

PREPARATION AND DESIGN OF THE PROCESS FOR THE PRODUCTION OF A HEALING CREAM FROM THE EXTRACT OF CROTON ELEGANS KUNTH LEAVES

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Abstract.

Ecuador being a megadiverse country, has plant species with uses in ancestral medicine, is the case of the plant *Croton elegans kunth* or its common name known as Mosquera that currently there is not enough information about its uses, however there is a study where they test their healing activity, giving good results in tests with mice, Thus, this study shows a process of obtaining ethanolic extract from the leaves of the Mosquera plant for use in the development of a healing cream and shows the study of the feasibility of business for its industrial production. The tests show that the extract of fly fruit leaves (*Croton elegans kunth*) contains phenolic compounds with important biological activity that can help the processes of skin healing, the most stable cream with better characteristics was the one containing 2.5% of leaf extract of the plant, with a pH value of 4.2, a density of 0.9607 g/mL and an extensibility of 3176.54 mm², and microbiological analyses of the extract and cream show results free of pathogenic microorganisms that can harm health. In addition, the product complies with the specifications of cosmetic regulations of the USA, Mexico and Ecuador. When performing the financial analysis, it shows that an investment of \$ 22,423.24 US dollars in the construction and start-up of a healing cream production plant is recovered in approximately 2 years, which indicates a business feasibility.

Key words: Healing cream, Extract, Maceration, Extraction, Mosquera leaves (*Croton elegans kunth*).

1 Introduction.

The tropical and Andean regions are considered to be of high diversity, a source of endemic plant species [1]. Ecuador is a South American country with great wealth of animal and plant species, its geographical location helps its development [2][3] and is considered among the 17 megadiverse countries, contains approximately 10% of plant species around the world with various applications with special medicinal and therapeutic interest[4][5].

According to studies, the indigenous people use 11 medicinal species of the genus Euphorbiaceae mainly in the South of Ecuador (province of Loja) with a development since the beginning of the colonial period where the *Croton* species is included [6][7]. It is known that the species *Croton mentodorum* is used in traditional Ecuadorian medicine where indications of inflammatory and antioxidant activity have been found [8]. There are also data on *Croton* species used in folk

medicine as healing, anti-inflammatory, anti-cancer, against gastric problems, to treat hemorrhoids and as agents to control uterine bleeding [9] [10]. In this species in addition to producing terpene compounds, mainly diterpenes, triterpenes and volatile isoprenoids that form essential oils, alkaloids are or other metabolites found to be of biological importance [11], [10]

This study has given importance to the plant *Croton elegans kunth*, which was discovered by Carol Sigsimund Kunth, was first published in 1817 in volume II in the book *Nova Genera et Species Plantarum*, has its heterotypic synonym *Croton ferrugineus Kunth* [12]. Research on this species is scarce, it is known that it is an endemic species of Ecuador, belongs to the Euphorbiaceae family and its common name is "Mosquera". In the morphological characterization it is considered as a shrub that reaches a size of up to 1.2 m in height and grows in the dry interandine region at an altitude between 1500 and 3500 m a.s.l., in Ecuador it is used in traditional medicine as an anti-inflammatory for toothache, wounds, warts and sore throat [13].

In 2019, a trial was carried out at the Polytechnic School of Chimborazo (ESPOCH)-Ecuador on the evaluation of healing activity in mice (*Mus musculus*) using Mosquera plant, in which they obtain an ethanolic extract at 80% of *Croton elegans kunth* and when performing The phytochemical screening shows the presence of secondary metabolites of pharmacological interest such as flavonoids (quercetin) and phenolic compounds such as is chlorogenic acid, which are metabolites related to anti-inflammatory and healing activity, when using this extract in mice, they obtain encouraging results in healing processes [14].

With this background, in the present research the ethanolic extract is obtained as the basis for the elaboration of a cream with healing function of the *Croton elegans kunth* plant, which requires a complex process in the laboratory, and its production process is designed.

2 Materials and methods.

Collection of plant material and extract

The plant material was taken based on its information in traditional medicine in May 2019, it collected 1 kg of *Croton elegans kunth* leaves from the Cusubamba area located in the Cayambe region -Ecuador. The material obtained was transported in plastic bags for analysis on a laboratory scale. In the laboratory, the best specimens under observation were selected, and impurities were removed from the sample by discarding the leaves that are in poor condition, then washed three times in distilled water to remove all soil residues and possible residues from other plants. A part was used for the physicochemical characterization of the raw material [15]. The remaining material was subjected to an oven drying at 40 °C for 6 hours until a constant weight of the samples was obtained, and the sheets were pulverized. For the maceration process, the sample was subjected to 96% ethyl alcohol for 48 hours, at this time the preparation was shaken 3 times a day using a magnetic stirrer, finally it was subjected to ultrasound for 1 hour and then filter the sample and obtain a liquid macerate. For the extraction of the liquid in the rotary vapor, ethyl alcohol was used as a solvent.

To obtain the best extract, 4 trials were carried out using 17 grams of pulverized leaves with different concentrations of alcohol in relation 1:6 1:8 1:10 and 1:12, of each experiment 3 repetitions were performed noting the value of pH [16], density, temperature and extraction time.

Laboratory scale cream production

It brought to melting the solid compounds (lanolin, cetyl alcohol, stearic acid and solid paraffin) using a water bath, then heated propylene glycol, castor oil (*Ricinus communis*) and glycerin. And for the aqueous phase distilled water was used at 80°C. With the prepared materials, we proceeded to shake and mix the oil phase (lanolin, cetyl alcohol, stearic acid, solid paraffin, propylene glycol, castor oil and glycerin) with the aqueous phase (distilled water), and at the end Dehyquart, the extract of leaves, preservative and perfume was added. The cream obtained was packaged in plastic containers at 67 °C to prevent the proliferation of microorganisms, and stored in a cool place.

3 Results and discussion.

Characterization of the raw material (*Croton elegans kunth leaves*)

The moisture content, total ash, water-soluble ash and hydrochloric acid-insoluble ash of *Croton elegans kunth* leaves was evaluated and compared with the specifications of the FEUM (Pharmacopoeia of the United Mexican States) and Project A1 of the Ecuadorian Standard (Mandatory) "Phytotherapeutics: Raw Drug. Test methods", described in Table 1, and all results are within the above specifications.

Table 1. Characterization of (leaves of *Croton elegans kunth*)

PARAMETERS	RESULT (%)	SPECIFICATIONS ACCORDING TO THE FEUM
Humidity on a wet basis	65,56	-
Dry-based moisture	6,219	6 – 14 %
Total ash	9,304	Up to 12%
Water-soluble ash	5,669	Up to 7%
HCl-insoluble ash	4,692	Up to 5%

Obtaining the leaf extract on a laboratory scale

Four tests were performed at different concentrations of alcohol, and the maceration process of the sample was obtained the maximum amount of 204 mL with 17g of sample at a ratio of 1:12 with 96% alcohol as shown in Table 2.

Table 2. Results of the maceration obtained at different concentrations of 96% alcohol

Weight (g)	Ratio of the macerated obtained (mL)			
	1:6	1:8	1:10	1:12
16	96	128	160	192
17	102	136	170	204

For the filtering process, the macerated material was passed through sterile gauze and filter paper, thereby reducing the amount of material to a maximum of 170 mL as shown in Table 3.

Table 3. Results of the filtering process obtained date different concentrations of 96% alcohol

Weight (g)	Obtained filtering (mL)			
	1:6	1:8	1:10	1:12
16	59	84	125	158

17	65	92	135	170
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Finally, a concentration process was carried out where a rotary evaporator was used at 40 ° C to partially remove the solvent (ethyl alcohol) from the extract [17], and a maximum volume of 83 mL was obtained as shown in Table 4.

Table 4. Results of the concentration process obtained date different concentrations of 96% alcohol

Weight (g)	Concentration obtained (mL)			
	1:6	1:8	1:10	1:12
16	25	75	50	58
17	31	83	60	66

At the end of the process, the extraction time, the largest amount of concentrate obtained, and the amount of alcohol used were evaluated optimizing resources, so the amount of 75 mL and 83 mL was considered at a ratio of 1:8 of alcohol to continue with the process.

Once the concentrate was defined, the organoleptic characterization shown in Table 5 was carried out, obtaining a dark green liquid appearance and an herbal odor characteristic of plant extracts.

Table 5. Organoleptic analysis of extract (Croton elegans kunth)

Parameter	Feature
Aspect	Liquid
Color	Dark Olive Green
Smell	Herbal (characteristic of Mosquera)

The determination of physical parameters of the leaf extract was performed, obtaining a pH of 5.89 which will not generate skin irritation, being within the range of 4.5 to 6.5 shown in table 6 [18]

Table 6. Physical Diameters of Croton elegans Kunth Leaf Extract

Parameter	Results	FEUM Specifications
<i>pH</i>	5.89	4.5 – 6.3
<i>Density</i>	0.8212 g/mL	0.8092 – 1.0627 (g/mL)
<i>Refractive index</i>	1.368	-
<i>Total solids</i>	6.39 %	6.37 – 16.8 (%)

It was considered important to perform the microbiological analysis of the leaf extract to ensure that there is no contamination with pathogens that may affect the obtaining of the cream, the results are shown in table 7, the same that were compared with the specifications of the Herbalist Pharmacopoeia of the United Mexican States 2nd edition 2013 (FHEUM) finding less than 60 CFU / mL of total aerobic and less than 10 CFU / mL of other microorganisms, This indicates that the extract is safe for use on the skin and is within acceptable ranges.

Table 7. Microbiological analysis of Croton elegans kunth leaf extract

Parameter	Results (UFC/mL)	Specifications according to the fheum
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Total Coliform Count	<10	10
Mold Count	<10	10 ³
Yeast Count	<10	10 ³
Total Aerobes Count	60	10 ⁵

When positive results were achieved in the ethanolic extract of *Croton elegans kunth* leaves, phytochemical screening was performed using the Shinoda method, finding the presence of flavonoids and anthocyanins as shown in Table 8.

Table 8. Phytochemical screening analysis of *Croton elegans kunth* extract

Secondary metabolites	Practice	Results
Flavonoids	Shinoda	Color change (+)
Group of flavonoids – anthocyanins	Anthocyanins	(+) of the phases

(+) presence.

According to [19], the wound healing process can be improved by using some plant species, this is due to the antioxidant, antimicrobial and/or bioestimulant properties of plants. Among these properties, there is evidence of the positive effect of polyphenols on tissue regeneration in some plant species [20], so the quantification of phenolic compounds in the hydroalcoholic extract of leaves of Mosquera grass (*Croton elegans kunth*) was carried out.) using the method of Folin-ciocalteau, gallic acid was used as a standard, and the determination of phenolic compounds was performed by ultraviolet spectroscopy. The content of phenols with respect to gallic acid was 2.0700 µg with an absorbance of 0.059. In the test where tannic acid was used as a standard, it indicates a total concentration of phenols with respect to tannic acid of 24.3600 µg with an absorbance of 0.152. In addition, an analysis of the infrared spectrum was performed showing bands of 3320.82 1382.71 cm^{-1} (0.05 Abs) and 1324.86 to confirm the presence of phenolic compounds in the sample and cm^{-1} therefore their healing action as shown in Table 9 and Figure 1.

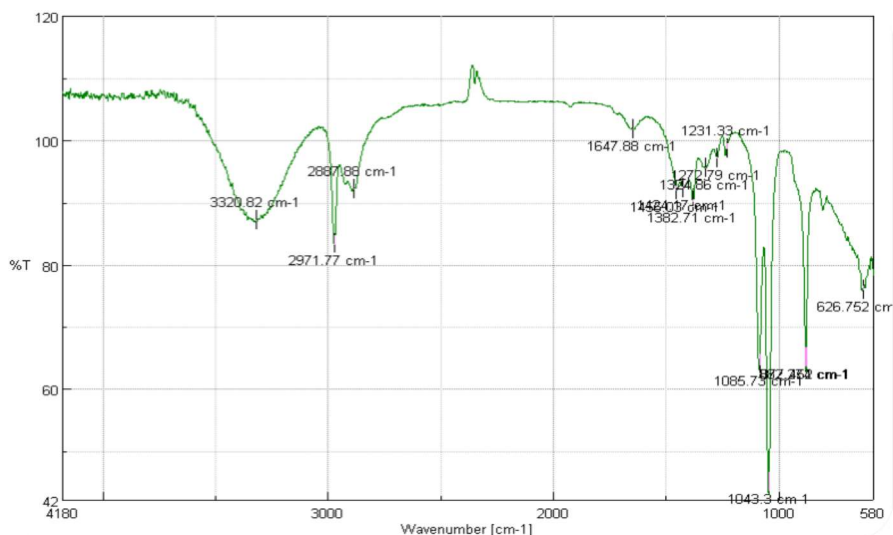




Figure 1. Infrared spectrum of *Croton elegans kunth* leaves extract.

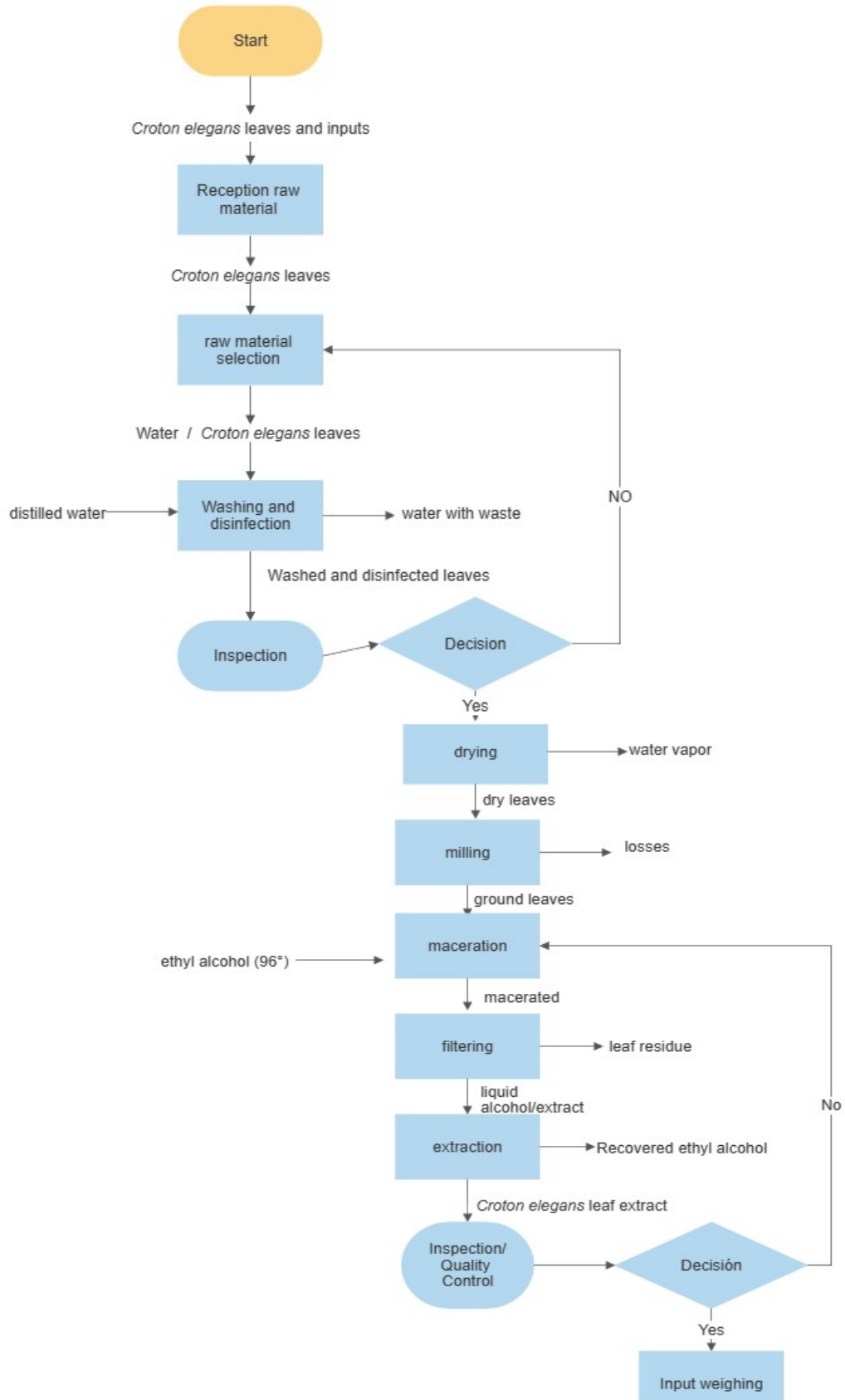
Table 9. Results of functional groups according to the infrared spectrum of Croton elegans kunth extract

Wavenumber [cm-1]	%T	Functional group
3320.82	87.1022	
2971.77	83.4617	-CH3, -CH2
2887.88	92.1505	
1647.88	101.725	C=N, C=C
1455.03	91.9418	CH2, NO2
1424.17	92.3446	CH3
1382.71	90.216*	
1324.86	95.5539*	
1272.79	97.1555	AR-O
1231.33	98.7249	C-O-C
1085.73	63.879	C-OH
1043.3	44.9336	

*Abs 0.05

Laboratory scale cream formulation

Figure 2 shows the flow diagram applied for the cream production process where a formulation of lanolin, cetyl alcohol, stearic acid, paraffin, glycerin, propylene glycol, distilled water, Dehyquart was used, and 3 formulas were made with different percentages of extract (2.5%, 5% and 10%). [21]; [18].



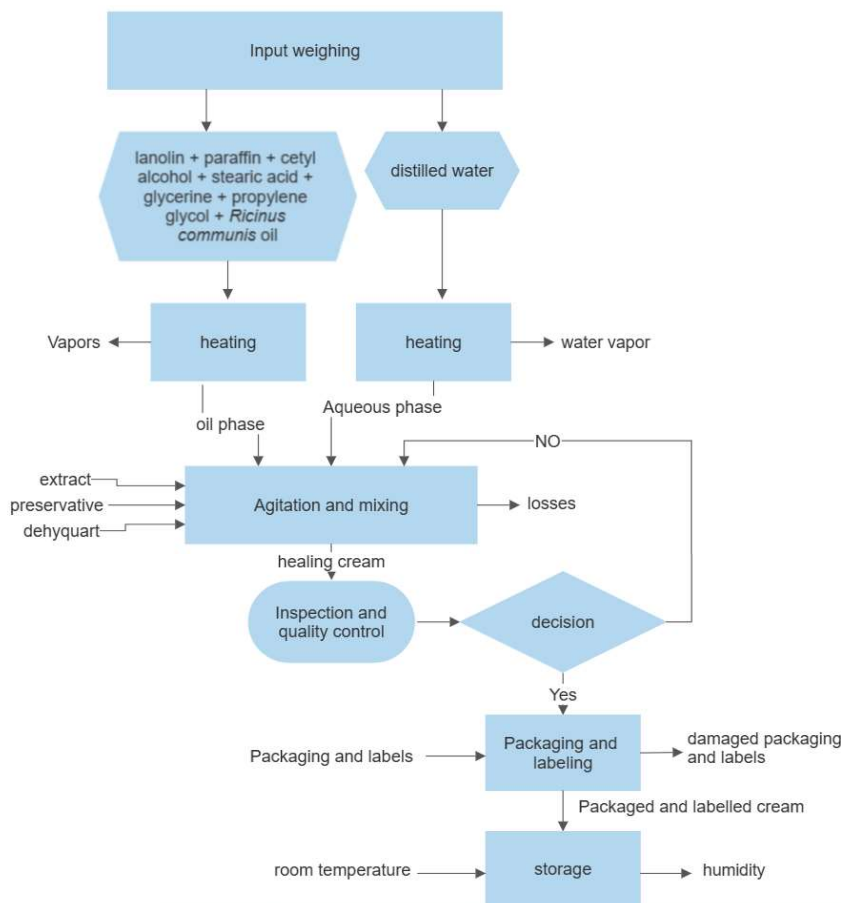


Figure 2. Process flowchart for obtaining cream from *Croton elegans kunth* leaves

Of the 3 trials performed, those formulated with 5% and 10% extract were discarded as there was no correct homogenization and the range between the maximum and minimum limits for the use of natural extracts in cosmetic creams is 0.50% to 4% [18]. Therefore, the assay containing 2.5% extractor for cream production was chosen.

Physical-chemical and microbiological characterization of the cream obtained from the extract of *Croton elegans kunth* leaves

For the characterization of the cream obtained, organoleptic tests were shown in Table 10 according to the Standard of Cosmetic Products of Ecuador. NTE requirements [22], which highlights a light green coloration, with a semi-solid consistency typical of a cream, and a pleasant herbal smell[23].

Table 10. Organoleptic analysis of the cream of Mosquera *Croton elegans kunth*

PARAMETER	RESULT
Aspect	Semisolid
Color	Light green
Smell	Herbal

As for the physicochemical characteristics of the cream obtained, they are shown in Table 1 1 where it is distinguished that the cream has a pH of 4 that is considered acidic and a filling temperature greater than 65 ° C was used to avoid possible contamination, according to [24] cream corporal must have a pH between 4, 3 to 6 to be considered safe for use and not cause skin irritation.

Table 1 1. Physicochemical analysis of the cream of Mosquera *Croton elegans kunth*

PARAMETER	RESULTS	SPECIFICATIONS INEN 2867:2015
pH	4,3	3
Density	0.9670 g/mL	-
Extensibility	3176,54 mm ²	-
Filling temperature	67 °C	≥ 65,0 °C

For microbiological analysis, it is important to determine if there is presence of microorganisms that can damage the product, for example, it can cause its separation, shrinkage of the product and influence its weight and the development of unpleasant odors[25]. Damage to the product can be caused by bacteria, yeast, or fungi [26]. The characteristics of microorganisms that have a high adaptability to the environment cause several natural organic components to be easily damaged or degraded, causing possible damage to the health of those who use it. In the results obtained, no pathogenic microorganisms were found, being a safe product for use, and it is within the parameters established according to the Cosmetic Products Standard of Ecuador. Requirements NTE INEN 2867:2015, the detail of the results is shown in table 12.

Table 12. Microbiological analysis of the cream of Mosquera *Croton elegans kunth*

PARAMETER	RESULTS (UFC/mL)	SPECIFICATIONS ACCORDING TO INEN 2867:2015
Total aerobic count	<10	Maximum 5x10 ³ CFU/g
Detection of <i>Pseudomonas aeruginosa</i>	Absence	Absence
Detection of <i>Staphylococcus aureus</i>	Absence	Absence
Detection of <i>Escherichia coli</i>	Absence	Absence

Distribution of the processing plant for obtaining cream of Mosquera *Croton elegans kunth*

The equipment was distributed according to the unit operations necessary to produce cream on an industrial scale as shown in figure 3. To produce cream, it starts with a sample of 3 kg of flytrap leaves, 22 l of alcohol and 34 kg of ingredients mentioned in section of cream mulation at laboratory scale, which will produce 50 l of cream per day. The equipment to be used will be : selection table, washing tank, maceration tank, mixing tank, aqueous phase tank, oil phase tank, agitation system and alcohol storage tank on an industrial scale, and it is recommended that the material of the equipment be AISI 304 stainless steel because it is a cosmetic according to the Cosmetic Products Standard. Requirements NTE INEN 2867:2015.

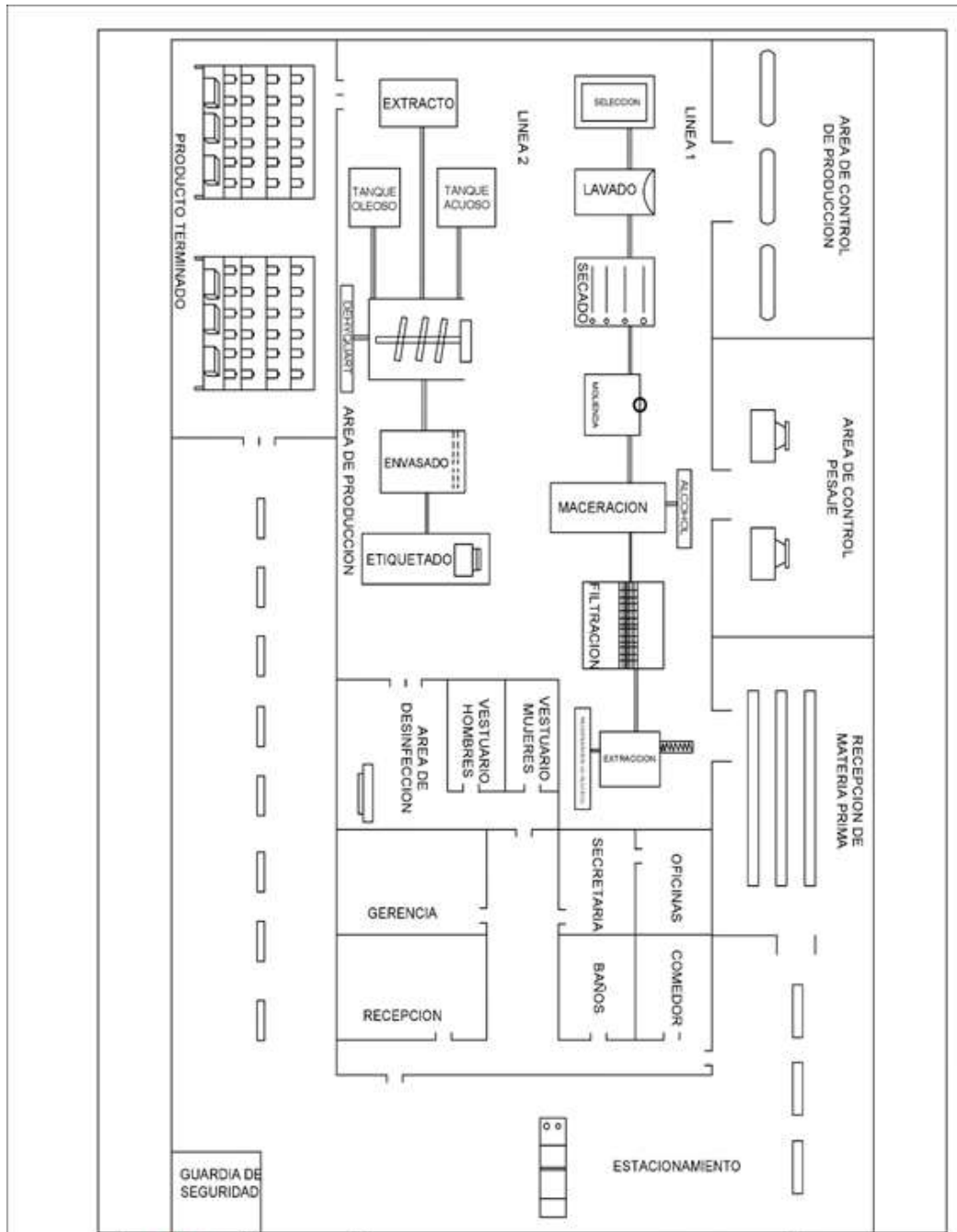


Figure 2. Distribution of the processing plant of Mosquera scar cream *Croton elegans kunth*
Budget and Project Viability

The most important financial indicators were calculated: IRR (Internal Rate of Return) 50% and NPV (Net Present Value) \$ 22,423.24, as shown in table 1 3, so it is determined that the project is economically viable, the cost / benefit ratio will be \$ 0.87 cents for each US dollar invested and the recovery period of everything invested will be approximately 1 year 10 months and 9 days. In addition, it was determined that the retail price of the cream will be \$ 2.00 US dollars per 50 mL of cream and a production of 1000 units per day is projected.

Table 14. Cash Flow

Values	YEARS					
	0	1	2	3	4	5
+ Net sales		480000	495092,8	502816,2	510660,1	518626,4
- Production costs		398723,6	398737,2	398744,0	398750,7	398757,5
- Administrative costs		7	3	1	9	6
- Profit sharing (15%)		32888,16	32889,28	32889,84	32890,4	32890,96
- Financial costs		700	700,024	700,036	700,048	700,06
Profits before distributing profits and taxes		100	100	100	100	100
= Profit sharing (15%)		47588,17	62666,28	70382,38	78218,96	86177,91
- Profit sharing (15%)		7138,23	9399,94	10557,36	11732,84	12926,69
= Pre-tax earnings		40449,94	53266,34	59825,02	66486,11	73251,23
- Income tax		0	0	32,36	113,62	593,71
= Net Income		40449,94	53266,34	59792,66	66372,49	72657,52
- Investment in machines and equipment		-	219756,9			
- Furniture and fixtures			7			
- Investment in a land and physical construction			-690			
- Vehicle			-70000			
- Incidentals			-30000			
- Partner Capital/Loan			13000			
			20000			
+ Cash flow		-	335035,1	53266,34	59792,66	66372,49
		287446,9	4			72657,52
		7				
Market Rate of Return		10,5%				
FROM SHOOTING		(\$22.423,24)				
		50%				
					Payback: 1,85796	Years the investment is recovered

4 Conclusions.

The extract of flycatchers (*Croton elegans kunth*) contains phenolic compounds with important biological activity that can help the processes of skin healing and serves as an input for the manufacture of a cream. 2.5% is the ideal concentration of extract for the manufacture of cream with good physicochemical characteristics with a pH value of 4.2, a density of 0.9607 g/mL and an extensibility of 3176.54 mm². Microbiological analyses show that the cream is free of pathogenic microorganisms that can harm health and complies with the specifications of cosmetic regulations used. When performing the financial analysis, it shows that an investment of \$ 22,423.24 US dollars in the construction and commissioning of a healing cream production plant is recovered in approximately 2 years, which indicates a business feasibility.

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