

ANALYSIS OF INVESTMENT AND PRODUCTION COSTS OF HOPS IN THE CAIUÁ SANDSTONE REGION

Recebido em: 21/10/2024

Aceito em: 11/11/2024

DOI: 10.25110/receu.v25i1.2024-11656



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ABSTRACT: Hops (*Humulus lupulus* L.) is an ancient crop widely distributed across much of the world. The use of hops is very diverse. They are utilized in the pharmaceutical industry, in popular uses such as teas, and notably in the brewing industry, which is one of the main interests in hop cultivation since they are a key ingredient in beer formulation. Brazil is a significant consumer of hops; however, a large portion of its consumption comes from imported products. The country has great production potential, but its current production is still modest. Thus, the main objective of this study was to evaluate the initial investment and maintenance costs for hop cultivation in the Caiuá Sandstone region in northwestern Paraná State. To achieve this, an experiment covering 1,100 m² was conducted in the city of Umuarama, PR, assessing initial investment and production costs over two years. A significant portion of the investment was allocated to seedlings and trellis structures, while the most evident cost was the need for labor to maintain the crop.

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It was concluded that hop cultivation can be implemented; however, the initial investment is high, and there is a need to mechanize part of the management to mitigate labor costs.

KEYWORDS: *Humulus lupulus*; Initial investment; Production; Hop culture.

ANÁLISE DOS CUSTOS DE INVESTIMENTO E PRODUÇÃO DE LÚPULO NA REGIÃO DO ARENITO CAIUÁ

RESUMO: O lúpulo (*Humulus lupulus* L.) é uma cultura antiga difundida em grande parte do mundo. O uso do lúpulo é muito diversificado, sendo utilizado na indústria farmacêutica, no uso popular como chás e pela indústria cervejeira, que aliás é um dos principais interesses pelo cultivo de lúpulo, visto que esse é um dos principais ingredientes da formulação cervejeira. O Brasil é um grande consumidor de lúpulo, porém grande parte do seu consumo é proveniente de produtos importados; o país pode ter um grande potencial de produção, mas sua produção ainda é tímida. Assim, o objetivo geral deste trabalho foi avaliar o investimento inicial e os custos para a manutenção da cultura de lúpulo na região do Caiuá Sandstone no Noroeste do Estado do Paraná. Para isso foi conduzido um experimento de 1.100 m² na cidade de Umuarama/PR, avaliado o investimento inicial e os custos de produção por dois anos. Grande parte do investimento foi em mudas e estrutura de palanques, enquanto o custo mais evidente foi a necessidade de mão de obra para manutenção da cultura. Concluiu-se que a cultura pode ser implementada, porém o investimento inicial é alto havendo também a necessidade de mecanizar parte do manejo para mitigar custos com mão de obra.

PALAVRAS-CHAVE: *Humulus lupulus*; Investimento inicial; Produção; Cultura do lúpulo.

ANÁLISIS DE LA INVERSIÓN Y COSTOS DE PRODUCCIÓN DE LÚPULO EN LA REGIÓN DE ARENITO CAIUÁ

RESUMEN: El lúpulo (*Humulus lupulus* L.) es un cultivo antiguo ampliamente distribuido en gran parte del mundo. El uso del lúpulo es muy diverso, ya que se utiliza en la industria farmacéutica, en usos populares como tés y, notablemente, en la industria cervecera, que es uno de los principales intereses en el cultivo de lúpulo, dado que es un ingrediente clave en la formulación de la cerveza. Brasil es un consumidor significativo de lúpulo; sin embargo, gran parte de su consumo proviene de productos importados. El país tiene un gran potencial de producción, pero su producción actual sigue siendo modesta. Así, el objetivo principal de este estudio fue evaluar la inversión inicial y los costos de mantenimiento para el cultivo de lúpulo en la región del Caiuá Sandstone, en el noroeste del estado de Paraná. Para lograr esto, se realizó un experimento en una superficie de 1.100 m² en la ciudad de Umuarama, PR, evaluando la inversión inicial y los costos de producción durante dos años. Una parte significativa de la inversión se destinó a plántulas y estructuras de enrejado, mientras que el costo más evidente fue la necesidad de mano de obra para el mantenimiento del cultivo. Se concluyó que el cultivo de lúpulo puede ser implementado; sin embargo, la inversión inicial es alta y hay una necesidad de mecanizar parte del manejo para mitigar los costos laborales.

PALABRAS CLAVE: *Humulus lupulus*; Inversión inicial; Pruducion; Cultura del lúpulo.

1. INTRODUCTION

Hops (*Humulus lupulus* L.) are widely recognized as a fundamental ingredient in the production of several varieties of beer. However, its chemical composition also makes it relevant in the pharmaceutical industry, due to its anti-inflammatory properties and the presence of prenylflavonoids, which act as phytoestrogens. These compounds are often used in the manufacture of hormonal supplements intended for menopausal women. Thus, in addition to its importance in beer production, hops can offer many benefits to human health (Sposito, 2019).

According to Rickli (2021), the plant is known for its female flowers (cones), where the lupulin glands are found, which produce resins that contain alpha and beta acids, xanthohumol, and essential oil (EO), responsible for the characteristic flavor and bitterness of the drinks.

In addition to its application in beer production, this plant has been used in traditional medicine as a remedy for inflammation, disinfection, fluid retention, colic, and increased sexual appetite (BLUMENTHAL, 2008), as well as hypnotic and sedative properties (ZANOLI; ZAVATTI, 2008; KOETTER; BIENDL, 2010). According to Cleemput *et al.* (2009), indigenous communities used to drink hop tea to reduce nervousness and heat a small bag of leaves to treat earache or toothache. Additionally, a variety of products containing hop extracts or their derivatives are commercially available for herbal purposes, including sleep difficulties, pain relief, and post-menopausal treatments.

According to Fagherazzi *et al.* (2018), hops are an essential component in beer manufacturing, as they provide aroma and flavor, contribute to foam formation, and act as a natural preservative. Art. 36 of Decree No. 6,871 of June 4, 2009, which regulates Law No. 8,918 of July 14, 1994, deals with the classification, registration, production, inspection, supervision, and standardization of beverages, including beer. The decree mentions that in the manufacture of beer, besides other ingredients, the addition of hops is mandatory (BRASIL, 2021).

Data from the Ministry of Agriculture and Livestock (MAPA, 2023) indicate that in 2023, beer sales volume was 16.1 billion liters, a growth of 4.5% compared to 2022, representing 1.6% of Brazilian GDP. These data demonstrate progress, even in the face of a challenging economic scenario, marked by high interest rates and rising inflation expectations. This growth is directly related to the increase in the number of breweries

registered in the country which according to the Ministry of Agriculture, Livestock and Supply, registered 1,847 beer-producing establishments in Brazil in 2023, a growth of 6.8% compared to 2022 (MAPA, 2024).

Another factor that deserves to be highlighted is the generation of jobs since the beer production chain contributes to more than 2 million direct, indirect, and induced jobs and generates 2% of the National GDP. For every job in a brewery, 34 new jobs are created throughout the production chain. Regarding numbers, the chain generates more than 27 billion in salaries. It is responsible for more than R\$49.6 billion (base 2022) in taxes per year, being one of the main contributors to Brazil's growth.

Success in hop cultivation depends on several factors, such as the level of technical knowledge of producers, management, soil and climate conditions, and, mainly, the selection of cultivars suitable for regional conditions, ensuring satisfaction for both producers and consumers.

According to Silva *et al.* (2016), breweries use hop cones in their production process, but a large part of this input comes from abroad. According to Canal Rural (2021), the Brazilian beer industry imports around 90% of the hops it needs. Data from the Ministry of Agriculture indicate that Brazil imported 3,243 tons of this product, which is equivalent to a value of 57 million dollars.

For Fagherazzi *et al.* (2018), hop cultivation in Brazil has gained visibility in the last five years, especially when some producers in the Serra da Mantiqueira, Brazil identified the economic potential of this commodity. Considering Brazil imports approximately two thousand tons per year, at a cost of around 36 million dollars. Currently, it is possible to find hop cultivation in states such as Rio Grande do Sul, Santa Catarina, Paraná, São Paulo, Rio de Janeiro, Minas Gerais, and the Distrito Federal. Although the exact value of national production is not yet known, the average price per kilo of dry hop cones is R\$200.00.

In Brazil, despite the first initiatives and incentives, hop cultivation still does not occur on a large scale, mainly due to the predominantly tropical climate. This represents a great challenge, especially when considering the implementation of this crop in places like Umuarama, in the northwest region of Paraná, which, according to the Koeppen classification, has a humid subtropical climate (Cfa) (WREGE *et al.*, 2012), with sub-warm variations (BRAGA; GHELLERE, 1999).

According to Rodrigues *et al.* (2015), hops are rarely cultivated in the southern hemisphere, partly because they are native to the northern hemisphere. The countries with the largest hop production include Ethiopia, Germany, the United States, the Czech Republic, and China. According to Atlasbig (2020), the world produces 142,154 tons of hops annually. Ethiopia leads with 40,074 tons, followed by the United States with 39,526 tons, with these two countries together producing 56% of the world's total, while production in Brazil is insignificant.

Volpato and Pasuch (2015) argue that international trade plays a crucial role in a nation's economy and the external sector can be decisive in balancing national accounts. In other words, it is preferable to export more and import less. The greater the import of goods and services, the greater the devaluation of the importing country's currency. Therefore, the greater the surplus in Brazil's trade balance, the greater the appreciation of the real to other currencies, contributing to the stabilization of the currency against the dollar.

In addition to the macroeconomic indicators that can benefit from the implementation of a culture that is currently mostly imported, microeconomic indicators, such as GDP and the Human Development Index (HDI), as well as the reduction of poverty and the increase in job and income generation, can also be boosted by encouraging new regional production models. Hop production can bring additional advantages, such as the creation of a new source of income for family farming, the formation of producer associations or cooperatives, and the strengthening of cooperatives in the Caiuá Sandstone region.

Thus, the general objective of this work is to evaluate the initial investment and costs for maintaining hop cultivation in the Caiuá Sandstone region in the northwest of the State of Paraná. For this evaluation, an experiment was conducted in an area of 1,100 m², and the values for 01 hectares were subsequently estimated. Thus, this work is justified by the growth of the beer market at an industrial and artisanal level; also by the possibility of strengthening the national and regional economy; and by the social factors that can be aggregated with the implementation of a new culture.

2. MATERIALS AND METHODS

2.1 Characterization of the experimental area

The experiment was conducted in a space of 1100 m² of an experimental area belonging to the State University of Maringá (UEM), Umuarama Regional Campus, located at 23°47' South latitude and 53°14' West longitude.

The soil where the hops were grown is derived from Caiuá Sandstone. This type of soil is classified as a Dystroferic Red Latosol and is characterized by a sandy loam surface with low clay and organic matter content (FIDALSKI et al., 2013).

2.2 Implementation and management of the culture

204 seedlings of four hop varieties were acquired from specialized nurseries, including 51 seedlings of the Cascade, Columbus, Nuget, and Comet varieties. Hop cultivation was carried out at a spacing of 3.0 m x 1.0 m, between rows and plants respectively, conducted in a single-stem planting system. To assemble the support system 30 eucalyptus stands measuring 9 meters in height were used. Wires were fixed to the top of the platforms, and sisal wires were placed between the plants in a “V” shape, serving as a guide for the plants.

Before planting, soil samples were collected at a depth of 0-20 cm for chemical characterization. After analyzing the soil, soil correction was carried out following the recommendations of Teixeira; Aquino; Macedo (2022). Soil analysis was performed between collections, and corrections were made as needed.

To plant the seedlings, beds were raised along the planting line, in such a way as to turn over a layer of soil so that it becomes more friable to facilitate the development of the root system, as recommended by Spósito *et al.* (2019). In the beds and following the spacing between plants, holes with a depth of approximately 20 cm were opened to plant the seedlings. Topdressing fertilization was carried out, dividing the crops according to the different phenological stages of the hop crop and according to the proportions recommended by the same authors. Hop cultivars were planted in November 2022.

2.3 Irrigation system and management

A localized drip irrigation system was used, using drip tapes with emitters presenting a nominal flow rate of 1.6 L h⁻¹ spaced at 0.15 cm.

2.4 Investment value analysis

For this initial study, an analysis was carried out of the value of the investment required to plant hops in 01 hectare, therefore it was necessary to carry out a simple rule of 3 to estimate the value invested in 10,000 m² through the area of the experiment which was 1,100 m², then for each quantity and value invested the equation was carried out which considered the Experimental Area (AE), Estimated Value (VE), Hectare (HA) and Value Invested in the experiment area (VI), represented in equation 01:

$$\text{Eq 01: } AE * VE = HA * VI$$

It is worth noting that investment is considered to be money spent on something with the expectation of generating a positive return in the future. An investment can be short, medium or long term (GITMAN; JOEHNK, 2016). Many people, especially those who do not have training in courses related to administration, accounting, and economics, confuse the concepts of investment and cost since the cost is the expense or outlay to acquire or produce a certain good or service, so the cost does not generate a direct financial return in the future, that is, the cost is the outlay necessary to keep the investment ongoing, but does not increase the net value of the business (HORNGREN; DATAR; RAJAN, 2015). Therefore, we can consider that the experiment up to now is an investment, given that the amounts spent on preparing the structure, purchasing, and planting the seedlings were taken into account.

2.5 Cost analysis in the first 4 semesters of cultivation

Cost analysis was determined over the first four semesters of cultivation. A detailed analysis of the direct and indirect costs associated with the maintenance and improvement of the experiment was carried out.

3. RESULTS

The results representing the investment in the structure for 1,100 m², also dimensioned for 01 hectare (10,000 m²) where the Cascade, Columbus, Comet, and Nuget varieties of *H. lupulus* were planted, are shown in Table 1.

Table 1. Investment in structure for experimental area (1,100 m²) and 01 hectare (10,000 m²), for the implementation of the *Humulus lupulus* crop

Unit	Items	Experimental Area (1,100 m ²)		Estimated Area (10,000 m ²)	
		Quantity	Value (R\$)	Quantity	Value (R\$)
Un	Sisal yarn 155/1 roll 9kg	3.00	720.00	27	6,545.45
Un	Drilling holes 1.5 m deep by 50 cm wide	30.00	1,000.00	273	9,090.91
Un	Tractor hours	2.00	600.00	18	5,454.55
Un	Double Ratchet Wire Tensioner	1.00	235.00	9	2,136.36
Mt	Oval wire 16x14	1000.00	780.00	9091	7,090.91
Un	Wire ratchet	25.00	212.25	227	1,929.55
Un	Drip system (drip tapes, lateral lines, main line and branch lines and separator filters)	01	4,050.00	01	38,000.00
Un	Untreated eucalyptus pallets, 30 cm in diameter, 7 meters long	30.00	3,000.00	1818	27,272.73
Lt	Gasoline for drilling holes	9.00	58.50	273	531,82
Un	Drill bits for drills	4.00	140.00	82	1,272.73
Un	Untreated eucalyptus stakes, 30 cm in diameter, 1.5 meters long	24.00	600,00	36	5,454.55
Hs	Munck truck	6.00	1,800.00	218	16,363.64
Total expenditure on structure			13,195.75		121,143.20

Un: units; Mt: meters; Lt: liters; Hs: Hours

To implement the hop culture, it was necessary to hire a qualified professional, the investment for which is detailed in Table 2.

Table 2. Investment in labor for an experimental area of 1,100 m² and 01 hectare (10,000 m²)

Unit	Item	Experimental Area (1,100 m ²)		Estimated Area (10,000 m ²)	
		Quantity	Value (R\$)	Quantity	Value (R\$)
Un.	Professional labor to drill and install 1.5 m eucalyptus stakes, drill stakes, and posts, as well as stretch the wires.	1	1,600.00	9	14,545.45
Daily Wage	Labor placing eucalyptus trees in the hole	4	480.00	36	4,363.64
Daily Wage	Sisal installation labor	4	480.00	36	4,363.64
Daily Wage	Labor for planting	4	480.00	36	4,363.64
Total labor costs			3,040.00		27,636.37

Un: units

The acquisition of seedlings of the four varieties of *H. lupulus*, as well as the inputs necessary for the correction and nutrition of the soil where the crop was planted, are detailed in Table 3.

Table 3. Investment in the acquisition of seedlings and supplies for an experimental area of 1,100 m² and 01 hectare (10,000 m²)

<u>Un</u>	<u>Item</u>	<u>Experimental Area</u> <u>(1.100 m²)</u>		<u>Estimated Area</u> <u>(10.000 m²)</u>	
		<u>Quantity</u>	<u>Valor (R\$)</u>	<u>Quantity</u>	<u>Value (R\$)</u>
Kg	Potassium chloride	1.00	18.73	25	458.95
Kg	Urea	4.40	118.80	108	2,911.76
Kg	Simple superphosphate	41.60	332.80	1020	8,156.86
Kg	Calcitic limestone	50.00	130.00	1225	3,186.27
Un	Shipping	1.00	30.00	25	735.29
Un	Hop seedlings	200.00	4,000.00	4902	98,039.22
Total spent on seedlings and supplies			4,630.33		113,488.35

Un: units; Kg: kilos

Chart 1. Comparison between the amount invested in the experimental area (1,100 m²) and the estimated investment required for 1 hectare (10,000 m²)

Total invested in the experimental area (1,100 m ²)	R\$ 20,866.08
Estimated total investment for 1 hectare (10,000 m ²)	R\$ 262,267.92

Table 4. Survey of the costs incurred over two years to conduct a hop cultivation experiment in an area of 1,100 m² and estimate of the costs for growing hops in an area of 1 hectare (10,000 m²), based on the experimental cost. These costs include inputs, labor, fertilization, and soil correction, among other essential elements for the maintenance and success of hop cultivation.

<u>Classification</u>	<u>Item (02 years of cultivation)</u>	<u>Experiment</u> <u>Cost</u>	<u>Estimated cost</u> <u>01 hectare</u>
Equipment	Pruning shears	88.00	800.00
Equipment	Drip tube	148.00	1,345.45
Soil correction	Soil analysis	320.00	3,200.00
Inputs (Materials)	Fertilization (Urea, simple superphosphate and potassium chloride) and	1,453.63	13,211.72
Inputs (Materials)	Ant control	500.00	4,545.46
Inputs (Materials)	Satin ribbon for identification	57.00	518.18
Inputs (Materials)	Sisal thread 155/1 roll 9kg	720.00	6,545.45
Inputs (Materials)	Replacement of seedlings	367.50	3,345.45
Inputs (Materials)	Crop identification plate	50.00	50.00
Labor	Labor maintenance	9,600.00	65,297.46
Total		13,216.13	98,059.17

4. DISCUSSION

This study is a pioneer in the northwest region of the state of Paraná; no other study on cultivation was found in the region. It is worth noting that, although modest, there are already some planting initiatives in the state. Carrying out a good investment

and cost analysis aims to compare the values needed to implement and fund a culture (SEBRAE, 2023).

In Table 1 it is possible to observe that a relevant part of the expenses with the assembly of the experiment occurred with the acquisition of the drip system (4,050.00), which is estimated for 01 ha generates a substantial amount (38,000.00), or a considerable investment was with the eucalyptus stands, either with stakes or posts (R\$3,000.00), which can also be observed in the investment estimate in structure for 01 ha. (R\$ 27,272.73).

As for labor (Table 2), the largest outlay was for specialized labor (R\$ 1,600.00) for the experimental area and R\$ 14,545.45 for the 10,000 m² area, since drilling the holes in the ground, drilling the stakes, and tying the wires it was necessary to hire a professional with prior knowledge in fence construction. It is worth noting that it is increasingly difficult to find labor in the countryside, given that mass migration to large centers has emptied a significant part of the human resources in rural areas (EMBRAPA, 2024).

Still regarding labor (Table 2), daily wages were contracted for the installation of sisal, to assist in the placement of eucalyptus posts and for planting. In the experiment, it was necessary to pay 12 daily wages. However, for the investment required in 01 ha, it is relevant to identify whether the property already has available labor or whether it will mechanize part of the work. With the reduction of labor in the field, the use of technological mechanization has been driven by a need for people with greater qualifications to operate such technologies (CNA, 2018)

An important part of the amount invested in hop cultivation was the acquisition of seedlings, while for the experimental area R\$ 4,000.00 was spent on 200 hop seedlings, an estimated outlay of R\$ 98,039.22 on 4,902 seedlings for 01 ha (Table 3). Of the inputs used in planting, simple superphosphate and calcitic limestone account for a significant portion of the outlay, but only account for 2.7% of the total amount invested. The average cost of purchasing hop seedlings is relatively high, justified by the added value of the propagation technique, which is more expensive than other crops such as peaches and apples. With the popularization of hop cultivation in Brazil, the tendency is for the cost of purchasing seedlings to decrease (FAGHERAZZI *et al.*, 2018).

In Table 1 it is possible to compare the total amount spent on the experimental area with the estimated amount for 01 ha, while R\$ 16,944.08 was spent on the

experiment, it is estimated that for each ha of planting it will be necessary to disburse approximately R\$ 262,267.92. It is worth noting that the larger the planting area, the lower the costs incurred with the structure. Thus, as Porter (1980) said, the larger the purchase, the greater the customer's bargaining power to reduce the outlays used in the investment.

The analysis of Table 4, which details the costs of a hop cultivation experiment in an area of 1,100 m² and projects these costs for a larger area of 1 hectare, is essential to assess the financial and operational viability of this crop.

In Table 4, costs over two years total R\$13,216.13, with a greater concentration on labor and material inputs. The monthly labor, responsible for maintenance activities, appears regularly, being the main cost component. This suggests that hop cultivation requires high manual labor intensity, which is feasible on smaller farms but can become challenging when scaling up the operation (EMBRAPA, 2022). The dependence on labor is linked to the constant maintenance of the crop, reflected in fixed monthly expenses of R\$400.00, which represents a significant portion of the total cost.

Material inputs, such as fertilization, ant control, and seedling replacement, are also important costs. Regular fertilization is vital for soil health and productivity, using inputs such as urea, simple superphosphate, and potassium chloride (NOBILE, 2024). Ant control is a recurring expense, highlighting the impact of pests on crop success. These variable costs show the importance of careful management to ensure financial sustainability.

The cost projection for an area of 1 hectare totals R\$98,059.17 over two years, as per Table 4. The substantial increase in costs, mainly in labor, reflects the difficulty of expanding cultivation without a proportional increase in operating expenses. Labor remains the largest cost factor, with each month of maintenance estimated at R\$2,839.02, a significant increase compared to the smaller area. The regional minimum wage for rural workers in Paraná in 2024 is R\$1,856.94, and, adding social charges and benefits, the monthly cost of a rural employee in Paraná can be estimated at around R\$2,839.02 (MTE, 2024). This data indicates that mechanization or automation could be a solution to reduce labor costs and improve economic viability in larger areas, considering that, in the 1-hectare estimate, the need for only 1 employee was predicted.

The costs of inputs, such as fertilization and pest control, increase proportionally. A adubação contínua, essencial para o bom desenvolvimento da cultura, eleva os custos,

principalmente pela necessidade de grandes quantidades de fertilizantes. Ant control remains an economic challenge, reflecting the difficulty of managing pests effectively.

The projection of equipment costs is also relevant. In Table 4, equipment costs are low, with items such as pruning shears and a basic irrigation system that required replacement. In the projection for 1 hectare, these costs increase significantly with the inclusion of drip tubes and more sisal to support the crop. These infrastructure investments are crucial to optimizing cultivation but require significant upfront capital.

Thus, the analysis of Table 4 shows that hop cultivation faces challenges to be expanded, due to the high dependence on labor and inputs. To ensure financial sustainability and viability in larger areas, it would be necessary to seek solutions that reduce the intensity of manual work, such as process automation, in addition to implementing more efficient strategies for managing pests and inputs.

5. CONCLUSION

Based on the results obtained in the experiment that was conducted in an experimental area of 1,100 m², the study aimed to evaluate the initial investment and maintenance costs for hop cultivation in the Caiuá Sandstone region, Northwest of Paraná. Thus, this work had the general objective of evaluating the initial investment and costs for maintaining hop cultivation in the Caiuá Sandstone region in the Northwest of the State of Paraná.

The results show that, although the initial implementation costs are relatively high, especially with the acquisition of seedlings and the construction of the support structure, there is potential for financial return in the medium and long term. In the experiment, the total amount spent was R\$20,866.08, and for the projection of 1 hectare, the estimated cost was R\$262,267.92, demonstrating the viability of expanding the crop. However, skilled labor and regular maintenance are relevant factors in the budget, highlighting the need to optimize these processes to increase profitability.

Furthermore, the data suggests that, with technical development and incentives for hop production on a local scale, it is possible to reduce dependence on imports, strengthening both the regional and national economies. Therefore, hop cultivation in the region may present itself as a promising alternative for agricultural diversification and income generation, especially if mechanization practices are adopted that reduce operational costs. It is recommended that further studies be carried out to reveal the

economic and market viability, given that hop production intensifies from the fourth year of planting.

6. CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this research.

7. ACKNOWLEDGMENTS

The authors would like to thank Universidade Paranaense (UNIPAR), the Postgraduate Support Program for Private Institutions (PROSUP), the State University of Maringá UEM Campus Umuarama, the Araucária Foundation, the Coordination for the Improvement of Higher Education Personnel (CAPES) – Finance Code 001 and the National Council for Scientific and Technological Development (CNPQ) – Finance Code 310105/2021-8.

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