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Potential Use of Mango Leaves Extracts Obtained by High Pressure Technologies in Cosmetic, Pharmaceutics and Food Industries

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The greater consciousness awakened in recent years on healthy and organic has led to increase “natural” products demand worldwide. The quality and high content on bioactive compounds have consolidated their penetration in cosmetic and food market, showing great potential within the pharmaceutical sector too. For this reason, food, cosmetic and pharmaceutical sectors have been forced to develop natural products manufactured by efficient and environmentally clean process. Mango leaves extract have showed potential use in food and cosmetic, and pharmaceutical industries due to its high content in potent antioxidant phenolic compounds. The aim of this work was analyse the valorization of pruning mango residues into valuable chemical products by high pressure extraction techniques. An economic feasibility study was realized including industrial scale up, manufacturing costs and financial study, showing the viability of mango leaves extraction by high pressure technologies at industrial scale and the applications of extracts in food, pharmaceutical and cosmetic industries.

1. Introduction

In recent years, pharmaceutical, cosmetic and food industries have shown a growing interest in the use of natural antioxidants (non-synthetic origin) obtained from sources like plants, microalgae and microorganism. Mango (*Mangifera indica L.*) leaves are a rich source of phenolic compounds with strong antioxidant power, particularly mangiferin, a special xanthone commonly called as “super-antioxidant” because of their potent antioxidant capacity, and other phenolic compounds like quercetin, widely studied by its pharmacological properties (Massibo et al., 2008),

Thanks to its “super-antioxidant properties”, mango leaves extract can be used as natural preservatives in food applications (Morsi et al., 2010) and as anti-aging compound in cosmetic products (Charrier et al., 2006). Also, mango leaves extracts present potential use in pharmaceutical applications as chemo-preventive agent of diseases relates with oxidative stress giving their numerous antioxidant and health-promoting properties scientifically demonstrated (Mohan et al., 2013).

The recovery of bioactive compounds from plants is frequently realized by conventional extractions methods. However, in the last decades, food, cosmetic and pharmaceutical industries have increased their safety requirements to protect the health of consumers and the environment, requiring more efficient and greener processes (Straccia et al., 2013). This work, evaluated a more effective an environmentally friendly extraction technique based on high pressure extraction techniques which present many advantages over conventional processes (Fernández-Ponce et al., 2012).

The present study shows important aspects related to the production of mango leaves extracts by high-pressure extraction techniques: global extraction yield, phenolic content and antioxidant activity of the extract. In addition, an economic feasibility study at industrial scale including scale up is realized. The cost of manufacturing (COM), demand of natural extracts and financial analysis, in order to know the viability of

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mango leaves extracts production by high pressure techniques with applications in food, cosmetic and pharmaceutics industries, is also analysed.

2. Demand of natural extracts

The market only for herbs for nutritional supplements, for example, green tea, blueberry, is about 6.7 Billion Euros in Europe and 17.5 Billion worldwide. The annual growth rates for nutraceuticals and pharmaceuticals derived by industrial products extraction is about 6 to 8 %. In 2002 the world market for pharmaceuticals from natural plants was estimated to be US$ 30.7 Billion and the market for only extracts from plants was to be US$ 2.0 Billion (Bart and Pilz, 2011).

The natural cosmetic segment shows a marked growth too. Market studies confirm the increasing trend for next years with 15 % over the only 5 % for the cosmetic products. In the United States it is estimated that demand of botanical extracts in cosmetics grows by 7% per year, reaching US$ 1.0 Billion in 2016.

In response to this demand, industrial sectors of food, nutraceutical, pharmaceutical and cosmetic have been forced to develop more natural products to replace synthetic chemicals considered harmful to health, and to implement green processes that do not pollute the environment.

3. Extraction of antioxidant compounds from mango leaves

3.1 Extraction techniques to obtain mango leaves extracts

Mango extracts are obtained at laboratory and industrial scale usually by traditional solvent extraction techniques. Cuba, for example, produces at industrial scale “Vimang”, an aqueous extract from mango steam bark whose mainly polyphenols is mangiferin (7 - 10 %) (Núñez Sellés et al., 2002) and its pharmacological properties such as anti-inflammatory and antioxidant activities have been demonstrated *in vitro* and *in vivo* (Wauthoz et al., 2007). Ling et al. (2009) obtained ethanolic extracts from mango leaves with 7 % of mangiferin and with antioxidant and anti-apoptotic activities. However, conventional extraction methods presents some drawbacks, among them low selectivity and/or low extraction yields, time consuming processes, use of large volumes of toxic organic solvents, and extended concentration steps that results possibly in loss or degradation of antioxidants (Fernández-Ponce et al., 2012).

High pressure extraction techniques, such as supercritical fluid extraction (SFE) and pressurized liquid extraction (PLE), have been used in recent years so result interesting alternatives to overcome the above mentioned drawbacks. These techniques uses green solvents such as carbon dioxide (CO_2), ethanol or water, allows the design of faster and more selective processes, reduces the use of organic solvents and concentration steps, and guarantees the conservation of the biological properties of phenolic compounds using mild operation conditions in absence of light and oxygen (Fernandez-Ponce et al., 2012). Table 1 shows performance of different high pressure extraction techniques used to obtain mango leaves extracts.

Table 1: High pressure extractions techniques used to obtain mango leaves extracts

Extraction method	Extraction conditions	Global Yield (%)	Mangiferin Content (%)	Authors
SC-CO_2	25 MPa, 45 ºC, 3.96 Kg/s, 1 h	1.0	--	Pereira and Miereles, 2005
SC-CO_2 + Ethanol	10 MPa, 55 ºC, 20 g/min, 3 h	4.2 – 8.7	1.9 - 7.25	Fernández-Ponce et al., 2012
SWE	4 MPa, 100 ºC, 10 g/min, 3 h	24 - 35	1.9-11.5	Fernández-Ponce et al., 2012

Pereira and Miereles (2007) studied the extraction from mango leaves using supercritical pure CO_2 (SC-CO_2) obtaining very low global yields, only 1.00 %. SC-CO_2 is a non-polar solvent, so the addition of polar-cosolvents is necessary to improve the extraction yields of phenolic compounds. Fernández-Ponce et al. (2012) showed the addition of ethanol as co-solvent improve global yield of the process between 4.2 - 8.2 %, however water extraction at 4 MPa, 100 ºC, 10 g/min, and 3 h resulted more efficient with global yields up to 35 %, similar to those obtained by conventional extraction techniques.

3.2 Characterization and of mango leaves extracts and applications at industrial scale

The antioxidant and pharmaceutical properties of aqueous and ethanolic extracts of this plant have been studied by different authors. Due to the high content in phenolic compounds, primarily mangiferin, mango by products, particularly leaves and bark, present anti-inflammatory, antioxidant, antibacterial, antidiabetic, immunomodulatory and analgesic properties (Mohan et al., 2013).

Mango leaves extracts can be also used in food applications as natural antioxidant additive replacing toxic synthetic antioxidants such as butylhydroxytoluene (BHT) (Morsi et al., 2010); and in cosmetic applications have showed anti-aging activity, and capacity to protect the skin against ultraviolet radiation and prevent or reduce the effects on the skin, lips and hair caused by heat stress (Charrier et al., 2006).

The high content on mangiferin of extracts obtained by supercritical carbon dioxide + ethanol extraction and SWE indicate the interesting applications of these extracts at industrial scale. In addition, according to Fernández-Ponce et al. (2012) subcritical water extracts have very potent antioxidant activity with AAI values of 7.92 ± 0.16 for Osteen variety, and up to 6.5 ± 0.01 for Kensington, Kent and Ataulfo varieties, showing superior activity than (+)-α-tocopherol (AAI = 3.65 ± 0.07) and similar to the pure phenolic compounds mangiferin and quercetin (AAI = 7.8 and 7.06 respectively).

These findings support the use of high pressure extraction techniques to obtain *M. indica* leaves extracts with high content on phenolic compounds and potent antioxidant properties showing their potential use in food, cosmetic, and pharmaceutical applications.

4. Scale up of high pressure extraction process

A design process requires the application of the results obtained on a laboratory scale to pilot plant and industrial scales. The scale up of extraction process required the application of similarity theory and dimensional analysis (Casas et al., 2009a). Some considerations are necessaries to change scale: the extractor is under isothermal conditions, chemical reaction does not take place, and similarity relationship corresponding to geometry and dynamics must be maintained. For this reason, is necessary to keep constant in each scale of operation the geometric factors and the dimensionless numbers related to the dynamic similarity.

Geometric factor consider constant geometric dimensions. The relationship shown in Eq(1) must be maintained:

$$\left(\frac{H}{d}\right)_{extractor1} = \left(\frac{H}{d}\right)_{extractor2} \quad (1)$$

Where H is the height and d the diameter of the vessel.

Dynamic similarity requires maintaining constant Reynolds number, Re on changing the process scale. This criterion is based on a combination of dimensional analysis and similarity, and one might reasonably expect to obtain similar flow patterns within the mixing volume provided that Re is the same for each scale of operation. Re values can be calculated from Eq(2):

$$\mathrm{Re}_{extractor\ 1} = \mathrm{Re}_{extractor\ 2} = \frac{\rho_d D_p v}{\mu_d} \quad (2)$$

Where ρ_d (g/mL) is the solvent density, μ_d (g/cm) the solvent viscosity, D_p (cm) the particle diameter and v (cm/min) is the average velocity of the solvent. Estimates of the average velocity can be calculated from Eq. (3):

$$v = Q_V / A \quad (3)$$

Where Q_v (cm^3/min) is the volumetric flow estimated as $Q_v=Q_m/\rho_d$ and A (cm^2) is the cross-sectional area of both extractors estimated as $A=\pi \cdot r^2$. Finally, the estimation of mass flow Q_m at industrial scale, keeping constant geometric and dynamic parameters, is necessary in order to ensure performance of process similar to laboratory scale. The scale up to a pilot plant with two extraction vessels of 5 L of capacity was realized for the best condition showed in previous studies with subcritical water at 4 MPa, 100 ºC, 10 g/min and 3 h. (Fernández-Ponce et al., 2012). Geometric dimensions are assumed as similar for both scales. The parameters for scale up are shown in Table 2.

Table 2: Characteristic parameters for the extraction process for dried samples

	Analytical Scale	Pilot Plant Scale
d (cm)	2.9	9.5
H (cm)	19	63
H/d	6.5	6.6
V (cm^3)	100	5000
Q_m (g/min)	10	86

5. Economic analysis of mango leaves extracts obtained by high pressure techniques

The high content on phenolic compounds and the very strong antioxidant activity of mango leaves extracts obtained by high pressure extraction techniques indicated they may be used in food, cosmetic and pharmaceutics applications. Increasingly, these industries require high quality, healthy and more natural products produced by methods that respect environment. High pressure extraction techniques complies these requirements so they use only green solvents and preserve natural properties of extracts. However, the choice of appropriate technique depends on the economic feasibility and suitability of processes too. Unfortunately, the elevate investment cost of this technology cause it would not be consider as an option in process design at industrial scale. The purpose of this section is to show, by the estimation of the cost of manufacturing (COM) and the economic analysis of the production of mango leaves extracts, high pressure extraction techniques are an interesting alternative to consider in the extraction process of antioxidants from mango leaves at industrial scale.

5.1 Investment cost for a high pressure extraction equipment

The basic requirements for high pressure extraction equipment are: a liquid CO_2 storage tank, a cooler to prevent CO_2 from evaporating in the pump, a pump for liquid CO_2, a heat exchanger to control the temperature of CO_2 entering the extractor, an extraction vessel, a heat exchanger to control the CO_2 plus solute mixture entering the separator, and a separation vessel. At laboratory scale condensing and recycling of CO_2 after separation is not needed but at industrial production level these are essential requirements. Besides, the use of at least two extraction vessels is necessary for a continuous process streamlining charging/discharging steps.

The investment cost of the equipment was estimated for a high pressure unit of 10 L of capacity as €200,000. The unit contains two extraction vessels of 5 L with a thermostatic jacket, two pumps with a maximum flow rate of 200 g/min, a back pressure valve regulator, tree cyclonic separators and a solvent recovery tank for CO_2. A schematic diagram of the equipment is shown in Figure 1.

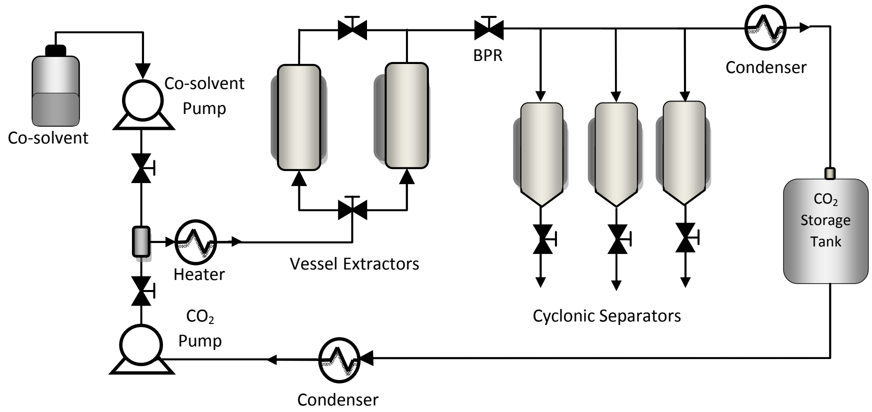

Figure 1: Schematic diagram of the high pressure equipment at pilot scale

5.2 Cost of manufacturing mango leaves extracts by high pressure extraction techniques

An accurate evaluation of production costs, including both capital and utility costs, must be performed before scaling up a process whose technical feasibility has been demonstrated at the laboratory level. The estimation of manufacturing cost (COM) can be realized using the expression proposed by Casas et al. (2009b) Eq (3):

$$COM = 0.304FCI + 2.73COL + 1.23(CUT + CWT + CRM) \quad (3)$$

Where FCI is the fraction of investment calculated as the product of the total investment and the depreciation rate, COL is the cost of operational labour, CUT is the cost of utilities, CWT is the cost of waste treatment, and CRM the cost of the raw material. At present, mango leaves are agricultural by-products without any value, but evaluation of CRM must include an estimation of the collection, transport and pre-treatment of raw material. CWT may be neglected so this technology does not produce solvent wastes to be treated and the solid reside, vegetable matrix, can be commercialized as a by-product. Table 3 shows the concepts used to estimate the COM by Eq (3).

Table 3: Manufacturing cost of mango leaves extracts at pilot scale

Concept	Description	Comments	€/y	€/h
Raw material	Mango leaves	Agricultural by-product	5,256	0.6
	SUBTOTAL		5,256	0.6
Labour	Labour cost	19,200 €/man y, 3 man/d	57,600	6.6
	Supervision	25 % of labour cost	14,400	1.6
	SUBTOTAL		72,000	8.2
Utility	Electricity	11.6 kWh 0.17 €/kWh	17,275	2.0
	Water	0.5 m^3/h, 1€/m^3	4,380	0.5
	SUBTOTAL		21,655	2.5
Investment fraction	Depreciation rate	10 %		
	Depreciation	10 y	2,000	0.2
	Tax-insurance	1.5 % of investment	3,000	0.3
	Maintenance	4 % of investment	8,000	0.9
	SUBTOTAL		13,000	1.5

The COM estimation according to Eq(3) was 24,71 €/h for a supercritical plant of 10 L. According to these data and considering an apparent density from mango leaves of 0.3 g/mL and extraction yield of 35 % the COM of subcritical mango leaves extract varied from 94.15 and 141.2 €/kg for semi-continuous extraction process using each vessel of 5 L between 2 and 3 h. This value was similar to COM estimated by Pereira and Meireles (2005) for SC-CO_2 mango leaves extracts, US$151.01/kg of extract for an extraction time of 2 h. The selling price at the market of conventional mango leaves extract is 80-280 €/Kg for extracts with mangiferin content between 40-80 %. Despite the low mangiferin content of subcritical mango leaves extract (around 12 %), the high antioxidant power of extract comparable with pure mangiferin allows to set a higher selling price even similar to high purity mango extracts with 95 % of mangiferin (400-500 €/Kg). In addition, optimization of the extraction conditions and estimation at industrial scale would cause an important decrease of COM and would improve the viability of the process.

5.3 Financial Analysis

The economic and financial analysis is also necessary for demonstrate the viability of the process at industrial scale. The financial analysis was realized estimating a sales volume between €150,000 and €500,000 for the first five years, also was consider an external funding for the acquisition of the high pressure technology. The financial projection gives the economic and financial ratios showed in Table 3.

Table 3: Economic and financial ratios at Pilot Scale

	1st y	2nd y	3rd y	4th y
Profitability Ratios				
Economic Profitability (ROI)	-53.44	41.44	60.99	50.85
Financial Ratios				
Solvency Ratio	0.84	1.12	2.03	3.74
Financial Independence	-0.19	0.11	0.51	0.73
Economic Ratios				
Profit Margin	-213.1	26.2	40.3	43.2

The analysis of the economic and financial ratios shows that the return on investment in the acquisition of this technology of extraction is high. In the fourth year can achieve a profit of 50 monetary units or higher for each unit invested. The solvency ratio also shows and adequate result with and increasing trend showing the assets are superior to borrowed funds. For this projection, the financial independence is very low the first year because of the borrowed fund considered for the investment. However, using owns

funding, the financial independence decrease and is possible improve the financial solvency. About economic ratios, the profit margin is negative the first year due to the low sales volume. Next years, the increases in sales volume improve the profits, but also an efficient administrative management is necessary to control the indirect cost of the process, such as commercial and administrative costs.
This financial and economic analysis of the process shows the viability of produce mango leaves extracts by high pressure techniques despite the investment cost of technology. The reasonable COM of the process allows a good profit margin; in addition, an efficient administrative and commercial management is also necessary to increase the sales, control the costs and improve the financial solvency and profitability.

6. Conclusions

High pressure extraction techniques using subcritical water as solvent system is an efficient alternative to extract antioxidant compounds from mango leaves. The quality of extracts with high content in mangiferin and other phenolic compounds and with potent antioxidant activity shows their potential applications in food, nutraceutical, pharmaceutical and cosmetic industries. In addition, the market of natural extracts with a growing demand, the COM estimation and the financial analysis indicate extraction from mango leaves by the above-mentioned technique is an economically viable alternative that meets market demand according to quality and low environmental impact processes.

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