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Research Article

Production of Lactobionic Acid Using Gold Nanoparticles Synthesized with Fruit *Myrciaria dubia* Extract

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Lactobionic acid (LBA) is a polyhydroxy acid with attractive properties in the pharmaceutical, cosmetic, food, medical, and chemical industries, making it a versatile product with multiple applications, which supports the various studies aimed at its production by increasingly more simple, efficient, and environmentally friendly processes. For this reason, the purpose of this research was to synthesize gold nanoparticles (AuNPs) by a synthesis process using *Myrciaria dubia* (Camu camu) fruit extract. Subsequently, AuNPs were used to produce LBA from lactose. The results demonstrate that the *Myrciaria dubia* extract manages to synthesize AuNPs that were characterized by UV/vis spectrophotometry, energy-dispersive X-ray spectroscopy (EDX), and Zetasizer. LBA was quantified by FTIR-ATR spectroscopy and ion chromatography. The results showed that AuNPs succeeded in producing LBA from lactose showing the highest LBA production efficiency at a dose of 0.5 g/L and a temperature of 60°C. It has been shown that the AuNPs obtained by synthesis using the *Myrciaria dubia* extract efficiently catalyze the production of LBA from lactose, with a yield of 45.24%, which can be used to produce LBA for industrial or research purposes.

1. Introduction

Lactobionic acid (LBA) is composed of gluconic acid linked by an ether bond to a galactose that, according to its structure and composition, has properties of great interest [1]. This LBA is a polyhydroxy acid with various proven applications in food, medical, pharmaceutical [2], cosmetic [3], and chemical [4] industries. Among its properties, its antioxidant, chelating, and moisturizing activities stand out [5] and have allowed this LBA to be applied in the development of nanomaterials with potential use in the treatment of some types of cancer [6–10]. On the other hand, thanks to its moisturizing properties, it has been shown that it can be used in cosmetics for sensitive skin, including couperose skin [11]. Another study showed that 10% LBA reduces the pH of the skin surface without causing irritation [12] and can even be used in the preparation of an effective biomaterial in injuries since it promotes healing of wounds in endoscopic submucosal dissection [13]. Among other properties, it has also been shown to be safe when used as a supplement in artificial tears for ocular surface diseases such as dry eye [14]. Likewise, it is known to have an antibacterial effect against *Staphylococcus aureus* [15]. These studies highlight the numerous applications of LBA in different areas, making this substance a versatile compound.

Regarding the production of LBA, various studies have been carried out using microorganisms such as *Pseudomonas taetrolens* [4, 16]. Similarly, LBA can also be prepared by oxidation of the free aldehyde group of lactose through the application of strains such as *Escherichia coli* [2, 17], *Pseudomonas fragi* [18], *Zymomonas mobilis* [19], *Gluconobacter* spp., and *Gluconacetobacter* spp. [20]. However, these methods imply procedures that involve more time and equipment for the LBA preparation process. For this reason,

the aerobic oxidation of lactose using gold nanoparticles has been developed as an alternative method of production [21]. These gold nanoparticles (AuNPs) have diverse chemical and physical properties [22], proving useful as important components for biomedical applications [23].

Nanotechnology has inspired many investigations and research studies aimed at the manufacture of nanoparticles [24, 25]. AuNPs can be obtained by chemical synthesis methods following complicated and strict protocols [26–29]. But, in addition, the use of reagents for synthesis can often be harmful to the environment, so there is an alternative to the ecological synthesis of nanoparticles, better known as green synthesis [30–32]. This is because nature is considered a biological laboratory due to the diversity of plants, algae, and microorganisms that are used to synthesize nanoparticles [33, 34] and is well received due to its speed, low cost, nontoxicity, and its environmentally friendly applications [35, 36]. The green synthesis of nanoparticles is feasible because plant species have secondary metabolites with high antioxidant or reducing capacity, as is the case of *Myrciaria dubia* known as Camu camu, which is an Amazonian fruit bush that produces various nutritional compounds such as essential amino acids, essential fats, vitamins, and minerals [37], and it is characterized by its excellent antioxidant capacity [38] due to its high concentration of ascorbic acid, flavonoids, and anthocyanins [39]. Therefore, in this study, the *Myrciaria dubia* fruit extract was used to synthesize AuNPs. Likewise, it was proposed to apply these AuNPs to produce LBA from lactic acid. Furthermore, a method was developed for the quantification of LBA by Fourier-transform infrared spectroscopy-attenuated total reflectance abbreviated as FTIR-ATR.

2. Materials and Methods

2.1. Reagents. Tetrachloroauric acid ($HAuCl_4{\cdot}3H_2O$), trisodium citrate, ethanol, lactose, LBA, and other reagents were obtained from Merck. HCl and HNO_3 were of suprapure quality (Merck). Ultrapure water was obtained from Merck Millipore's Simplicity® system purification unit.

2.2. Preparation of the Extract. To obtain the *Myrciaria dubia* extract, the shelled fruit was cut into pieces and then dried in an oven at 40°C for seven days. Once dry, the samples were crushed in a mortar until a fine powder was obtained. Then, 1 g of the powder was weighed in a 15 mL tube, and 3 mL of 96% ethanol was added; then, the samples were taken to a Branson ultrasound bath (40 kHz) for 15 min (final temperature = 25°C). The extract was centrifuged at 4000 rpm for 15 min; then, the supernatant was removed from the tube and placed in a 10 mL volumetric flask where it was made up to volume with 96% ethanol. This procedure to obtain the extract was repeated three times.

2.3. Synthesis of Gold Nanoparticles. The materials used were first washed with aqua regia (HNO_3 : HCl; 1 : 3) for the synthesis of gold nanoparticles, then rinsed with ultrapure water, and dried [40].

The process consisted of measuring 10 mL of 0.001 M $HAuCl_4{\cdot}3H_2O$ in a 50 mL beaker and then stirring at 250 rpm for 1 minute before adding 2 mL of 38.8 mM trisodium citrate [41]. Stirring continued for 1 more minute, 1 mL of the *Myrciaria dubia* extract was added, and stirring was left constantly for 90 minutes. Ultrasound was performed for 3 minutes using a high-power sonicator with a Model CV 188 probe, SERIAL 201502, with parameters of 130 watts and 20 kHz. At the end of that time, the suspension of AuNPs was centrifuged at 6000 rpm for 20 minutes. The supernatant was removed, the pellet was redispersed with ethanol, and ultrasound was performed again (Figure 1). Then, it was centrifuged again, and the process was repeated twice more. The synthesized AuNPs were dried at 40°C for subsequent experiments.

2.4. Characterization of Gold Nanoparticles. The characterization of the AuNPs was performed using different pieces of equipment. First, a spectrophotometric scan from 400 to 800 nm [42] was performed on the Agilent Cary spectrophotometer. AuNPs show a peak of maximum light absorption around 530 nm. The average size of the AuNPs synthesized in the Zetasizer Nano ZS90 equipment was also determined. The nanoparticles were also analyzed under a Thermo Scientific Talos F200i transmission electron microscope. Finally, elemental analysis was performed in SEM-EDX equipment, model: ZEISS MA LS 10, brand: Zeiss, with an X-ray diffraction detector.

2.5. Production of Lactobionic Acid. The production of LBA was made from lactose [2]. For this, 20 mL of a 50 g/L lactose solution adjusted to pH = 9 was reacted with the AuNPs (Figure 1).

For the lactose oxidation process, a $2^2 \times 3$ factorial design was carried out (Table 1) taking as one of the factors of the dosage of AuNPs with a minimum (–1) and maximum (+1) value of 0.125 and 0.5 g/L, respectively. The second factor evaluated was temperature, with minimum (–1) and maximum (+1) values being 20 and 60°C, respectively. Subsequently, the systems were allowed to cool down as appropriate and were analyzed in the Agilent Cary 630 FTIR-ATR spectrometer.

2.6. Determination of Lactobionic Acid by FTIR-ATR. A method was developed for the quantification of LBA by FTIR-ATR which consisted of preparing LBA solutions of 16, 21.6, 27.2, 32.8, and 38.4 g/L in ultrapure water since it is soluble in water [43]. These solutions were analyzed on Cary 630 FTIR using a single diamond reflection attenuated total reflectance (ATR) device. The measurement was made in the wave number interval of 4000–650 cm^{-1}.

2.7. Determination of Lactobionic Acid by Ion Chromatography. An ion chromatography (IC) method was developed for the determination of LBA by preparing LBA calibration solutions of 2, 3.5, 5, 5, 6.5, and 8 mg/L in ultrapure water and adjusting the pH to 6.5 with 0.1 N NaOH.

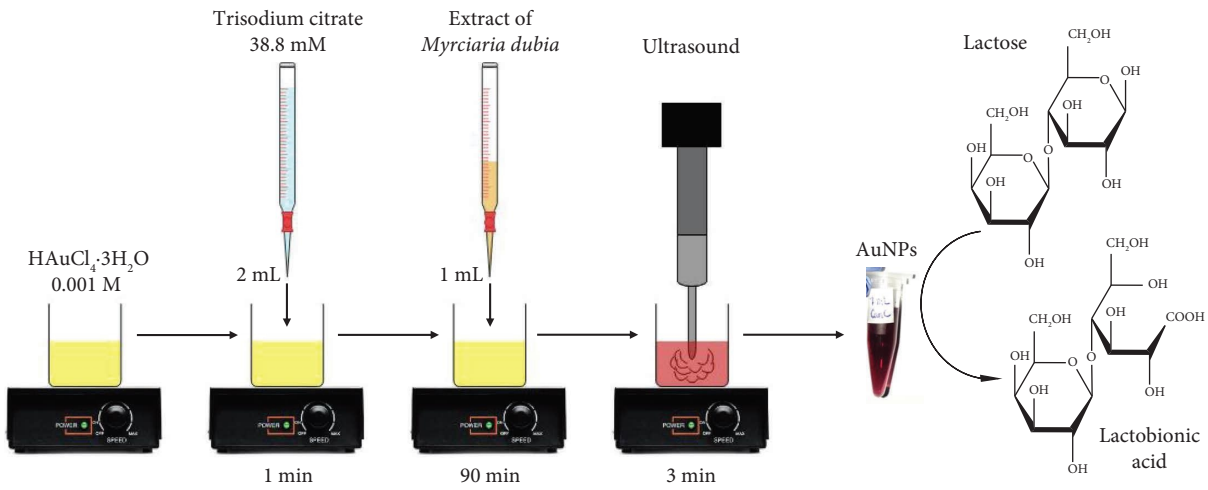


Figure 1: Graphic summary of the synthesis of gold nanoparticles from *Myrciaria dubia* and production of lactobionic acid from lactose.

Table 1: Factors and levels for factorial design $2^2 \times 3$.

Factors	Level	
	−1	+1
A: dosage (g/L)	0.125	0.5
B: temperature (°C)	20	60

Measurements were performed on the 930 Compact IC Flex ion chromatograph with chemical and sequential suppression with a conductivity detector. A Metrosep A sup 5 100/4 column was used using carbonate/bicarbonate as eluent. The injection volume was 20 μL, and the flow rate was 0.7 mL/min.

3. Results and Discussion

3.1. Characterization of Gold Nanoparticles. Figure 2 shows the result of the synthesis process of AuNPs from the *Myrciaria dubia* extract. The formation of AuNPs is evidenced by the formation of the purple hue. The UV-vis spectrum of the synthesized AuNPs is represented in Figure 2(a), which shows at 535 nm a maximum absorption peak corresponding to the AuNPs. This absorption band responds to the exposure of the nanoparticles to light, since an oscillation of the electrons around the nanoparticle is produced, causing a separation of charges concerning the ionic network, thus forming a dipolar oscillation in the direction of the field of light. The amplitude of the oscillation reaches a maximum of a specific frequency known as surface plasmon resonance (SPR), and this induces a strong absorption of incident light [44], which causes the spectrum to form with an absorption band centered at 535 nm in Figure 2(a). This is explained by [45] where they mention that gold nanostructures present SPR bands at 646 nm, 653 nm, and 535 nm, and they would present forms of nanoboxes, nanobars, and quasi-spheres, respectively. A similar study where an ethanolic extract of *Galaxaura elongata* was used to synthesize AuNPs also showed strong localized SPR at approximately 535 and 536 nm [46].

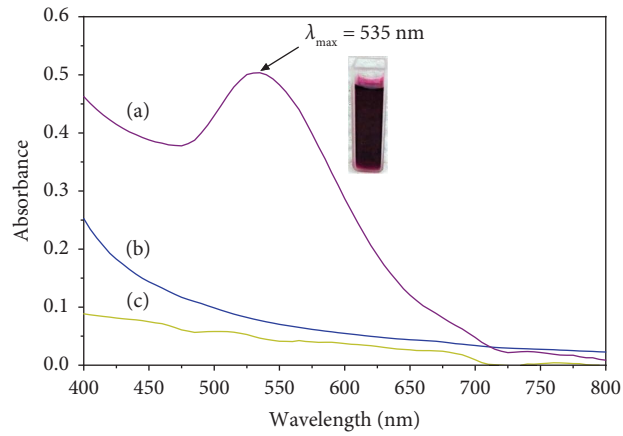


Figure 2: UV-vis spectra of (a) gold nanoparticles synthesized using *Myrciaria dubia* extract, (b) *Myrciaria dubia* extract, and (c) $HAuCl_4$ solution.

On the other hand, spectrophotometric scans were also carried out under the same conditions on the *Myrciaria dubia* extract (Figure 2(b)) and on the $HAuCl_4$ precursor solution (Figure 2(c)), noting that the absorption band of the AuNPs was not found, thus confirming the formation of the AuNPs.

The measurement of the hydrodynamic diameter of the AuNPs synthesized by the *Myrciaria dubia* fruit extract was carried out by Zetasizer, showing a size of 77 nm. This result was similar to that obtained by [46], where an ethanolic extract of the *Galaxaura elongata* algae was used, achieving nanoparticles of 77.13 nm determined in Zetasizer. It can be confirmed, therefore, that the extracts of fruits and algae turn out to be effective for the synthesis of AuNPs (Figure 3).

However, when TEM micrographs were taken (Figures 4(a) and 4(b)), most of the AuNPs were observed to be approximately 10 nm in size; also, most of the AuNPs were observed to be agglomerated, which could explain why the Zetasizer analysis showed average sizes of 77 nm.

		Size (d.n...	% Intensity:	St Dev (d.n...
Z-Average (d.nm): 77.36	Peak 1:	107.3	100.0	50.72
PdI: 0.279	Peak 2:	0.000	0.0	0.000
Intercept: 0.910	Peak 3:	0.000	0.0	0.000
Result quality Good				

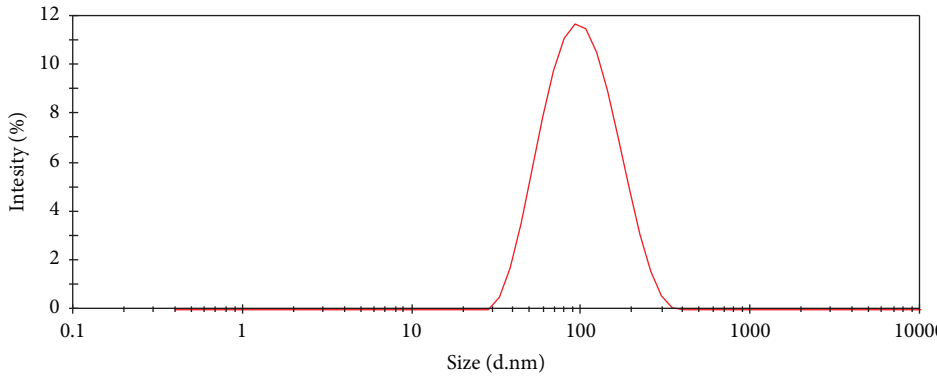
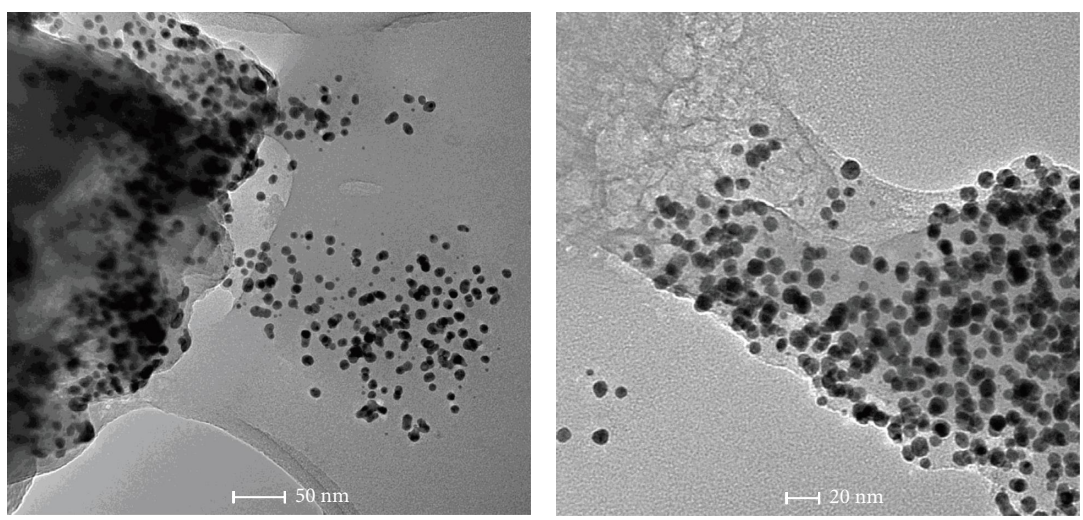
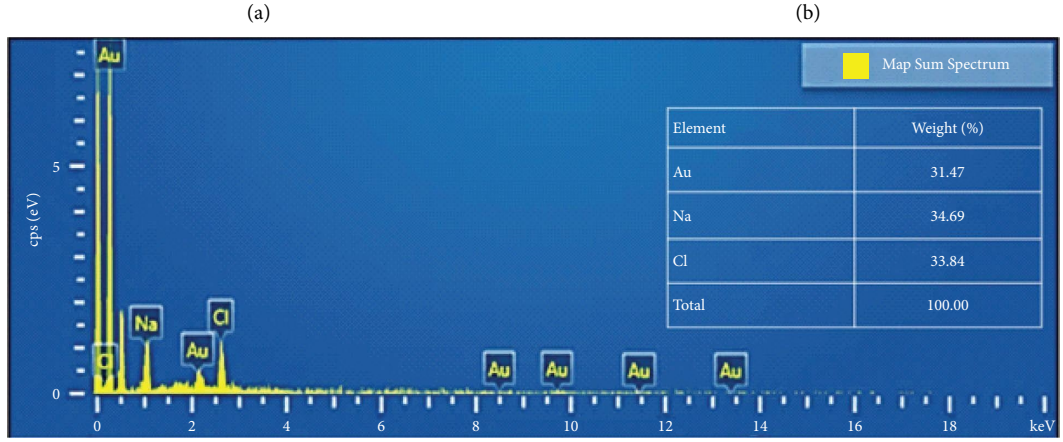


Figure 3: Particle size distribution of gold nanoparticles synthesized with *Myrciaria dubia* extract.



(a) (b)



(c)

Figure 4: (a, b) TEM micrographs; (c) EDX spectrum of gold nanoparticles synthesized with *Myrciaria dubia* extract.

The synthesis of AuNPs with the *Myrciaria dubia* extract was confirmed by EDX, as shown in Figure 4(c). A strong gold signal is observed with %wt of 31.47%. In addition, EDX shows sodium and chlorine which could correspond to trisodium citrate and the $HAuCl_4 \cdot 3H_2O$ precursor, respectively. Similar results regarding the gold signal were obtained in other studies such as the one by [47] who synthesized AuNPs using *Ganoderma* spp.

3.2. Method for Quantification of Lactobionic Acid by FTIR-ATR. Figure 5 shows the FTIR-ATR spectra of LBA corresponding to the calibration solutions of 16, 21.6, 27.2, 32.8, and 38.4 g/L, and it was observed that, at 1729 cm^{-1}, the peak corresponding to the C=O group of the carboxylic acid of LBA appears. Between 3550 and 3200 cm^{-1}, the presence of -OH groups is evident. Similar results were found in [48], who also carried out an FTIR-ATR analysis of LBA, where they found similar results. On the other hand, it can be seen that at 2935 cm^{-1} there would be -CH groups, 780 to 870 cm^{-1} show the vibration of the LBA ring, between 1177 and 1067 cm^{-1} the vibration of the C-O, 1283 cm^{-1} would give the vibration of the C-O of the acid and at 918 cm^{-1} the vibration of the C-O-H. These vibrations are also observed in LBA produced by the AuNPs in Figure 6(b).

It is also evident that, as the concentration increases, the intensity of this peak to 1729 cm^{-1} also grows, which allowed for the setting up of a calibration graph.

Figure 7(a) shows the spectrum of LBA in a wave number range of 1500–2000 cm^{-1} in which the spectra were superimposed at the different concentrations of LBA. As a result, it can be confirmed that, as the concentration increases, transmittance (%) also increases proportionally. Figure 7(b) shows that there is also a linear correlation between the LBA concentration and the peak area at 1729 cm^{-1}. The coefficient of determination R^2 was 0.9956, and the equation of the line is $y = 31.293x + 268.33$ with limits of detection and quantification of 4.42 and 5.78, respectively. With this equation of the straight line, LBA obtained by the AuNPs was quantified. Taking into account that "y" is the area of the peak and "x" is the concentration of LBA in g/L, the equation for quantification would be as follows:

$$\text{lactobionic acid}\left(\frac{g}{L}\right) = \frac{\text{peak area at } 1729\text{cm}^{-1} - 268.33}{31.293}. \quad (1)$$

3.3. Production of Lactobionic Acid Using AuNPs as Catalysts. Finally, the production of LBA from lactose was carried out using the AuNPs synthesized with the *Myrciaria Dubia* extract. Figure 6(a) shows the FTIR-ATR spectrum of lactose used as an LBA precursor. Figure 6(b) shows the FTIR-ATR spectrum of LBA produced from lactose using AuNPs as a catalyst. This is evidenced by the presence of the characteristic peak of LBA at 1729 cm^{-1}, which is not present in the lactose spectrum, although it also presents peaks similar to LBA. However, it is possible to highlight in the lactose

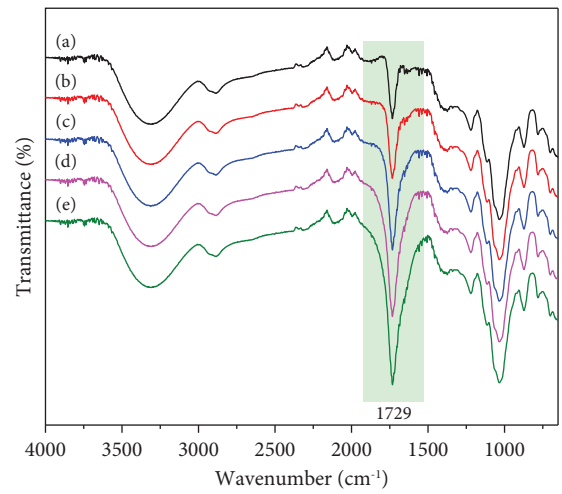


Figure 5: FTIR-ATR spectrum of lactobionic acid corresponding to calibration concentrations of (a) 16 g/L, (b) 21.6 g/L, (c) 27.2 g/L, (d) 32.8 g/L, and (e) 38.4 g/L.

spectrum bands at 2925–2927 cm^{-1} that would correspond to the $-CH_2$ groups, and the bands at 800–1000 cm^{-1} and 1150–1030 cm^{-1} would be characteristics of carbohydrates. Likewise, the peak of 1700 cm^{-1} would also be the characteristic of lactose [49, 50].

Table 2 shows the LBA concentrations in g/L produced by different doses of AuNPs and different temperatures corresponding to the $2^2 \times 3$ factorial design.

The analysis of the mean-normal graph is presented in Figure 8(a), where it can be seen that the dose of AuNPs has a greater influence on the production of LBA, achieving a positive effect on the process. In the same way, the second most important factor is the temperature, which also has a positive effect. However, the interaction of these factors has a negative effect on the production of LBA. On the other hand, the perturbation graph (Figure 8(b)) indicates that the interaction does achieve a significant effect on LBA production, making the overall effect negative.

The variance analysis of the $2^2 \times 3$ factorial design model is shown in Table 3, which turned out to be significant ($p < 0.05$). Likewise, the AuNPs dose factors, temperature, and AB interaction also present a significant effect ($p < 0.05$) in LBA production.

Once it has been identified that the two factors studied affect LBA production, the following mathematical model is obtained from the chosen factorial design:

$$\text{LBA}\left(\frac{g}{L}\right) = 5.61 + 33.37\text{AuNPs}_{\text{Dosage}} + 0.143\text{Temperature} - 0.27\left(\text{AuNPs}_{\text{Dosage}} \cdot \text{Temperature}\right). \quad (2)$$

This model can be used to make predictions of LBA production at different dose and temperature values under the conditions studied. With the abovementioned mathematical model, the surface graph was obtained (Figure 9(a)), in which it can be observed that while the dose of AuNPs increases, the

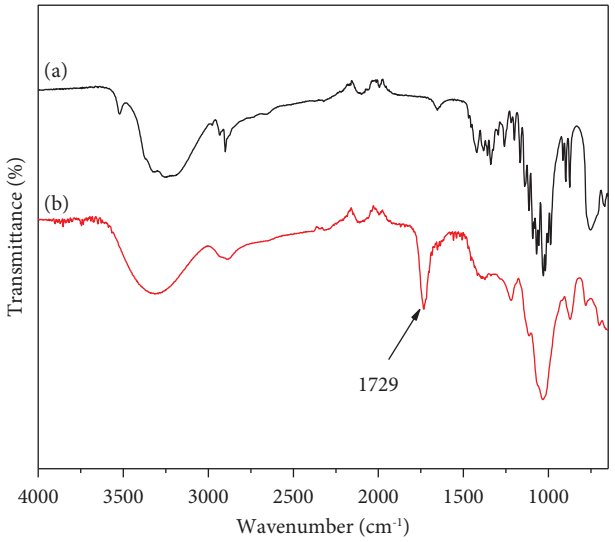


Figure 6: FTIR-ATR spectra of (a) lactose and (b) lactobionic acid produced using AuNPs synthesized with *Myrciaria Dubia* extract.

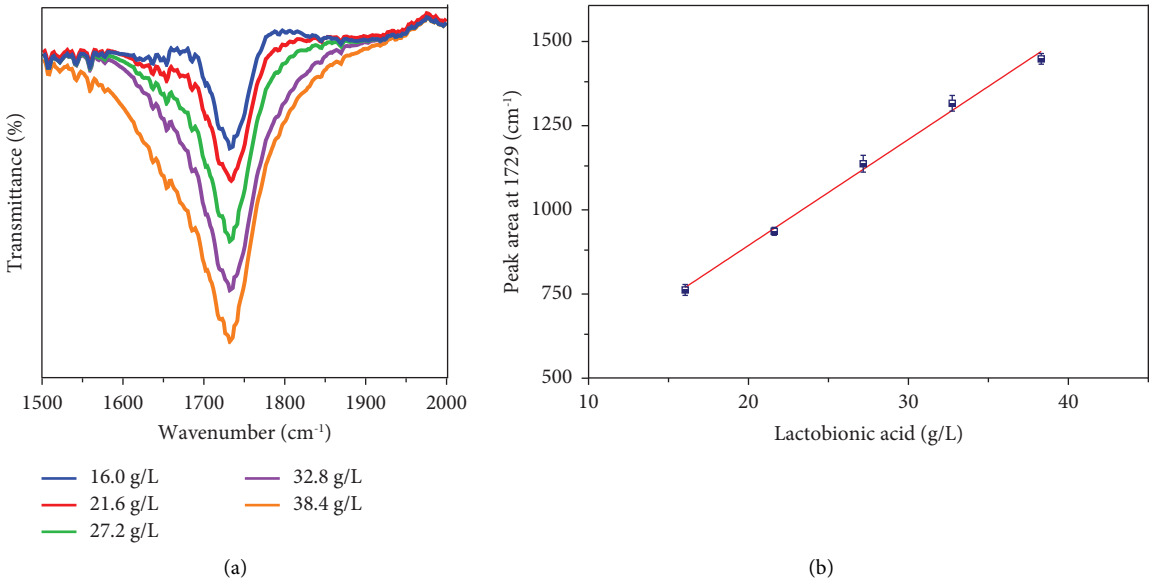


Figure 7: Method for the determination of lactobionic acid (LBA) by FTIR-ATR: (a) overlaid spectra at different LBA concentrations and (b) LBA concentration calibration plot with linear response.

Table 2: Results of the concentration of lactobionic acid produced at different conditions of doses of AuNPs and temperatures of the $2^2 \times 3$ factorial design.

N	Coded factors		Real factors		Lactobionic acid (g/L)
	A : dosage of AuNPs	B : temperature	A : dosage of AuNPs (g/L)	B : temperature (°C)	
1	+1	−1	0.5	20	22.43
2	+1	+1	0.5	60	22.62
3	−1	−1	0.125	20	11.84
4	+1	−1	0.5	20	22.36
5	−1	+1	0.125	60	16.86
6	−1	+1	0.125	60	15.7
7	−1	−1	0.125	20	12.14
8	+1	+1	0.5	60	22.62
9	−1	−1	0.125	20	11.92
10	+1	−1	0.5	20	22.48
11	+1	+1	0.5	60	22.78
12	−1	+1	0.125	60	16.44

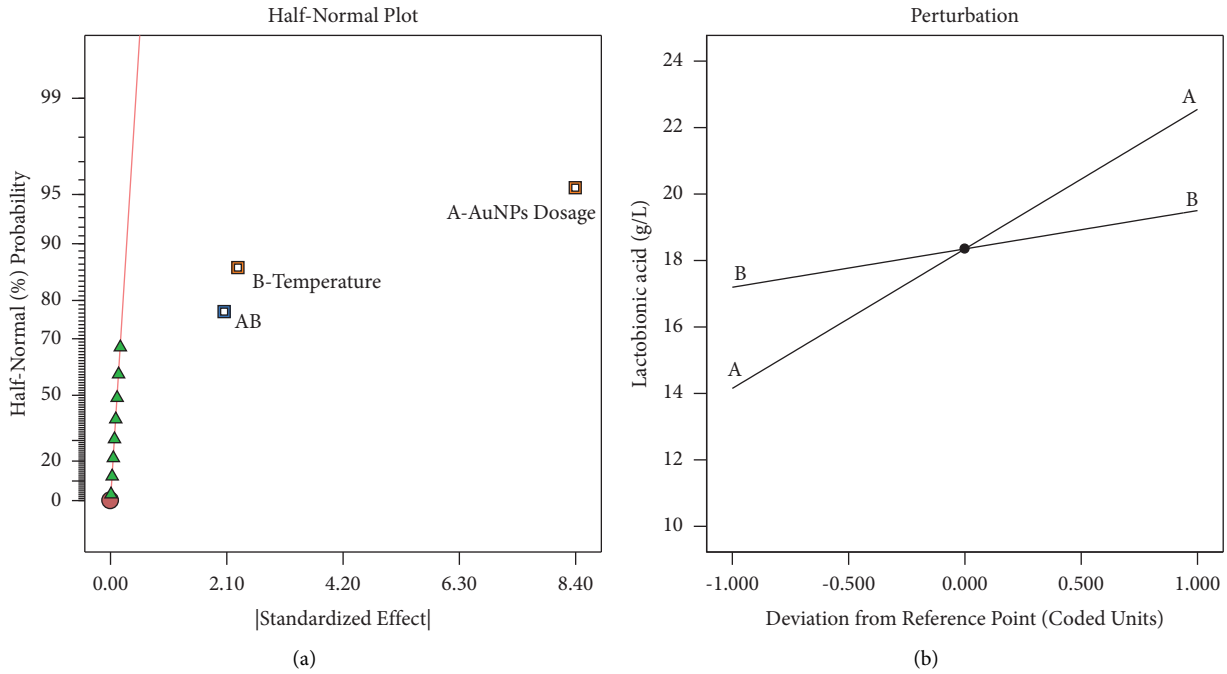


Figure 8: (a) Mean-normal plot and (b) perturbation plot for the production of lactobionic acid from lactose using AuNPs as a catalyst.

Table 3: Analysis of variance for the $2^2 \times 3$ factorial design.

Sources	Sum of squares	df	Mean square	F value	p value	Interpretation
Model	240.29	3	80.1	840.4	<0.0001	Significant
A: dosage	211.6	1	211.6	2220.12	<0.0001	Significant
B: temperature	15.99	1	15.99	167.72	<0.0001	Significant
AB	12.71	1	12.71	133.36	<0.0001	Significant
Pure error	0.7625	8	0.0953			
Cor. total	241.05	11				

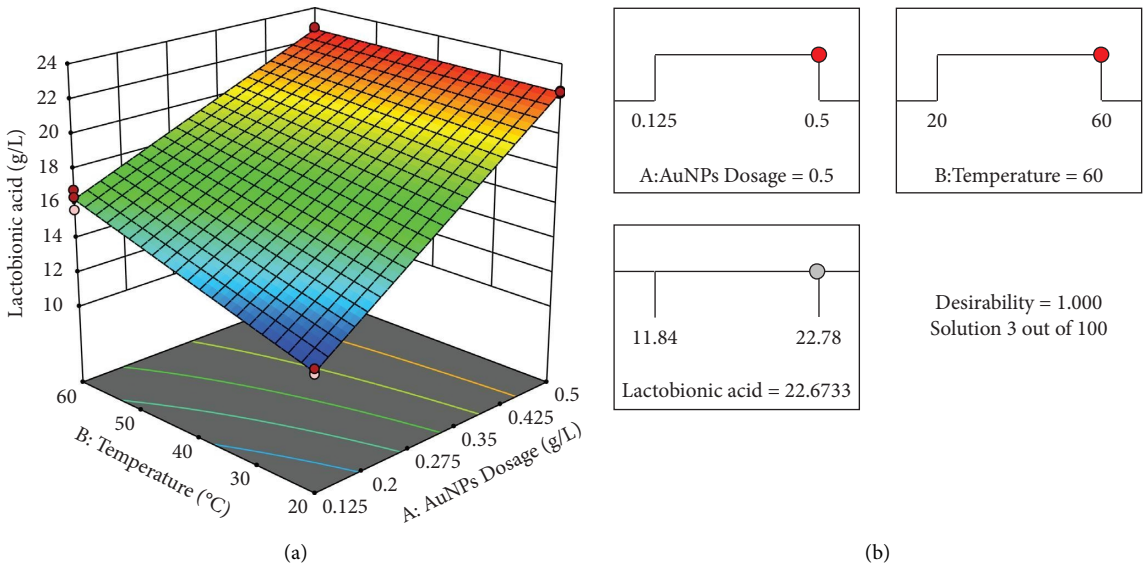


Figure 9: (a) Surface diagram corresponding to the $2^2 \times 3$ factorial design and (b) ramp graph to determine the optimal factors of AuNPs dose and temperature for the highest production of lactobionic acid.

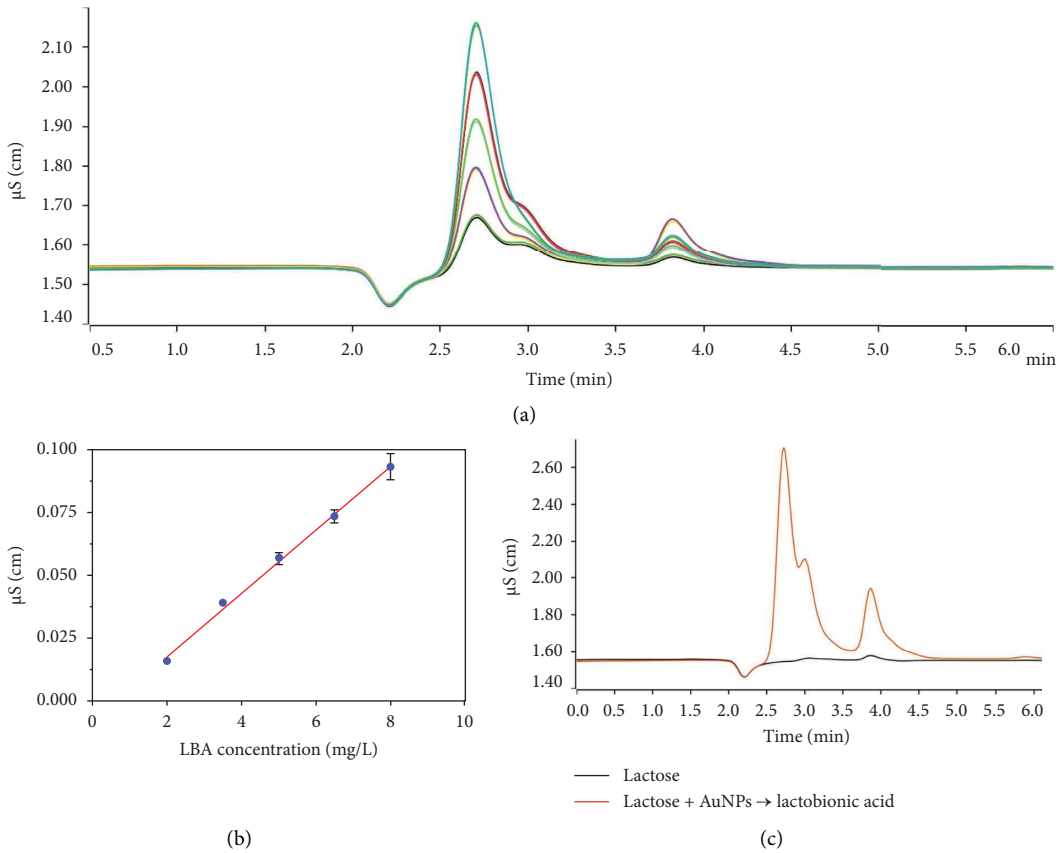


Figure 10: (a) Chromatograms of lactobionic acid calibration solutions (2–8 mg/L) after analysis by ion chromatography. (b) Calibration graph for the quantification of lactobionic acid by ion chromatography. (c) Chromatogram of lactobionic acid production from lactose.

production of LBA increases. In the same way, as the temperature increases, the production of LBA also increases. It can also be observed that, at the maximum dose of AuNPs and lower temperature, a high production of LBA is obtained, which is similar when the dose interacts with a higher temperature. For this reason, it was intended to optimize the process by taking into account that it seeks to achieve the highest production of LBA, for which the Design Expert software was allowed to suggest the ideal values for each factor. It was determined that, to achieve the maximum production of LBA (22.67 g/L) with a desirability of 1.000 (solution 3), a AuNP dose of 0.5 g/L and a temperature of 60°C should be considered (Figure 9(b)). Likewise, with the maximum concentration of LBA obtained, the yield of LBA produced was calculated concerning the amount of lactose used in the process, resulting in 45.24%. This result is very close to that found in [21] who achieved a 50% conversion of sodium lactobionate to lactobionic acid by also using gold catalysts. In another current study, they used *Escherichia coli* which was able to produce lactobionic acid with 100% yield [17].

3.4. Comparison of the Lactobionic Acid Determination Method by FTIR-ATR with Ion Chromatography. Figure 10(a) shows the chromatogram of LBA calibration solutions at concentrations from 2 to 8 mg/L. Figure 10(b) shows that LBA concentration and the peak area gave a linear response ($R^2 = 0.997$, $y = 0.0127x - 0.0079$). Figure 10(c) shows the chromatogram of lactose and the chromatogram evidencing the formation of LBA produced from the reaction between lactose with AuNPs, demonstrating the usefulness of these AuNPs for the production of LBA.

Table 4: Comparison of lactobionic acid production from lactose determined by FTIR-ATR and ion chromatography (IC).

Methods	Concentration of lactobionic acid (g/L)	
	Experimental value (mean ± standard deviation)	Theoretical value
FTIR-ATR	20.42 ± 0.57	22.67
IC	21.90 ± 0.37	

Subsequently, the comparison of the methods by FTIR-ATR and IC was carried out, using the biosynthesized AuNPs to produce lactobionic acid from lactose at optimum conditions obtained in Figure 9. The results are shown in Table 4, where the theoretical value is 22.67 g/L, and the obtained concentration of LBA obtained experimentally determined by FTIR-ATR is 20.42 ± 0.57 g/L and by IC is 21.90 ± 0.37 g/L, being the results similar. Therefore, it is possible to use FTIR-ATR to quantify LBA at the conditions exposed in this research.

4. Conclusions

It was possible to synthesize AuNPs using the *Myrciaria dubia* fruit extract as a reducing agent and sodium citrate as a stabilizing agent, obtaining particles with a size of 10 nm by TEM analysis. Likewise, a method was developed for the determination of lactobionic acid (LBA) by FTIR-ATR spectroscopy, which resulted to have a linear correlation ($R^2 = 0.9956$) between the concentration of LBA and the area of the peak at 1729 cm^{-1} at concentrations between 16 and 38.4 g/L of LBA; likewise, this method was compared with a method developed by ion chromatography at concentrations of 2–8 mg/L of LBA with a linear response ($R^2 = 0.997$), finding that both methods achieve evidence of LBA production from lactose using AuNPs as catalysts, giving similar results. It was also possible to produce LBA from lactose using AuNPs as a catalyst, being the optimum factors that achieve the highest concentration of LBA at a dose of AuNPs of 0.5 g/L at a temperature of 60°C. Through this research, it is demonstrated that AuNPs synthesized using the *Myrciaria dubia* fruit extract possess reductive properties capable of synthesizing LBA from lactose with a yield of 45.42%, which can be taken into account in future studies or processes that focus on the production of LBA in pharmaceutical, cosmetic, and food industries, as well as in any other related industries.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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