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Ultrasonic incorporation of cinnamon essential oil into pre-gelatinized cassava starch oral films

Incorporação ultrassônica de óleo essencial de canela em filmes orais de amido de mandioca pré-gelatinizados

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ABSTRACT

The present work aims to produce oral films (OFs) based on pre-gelatinized starch with incorporation of cinnamon essential oil (CEO). For this purpose, the effectiveness of ultrasound in incorporating the CEO into the filmogenic solution was evaluated, in comparison with the use of magnetic stirring. The OFs were characterized in relation to physical properties, disintegration time, surface pH and total phenolic compounds content. In general, all formulations showed film-forming capacity, however, the distribution of the CEO in the polymer matrix was not efficient, regardless of the incorporation method used. The OFs had a disintegration time <32.17 seconds and the surface pH remained close to the oral pH, regardless of the formulation. All formulations produced with the CEO addition can be considered sources of total phenolic compounds, with the highest concentration observed (86.17±2.53 mg.100 g^{-1} OF) being produced by ultrasound. OFs based on pre-gelatinized starch can be considered an innovative way for the delivery of cinnamon essential oil, as a source of total phenolic compounds.

Keywords: Bioactive compounds. Phenolics. Ultrasound processing.

RESUMO

O presente trabalho tem como objetivo a produção de filmes orais (FOs) a base de amido pré-gelatinizado com incorporação de óleo essencial de canela (OEC). Para tanto, avaliou-se a eficácia do ultrassom na incorporação do OEC à solução filmogênica, em comparação com o uso de agitação magnética. Os FOs foram caracterizados em relação às propriedades físicas, ao tempo de desintegração, ao pH superficial e ao teor de compostos fenólicos totais. Em geral, todas as formulações apresentaram capacidade filmogênica, porém a distribuição do OEC na matriz polimérica não foi eficiente, independentemente do método de incorporação utilizado. Os FOs tiveram um tempo de desintegração <32,17 segundos e o pH de superfície permaneceu próximo ao pH oral, apesar da formulação. Todas as formulações produzidas com a adição de OEC podem ser consideradas fontes de compostos fenólicos totais, sendo a maior concentração observada (86,17±2,53 mg.100 g^{-1} FO) produzida por ultrassom. Os FOs à base de amido pré-gelatinizado podem ser considerados uma forma inovadora de liberação de óleo essencial de canela, como fonte de compostos fenólicos totais.

Palavras-chave: Compostos bioativos. Fenólicos. Processamento por ultrassom.

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INTRODUCTION

The oral route is one of the most used for the administration of dosage forms, and the oral films are presented as alternatives for drug administration, mainly for pediatric, geriatric, bedridden and/or dysphagic patients (Gupta et al., 2010). According to Bala et al. (2013), orally disintegrating films are noteworthy for having a fast disintegration time and mainly due to the incorporation of active compounds obtained from different sources, which can be incorporated into synthetic compounds (Brniak et al., 2015) or obtained from natural sources (Borges et al., 2016).

For the production of oral films, the most used technique is casting (Garcia et al., 2020), which consists of mixing the polymer with the solvent, in order to obtain the filmogenic solution, dispersing the solution in a container (e. g. petri dishes), followed by drying to evaporate the solvent (Arya et al., 2010). The typical composition of oral films consists of a drug or active compound, polymer and plasticizer, the addition of saliva stimulating agents to increase salivation and facilitate disintegration is optional (Saini et al., 2012). Generally, the active compounds incorporated in oral films are of synthetic origin, however, essential oils have been highlighted in the literature as a potential source of active compounds, especially cinnamon oil (Oussalah et al., 2006; Cansian et al., 2010; Andrade et al., 2012; Jayaprakasha et al., 2013; Souza et al., 2013; El Amrania et al., 2019), since the consumption of this oil in natura is reduced.

Essential oils make an important role as a source of active compounds (Burt, 2004). The presence of these compounds in cinnamon essential oil gives it the characteristic flavor and aroma of this spice. Coming mainly from the bark of the plant, the biological activity of this essential oil was previously studied with potential as an antioxidant, antifungal and antibacterial agent being reported (Sienkiewicz et al., 2014; El Atki et al., 2019). In particular, cinnamon essential oil has been reported to contain significant amounts of compounds such as monoterpenes, sesquiterpenes and phenols (Cardoso-Ugarte et al., 2016). Furthermore, some studies have reported that its main components, eugenol and cinnamaldehyde, effectively work as agents with antioxidant and antimicrobial activity (Sangal, 2011; Ranasinghe et al., 2013). Eugenol is used as a food additive and it is classified as a safe substance according to the United States Food and Drug Administration (FDA) (Falleh et al., 2020).

As an additive in orally disintegrating films, there are no regulations that establish limits for the use of essential oils. In addition to being an underexplored segment, its application is still challenging, considering the high volatility and reactivity of these compounds (Cardoso-Ugarte et al., 2016). Relevant international bodies such as the FDA, the Codex Alimentarius, the Council of Europe (CoE), the Food Chemical Codex (FCC), the International Organization of the Flavor Industry (IOFI) and the Flavor and Extract Manufacturers Association on the United States (FEMA) have established safety limits for the use of essential oils as food preservatives for consumption by mammals (Jemaa et al., 2018), since a synergistic and antagonistic effect may arise in some cases (Dima & Dima, 2015).

During the production of films, the loss of active compounds can occur (Genina et al., 2013; Low et al., 2013). Therefore, one way to minimize these losses is the use of ultrasound, which is considered an effective technique for microencapsulation of compounds of interest (Fernandes et al., 2016; Pieczykolan & Kurek, 2019; Teodoro et al., 2019). Cruz-Diaz et al. (2019) reported that the use of ultrasonic irradiation in the preparation of films based on whey protein promoted the formation of films less permeable to water vapor, thinner and with greater mechanical resistance, as ultrasound promoted the modification of the structure of proteins and consequently the properties of the films obtained. Fabra et al. (2017) and Liu et al. (2021a) also verified that the use of ultrasound improved the properties of corn starch-based films, as increased breakdown of the cell wall of the matrix with greater release of active compounds and moisture, producing films with improved barrier properties.

Although the effect of ultrasound in the production of films with different polymers has already been reported, it was found that the evaluation of ultrasonic irradiation in the production of films based on pre-gelatinized starch with the addition of essential oil is incipient. In this context, based on pre-gelatinized starch, the objective of this work was to evaluate the incorporation of cinnamon essential oil in oral films (OFs), comparing the techniques of ultrasound and magnetic stirring. The films obtained were characterized in relation to visual appearance, thickness, disintegration time, color parameters, surface pH and total phenolic compounds content.

MATERIALS AND METHODS

In the production of the OFs, pre-gelatinized cassava starch (Cargil), glycerol (Synth) and cinnamon essential oil (Laszlo) were used. For characterization and quantification of phenolic compounds in oral films, the following were used: sodium chloride (Synth), potassium chloride (Vetec), potassium phosphate monobasic (Vetec), sodium phosphate dibasic (Vetec), methanol (Vetec), n-hexane (Vetec), sodium carbonate (Synth), Folin-Ciocalteu (Sigma-Aldrich) and gallic acid (Sigma-Aldrich).

Production of oral films

OFs were produced by casting technique, with constant concentration of pre-gelatinized starch ($2g.100g^{-1}$ filmogenic solution), according Garcia et al. (2017), and glycerol (0.4g.100g^{-1} pre-gelatinized starch). Initially, the pre-gelatinized starch was solubilized in distilled water for 30 minutes under magnetic stirring (Marconi MA 085). Then, the solution was heated at 90 °C for ten minutes in a thermostabilised bath (New Ethics) and glycerol was added to the filmogenic solution under magnetic stirring.

For oral films with the addition of cinnamon essential oil (CEO), the filmogenic solution was cooled to 30 °C and it was added at different concentrations in the films (Table 1). Intending to compare different forms of essential oil incorporation in the filmogenic solution, two methods were used: (1) magnetic stirring (Gehaka, AA-1840) and (2) ultrasonic bath (Ultranique Q5. 9/40 A, frequency of 40 kHz and power of 123 W). In both methods, the incorporation time was ten minutes. The filmogenic solution (with or without the addition of CEO) was dispersed in petri dishes and subjected to drying in an oven (Marconi MA 35) for 24 hours at 30 °C.

Table 1
Production of oral films based on pre-gelatinized starch with different concentrations of cinnamon essential oil (CEO).

Formulation	F1	F2	F3	F4	F5
CEO concentration (mg mL^{-1})	0	0.5	0.5	5.0	5.0
Magnetic agitation (300 rpm)		x		x	
Ultrasonic irradiation			x		x

Source: The authors.

Characterization of oral films

The visual aspect was evaluated for homogeneity (absence insoluble particles), on capacity for film formation (absence of discontinuous zones) and for manageability, according to Garcia et al. (2018). Thickness determination was performed using a digital micrometer (Western), evaluating ten random points on the sample (5 x 5 cm).

The disintegration time was determined in according with Garsuch and Breitkreutz (2010). Firstly, the OFs were fixed on a slide frame and deposited in Petri dishes with the addition of 250 µL of distilled water on the film surface. The time required for the drop to dissolve the film and to form a hole was fixed as the disintegration time.

The color parameters were evaluated using a colorimeter (Koncka Minolta) in relation to L* (brightness, black to white), chroma a* (green to red) and chroma b* (blue to yellow). The difference found in the colors of the OFs with addition of CEO, in relation to the OFs without the addition of CEO, was calculated by the Equation.

$$\Delta E^{*} = \sqrt{\Delta a^{*2} + \Delta b^{*2} + \Delta L^{*2}}$$

In order to determine the surface pH, the oral films (2 x 1 cm) were added to a container containing 15 mL of phosphate buffer solution (pH 6.8). They were prepared as described by Föger et al. (2008) and the pH was recorded at times of 0, 1, 2, 3, 5, 7, 12 and 15 minutes (Manhar & Suresh, 2013).

The content of total phenolic compounds incorporated in the OFs was determined according to Singleton et al. (1999), having gallic acid as standard. To extract the compounds, 1 g of film was added in 3 mL of methanol/water solution (70:30, v/v) and 1 mL of n-hexane, then this solution was homogenized in a vortex (Phoenix/AP-56) for ten minutes. The hydroalcoholic phase was separated by centrifugation (Quimis/0222TM1) at 3500 rpm for 15 minutes. Subsequently, in a tube containing 2.5 mL of Folin-Ciocateu reagent (1:10), an aliquot of 0.5 mL of the hydroalcoholic solution was added, and, after five minutes, it was added 2 mL of sodium carbonate (7.5%). The solution was homogenized and kept in the absence of light for two hours. The absorbance of the samples was determined in a spectrophotometer (Kasuaki, IL-227) at 740 nm and the results were expressed in mg gallic acid equivalent to 100 g^{-1} OF.

The analyzes were performed in triplicate and analysis of variance (ANOVA) was performed using the SAS software (Version 9.2) the difference between them was determined by the Duncan test (95%).

RESULTS AND DISCUSSION

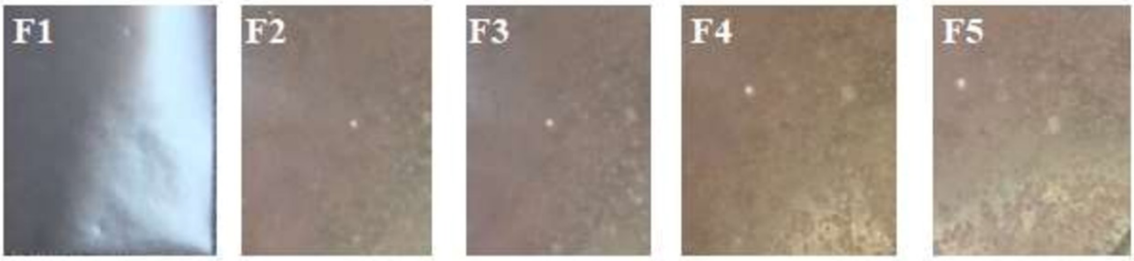
From this Table, it is possible to notice that all the formulations evaluated presented film formation capacity, however, maneuverability was not efficient for all of the OFs obtained. This fact corroborates the data that can be seen in the images presented in Figure 1.

Table 2
Visual aspect[1] of oral films based on pre-gelatinized starch with different concentrations of cinnamon essential oil.

Formulation	F1	F2	F3	F4	F5
Homogeneity.	+	-	-	-	-
Capacity for film formation.	+	+	+	+	+
Manageability.	+	-	-	-	-

Source: The authors.
Note: [1](+) Yes; (-) No.

Figure 1
Oral films with and without the addition of cinnamon essential oil.



Source: The authors.

In general, all formulations showed film-forming capacity, however, in relation to homogeneity and workability, only oral films without the addition of CEO showed positive aspects. Guerra et al. (2019) also observed that starch-based films plasticized with glycerol have high film-forming capacity, they are homogeneous and they are easy to handle.

The formulations F2, F3, F4 and F5 not provided OFs with uniform distribution of the CEO on the surface, possibly because the incorporation time or the techniques used were not efficient for the concentration of essential oil added, due to the possible occurrence of the formation of hydrophobic CEO microdroplets, producing heterogeneous films. A possible alternative for the incorporation of essential oil into a polymeric matrix in OFs would be the use of microparticles, which are easier to solubilize the polymeric matrix, or the use of a surface-active agent to improve the interaction of the essential oil with the water in the solution filmogenic, used in the production of OFs, before the drying process.

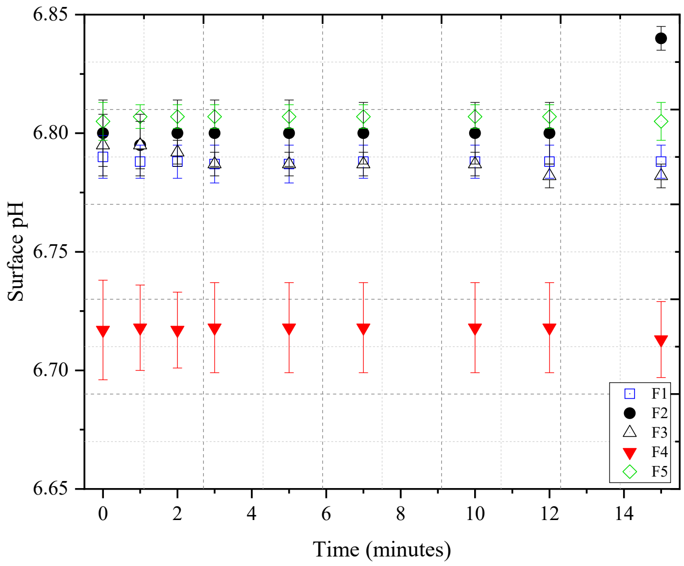
According to Borges et al. (2016), the presence of oil droplets on the surface can cause an interruption in the protein-protein interactions, causing an incomplete incorporation between the oil and the polymer matrix due to roughness in the cross sections of the film. Gonçalves et al. (2020) also reported an incompatibility of the polymer matrix of cellulose acetate films with the addition of fennel essential oil, reporting that possibly the oil was trapped between the polymeric chairs. On the other hand, Zhou et al. (2021) produced starch-based cassava edible films with the addition of cinnamon essential oil and reported the homogeneous distribution of the CEO on the surface of the films, however, the authors reported the incorporation of emulsifier (Tween 80%) in the production of the films. Rodrigues et al. (2020) produced films based on mangarite starch with incorporation of essential oil from copaiba and also reported that the films had a homogeneous surface, however, the incorporation of the oil was through an ultra-turrax.

Regarding the thickness of the OFs, no significant differences were observed, indicating an efficient control during the production process. The addition of essential oil to the OFs increased the disintegration time ($p<0.05$), and this increase is possibly related to the heterogeneity of the films after drying, due to the increase in the CEO concentration. It is believed that the addition of CEO has given hydrophobic characteristics to the OFs, causing an increase in the disintegration time. In accordance with Ju and Song (2019), the presence of phenolic compounds in extracts can increase the hydrophobicity of the films, which is possibly related to the increase in disintegration time values with the addition of different concentrations of CEO. Hoqque et al. (2011) also reported that the presence of phenolic compounds in the oil, which interact with the polymeric matrix, reduces the solubility of the material, consequently leading to an increase in the disintegration time.

Borges et al. (2019) verified an increase in the disintegration time of gelatin-based films with the addition of ethanolic propolis extract, and attributed this increase to the presence of phenolic compounds in the extract. However, the OFs obtained are classified as rapid release (Jyoti et al., 2011), with disintegration time of less than 60 seconds. According to Liang et al. (2001), the rapid disintegration of films prepared from macromolecules, such as starch, is due to the high porosity of starch, which facilitates the entry of water, resulting in a shorter disintegration time.

The surface pH of the oral films over time, regardless of the formulation, varied from 6.78 to 6.81 (Figure 2). Regardless of the formulation, the OFs presented pH close to the buccal, indicating that the addition of the CEO did not change the surface pH of the films (Figure 2). Oral films can present, at acidic or alkaline pH, adverse effects during consumption, such as irritation in the oral cavity, however, they do not cause irritation at pH close to neutral (Daud et al., 2011). In studies carried out by Manhar and Suresh (2013), the authors observed that the surface pH of the OFs remained close to neutral, as observed by Chevala et al. (2015). Garcia et al. (2017) reported that the OFs produced with isolated starch had a surface pH close to the buccal.

Figure 2
Evaluation of the surface pH of oral films based on pre-gelatinized starch with addition of cinnamon essential oil as a function of time.



Source: The authors.

In Table 3, it shows the values for thickness, disintegration time, color parameters (L*, chroma a* and chroma b*), difference color and total phenolic compounds content of the OFs obtained. The thickness remained between 0.07 and 0.08 mm. An increase in disintegration time was observed after addition of cinnamon essential oil. In general, no significant changes were observed in the color parameters of the films. The increase in the concentration of essential oil in the formulations provided OFs with higher levels of total phenolic compounds. Formulations F3 and F5 that underwent ultrasonic treatment presented a higher concentration of phenolic compounds after drying, when compared to OFs with the same concentration of oil incorporated by magnetic stirring.

Table 3
Thickness, disintegration time (DT), color parameters (L*, a*, b*), difference color (ΔE) and content of total phenolic compounds of oral films based on pre-gelatinized starch with different concentrations of cinnamon essential oil.

F[1]	Thickness (mm)	DT (s)	Color parameters				TPC[2] (mg 100 g^{-1} OF)
			L*	a*	b*	ΔE	
F1	0.08^{a}±0.01	11.05^{c}±3.55	97.80^{a}±0.26	0.49^{a}±0.03	2.26^{b}±0.15	nd	nd
F2	0.08^{a}±0.01	30.41^{a}±2.35	97.73^{a}±0.14	0.53^{a}±0.01	2.45^{a}±0.12	0.35^{b}±0.06	52.53^{d}±0.86
F3	0.08^{a}±0.02	23.81^{b}±3.04	97.62^{a}±0.17	0.50^{a}±0.02	2.39^{ab}±0.05	0.33^{b}±0.09	54.79^{c}±0.05
F4	0.08^{a}±0.01	32.17^{a}±5.41	97.66^{a}±0.14	- 0.55^{b}±0.06	2.47^{a}±0.12	1.39^{a}±0.26	79.45^{b}±2.16
F5	0.07^{a}±0.02	26.25^{b}±0.45	97.52^{a}±0.32	-0.47^{b}±0.05	2.44^{a}±0.14	1.46^{a}±0.37	86.17^{a}±2.53

Source: The authors.
Note: [1]Formulation (F). [2]Total phenolic compounds (TPC). Means with the same letters, in the same column, do not differ statistically from each other at the 5% level of significance. nd: not determined.

When compared to the control, the incorporation of CEO caused changes mainly in the chroma b* parameter ($p>0.05$) due to the characteristic color of the essential oil, showing a tendency to yellow, that is the characteristic color of cinnamon essential oil. Regarding the L* (luminosity) and a* chroma parameters, in general, no significant differences were observed between the films ($p>0.05$) obtained from the evaluated formulations. If they are formed from starch, the films without the addition of essential oil are generally transparent or opaque, and they have a characteristic coloring of the extract incorporated in the formulation (Darji et al., 2018). Zhou et al. (2021) reported that the color of starch-based edible films changed from clear to pale yellow after addition of cinnamon essential oil. The results obtained for the difference in color (ΔE) indicate that the OFs with different CEO concentrations had a very different color, indicating that the CEO incorporation technique interfered with the OFs color, especially when ultrasound was used.

With the incorporation of CEO by ultrasound, the formulations F3 and F5 showed higher concentrations of total phenolic compounds ($p<0.05$), an effect resulting from the greater incorporation of essential oil by the sonication process. This mechanism involves formation, rapid growth, oscillation and implosion of small vapor bubbles, in which promote cavitations and the action of shear forces in the liquid medium (Borah et al., 2017), breaking and reducing the droplet size in emulsions (Chu et al., 2020). The increase in local pressure in a very short time is verified, causing the uniform dispersion of the emulsion droplets in the system, contributing to the retention of the compounds in the film structure (Fang et al., 2020). Yuan et al. (2021) evaluated the ultrasound efficiency for incorporation of Sargassum pallidum polysaccharides into chitosone edible films. They reported that the ultrasonic treatment provided films with greater antioxidant activity.

The CEO is predominantly composed of phenolic compounds, such as eugenol and cinnamaldehyde (Du et al., 2009; El-Baroty et al., 2010; Ojagh et al., 2010; Li et al., 2013; Haghighi et al., 2019), which are compounds that have the ability to reduce the formation of reactive oxygen species preventing lipid peroxidation (Mateen et al., 2019). Ayala-Zavala et al. (2012) reported that the increase in the concentration of cinnamon leaf essential oil (7.3 to 36.1 $g.L^{-1}$) in pectin films resulted in an increase in eugenol in the produced films (4 to 71 $mg.g^{-1}$). Other works reported in the literature also identified the presence of total phenolic compounds in films incorporating essential oils, such as thyme essential oil (Liu et al., 2021b) and clove essential oil (Shen et al., 2021).

CONCLUSION

The use of ultrasound showed efficiency in the incorporation of cinnamon essential oil in oral films, since the formulations presented a higher concentration of total phenolic compounds, when compared to the stirring technique. In addition to the high concentration of total phenolic compounds, the oral films had a surface pH close to the buccal and they reduced disintegration time, thus being considered carriers of active compounds from natural sources.

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