanotechnology has taken an important role in the development of new materials, the synthesis of nano-particles has increased in the last decades since at this scale the materials enhance their properties such as hardness, elasticity, thermal conductivity among others, which favours their diverse applications [1-4].

The use of nanoparticles in various areas of technology is very broad, an example of this is the production of a number of TiO_2-based materials, functionalised TiO_2 and TiO_2-Ag, TiO_2-Zn, TiO_2-SiO_2 composites, which have been used as photo-degraders of pollutants in wastewater treatment [1-12]. The interest in the study of TiO_2 particles lies in the fact that its photocatalytic properties make it so useful in fields such as microbiology, medicine, environmental and materials science.

TiO_2, a semiconductor material that absorbs electromagnetic radiation mainly in the Uv region, tends to be thermally and chemically stable, as well as having photocatalytic properties as mentioned above; it is considered a non-toxic oxide, is corrosion resistant and bio-compatible [1-13-15]. It is currently used as a white pigment for paints, as it scatters light more efficiently and is more stable and durable than classical pigments. TiO_2 coatings have high photoactivity and are used in the water and air purification industry by photocatalysis. [12]

Today's increasing pollution has led to the development of new possibilities for remediation procedures. Heterogeneous photocatalysis has been an environmentally friendly method, as it has been shown to degrade organic pollutants at low and medium concentrations [2-10, 17], both in the liquid and gas phase. One of the main materials used in these processes is TiO_2. [16]. In general, this method consists of the degradation of the pollutant through the use of catalysts such as semiconductor oxides (TiO_2, ZnO, among others), ultraviolet and/or solar radiation, generating radicals (O_2·, HO_2·, OH·), which cause the oxidation of the pollutants [17].

Therefore, it has the characteristic of having a particulate photocatalyst suspended in a solution or it can be in contact with a substrate that is in the gas phase, it is irradiated with sufficient energy for photo-excitation to occur. It has been reported that, in order to exploit the visible spectrum, methodologies for material modification, such as the addition of dopant species, have been developed. [15]

The photocatalytic and photodegradation activity of TiO_2 has been enhanced by doping or forming composites with TiO_2 and various additives such as Fe3O4, graphene, silica, Ag, Ru, N, C, Fe, Mo, V, Co and Cu. [3-11]. It is well known that the mechanism by which photo-degradation is generated with semiconductors such as TiO_2, occurs when they adsorb a photon with greater or equal energy than the bandgap energy, an electron from the valence band moves to the conduction band, then the electron and positive hole that was generated migrate to the surface of the catalyst where they participate in oxide-reductive reactions with the absorbed species (pollutant) leading to their degradation and sometimes to their complete mineralisation. [18]

The present work shows the study of the photo-degradation of the AMARATH dye with synthetic TiO_2 obtained by sol-gel process.

Methodology

All the reagents used were reagent grade from Sigma-Aldrich and no purification process was carried out for their use in the syntheses developed.

Synthesis of TiO_2

In a 250 mL ball flask, adapted with a cooler (Figure 1), 70 mL of butanol and 10 mL of titanium terbutoxide were placed, maintaining the temperature at 80°C for 30 minutes, 1 mL of concentrated nitric acid was added to the solution and kept under constant agitation for 5 minutes to homogenise the solution. Slowly add 5 mL of deionised water over a period of 15 minutes until gel formation is observed in the system. Once the gel is obtained, the system is kept under reflux for 30 minutes. The obtained gel is recovered and dried at 70ºC for 12 h. The solid obtained is subjected to heat treatment for 1 and 2 h at 500, 550, 600, 650 and 700 ºC.

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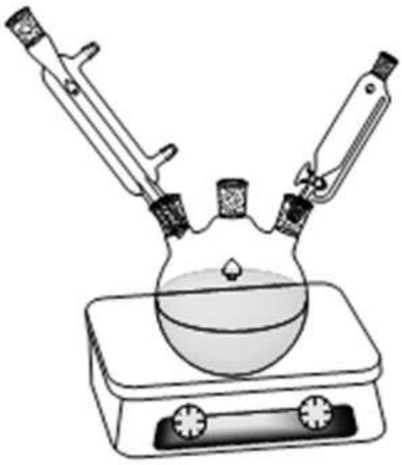

Figure 1 Reaction system for the production of TiO_2

Characterisation

The characterisation of TiO_2-c and TiO_2-s was performed by X-ray Diffraction (XRD) and Scanning Electron Microscopy (SEM). Morphology was evaluated using a Joel-6510 plus microscope and XRD was obtained on a RIGAKU ULTIMA IV diffractogram.

AMARANTH® Dye Photo-Degradation Studies

The photo-catalytic degradation tests of the dye were evaluated by degradation kinetics, against commercial TiO_2 (TiO_2-c) and synthesised TiO_2 (TiO_2-s). 0.2 g of the material to be evaluated (TiO_2-c and TiO_2-s) is added with 20 mL of a 3.52X10-3M Amaranth dye solution. The residual concentration of the dye in the solution is evaluated every 20 min by Uv-visible spectroscopy at 520 nm.

Results

The XRD characterisation of commercial and synthesised TiO_2 showed the presence of the anatase phase, which is the phase with the highest conduction band (3.2 eV) (Figure 2), the rutile phase presents a conduction band of 3. 0 eV, lower than that of the anatase phase, which is why this phase is preferable for photocatalytic applications in the degradation of pollutants; for this reason, the effect of heat treatment at 500, 550, 600, 650 and 700 ºC on the synthesis of the material was evaluated. The formation of the rutile phase was observed from 550ºC onwards, favouring it from 600 ºC, where a composition of 70% of the rutile phase was observed in the material (Figure 3).

At 700 ºC a composition of 80% of the rutile phase was observed, so it could be considered a quantitative composition of the rutile phase with thermal treatments above 700ºC, however at these high temperatures the sintering process of the materials is observed, which considerably reduces the surface area of these, disfavouring the contact area of the material with the analytes to adsorb or degrade in a photo-degradation process, that is why the temperature at 600-650ºC was considered as the most suitable for the synthesis of the material.

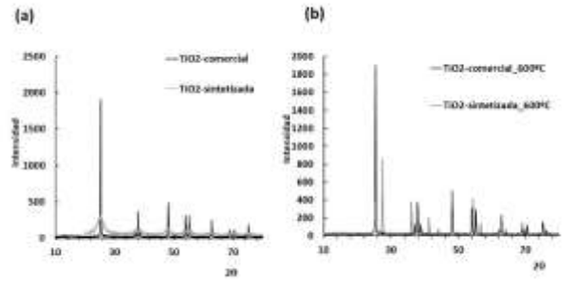

Figure 2 XRD TiO_2-c and TiO_2-s

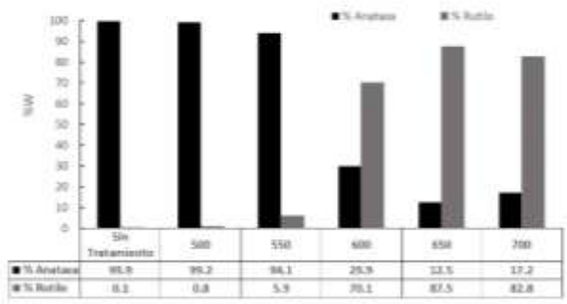

Figure 3 Effect of temperature on the formation of rutile phase

Figure 4 shows the characterisation of the material by SEM, where the presence of condensed particles is observed, as well as no change in the texture and morphology of the material with the thermal treatment (Figure 4b).

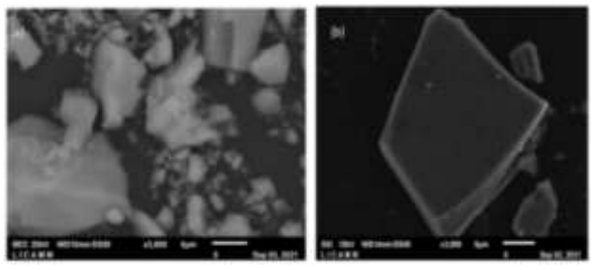

Figure 4 SEM characterisation of TiO_2 synthesised (a) without heat treatment and (b) treated at 600°C

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AMARANTH Dye Photo-Degradation Studies

The degradation of the AMARANTH dye with synthetic and commercial TiO_2 was evaluated by following the concentration of the dye with respect to time once in contact with the material and UV light. It should be mentioned that both materials (TiO_2-c and TiO_2-s) were placed in contact with the dye without UV radiation, showing a decrease in the dye concentration by 2.5 %, in an initial period of 20 minutes of contact, this is due to the adsorption of the dye on the materials and not to photo-degradation.

Figure 5 shows the degradation kinetics of AMARANTH, where it can be observed that TiO_2-c shows a higher degradation of the dye by 37%, reaching equilibrium after 140min, while TiO_2-s only reached 22% degradation, however the equilibrium of the system is not observed, so the degradation kinetics that this material offers is slower. The experimental data were adjusted to the second order model, observing rate constants of 1.39 Lmol-1min-1 and 0.345 Lmol-1min-1, being 4 times higher the degradation rate offered by TiO_2-c than the one observed with TiO_2-s. This difference could be due to the textural properties of the materials, considering that TiO_2-s could have a lower surface area than TiO_2-c due to the sintering of the surface caused by the heat treatment temperature.

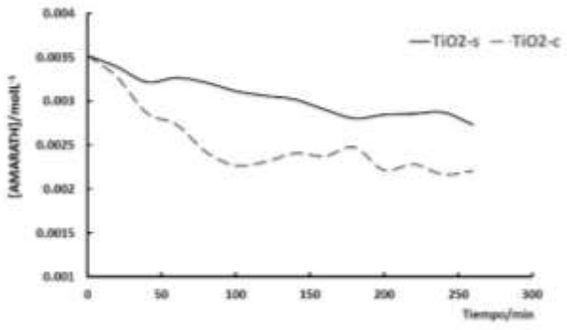

Figure 5 Photo-degradation kinetics of the dye AMARANTH

Conclusions

The formation of the rutile phase, which is the crystalline phase with the lowest conduction band, is favoured by treatments at 600ºC.

The comparative study of the photocatalytic degradation kinetics of the AMARANTH dye TiO_2-c and TiO_2-s showed the degradation of 37 and 22% of the dye with TiO_2-c and TiO_2-s respectively, with TiO_2-c reaching equilibrium at 140 min of exposure. The experimental data were fitted to the second-order model, observing rate constants of 1.39 Lmol-1min-1 and 0.345 Lmol-1min-1, with the degradation rate offered by TiO_2-c being 4 times higher than that observed with TiO_2-s.

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Hand orthosis design for the rehabilitation of people with rheumatoid arthritis

Diseño de órtesis de mano para la rehabilitación de personas con artritis reumatoide

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Abstract

This project is based on the design and development of a hand orthosis controlled by wireless communication through a mobile application, developed in MIT AppInventor, and a web interface, designed in HTML and CSS; using a NODEMCU ESP8266 V3 development board as a microcontroller in order to obtain the benefit of Wi-Fi communication without ruling out the use of Bluetooth technology. This medical device is focused on the rehabilitation of patients with Rheumatoid Arthritis, or some other pathology that directly affects mobility in the joints of the hands. Similarly, the device has an electromyography module, designed from scratch, in order to monitor the patient's muscle activity and, in the future, achieve control of the orthosis through the possible actions issued by the user or patient. On the other hand, a "Local Network" was implemented with the aim of migrating or embodying the project within a rehabilitation center and having its own communication network, isolated from the outside. Thus, the rehabilitation doctor or physical therapist will be the only person who can control the device when the patient comes to the clinic for therapy or progress review.

Biological samples, Cold chain, Temperature

Resumen

El presente proyecto se basa en el diseño y desarrollo de una órtesis de mano controlada por comunicación inalámbrica mediante una aplicación móvil, desarrollada en MIT AppInventor, y una interfaz web, diseñada en HTML y CSS; usando como microcontrolador una placa de desarrollo NODEMCU ESP8266 V3 con el fin de obtener el beneficio de una comunicación Wi-Fi sin descartar el uso de la tecnología Bluethoot. Este dispositivo médico va enfocado a la rehabilitación de pacientes con Artritis Reumatoide, o alguna otra patología que afecte directamente la movilidad en las articulaciones de las manos. De igual forma, el dispositivo cuenta con un módulo de electromiografía, diseñado desde cero, con el fin de monitorear la actividad muscular del paciente y, en un futuro, lograr un control de la órtesis mediante los potenciales de acción emitidos por el usuario o paciente. Por otra parte, se implementó una "Red Local" con el objetivo de migrar o plasmar el proyecto dentro de un centro de rehabilitación y contar con una red de comunicación propia, aislada del exterior. Así, el médico de rehabilitación o fisioterapeuta será la única persona que pueda controlar el dispositivo cuando el paciente acuda a la clínica para terapia o revisión de avance

Biological samples, Cold chain, Temperature

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1. Introduction

Rheumatoid arthritis (RA) is produced when the immune system does not work properly, hence the term systemic autoimmune disease, and is characterized by synovitis and progressive destruction of articular cartilage and underlying bone, along with other extra-articular manifestations such as pain and stiffness (Díaz et al, 2002).

This disease is one of the most common worldwide, Belmonte Serrano in 2013 and Duró Pujol in 2010 report an incidence of 6-10 cases per 100,000 inhabitants; thus affecting 0.5% to 1% of the population (Mitchell & Kumar, 2017). Currently in our country, more than 1 million people are affected by RA, and three out of four people who present it are women according to the National Institute of Statistics and Geography (INEGI) in 2019. Statistics indicate that of the 100% of Mexican women who suffer from this condition, 75% are of productive age (between 25 and 50 years old). In contrast, in men it is only 25%.

The manifestations of RA are usually treated symptomatically and exclusively, although effective and consistent control is sought through the use of disease-modifying antirheumatic drugs (Gamero D. 2018).

Delayed treatment of this disease is associated with rapid progression of joint damage and an unfavorable outcome for the patient (Diaz E., et. al, 2005). Figure 1 shows the comparison between a healthy joint and a joint affected by *RA.*

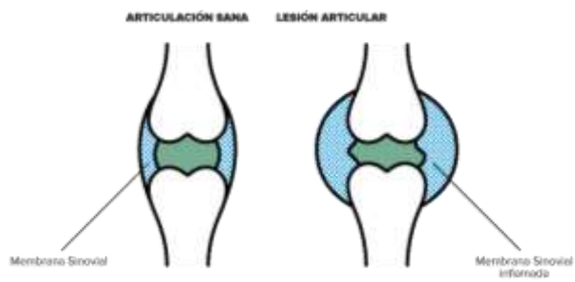

Figure 1 Comparison of a healthy joint with a joint affected by *RA*

The therapeutic approach to the rheumatologic hand is based on the fact that it is palliative, that is to say that none of the therapeutic interventions are curative in nature, their purpose being to reduce the signs and symptoms in order to improve the patient's quality of life. It is for this reason that the treatment of the rheumatologic hand must be individualized, periodic and permanent. It is worth mentioning the importance of assessing the patient in each of the different stages of the disease in order to carry out a more effective treatment.

For the physiotherapist, the treatment of the rheumatologic hand aims to increase its functional capacity. It is essential to identify, first of all, the state of each process: hand with osteoarthritis (with or without additional synovitis) or arthritic hand (in flare-up or remission phase, with slow or rapid progression), as this will condition the choice of one or another therapeutic modality (Miralles et al, 2002). That is why in effort to improve the quality of life of patients with RA, devices have been developed to assist in the patient's rehabilitation process, decreasing symptoms of the disease such as joint pain and preventing synovitis (Iturriaga, V, et al 2018).

There are different therapeutic modalities, whose use should stick to the phase of evolution of the rheumatologic hand (Montull S., et al 2004). Some modalities are:

– ***Orthoses***. *Orthoses* are defined as treatment modalities very useful to affect pain (rest splints), to control the progression of deformities (corrective) and to maintain the joint path (dynamic or static) in the rheumatologic hand (Bressel A.E, 2018). For the application of an *orthosis*, the aspects of a functional hand corresponding to an intermediate position of the hand and wrist, resting position and hand muscles must be considered (Braddom R.L, 1996).

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– ***Thermotherapy***. It is a modality used for its analgesic effect and favoring the extensibility of collagen, although it is important to know well the situations in which this modality can be used, because if it is used in inflammatory phases it can aggravate the consequences of inflammation (Apolo M.D, et. al 2006).

– ***Electrotherapy***. Electrostimulation is effective in improving functionality (avoiding atrophy, increasing fatigue resistance, increasing pressure strength) and TENS (Transcutaneous Electrical Nerve Stimulation) may be the most useful modality to reduce pain and increase muscle strength (Crépon F., et al, 2008).

However, certain disadvantages have been detected in these devices:

– High equipment price, due to the fact that the development and design of these devices is in other countries.
– Limitation to device functions, implementing only movement functions.
– There is no monitoring of the patient's biomedical signals.

They are not self-adjustable, since exact measurements have to be taken for a personalized design for each patient, making the process of design, development and acquisition of the device longer.

This is why the need arises to develop new methods and alternatives to provide an auxiliary rehabilitation in the search for restoring the level of movement in the affected joints; for this purpose, the design of an automated orthosis that allows measuring force levels and obtaining Electromigraphic (EMG) signals is proposed in this project, which is expected to provide the following benefits:

– Provide an automated system in the rehabilitation of patients with RA.
– Manage the progress of the rehabilitation of patients with RA.
– Provide stages and degrees of movement according to the damage and progression of the pathology in patients.
– Enable the patient to perform functions related to the rehabilitation of joint strength.

This article will discuss the methodology and results obtained in the development of a hand orthosis for rehabilitation in people with RA.

2. Methodology

The following activities were carried out to develop this project.

2.1 To perform the characterization of the sensors to be implemented in the orthosis

For the characterization of sensors and actuators, different methods were used according to each type of sensor and actuator to be implemented. For the part in question of sensors will be implemented:

2.1.1. Muscle sensor or EMG module

This module will be developed from 0 with the implementation of Bioinstrumentation; in order to have a complete processing of the myographic signal (representative signal of the muscular activity of the human body).

The characterization in this sensor will be deduced according to the Motor Unit Action Potential (MUAP) emitted by the patient. The signals will be acquired in the forearm, specifically in the muscles that are responsible for finger movements (superficial flexor muscle of the fingers).

In this module 4 stages were implemented: pre-amplification, filtering, rectification and final amplification.

2.1.1.1 Pre-amplification

Signal pre-amplification is the first stage in the development of the EMG module. In this stage, the myoelectric signal (electrical signal from the muscle) is obtained using patch electrodes and an instrumentation amplifier. These are three-lead electrodes: two for signal acquisition and a third as a reference.

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The instrumentation amplifier is basically a differentiating amplifier, since its output is the difference of the two input signals. It is also known that this amplifier has a practically infinite gain, although for this stage a gain (AV) of between 10 and 20 is used.

This amplifier is composed of three amplifiers, and its design consists of 7 resistors, 6 of them set by the designer with values of an order of K Ω. Figure 2 shows the schematic or design of an instrumentation amplifier, with three operational amplifiers.

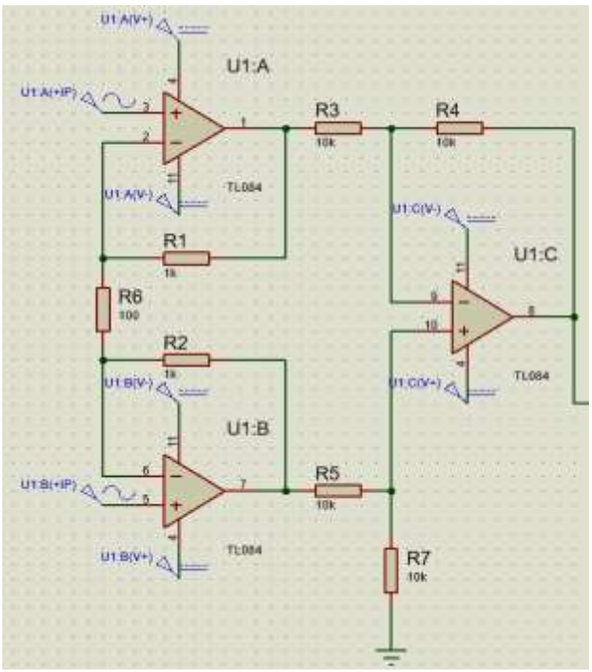

Figure 2 Instrumentation amplifier (Own Authorship)

Considering the previous design, it is essential to consider the following:

$$Y_{ij} = \alpha + \sum_{h=1}^{r} \beta_h X_{hij} + u_j + e_{ij}$$

R1 = R2 = R = 1kΩ

R3 = R4 = R5 = R6 = 10kΩ

AV = 20

$$\boldsymbol{RG} = \boldsymbol{AV}\_\_\_\_\boldsymbol{2R}-\boldsymbol{1}$$

Applying the formula and substituting the established resistor values, a Gain Resistance (RG) of approximately 100Ω is obtained.

In this way, the preamplification stage would be complete, having at the output a signal amplified 20 times. It should be remembered that the signals obtained from a muscle have an amplitude in the order of micro volts (μV).

2.1.1.2. Filtering

The filtering of a myoelectric signal is fundamental, since the filters are used to obtain selected data that are of interest for the correct processing of the signals obtained, taking into account the needs of the device. There are passive and active filters, which differ in their design.

For this application it is necessary to use active filters. This type of filters are used only when the quality factor is higher than 0.5. Figure 3 shows the design of an active narrow band pass filter.

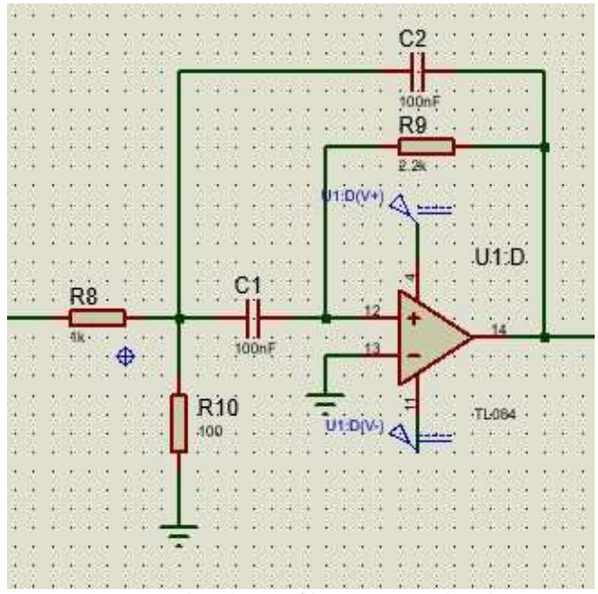

Figure 3 Narrow band-pass filter (Own authorship)

The design conditions of this filter are as follows:

- C1 = C2 = C = 0.1uF
- R1 = 1kΩ
- R2 = 2R1= 2kΩ

In addition to these conditions, it is necessary to establish certain frequencies for the filter design, such as the upper frequency (fs), lower frequency (fi) and resonant frequency (fr). In this design, bands with a frequency range between 150 and 100 Hz will be used.

The equation to be calculated is:

$$fr = \sqrt{fsxfi}$$

fr = 122.47 Hz

The bandwidth (B) is the difference between the upper frequency and the lower frequency. Therefore, the bandwidth (B) is the difference between the upper frequency and the lower frequency.

$B = fs - fL$ i = 50 Hz

The quality factor (Q) indicates the degree of selectivity the filter will have. If Q is greater than 0.5 Hz, the filter will be more selective, i.e., the waves it will allow to pass will have a narrower aspect. To obtain Q the following is done:

$$Q = \frac{fr}{B}$$

Q = 2.44

Once we have these values we can deduce that the filter will have a higher selectivity factor in the relation between reactive energy and the energy it dissipates in a complete cycle of the signal, and the Resonance Resistance (Rr) is calculated in order to obtain the frequency of the narrow band pass filter (FPBA), following equation:

$$Rr = \frac{R}{2Q^2-1}$$

Rr = 91Ω

The second order high-pass filter is intended to let only the higher frequencies pass at the selected cutoff frequency (1.5KHz), thus cleaning the signal and obtaining better filtering results. Figure 4 shows the design of a second order high pass filter, according to the needs of the project.

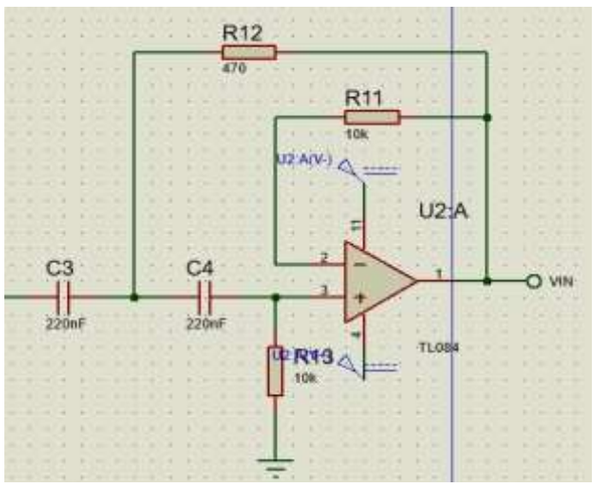

Figure 4 Second order high-pass filter
Own Authorship

2.1.1.3. Rectification

The rectification of the signal is very important, since the signal obtained has both positive and negative voltage peaks (Vp), and these negative Vp could damage the Microcontroller Unit (MCU). Because of this, a full-wave precision rectifier was implemented. In the design of this rectifier the resistors are equal except for the feedback resistor of the second operational amplifier (RF2) and the load resistor (RL). RF2 will have twice the Ω value as the other resistors. Figure 5 shows the design of a full-wave precision rectifier.

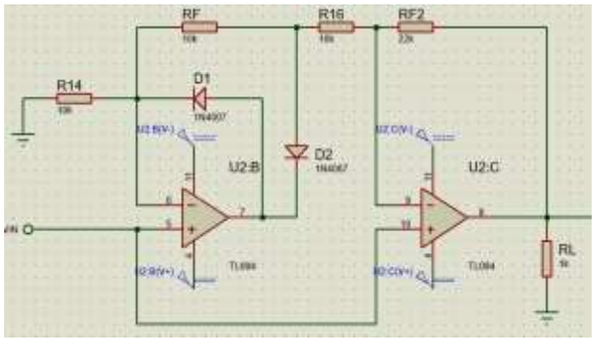

Figure 5 Full wave precision rectifier
Own Authorship

2.1.1.4 Final Amplification

Once the signal is rectified, it is necessary to amplify the voltage in order to have a better use of the signal and continue with its processing inside the MCU. For this, an inverting amplifier was implemented, since the output signal was negatively rectified. The gain in this final amplification stage was 1500 Hz. Figure 6 shows the design of an inverting amplifier.

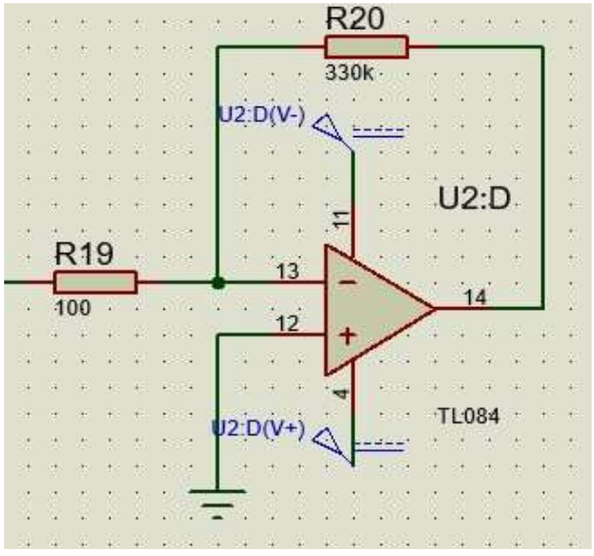

Figure 6 Inverter amplifier
Own Authorship

For the actuator part, the following was implemented:

– Servomotor Micro servo MG90S. The servomotor will help in the project for the mobility of the fingers. The operation of this component is by means of pulses, by means of which the servomotor achieves a rotation from 0° to 180°. The proprietary connections for the MG90S Servomotor are:

1. VCC: 5V to 6V power supply.
2. GND: ground.
3. SIGNAL: write pin for the servo.

A person with correct hand mobility can generate degrees of inclination ranging from zero degrees, 0° degrees being a straight hand position, to 90° degrees, always using the proximal phalanges. By means of quantitative tests, 15 test subjects were taken to analyze the degrees of inclination presented by people with correct hand movement. These tests were done through a geometric measurement to verify up to what degrees of inclination the test subjects can reach when the phalanges are in a straight position.

As well as, the verification that the orthosis gives the exact degrees of inclination that were made to the subjects. This in order that at the time of performing a rehabilitation in a person who is losing the degrees of mobility to recover the full movement.

The characterization of this actuator is based on the degrees of mobility of the patient's fingers. For this purpose, a variable electrical resistor and a programming loaded on the Wi-Fi development board were used.

The objective of the programming was to read the voltage provided by the variable resistor, connecting one of the side pins to VCC, the second side pin to GND and the central pin to the analog input of the Wi-Fi module; and by means of a programmed mapping, to match the maximum and minimum values of the potentiometer with the degrees from 180° to 0°, respectively.

In this way, and by varying the values of the potentiometer, the minimum and maximum degrees of mobility applicable to a patient's finger were deduced, taking as a reference the patient's comfort when experiencing these movements.

2.2 Generate polypropylene-based orthosis structure to start the prototype model.

The prototype structure was designed using polypropylene, in order to optimize the process and reduce manufacturing and modification costs of the structure.

This structure is designed to place the servomotors in a horizontal orientation in order to facilitate the execution of the movements of each of the fingers.

The parts designed were:

– **Palm of the hand:**

This is the part that holds the servo motors and the phalanges of the fingers. It is basically the largest part of the device, and is sized representative to the palm of an adult person's hand.

– **Phalanges**:

This piece is responsible for the characteristic movement of the finger, when opening or closing the fist. It was designed with a curvature, in order to generate the movement as similar as possible, anatomically speaking, to that of the joints in question. It has a length of approximately 12 cm, with an angle of inclination of ≈75°.

– **Phalangeal support**:

The purpose of this support is to hold the phalanges of the patient's fingers to the previously designed representative piece of the same. There are two supports, which are placed one on the proximal phalanges and the second on the middle phalanges. It is worth mentioning that the distal phalanges do not need to be supported with the brackets since these joints can hardly be moved voluntarily by the patient.

2.3 Carry out the specific programming for the control of the device and signal acquisition in the software

Once the prototype is assembled, and having the degrees of mobility representative of the joints, it is necessary to implement programming in order to control the device as planned. For this purpose, a development interface was used in combination with the mobile application. As part of the hardware, it was necessary to use the Wi-Fi module development board, an MG90S servo motor, a 1-inch OLED screen to display important data, a Bluethoot HC-05 module for communication with the mobile application, a push-button to perform the connection and disconnection to a specific Wi-Fi network.

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4. Results

The results obtained in the project are presented below.

4.1 Characterization of sensors and actuators

Table 1 shows the representative values of the minimum and maximum degrees of mobility obtained in the characterization performed with the potentiometer.

Limit.	Value.
MIN	**80**
MAX	**180**

Table 1 Characterization of the servomotor with potentiometer (Own authorship)

In order to establish a reference of mobility degrees characteristic of patients with correct mobility, quantitative measurements of the movement of the fingers of 3 persons were performed, having as a reference an angle measurement. Table 2 shows the results obtained from this test. The statistical analysis performed showed that there is no significant difference between the angle obtained from the prosthesis and that of the programming.

Subject	Mobility grades				
	0°	*25°*	*50°*	*65°*	*90°*
1					X
2					X
3					X

Table 2 Obtaining degrees of mobility of healthy patients, starting from 0 to 180 (Own authorship)

Figure 7, 8 and 9 show the results obtained from the characterization of the servos according to the degrees of mobility supported by the persons subjected to the quantitative measurements, shown in the previous table.

Figure 7 180-degree script in servo characterization *Own Authorship*

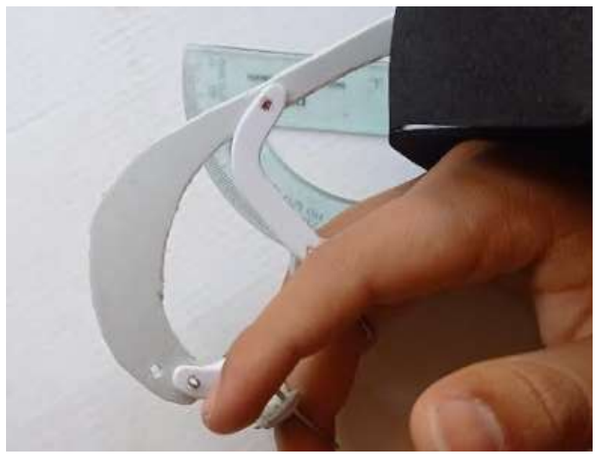

Figure 8 135-degree script in servo characterization *Own Authorship*

Figure 9 80-degree script in servo characterization *Own Authorship*

4.2 Wireless Communication

The device is controlled by a mobile application implementing Bluetooth technology. This application will also be able to monitor the biological measurements obtained corresponding to electromyography signals. Similarly, Wi-Fi technology will be implemented, focused on controlling or monitoring the progress of the patient, by a specialist, throughout his rehabilitation, using a local network to have a patient management within a clinic or rehabilitation area.

4.3 Collection of Electromyogram signals

Obtaining EMG signals will be very useful when evaluating and monitoring the patient's progress in the rehabilitation process. Figure 10 shows the design of the EMG module designed to obtain these signals and Figure 11 shows the circuit assembly on a breadboard.

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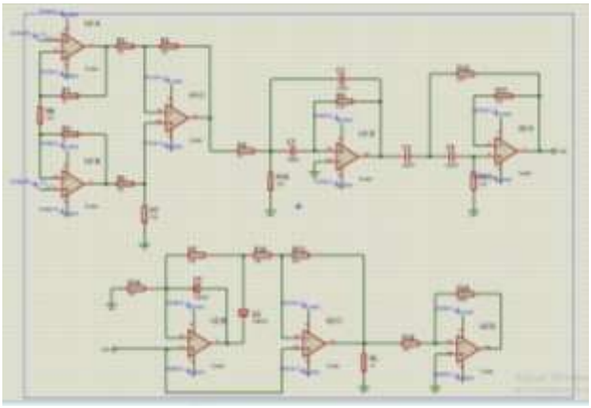

Figure 10 EMG module design
Own Authorship

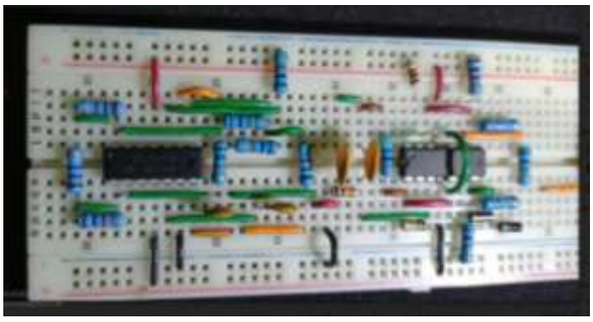

Figure 11 Physical assembly of the EMG module
Own Authorship

With the EMG module it was possible to obtain a satisfactory signal processing. Figure 12 shows the waveform obtained from the myoelectric signal processed by the EMG module.

Figure 12 Non-inverted myoelectric signal processed by the EMG module
Own Authorship

4.4 Programming of rehabilitation sessions

A mobile application was developed where the type of rehabilitation will be configured at different levels, a time selected by the patient can be established in order to schedule rehabilitation sessions; speeding up this process, automating it and avoiding setbacks caused by non-compliance with the recommended times for each movement or stimulation time. Figures 13, 14 and 15 show the design of the interfaces of the mobile application to control the device.

The home screen of the interface has a user name and password for access (see Figure 13). Within the application it will be possible to choose the level of rehabilitation based on the degree of mobility of the subject, based on the recommendation of the specialist, Figure 14.

After selecting the level, a window appears to start the therapy, in which the play and stop icon appears, as well as the number of repetitions corresponding to each level (Figure 15).

Figure 13 Home screen interface of the mobile App
Own Authorship

Figure 14 Interface of the mobile App menu screen
Own Authorship

Figure 15 Screen interface representative of the first level of movement of the device
Own Authorship

4. Conclusions

According to the functional tests performed, it can be concluded that the objectives set at the beginning of the project were achieved, since a functional device was obtained in terms of control with web and mobile interfaces and good aesthetics, as well as the interfaces, which fulfilled the purpose of controlling the orthosis.

The electromyography module was completed in a prototype approach, since the module is able to observe the waveforms corresponding to muscle contractions, but a complete digitalization of the signal has not been achieved

At the moment it has not been tested with patients suffering from this type of arthritis or affected by a pathology that affects the movement in the joints of the hand, but the movement sessions have been achieved and executed using the wireless control of web pages and mobile applications.

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Article **ECORFAN-Journal Bolivia**
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Antimicrobial effect of *Eysenhardtia polystachya* homemade extracts on bacteria causing urinary tract infections

Efecto antimicrobiano de extractos caseros de *Eysenhardtia polystachya* sobre bacterias causantes de infecciones del tracto urinario

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Abstract

Objective: To evaluate the *in vitro* antimicrobial effect of homemade preparations of *Eysenhardtia polystachya*, obtained by maceration or by infusion, on bacteria that cause urinary tract infections. Methodology: Microdilution assays were performed in 96-well plates where bacterial suspensions were co-incubated with different dilutions of homemade extracts, as well as a control for comparison using a commercial extract of the plant. Subsequently, the absorbance at 600 nm was measured to be considered as a direct measure of bacterial growth. For each culture, the values were normalized to growth percentage from the absorbance value obtained in the wells without extract. Contribution: The results show that the homemade extracts have a partial antimicrobial effect on the growth of the bacteria used in this work. The effect was the same between the extract by infusion and the extract by maceration against Gram negative bacteria. On the other hand, the extract by infusion showed a better effect than the extract by maceration on Gram positive bacteria. None of the homemade extracts achieved the antimicrobial effect of the commercial extract. This work corroborates the empirical knowledge of the use of homemade preparations of *Eysenhardtia polystachya* to treat urinary tract infections.

***Eysenhardtia polystachya* extract, Antimicrobial effect, Urinary tract, Bacterial infection**

Resumen

Objetivo: Evaluar el efecto antimicrobiano *in vitro* de preparaciones caseras de *Eysenhardtia polystachya*, obtenidas por maceración o por infusión, sobre bacterias causantes de infecciones del tracto urinario. Metodología: Se realizaron ensayos de microdilución en placas de 96 pozos donde se co-incubaron suspensiones bacterianas con diferentes diluciones de extractos caseros, así como un control para comparación usando un extracto comercial de la planta. Posteriormente, se midió la absorbancia a 600 nm para considerarla como una medida directa del crecimiento bacteriano. Los valores se normalizaron a porcentaje de crecimiento a partir del valor de absorbancia obtenido en los pozos sin extracto para cada cultivo probado. Contribución: Los resultados muestran que los extractos caseros tienen un efecto antimicrobiano parcial sobre el crecimiento de las bacterias utilizadas en este trabajo. El efecto fue el mismo entre el extracto por infusión y el extracto por maceración contra bacterias Gram negativas. Por otro lado, el extracto por infusión mostró tener mejor efecto que el extracto por maceración sobre bacterias Gram positivas. Ninguno de los extractos caseros logó el efecto antimicrobiano del extracto comercial. Este trabajo corrobora el conocimiento empírico del uso de preparaciones caseras de *Eysenhardtia polystachya* para tratar infecciones del tracto urinario.

Extracto de *Eysenhardtia polystachya*, Efecto antimicrobiano, Tracto urinario, Infección bacteriana

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Introduction

Mexico has a history of the use of ethnomedicine, whose origins go back to pre-Hispanic cultures where archaeological finds have demonstrated its influence and anthropological impact on Mexican culture. (Esquivel-García *et al*., 2018).

In Mexico, the National Commission for the Knowledge and Use of Biodiversity (Conabio, for its name in spanish), states that there are registered more than four thousand species of plants to which medicinal properties are attributed, representing almost 15% of the total flora of the country (CONABIO, s/f).

The World Health Organization (WHO) defined traditional medicine as "the set of knowledge, skills and practices based on the theories, beliefs and experiences of different cultures, whether explicable or not, used to maintain health and prevent diagnosing, ameliorating or treating physical and mental illnesses" (Organización Mundial de la Salud, 2013).

In recent years, the use of medicinal plants has increased for the treatment of various pathologies or as an adjuvant in medical treatments, an example of this is *Eysenhardtia polystachya*. This plant is commonly known as "blue wood" or "sweet wood", it belongs to the Leguminosae family. It is a deciduous tree or shrub 3 to 9 m tall with a diameter of 15 to 35 cm (Silva Guzmán *et al*., 2007). It has alternate, compound, pinnate crown and leaves, elliptic leaflets and aromatic resins.

The bark is rough and scaly with a dark color on the outside and reddish-brown on the inside (Silva Guzmán *et al.,* 2007). It presents inflorescences in pointed, lobed clusters with a white corolla. Its fruit is shown in a curved pod that houses a thin seed susceptible to water and is a hermaphrodite. It is distributed throughout Mexico, mainly in the states of Colima, Chiapas, Chihuahua, Coahuila, Mexico City, Durango, Guanajuato, Guerrero, Hidalgo, Jalisco, State of Mexico, Morelos, Oaxaca, Puebla, Querétaro, San Luis Potosí, Sinaloa, Sonora, Tamaulipas, Tlaxcala, Veracruz and Zacatecas. It has also been found in the southeastern United States (Gutierrez *et al*., 2015).

The recurrence of traditional medicine throughout Mexico is very common, since it is an essential part of Mexican culture as an alternative for the treatment of various pathologies or as an adjuvant in medical treatments. *Eysenhardtia polystachya* is used in traditional medicine to treat urolithiasis and other urinary diseases, such as urinary tract infections or the popularly called "urinary ailment". Commonly, the bark is boiled with water, obtaining a golden-colored liquid, which presents blue fluorescence and is administered orally (Pérez-Gutiérrez *et al*., 2002).

Urinary tract infections are a frequent problem in primary care and are among the most common infectious diseases worldwide. They are one of the leading causes of morbidity, only below respiratory infections (Tamadonfar *et al*., 2019). *Escherichia coli* is the main causative agent, being responsible for more than 90% of this type of infection. Other bacterial genera that also cause urinary tract infections include: *Klebsiella, Proteus* and *Staphylococcus* (Lee *et al*., 2018; Simões e Silva *et al*., 2020).

Until now, some biological properties of the ethanolic extracts of this plant have been reported, including antimicrobial activity. However, there are no studies that consider the dosage obtained in traditional preparations, which is how the population that uses traditional medicine consumes it. It is important to provide scientific evidence that supports the efficacy of the plant consumed in a traditional way, therefore, in this work the in vitro antimicrobial effect of the traditional preparation of *Eysenhardtia polystachya* against microorganisms that cause urinary tract infections is evaluated, in its preparations by infusion and maceration, taking as a reference the effect produced by a commercial extract of the same plant.

Methodology

Microorganisms and culture media

Three strains of Gram negative bacteria were used: *Escherichia coli* (ATCC 25922), *Proteus mirabilis* (ATCC 29906) and *Pseudomonas aeruginosa* (ATCC 27853) and two strains of Gram positive bacteria: *Enterococcus faecalis* (ATCC 29212) and *Staphylococcus aureus* (ATCC 29213).

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All strains were propagated from a stock suspension stored at -80°C and streaked for colony isolation. For the propagation and maintenance of the bacteria, LB agar plates (1% peptone biotryptase, 1% yeast extract, 0.5% NaCl and 2% bacteriological agar) were used, where the strains were inoculated and incubated at 37ºC. For the determination of the minimum inhibitory concentration (MIC) by the broth microdilution method, Mueller-Hinton broth was used. To count the bacteria on the plate, peptone water (1% meat peptone and 0.5% NaCl) and tryptone glucose yeast extract agar (TGEA, 0.3% meat extract, 0.5% casein peptone, 0.1% glucose, extract of yeast 0.1% and bacteriological agar 2%).

***Eysenhardtia polystachya* extracts**

The homemade extracts were made following the traditional preparation recommended by oral tradition. For this, the bark of the plant was purchased in a herbal medicine store and two extracts were prepared. For the first, a heaping tablespoon (15 g) of the bark was macerated in a liter of purified water overnight. For the second, 1 L of boiling purified water was added to 15 g of the bark and allowed to cool to room temperature. Both preparations were filtered separately and stored protected from light at 4°C until use.

To compare the results, a commercial extract that was purchased in the same herbal medicine store was used as a control (microdose of Palo azul, herbal extract, from the Tierra de vida brand). To use similar concentrations of the extracts (homemade and commercial) in the experiments, an aliquot was analyzed by UV-Vis spectrophotometry. From the spectrogram of the extracts, the commercial extract was adjusted by dilution until similar absorbance values were obtained. The highest concentration used in the experiments was that obtained in the undiluted traditional preparations.

Inoculum preparation

To obtain the inoculum from 0.5 MacFarland scale suspensions, 5 to 10 equal colonies were taken from the culture plate and diluted in 10 mL of peptone water.

Six decimal dilutions were then made using peptone water as diluent. 1 mL of the corresponding dilution was inoculated in duplicate in each box of medium and 18 to 20 mL of TGEA, melted and tempered in a water bath at 45 ± 1.0 ºC, were added. To homogenize, it was mixed with movements from right to left, clockwise and counterclockwise, and from back to front, on a smooth and horizontal surface until the complete incorporation of the inoculum was achieved in the medium, and they were left at rest until solidified.

One box without inoculum was included for each batch of medium and diluent prepared as a sterility control. The plates were incubated in an inverted position at 37 °C for 14 to 16 hours. To obtain an inoculum of 5 x 10^5 CFU/mL, the dilutions from which 50 colonies grew on the solid medium plate were considered. Based on this, the initial suspension was diluted in Mueller-Hinton broth for a concentration of 1 x 10^6 CFU/mL, so that when diluting the inoculum with an equal volume of extract, the final concentration would be 5 x10^5 CFU/mL.

Plate microdilution

The assay was performed in 96-well microplates using the serial dilution procedure as follows: for each extract, 100, 80, 60, 40, 20, and 0 µL of extract were placed in each well of the column, in duplicate. For those volumes less than 100 µL, the volume was completed with Mueller-Hinton broth. The same procedure was followed for the sterility control (100 µL broth + 100 µL of the extract dilution) and the negative control (100 µL broth + 100 µL water). Subsequently, 100 µL of the inoculum suspension were inoculated in all the columns except for the sterility controls, completing a final volume of 200 µL in the culture plate, thus adjusting the microbial population to 5x10^5 CFU/mL, and the extract/culture ratio at 1.0, 0.67, 0.43, 0.25 and 0.11. The plates were sealed and incubated at 37°C for a period of 18-24 hours. Bacterial growth was determined by measuring absorbance by UV-Vis spectrophotometry in a plate reader at a wavelength of 600 nm, to determine the lowest extract/culture ratio at which bacterial growth was inhibited.

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Statistic analysis

The absorbance values were normalized as a percentage of bacterial growth taking as reference the absorbance of the control without extract as 100%, for each condition (extract and bacteria) tested. All experiments were performed in duplicate and data from at least four independent experiments were used to report values as arithmetic mean ± standard deviation. Data were analyzed with a two-way ANOVA followed by Tukey's multiple comparison test using GraphPad Prism8 software for Windows. A *P* value less than or equal to 0.05 was considered significant.

Results

Concentration of homemade extracts

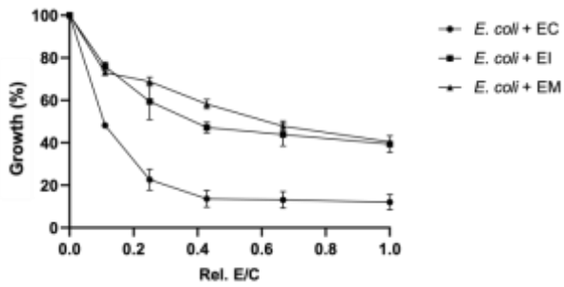
UV-Vis spectrograms of the two homemade extracts, obtained by maceration and by infusion, as well as the commercial extract used as control, were obtained. It was observed that the maximum absorbance peak was at the beginning of the visible range, at 400 nm of wavelength. And that both home preparations, infusion and maceration, reached similar concentrations (A_{400} ~ 0.130), while the commercial preparation was out of linearity.

Therefore, it was diluted until absorbance values below 1.0 were obtained. Thus, it was determined, in a 1:400 dilution, that the absorbance at 400 nm was 200 times greater for the commercial extract than for the homemade extracts. This suggests that home preparation methods do not allow optimal extraction of plant compounds.

Antimicrobial effect against Gram negative bacteria

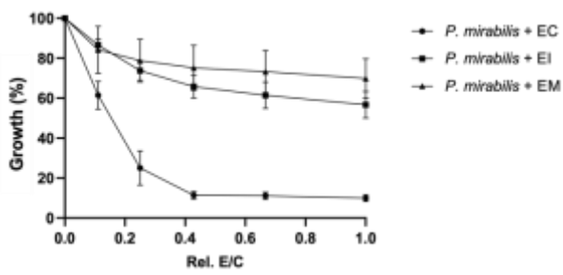
The antimicrobial effect of the homemade extracts obtained by infusion and by maceration on Gram negative bacteria that are commonly associated with urinary tract infections was tested. A commercial extract was used as a reference in each experiment. In Graph 1 it can be seen that the highest concentrations of home extracts manage to reduce almost 60% of the growth of the bacterial culture in vitro.

The statistics show that there is no significant difference in the effect of the homemade extracts among themselves (p = 0.4146), but there is a significant difference when any of the two homemade extracts is compared with the commercial extract in the same concentration (p < 0.0010). The commercial extract in a ratio of 0.11 extract/culture achieves the same effect as homemade preparations with a ratio of 1.0 extract/culture. The commercial extract in this last relationship manages to reduce bacterial growth by more than 80%.



Graph 1 Effect of *Eysenhardtia polystachia* extracts on the growth of E. coli. Rel. E/C: extract/culture ratio; EC: commercial extract; EI: extract by infusion; EM: extract by maceration
Source: Self Made

Graph 2 shows an effect similar to that observed for *E. coli* but in this case for *P. mirabilis*. Both homemade preparations manage to reduce almost 50% of bacterial growth, with no significant difference between them (p = 0.6192). There is a significant difference (p < 0.0001) when comparing any of the homemade extracts with the commercial extract, which manages to reduce 90% of bacterial growth from a ratio of 0.43 extract/culture, onwards.



Graph 2 Effect of *Eysenhardtia polystachia* extracts on the growth of P. mirabilis. Rel. E/C: extract/culture ratio; EC: commercial extract; EI: extract by infusion; EM: extract by maceration
Source: Self Made

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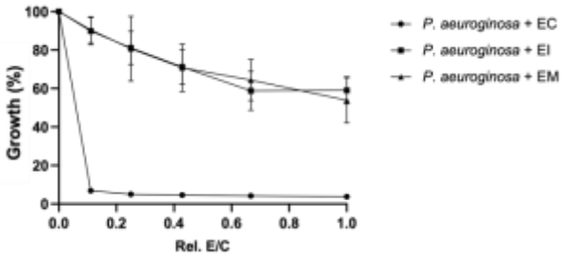
In the case of *P. aeuroginosa*, very low concentrations of the commercial extract managed to reduce around 95% of bacterial growth, contrasting with the effect that was observed with the homemade extracts where only a maximum reduction of 40% of bacterial growth was observed (Graph 3). There was no significant difference between both extracts ($p = 0.9849$), but there was between them and the commercial extract ($p < 0.0008$).

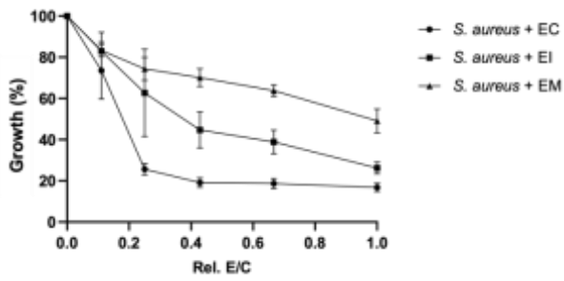


Graph 3 Effect of *Eysenhardtia polystachia* extracts on the growth of P. aeuroginosa. Rel. E/C: extract/culture ratio; EC: commercial extract; EI: extract by infusion; EM: extract by maceration
Source: Self Made

Antimicrobial effect against Gram positive bacteria

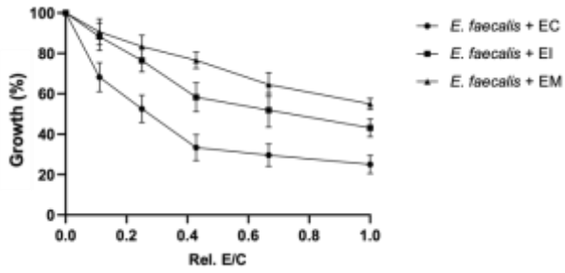
Unlike the almost homogeneous behavior shown by the home-made extracts by infusion and by maceration on the growth of Gram-negative bacteria, in the case of the Gram-positive bacteria used in this work, there were significant differences between the effect achieved by each of the preparations. homemade.

Graph 4 shows that the effect of the extract by infusion reduces the growth of *S. aureus* to levels very close to those achieved by the commercial extract (75% and 80%, respectively), both in the 1.0 extract/culture ratio; unlike the effect achieved by the extract by maceration that reduced growth by 50% in the extract/culture ratio of 1.0. The differences in the effect between the three extracts are statistically significant ($p < 0.0008$).



Graph 4 Effect of *Eysenhardtia polystachia* extracts on the growth of S. aureus. Rel. E/C: extract/culture ratio; EC: commercial extract; EI: extract by infusion; EM: extract by maceration
Source: Self Made

In Graph 5 it can be seen that the highest concentrations of the home extracts by infusion and by maceration manage to reduce almost 45% and 40%, respectively, of the growth of *E. faecalis*. The statistics show that there is a significant difference in the effect of the homemade extracts among themselves ($p < 0.0296$), and there is also a significant difference when comparing any of the two homemade extracts with the commercial extract at the same concentration ($0.0005 < p < 0.0120$). The commercial extract in a 0.25 extract/culture ratio achieves the same effect as home-made preparations by infusion with the highest extract/culture ratio. The commercial extract in this last relationship manages to reduce bacterial growth by more than 60%.



Graph 5 Effect of *Eysenhardtia polystachia* extracts on the growth of E. faecalis Rel. E/C: extract/culture ratio; EC: commercial extract; EI: extract by infusion; EM: extract by maceration
Source: Self Made

Discussion

Naturally, the microbiota only exists in the distal portion of the urethra, while the rest of the urinary tract remains sterile.

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This microbiota is different in men and women. In the latter, due to the anatomical proximity of the urethral orifice to the perianal region, it is common to find *E. coli* that comes from the intestinal microbiota.

In the case of men, *P. mirabilis* is the bacterium most frequently found in the urethra. However, although it is common to find this type of bacteria in the urethra, an imbalance in their control usually precedes the development of urinary tract infections (Tamadonfar *et al*., 2019).

Among the plants most frequently used in traditional medicine to treat conditions related to the urinary tract, including infections, is *Eysenhardtia polystachya*. This is usually used in home extractions obtained by infusion or by maceration in drinking water. However, little has been studied about the antimicrobial capacity of this type of preparation to validate the effects attributed to this plant.

In this work we observed that home preparations do have an antimicrobial effect on both Gram negative and Gram positive bacteria, frequently associated with urinary tract infections, and that the effect they exert on the former is very similar between home preparations, regardless if they were obtained by infusion or by maceration. On the contrary, the homemade extract obtained by infusion has a greater effect than the one obtained by maceration on Gram positive bacteria. However, when comparing the effect of homemade preparations with a commercial extract of the same plant, it was observed that none of these was able to match the antimicrobial effect of the commercial extract. This may be due to the extraction method since both homemade preparations are aqueous and with very simple techniques. The extraction method of the commercial product is unknown, but it is likely that it comes from a larger amount of biomass and includes several processes, including purification.

According to the results of this work, it was verified that the home-made extracts of *Eysenhardtia polystachya* have a broad spectrum, since they act on Gram-positive and Gram-negative bacteria, which agrees with what was reported for methanolic extracts obtained from leaves of this plant (Rivas-Morales *et al.,* 2016).

Conclusions

Until now there are several studies on the biological activities of the alcoholic extracts of *Eysenhardtia polystachya*. However, little has been studied about the effects of the homemade extracts of this plant, which are frequently consumed in traditional medicine. In this work it was verified that the homemade extracts obtained by maceration and by infusion have an antimicrobial effect on Gram-positive and Gram-negative bacteria that cause urinary tract infections. Additionally, it was observed that the concentrations obtained in these homemade extracts are lower than those of the commercial extract, therefore, although they cannot replace pharmacological therapy, they can function as auxiliaries in the treatment of this type of infection.

Taken together, our results corroborate the empirical use given to the extracts by infusion or by maceration of this plant. Studies that include the administration of this type of infusion together with different doses of antibiotics can provide information on the synergistic or combined effect that these infusions can have when used as adjuncts in the treatment of urinary tract infections. All this with the purpose of reducing the doses of antibiotics necessary to achieve the therapeutic effect and thus reducing bacterial resistance to antibiotics.

Acknowledgments

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What is your added value with respect to other techniques?

Clearly focus each of its features

Clearly explain the problem to be solved and the central hypothesis.

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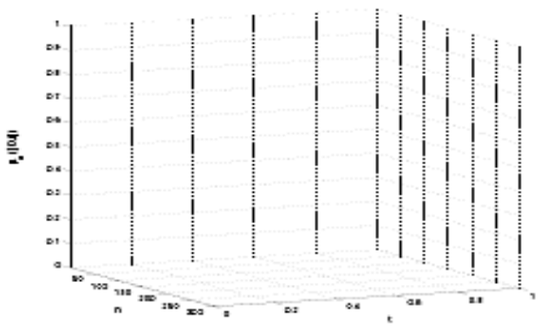

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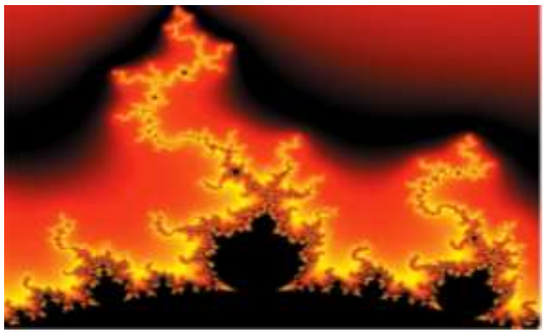

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