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Challenges in research and development of phytomedicines in semisolid pharmaceutical forms

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The research and development of new drugs is a slow process that involves costs, requires physical, material and qualified human resources. The purpose of this study was to examine the research of recent years exposed on the challenges and obstacles to production and design of semisolid pharmaceutical forms from extracts or isolated compounds from medicinal plants. This study is an integrative review. The sample consisted of scientific articles found on the databases (Lilacs, Scielo, Science Direct and PubMed) from January 2002 to September 2012. The following descriptors were used: phytomedicines, stability of medicines and pharmaceutical preparations. The design of semisolid pharmaceutical forms, especially those in phytocosmetics, is relevant in Brazil, a major producer country by the pharmaceutical industry. However, due to the peculiarity of each drug and medicine, the study design may become one of the great difficulties of its accomplishment, as well as being a challenge to professionals in developing new pharmaceuticals. Thus, it can be suggested that despite the vast Brazilian biodiversity, there is no investment and cooperation in research and development of new medicines.

Key words: Phytomedicine, drug stability, pharmaceutical preparations.

INTRODUCTION

The use of products extracted from medicinal plants occurs since the dawn of civilization. From the late 19th century, natural products have been used on an industrial scale as a source of medicines. Despite advances, research on natural compounds for the pharmaceutical market is still restricted to academic institutions, government laboratories and/or small to medium businesses that produce herbal medicines. In this scenario, it highlights the production of semisolid pharmaceutical forms, mainly cosmetic, with Brazil being one of the major producing countries of that area (Seild, 2002).

From the physicochemical point of view, pharmaceutical forms may be liquid, solid or semisolid consistency. In general, the semisolid pharmaceutical compositions are complex formulations and sometimes constitute substances whose structure also has some degree of complexity. Often, they are composed of two phases (water and oil), one continuous-external phase and the other dispersed-internal phase. In most cases, the active substances are dissolved in one of the phases, although occasionally the drug is not completely soluble in the system being dispersed in one or both phases, thus...
originating a three-phase system (Prista and Alves, 2003).

The development of new formulations in the pharmaceutical and cosmetic market has been increasingly in recent years with emulsions being widely used for the incorporation of drugs and cosmetic actives, which emphasizes the use of semisolid pharmaceutical forms in the development of new therapeutic agents (Lange et al., 2009).

Research and development of new drugs is a long process that involves costs, requires physical structure, equipment and skilled manpower. Thus, due to the peculiarity of each drug and medicine, the study design can be one of the great difficulties in its implementation, and at the same time it is a challenge to professionals in the development of pharmaceutical products (Silva et al., 2009).

For Brazil being among the countries with the richest floras in the world, the search for medicinal plants and their inputs with applicability in dermal-formulations and other pharmaceutical forms is enabled (Pereira, 2008).

Therefore, this study aimed at analyzing the research of recent years that expose the challenges and obstacles to production and design of semisolid dosage forms from medicinal plants.

Development of phytocosmetics in Brazil

Currently, there is a trend of incorporating plant extracts in cosmetic formulations, in order to obtain formulas that can be used by a growing number of people looking for an effective alternative and less aggressive in the nature. This enhancement of plant caused increased demand for scientifically substantiated information about its safety and therapeutic efficacy (Cunha et al., 2009; Crespo, 2012).

On the world stage, numerous cosmetics industries seek innovation, making use of raw materials of diverse origins, mostly derived from plants, representing an alternative replacement of natural by synthetic materials. The incorporation of plant extracts on the bases for cosmetic purposes is a widespread practice, being of fundamental importance to the proper choice of the base to which the active ingredients of topical will be incorporated, thus ensuring the stability and absorption of the active ingredients and consequently, obtaining its pharmacodynamic effects expected (Sousa and Ferreira, 2010).

Other studies also mention the increasing use of natural products in the cosmetic industry, as the study by Fennar et al. (2006), which states that the plant extracts incorporated into cosmetic formulations, should be standardized, requiring rigorous study on the plant composition, or plants which comprise it, thus originating the phytocosmetics. According to Almeida and Bahia (2003), the plant extracts can be incorporated into various cosmetic preparations and depending on the chemical class of its active ingredients may be responsible for the product activity and may or may not change the cosmetic form and the rheological behavior of the preparation.

In Brazil, studies have been conducted on phytocosmetics in order to evaluate its stability and physicochemical properties. Thus, creams containing 5 to 10% glycolic extract of Isabel grape bagasse (Vitis labrusca L.) and gels containing 10% ground seeds were evaluated for 60 days, there being no physicochemical instability. An antiseptic formulation containing ethanol extract of Plinia cauliflora Mart. was also analyzed for stability showing satisfactory results in the physicochemical analysis (Oliveira et al., 2011; Sousa and Ferreira, 2010).

Phytocosmetics can be defined as a cosmetic containing natural active of plant origin, or an extract, fatty acid, essential oil, whose action defines the pharmacological activity of the product (Isaac et al., 2008).

The emulsions represent historically the oldest form of cosmetic application, being the first one cream that one created by Galeno for facial application (Isaac, 2009). Emulsion is a system consisting of two immiscible liquids, containing one aqueous or hydrophilic part and another oily or lipophilic, where one of the parts is dispersed in another as droplets, becoming homogeneous by the addition of surface-active substances which emulsify the system (Cefali, 2009).

A phytocosmetic must pass all stages of research as the proposition, the creation and development, including stability tests to ensure the activity throughout its lifetime. Stability is a parameter of validation needed to ensure the quality of phytocosmetic, although rarely described in standards validation of analytical methodology (Isaac et al., 2008).

Stability is defined as the time during which the medicinal product or the raw material considered individually maintain, within the specified limits and throughout the period of storage, and use the same conditions and features as when it was manufactured. The stability of pharmaceuticals depends on environmental factors such as temperature, humidity, light and other factors related to the product itself as physical and chemical properties of active substances and pharmaceutical excipients, pharmaceutical form and its composition, manufacturing process, type and properties of packaging materials (Brasil, 2005).

During the development of new cosmetic formulations, the stability testing should be performed. The study of stability helps to guide the development of the formulation and packaging material; provide input for improvement of formulations; estimate the validity and provide information for its confirmation; assist in monitoring the organoleptic, physicochemical and microbiological stability, producing information on the reliability and safety of products. Note that the stability tests involve preliminary stability testing, which aims at assisting and guiding the choice of accelerated stability testing formulation, which provides
Table 1. Representation of integrative review on databases from the search of the following keywords: phytomedications, drug stability and pharmaceutical preparations.

<table>
<thead>
<tr>
<th>Database</th>
<th>Keywords</th>
<th>Articles</th>
<th>Theses/Dissertation</th>
<th>Abstracts</th>
<th>Book</th>
<th>Repeated</th>
<th>Publications used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lilacs</td>
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<td>7</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Drug stability</td>
<td>206</td>
<td>44</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Pharmaceutical preparations</td>
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<td>754</td>
<td>94</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
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<td>Phytomedicine</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<td></td>
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<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

The present study was designed as an integrative review, which is a method to gather and organize search results on a particular topic or issue, in a systematic and orderly manner, contributing to the deepening of the research theme (Roman and Friedlander, 1998). This study has established the following guiding question: "What are the challenges for design and production of semisolid pharmaceutical forms from medicinal plants?"

The sample consisted of scientific articles found in databases (Lilacs, SciELO, Science Direct and PubMed) from January 2002 to September 2012. The descriptors phytomedications, drug stability and pharmaceutical preparations were used in English and Portuguese.

The selection of articles was made by reading their abstracts and selecting those related to the research topic. As inclusion criteria, articles available in full and for free on selected databases in English, Portuguese and Spanish were used. Dissertations, theses, abstracts in conference proceedings and/or books, as well as the repeated articles were excluded from the sample. For analysis of the articles was reading the abstracts and selecting those who reported the design of phytomedicines in semisolid forms, emphasizing the stages of development of phytomedicines.

RESULTS AND DISCUSSION

The study sample composed of 15 articles, most from Lilacs database, as shown in Table 1. On the database (Science Direct), after searching with keywords phytomedications, drug stability and pharmaceutical preparations, 31 articles were found, but these articles were not related to the theme proposed in this study. On the LILACS database, among 1318 articles found, only 12 were related to the theme. On another database searched, SciELO, only one article related to the topic was found but excluded for having been found in other databases. Finally, the research on Pubmed, showed 41146 articles with three items being related to the research problem.

Most publications was conducted between 2009 and 2010 in Portuguese and reported, among other aspects, methods and techniques to control production and phytomedicines. The articles demonstrate the importance of conducting preliminary studies on stability and quality control of phytomedicines as a key step in the production and design of these pharmaceutical forms.

It is known that the major sources of biodiversity are rainforests located in developing countries like Brazil, which holds about a third of the world flora. However, developed countries like the United States (U.S.) and Japan are the ones that most manufacture and market...
natural products, given their greater investment in research and development of pharmaceuticals. In this context, it is expected that new products can be produced in Brazil from native species through institutional commitments (universities and companies), with the application of resources to ensure that the work of experts in the fields of botany, biology, pharmacy, medicine, chemistry, among others (Klein et al., 2009).

The design of semisolid pharmaceutical forms, especially phytocosmetic, gains prominence in Brazil, one of the major producing countries in the field of cosmetics. This large-scale production can be related to the strong ties with companies that are sources of natural products for preparation of formulations, as well as due to the commitment that producing industries have with the conservation of natural resources and promotion of sustainable development practices, which demonstrates that good relationships between companies and ensuring of raw material are important for success in the production of phytomedicines (Seild, 2002).

The production of phytomedicines necessarily passes through the stage of research and development (R & D) of drugs. Studies point to the idea that the success of R & D activity depends largely on its planning and organization. This requires the definition of objectives, adequate budget, leadership, effectiveness, safety, size of the research team and ease of internal and external communication. Moreover, the entire process involved in the production should be monitored, including the environment control, manufacturing control and final control of production. The failure of these criteria, due to poor human resources and/or materials can be an obstacle in the design of pharmaceutical forms (Cardoso et al., 2002; Martinelli et al., 2005).

According to the protocols of drug stability, the parameters evaluated in the products subjected to stability tests should be defined by the formulator and depend on the characteristics of the test and components used in the formulation. The organoleptic characteristics determine the parameters of acceptance of the product by the consumer. In general, the appearance, color, flavor, smell and feel to the touch were evaluated. The product must remain intact in the test while maintaining its original aspect in all conditions except at high temperatures, freezer or cycles in which small changes are acceptable. The color and smell should remain stable for at least 15 days to sun light. Minor changes are acceptable at elevated temperatures.

The rheological features are important properties to consider in the manufacture, storage and application of topical products. Studies on rheology of pharmaceutical formulations for topical use have become increasingly frequent in research conducted by the scientific community, because even today it is clear that the physical stability of a formulation is fundamental to the quality control, consumer acceptance and its effectiveness (Correa et al., 2005).

Previous studies have already demonstrated the importance of the rheology of the pharmaceutical product, stating that the determination of the rheological behavior of the formulation aids in the evaluation of the physicochemical nature of the vehicle in such a way that makes it possible to detect early signs of physical instability allowing control quality of constituents, testing formulations and final products (Cefali, 2009).

Cosmetic products may also be subjected to thermal analysis comprising a group of techniques by which a physical property of a substance or its reaction products is measured depending on temperature, while the substance is subjected to controlled propagation of the temperature. This analysis enables a wide range of application for physical measurements, study of chemical reactions, thermal stability evaluation, determination of the chemical composition of materials and development of analytical methodology (Guillen et al., 2006).

Thermoanalytical techniques have great importance in cosmetic scope due to the large variety of applications and the most used methods are the differential scanning calorimetry (DSC), thermogravimetry (TG) and derivative thermogravimetry (DTG). Thermal analysis can be used both in control of raw material as the finished product having potential use in the development and characterization of new products (Guillen et al., 2006; Silva et al., 2007).

The different phytocosmetic formulations still require testing related to their stability, as shown by different studies. The formulation of a proniosomal gel, with the aim of improving its transdermal permeation, brought positive results with improved permeation. In this study, there was a need for short-term stability tests, which demonstrated the chemical and physical stability of the product. Studies on the development of a gel from the extract Cacalia hastata L. also show the results of phytomedicines’ stability indicating that the product is stable at room temperature with preserved appearance and viscosity (Thomas and Viswanad, 2012; Jambaninj et al., 2012).

In a study with a cream developed from Allamanda catharica L. was also performed in accelerated stability tests, lasting 60 days. The samples were subjected to heating in an oven, cooling in refrigerators, exposure to light radiation and environment, with temperature control being subsequently analyzed, showing a positive result to the product stability (Crespo, 2012; Terra et al., 2009).

Faced with these new requirements with respect to the development and validation of stability indicating method, pharmaceutical industries and the Research & Development Centers must perform stress tests in order to isolate, identify and characterize the degradation products obtained by variable adverse conditions.

However, due to the peculiarity of each drug and medicine, the study design may become one of the major difficulties of its accomplishment at the same time it is a challenge necessary to professionals in the development of pharmaceutical products (Silva et al., 2009).
Also, regarding the stability studies, the need for better packaging and storage conditions of raw materials and finished products in masterful establishments, lighting conditions and packaging standardization are scored as difficulties to perform more effective stability testing (Kato et al., 2010).

Conclusion

The development of phytopharmaceuticals, especially those phytopharma, is increasing in Brazil, but there are still many barriers to production and design of these semisolid dosage forms. The study showed that lacked investment and cooperation in research and development of new drugs, despite the vast Brazilian biodiversity. The integration between business and universities and research centers is still a difficulty for production and design of pharmaceutical forms. There is also shortage of human and material resources in the studies of drugs stability, necessary procedure for their design.

Conflict of interest

Authors declare that they have no conflicts of interest.

REFERENCES

Physicochemical characterization and in vitro evaluation of the photoprotective activity of the oil from *Opuntia ficus-indica* (L.) Mill. seeds

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*Opuntia ficus-indica* (L.) Mill. is a cactus widely cultivated in northeastern Brazil due to its enormous growth potential and multiple uses. This study aimed to perform physicochemical characterization and in vitro evaluation of the photoprotective potential in the region of ultraviolet B (UVB) radiation of the oil from *O. ficus-indica* (L.) Mill. seeds. For physicochemical characterization of the oil, the following techniques were used: thermal analysis (TA), infrared spectrometry (IR) and gas chromatography-mass spectrometry (GC-MS). The photoprotective potential was determined by UV spectrophotometry. It was observed that *O. ficus-indica* (L.) Mill. oil is rich in saturated and unsaturated fatty acids, primarily linoleic acid (~65%), which may be related to the protection against ultraviolet rays (UVB). However, the results of evaluation of in vitro sun protection factor (SPF) indicated that under the conditions studied the oil from the *O. ficus indica* (L.) Mill. seeds does not have photoprotection activity.

Key words: *Opuntia ficus-indica* (L.) Mill., phytochemistry, physicochemical characterization, fatty acids composition, photoprotection.

INTRODUCTION

*Opuntia ficus-indica* (L.) Mill. is a cactus native to Mexico’s arid regions and is widespread through South America, Australia, South Africa and throughout the Mediterranean region (Leo et al., 2010). Members of the cactus family are biologically adapted to resist intense sunlight, drought and extreme temperature variations...
through day and night. In the Northeast of Brazil, a common species is *O. ficus-indica* that has been used as animal feed (Barbera et al., 2001). In many countries *O. ficus-indica* fruits have been used in human food due to the sweet taste and high content of nutritional compounds, such as the ascorbic acid, polyphenols, amino acids, minerals, vitamins and others; besides these products are juicy (Leo et al., 2010; Ozcan and Al Juhaimein, 2011).

Current researches with this species revealed their antiviral, anticancer, anti-inflammatory, hypoglycemic, antioxidant and diuretic properties (Guevara-Arauza, 2009; Galati et al., 2003; Zou et al., 2005; Chavez-Santoscoy et al., 2009). Furthermore, studies on nutrition indicated that this seeds are sources of natural fibers and due to the high concentration of essential fatty acids, sterols, carotenoids and fat soluble vitamins, the oil seeds can be used as nutraceutical agent (Ramadan and Mörsel, 2003; Ozcan and Al Juhaimein, 2011).

It is remarkable that current studies with *O. ficus-indica* have been performed in the researches for development of new drugs and functional foods. However, there is a need of studies for physicochemical characterization of the oil from *O. ficus-indica* seeds (Ennouri et al., 2005) and demonstrate potential activities and employability of this raw material in the area of new cosmetic development, such as the study performed by Schmid et al. (2005) which created a moisturizing, soothing and protective from ultraviolet A radiation –UVA- product. Species such as *O. ficus-indica*, which have phenolic constituents and fatty acid composition of its oils may be capable to absorb the ultraviolet light and when associated with the possible antioxidant activity can express photoprotective activity (Violante, 2009; Wagemaker et al., 2011). The photoprotective preparations for topical use are designed to protect the skin from the deleterious effects of solar radiation (Rangel and Corrêa, 2002). A promising tendency is the association of natural products in sunscreens to improve their photoprotective activity by intensifying the sun protection factor (SPF) into the final product (Ferrari et al., 2007). The SPF determination of sunscreens can be performed by *in vivo* or *in vitro* methods. In Brazil, *in vivo* method is highly recommended, according to the Resolution RDC n. 30/12, that presents the Mercosul technical regulation of sunscreens in the cosmetics area (Brasil, 2012). However, there are other *in vitro* methodologies developed which are based on absorbing or reflecting filter properties that can be used in a preliminary evaluation of the SPF during the development of formulations and for a routine quality control, bath to bath. These methods present the advantage of not requiring the use of human volunteers to determine the SPF (Nascimento et al., 2009). The spectrophotometric method developed by Mansur et al. (1986), proved to be effective and fast, besides showing a good correlation with *in vivo* results that are phototests (Mansur et al., 1986; Ferrari et al., 2008). The present study aimed to perform physicochemical characterization and *in vitro* evaluation of the photoprotective potential in the region of UVB radiation of the oil from *O. ficus-indica* (L.) Mill. seeds cultivated in the Northeast of Brazil.

**MATERIALS AND METHODS**

**Extraction of vegetable oil**

Ripe fruits of *O. ficus-indica* (L.) Mill. were collected in Juazeirinho - PB (Brazil), on March, 2011 and identified by Ivan Coelho Dantas. The voucher specimen was stored at the plant Manoel de Arruda Camara Herbarium (ACAM) of the State University of Paraíba, under registration number 907. The seeds were dried in a forced air circulation at 40°C and subsequently crushed in a Whitley® knife mill. The oil from *O. ficus-indica* seeds was extracted with hexane in a Soxhlet apparatus for nine hours. The organic phase was removed using a rotary evaporator under reduced pressure.

**Physicochemical characterization**

**Analysis of fatty acids**

The fatty acid content of oil from *O. ficus-indica* seeds was determined by gas chromatography (GC) after the esterification process, according to the methodology of Maia (1992). This process consists of replacing the reactive hydrogen of the carboxylic acid by a methyl, in order to get a derived product, which could be measured with more sensitivity and exactness and easily separated from the interferents (Lanças, 1993). Thus, a solution of acid (H2SO4) with methanol (MeOH) was used as esterifying reagent. The esterified oil was used only for the GC analysis. Qualitative analysis of the substances was carried out in gas chromatograph couple to a mass spectrometer (GC-MS, Shimadzu, QP-5000), equipped with a fused silica capillary column OV-5 (30 m × 0.25 mm × 0.25 μm Ohio Valley Specialty Chemical, Inc.), operating by electrons impact (70 eV). The analysis conditions were: injector: 240°C; detector: 230°C; carrier gas: He; flow rate: 1.0 ml min⁻¹, dilution: 1 μl fixed oil/1.0 ml ethyl acetate, volume injection: 1 μl, Split: 1/20. The oven temperature program was: 110°C (1 min), 110 to 170°C, 10°C/min; 170°C (2 min); 170 to 173°C, 1.5°C/min; 173 to 180°C, 1.0°C/min; 180°C (7 min); 180 to 230°C, 6°C/min; 230°C (20 min). Quantitative analysis was conducted in gas chromatography with flame ionization detector (GC-DIO), using the same condition as stated. The identification of substances was performed by comparing their mass spectra with database system GC-MS (Nist. 62 lib.) and retention index (Adams, 2007) and comparison with commercial standards of methyl esters fatty acids.

**Thermal analysis (TA)**

The thermal analysis was determined through the differential scanning calorimetry (DSC) using a DSC Q20 of the TA Instruments®. The heating rate was 10°C/min, under nitrogen atmosphere of 50 ml/min. A sample of 2 mg was weighed and subjected to a temperature range from 25 to 500°C. For the thermogravimetry (TG) an SDT Q600 was used, TA instruments® brand, with a heating rate of 10°C/min under nitrogen atmosphere (50 ml/min). There were weighed 8.5 mg of oil sample in alumina crucibles and subjected to a temperature range from 25 to 900°C. For the analysis of DSC and TG curves we used the TA Universal Analysis


Infrared absorption spectroscopy (IR)

The spectrum of absorption in the mid-infrared region was obtained using the equipment PerkinElmer® (Spectrum 400) with attenuated total reflectance device with crystal of selenium (ATR). The analysis was performed with 16 scans and resolution 4 cm\(^{-1}\) in the region between 4000 and 650 cm\(^{-1}\).

Evaluation of the potential photoprotective

SPF evaluation of vegetable oil

The SPF evaluation followed the methodology proposed by Mansur et al. (1986). The SPF was measured at different oil concentrations (screening). For this, the oil from the *O. ficus-indica* seeds was dissolved in hexane (Merck\(^{®}\)) analytical grade, at concentrations of 50, 40, 30, 20, 10, 5, 2, 1, 0.5 and 0.2 µl/ml. It a spectrophotometer UV/VIS (Schimadzu, model 1240) was used in quartz cuvette of 1.0 cm optical path in the range of 290 to 320 nm, at intervals of 5 nm. The absorbances obtained were added to the equation proposed by Mansur (Equation 1).

\[
SPF = \frac{320}{E_{\lambda}} \cdot EE(\lambda) \cdot i(\lambda) \cdot Abs(\lambda)
\]

Equation 1. Calculation of SPF according to Mansur et al. (1986).

Where CF = correction factor (equal 10); EE (\(\lambda\)) erythemal effect of solar radiation at each wavelength \(\lambda\); \(i(\lambda)\) = sunlight intensity at wavelength \(\lambda\); \(Abs(\lambda)\) = spectrophotometric reading of sample's absorbance at each wavelength.

The correction factor (CF) was determined so that a standard sunscreen formulation containing 8% homosalate presented a SPF value of 4, determined by UV spectrophotometry (Mansur et al., 1986). The relation between the erythemal effect and the sunlight intensity at wavelength \((EE \times i)\) is constant and was determined by Sayre et al. (1979). The experiment was performed in triplicate. The results of the SPF were expressed by the arithmetic mean of three determinations.

Evaluation of SPF of emulsion with oil of *Opuntia ficus-indica* (L.) Mill.

The SPF emulsion base was evaluated with 10% oil as well as the SPF photoprotective emulsion with 10% oil addition in order to verify the occurrence of SPF potentialization. As a vehicle for incorporating the derivative of *O. ficus-indica* self-emulsifying base, Aristoflex AVL\(^{®}\) (Clariant Brazil), was used which is a mixture of emulsifiers, emollients and thickening polymer. The emulsions were prepared by the method of reverse phase cold and the preservative methylparaben and the surfactant polysorbate 80 were used as adjuvants. Octyl methoxycinnamate was used as synthetic sunscreen (Table 1). To evaluate the SPF of these formulation, 1.0 g of all samples was weighed, transferred to a 100 ml volumetric flask, diluted to volume with ethanol (Merck\(^{®}\)) analytical grade, followed by ultrasonication for 5 min and then filtered through cotton, rejecting the first 10 ml. A 5.0 ml aliquot was transferred to 50 ml volumetric flask and diluted to volume with ethanol. Then a 5.0 ml aliquot was transferred to a 25 ml volumetric flask and the volume completed with ethanol. The absorption spectra of samples in solution were obtained in the range of 290 to 450 nm using 1 cm quartz cell, and ethanol as a blank. The absorption data were obtained in the range of 290 to 320, every 5 nm, and 3 determinations were made at each point, followed by the application of Mansur equation. The results of the SPF were expressed by the arithmetic mean of three determinations.

### RESULTS AND DISCUSSION

**Composition of fatty acids**

The saturated and unsaturated fatty acids content of the oil from the seeds of *O. ficus-indica* can be viewed in Table 2. It was observed that the oil in this study has predominantly unsaturated fatty acids 79.61%. This result is in agreement with those of Ramadan and Mörsel (2003), who previously reported the major saturated and unsaturated fatty acids present in the oil of *O. ficus-indica* cultivated in Germany. The pattern of lipids in the cactus is comparable to that of sunflower (*Helianthus annuus*) and grape (*Vitis vinifera*) oils seeds (Tan and Che Man, 2000). Recently, Ennouri et al. (2005) reported levels of linoleic and palmitic acid superior to the present study: (74.00% vs. 64.78%) and (7.20% vs. 4.84%), respectively. However, to oleic acid, the concentration detected by this study was lower (12.80% vs. 14.83%). According to Faria et al. (2002), the proportion of different unsaturated and saturated fatty acids found in vegetable oil from the same species may vary according to climatic conditions and soil types in which these species are cultivated. Epidemiologically, the linoleic acid (omega-6)
Table 2. Chemical composition of esterified oil from the seeds of *Opuntia ficus-indica*.

<table>
<thead>
<tr>
<th>Peak</th>
<th>Substance</th>
<th>Saturation</th>
<th>Retention Time*</th>
<th>Relative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-Undecane</td>
<td>-</td>
<td>3.2</td>
<td>5.52</td>
</tr>
<tr>
<td>2</td>
<td>n-Dodecane</td>
<td>-</td>
<td>3.8</td>
<td>1.95</td>
</tr>
<tr>
<td>3</td>
<td>n-Tridecane</td>
<td>-</td>
<td>4.1</td>
<td>2.60</td>
</tr>
<tr>
<td>4</td>
<td>Palmitic acid</td>
<td>C16:0</td>
<td>18.4</td>
<td>4.84</td>
</tr>
<tr>
<td>5</td>
<td>Linoleic acid</td>
<td>C18:2 (9c,12c)</td>
<td>27.3</td>
<td>64.78</td>
</tr>
<tr>
<td>6</td>
<td>Oleic acid</td>
<td>C18:1 (9c)</td>
<td>27.5</td>
<td>14.83</td>
</tr>
<tr>
<td>7</td>
<td>Us**</td>
<td>-</td>
<td>27.8</td>
<td>4.95</td>
</tr>
<tr>
<td>8</td>
<td>Stearic acid</td>
<td>C18:0</td>
<td>28.6</td>
<td>0.52</td>
</tr>
</tbody>
</table>

*Retention time in minute. **Unidentifiable substances.

Figure 1. DSC curve of the oil from the seeds of *Opuntia ficus-indica*.

plays an important physiological role as a potent mediator of the inflammation and the beneficial effect upon the immune system (Luzia et al., 2010). Furthermore, the presence of oleic and linoleic acids on skin is essential for maintenance of skin hydration, skin barrier and hydrolipidic mantle (Pianovski et al., 2008). And for presenting absorption band at UV region, these essential fatty acids are strong candidates for raw material in sunscreen industry (Remédios et al., 2006). Then, that several layers of fat-cells formed the skin, as the more lipophilic the sunscreen, the greater its substantivity. In other words, the product has the ability to retain its effectiveness for prolonged periods of time, especially when exposed to water (Wagemaker et al., 2011).

**Thermal behavior**

In the DSC curve (Figure 1) of the oil from *O. ficus-indica* seeds two events were observed: one exothermic with peak at 159.56°C and another endothermic with peak at 432.57°C. The first event may be associated with a crystallization peak favored by the power supply to the sample in sufficient quantity to promote a structural reorganization of the oil molecules (Herrera, 2005). According to Prado et al. (2007), the main factors that influence on the crystallization temperature of lipids are...
the size of their molecules and the presence of double bonds in carbon chains. Considering the palm oil is rich in saturated and unsaturated fatty acids, the endothermic event can match the thermal decomposition of these compounds, since according to Reda and Carneiro (2007) at temperatures above 200°C maximum decomposition of the oils occurs. Faria et al. (2002) analyzed the thermal stability of some seed oils typical of the cerrado and observed similar results to the present study about the final temperature of decomposition of guariroba (Syagrus oleracea) (433°C), babaçu (Attalea ssp) (440°C) murici (Pterogynne nitens) (477°C), araticum (Annona glabra L.) (478°C) and buriti (Mauritia flexuosa L.) (483°C).

According to Kasprzycha-Guttman and Cozeniak (2010), the thermal decomposition of saturated fatty acids requires more energy than the unsaturated acids. Then, as shown in the results of this study, the oil from *O. ficus-indica* seeds contains mainly unsaturated fatty acids (~80%), then we can try to justify that the enthalpy (ΔH) required for decomposition of this oil was relatively low (27.11 cal/g). The ΔH required for transition from decomposition of palm oil was higher than that of soybean (Glycine Max (L.) Merrill) oil (19.00 cal/g), corn (Zea mays) (11.60 cal/g), sunflower (H. annuus) (21.61 cal/g) and less than the canola oil (Brassica napus L.) (35.30 cal/g), rice (Oryza sativa) (51.13 cal/g) and olive (Olea europaea) (46.37 cal/g), which has significant levels of antioxidants (Santos et al., 2002). The thermal decomposition of oil from *O. ficus-indica* seeds (Figure 2) occurs in two main steps. The first stage begins at 219.39°C and has a weight loss of 17.74%. The second phase begins at 336.25°C and has a mass loss of 76.15%.

The first step is probably the decomposition of compounds with chains from 8 to 16 carbon atoms, and the second step is probably the decomposition of other saturated fatty acids and higher unsaturated carbon chains such as stearic acid (C18:0), oleic (C18:1) and linoleic (C18:2) (Santos, 2008). It is observed that there was no formation of residue, which may correspond to the complete decomposition and carbonization of the sample. Similar results were found in the thermal stability study by Santos (2008) with babaçu (Attalea speciosa) oil, which also breaks down into two stages and has thermal stability up to 209.30°C. Comparing the DSC with TG curve it was observed that the first event registered in the DSC (15°C) was not accompanied by significant mass loss. Therefore, it was just a physical change, which contributes to the proposition of an event of crystallization.

### Infrared absorption spectroscopy

The analysis of the IR spectrum of the *O. ficus-indica* oil (Figure 3) shows the presence of intense bands around 2900 cm⁻¹, which are characteristic of methyl groups (-CH₃); methylene (-CH₂) and methyl (-CH), similar to the spectral bands of sesame and buriti oils (Albuquerque et al., 2003; Barros et al., 2007). The greater intensity of these bands may be related to the accumulation of signal generated by the large amount of lead type C-H. The band of low intensity at 3009 cm⁻¹ refers to the asymmetric...
stretch of C-H bond sp² carbon (Silverstain and Webster, 2000). It also marks the existence of a band at 1744 cm⁻¹ characteristic of the carbonyl group (C=O) of esters, often long-chain fatty acids are also found in oils such as cotton and buriti (Albuquerque et al., 2003; Salgado et al., 2007). The bands at 1464 and 1377 cm⁻¹ may be related, respectively, the angular deformation of the asymmetric and symmetric methylene group (-CH₂). And the band in the range of 1161 cm⁻¹ is characteristic of stretching C-O (Silverstain and Webster, 2000). The band observed around 722 cm⁻¹ can be related to the synchronous vibration of the sequence of aliphatic chains of fatty acids (Albuquerque et al., 2003; Silverstain and Webster, 2000). Therefore, the bands observed in this IR spectrum are characteristic of the fatty acids detected in the GC-MS of the O. ficus-indica oil.

Evaluation of SPF of vegetable oil

According to the literature, polyunsaturated fatty acids present in the plants might absorb ultraviolet light. This shows the possibility to use the vegetable oils as sunscreens in photoprotection preparations (UVA/UVB) (Wagemaker et al., 2011). Corroborating with this assertion, it was detected that O. ficus-indica seed oil showed significant SFP on different oil concentrations. According to Figure 4, the SPF is directly related to the amount of oil in the solution spectrophotometric reading. Thus, the higher the concentration of oil, the higher the SPF. Given the data, it is important to point out that on the concentration of 50 µg/ml a 22 FPS was observed, which is quite useful on photoprotection, since vegetable products that have SPF > 4 compared to homossalato, could be applied for the same purpose, since its production follow current legislation marketing of sunscreens (Rosa et al., 2008).

Evaluation of SPF of emulsions with oil of Opuntia ficus-indica (L.) Mill.

The positive control (F2) performed with the incorporation of 7.5% (w/w) of octyl methoxycinnamate (synthetic sunscreen) showed in vitro SPF is equal to 12.53, which is in agreement with results of the literature 13.21 ± 1.07 (Violante, 2009). However, the formulation with oil from O. ficus-indica seeds incorporated at a concentration of 10% (w/w) showed no significant SPF (F3) and was not capable of increasing the SPF of the formulation with synthetic filter (F4) (Table 3). Similar results were found by Violante et al. (2009) while working with dry ethanol extracted from Macrosiphonia velame. This vegetable species was presented in UVB absorption, but when it was subjected to the in vitro determination of SPF developed by Mansur test, the result was 0.36 ± 0.01. Thus, at the concentration used and standardized to Macrosiphonia velame, it cannot be considered a plant
Figure 4. Correlation between the concentration of Opuntia ficus-indica oil and SPF value.

Table 3. Results of the SPF of the formulations studied.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>SPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.18 ± 0.01</td>
</tr>
<tr>
<td>F2</td>
<td>12.53 ± 0.03</td>
</tr>
<tr>
<td>F3</td>
<td>0.23 ± 0.01</td>
</tr>
<tr>
<td>F4</td>
<td>12.72 ± 0.06</td>
</tr>
</tbody>
</table>

F1 = Emulsion base; F2 = base + 7.5% sunscreen, F3 = base + 10% oil, F4 = base + 10% oil + 7.5% sunscreen.

with sunscreen potential. Wagemarker et al. (2011) investigated the photoprotective activity of 10 different species of Coffea oil by the method of Mansur. These species showed significant concentrations of linoleic and oleic fatty acid type. The highest SPF values were found in Coffea eugeniioides (2.6), Coffea salvatrix (2.2 to 3.1) and Coffea stenophylla (0.9 to 4.1), and the lowest in Coffea kapakata (0.0 to 0.1), Coffea liberica var. liberica ‘Passipagore’ (0.3), C. liberica var. dewevrei Abeokutae (0.2 to 0.6) and Coffea canephora (0.2 to 0.6). So, it was found that the employment of the latter species in the cosmetic field is remote. These results can be explained by the comments made by different researchers that showed that the effectiveness of sunscreen depends on the ability of absorbing radiant energy allocated to the chromophore groups, which is proportional to its concentration, range of absorption, and wavelength, which occurs at maximum absorbance (Silva Filho et al., 2003; Violante, 2009). Furthermore, according to Coelho (2005), the potential photoprotection not detected at formulations with oil could be related to chemical interactions which could have occurred between the metabolites of plants and the formulation chemical components. Therefore, given the aforementioned, it was observed that the IR and TA of the oil from O. ficus-indica seeds allowed us to characterize it physicochemically and check their thermal stability, in order to obtain parameters for quality control during oil processing and storage. Through the GC it was detected that the oil of O. ficus-indica is rich in saturated and unsaturated fatty acids, especially linoleic acid (~65%). The scientific literature indicates that fatty acids conferred UVB protection as well as maintaining hydration of the skin. However, the results of evaluation of in vitro SPF of formulations with O. ficus-indica oil indicated that, in the conditions of the study, this oil does not have photoprotection activity.

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Conflict of interest

Authors declare that they have no conflicts of interest.
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