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Development and characterisation of semisolid systems to deliver propolis in the oral cavity

Hirata, A.N.[1]; Bruschi, M.L.[2]*

[1]Curso de Farmácia, Departamento de Farmácia, Centro de Ciências da Saúde, Universidade Estadual de Maringá, Paraná, Brasil.
[2]Departamento de Farmácia, Centro de Ciências da Saúde, Universidade Estadual de Maringá, Paraná, Brasil.

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ABSTRACT

Pharmaceutical formulations containing poloxamer 407 (P407), Carbopol 934P (C934P) or gelatin (GELA), with ethanolic propolis extract (PE), were designed for the treatment of oral mucosal diseases. PE was produced and its quality was assessed by measuring its specific gravity, pH, weight of dry residue and total flavonoid content. Monopolymeric and binary polymeric formulations were prepared and their gelling temperature ($T_{sol/gel}$), pH, continuous flow rheology and mucoadhesion were studied. PE exhibited good quality and the formulations were easy to prepare and showed a wide range of consistency. Most of the formulations showed thermoresponsive behaviour and only those containing 15% P407, plus 0.20% C934P or 1.0 % GELA, displayed $T_{sol/gel}$ suitable for application to the oral mucosa. Monopolymeric formulations, containing C934P or GELA, and binary formulations exhibited pseudoplastic flow and low degrees of thixotropy. Monopolymeric formulations containing P407 exhibited pseudoplastic flow and rheopexy. The mucoadhesive properties of the systems could not be assessed. Fragments of formulation were found to remain stuck to parts of the mucin disc, owing to cohesive failure of the samples and of the sample/mucin interface. The data obtained on these formulations indicate a potentially useful role in the treatment of oral mucosal diseases.

Keywords: Propolis. Mucoadhesion. Poloxamer 407. Carbopol 934P. Gelatin.

INTRODUCTION

Bioadhesion is defined as the state in which two materials, at least one of which is biological, are held together for extended periods of time by interfacial forces. When the biological substrate is mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion (Gu et al., 1988; Lim et al., 2000).

Mucoadhesive materials can be incorporated in drug formulations, to hold the dosage form on the absorbing epithelial membrane, thereby prolonging and/or controlling the release rate of the drug and allowing a lower dosing frequency than is required with a more conventional dosage form (Bruschi & Freitas, 2005). Moreover, these materials can also be used as therapeutic agents in their own right, to coat and protect damaged tissues (e.g. gastric ulcers or lesions of the oral mucosa) or to act as lubricants (in the oral cavity, eye and vagina) (Smart, 2005). The most widely investigated group of mucoadhesives are hydrophilic macromolecules containing numerous hydrogen bonding groups. The presence of hydroxyl, carboxyl or amine groups on these molecules favours adhesion. They are called wet adhesives in that they are activated by moistening and will adhere non-specifically to many surfaces (Smart, 2005). Such bioadhesive polymers have been incorporated in dosage forms administered via almost all accessible routes, including the eye (Middleton et al., 1990; Bonferoni et al., 2004), nose (Lim et al., 2000), rectum (Kim et al., 1998), vagina (Chang et al., 2002), periodontal pocket (Bruschi et al., 2007) and oral cavity (Akbari et al., 2004).

The oral cavity is a propitious environment for microorganism infections, inflammations and aphthae. The buccal mucosa (lining the cheeks) is less permeable than the sublingual mucosa (floor of mouth) and generally incapable of mediating the same fast absorption and good systemic bioavailability. However, topical application of drug dosage forms to the tissues of the oral cavity is used in the treatment of a variety of conditions, including toothache, periodontal diseases, bacterial and fungal infections, aphthae and stomatitis (Bruschi & Freitas, 2005).

In this context, propolis has been used to treat oral cavity disorders, such as endodontal and periodontal diseases, microbial infections, cheilitis and aphthae. It is a sticky, resinous substance gathered by *Apis mellifera* L. bees, with many therapeutic properties, such as antibacterial, anti-inflammatory, antiviral, antifungal, immunostimulating and cytostatic activity. It is also reported to aid tissue regeneration and the healing of ulcers and to act as an analgesic (Burdock, 1998; Bruschi et al., 2007).

It has been shown to be possible to release propolis

Corresponding Author: Professor Dr. Marcos Luciano Bruschi - Universidade Estadual de Maringá - Departamento de Farmácia - Laboratório de Pesquisa e Desenvolvimento de Sistemas de Liberação de Fármacos - Bloco K80 - sala 16 Maringá - PR - Brasil. CEP.87020-900 - e-mail:mlbruschi@uem.br - telefones: (44) 3261-4817 / 3261-4870 - fax: (44) 3261-4999.

in the oral cavity from bioadhesive systems (Ceschel et al., 2002; Bruschi et al., 2007). These systems are composed of mucoadhesive polymers, which should be biocompatible, non-toxic, unabsorbed, economical and exhibit strong non-covalent adhesion. Natural polymers such as gelatin, sodium alginate, and guar gum, and synthetic and semi-synthetic polymers, such as hydroxypropylmethylcellulose, Carbopol 934 and sodium carboxymethylcellulose, and also various blends of two or more adhesive polymers, may be used as mucoadhesive systems (Bruschi & Freitas, 2005; Mohammadi-Samani et al., 2005; Smart, 2005). Moreover, *in situ*-gelling polymers, such as poloxamer 407, have been used together with Carbopol 934 to enhance the retention time of the pharmaceutical system at the site of application (Kim et al., 1998; Bruschi et al, 2007; Bruschi et al., 2008). Hence, the aim of this study was to develop and characterise mucoadhesive semisolid preparations containing poloxamer 407, Carbopol 934P and/or gelatin to deliver propolis in the oral cavity.

MATERIAL AND METHODS

Material

Propolis was collected at the experimental farm of the State University of Maringá (UEM), Paraná State, Brazil. Poloxamer 407 (P407), Carbopol 934P (C934P) and type A gelatin (GELA) were purchased from Sigma (St. Louis, MO, USA), B. F. Goodrich (Brecksville, OH, USA) and Royal (São Paulo, SP, Brazil), respectively. Triethanolamine (TEA), purchased from Galena (Campinas, SP, Brazil), was used as a neutralizing agent. All other chemicals were purchased from Merck (Darmstadt, Germany) and were of AnalaR, or equivalent, purity.

Preparation and characterisation of the propolis extract

Propolis extract (PE), with a propolis/ethanol ratio of 30/70 (w/w), was prepared by turbo extraction, filtered through filter paper and made up to the initial weight with ethanol (Bruschi et al., 2002). Exactly 10 g of PE was weighed and concentrated on a water bath (100°C) with occasional shaking. The concentrated material was dried on the Ohaus–MB 200 infrared analytical balance (Pine Brook, NJ, USA) at 110°C and the final % weight was designated the dry residue value (DR). In addition, the pH of PE was determined with a pH meter (Gehaka, São Paulo, Brazil), calibrated with buffer solutions (pH 4.0 and 6.86), and its specific gravity was determined in a pycnometer at 20°C (Bruschi, 2006). The total flavonoid content of PE was measured by a technique described elsewhere (Bruschi et al., 2003). Equal volumes (3.0mL) of distilled water, acetone and PE were mixed in a separating funnel. This mixture was extracted three times with 15 mL ethyl acetate. These extracts were pooled and made up to 50.0 mL with ethyl acetate (S1). Exactly 1mL of an ethanolic solution of aluminium chloride (2% w/v) was added to 10mL of S1, followed by a methanolic solution of acetic acid (5% v/v, MS) to a total volume of 25.0 mL. In parallel, 10.0 mL of S1 was made up to 25.0 mL with MS alone, as a compensatory solution. After 30 min, the solutions were analysed in a Shimadzu UV-1650PC spectrophotometer (Tokyo, Japan) at λ = 425 nm. The total flavonoid content of PE was calculated in grams of quercetin (specific absorptivity: 500) extracted from 100g of dried propolis. For all assays, three replicates were carried out to estimate the inherent variability of the determination.

Preparation of monopolymeric formulations

Monopolymeric formulations, containing P407, C934P or GELA, were prepared with a mechanical stirrer: P407 (10, 15 or 20%, w/w) was added to distilled water and the mixture was stored at 48°C for 12 h to ensure complete wetting; C934P (0.10, 0.15, 0.20 or 0.25%, w/w) was dispersed in distilled water and then neutralized with TEA; GELA (0.5, 0.75 or 1.0%, w/w) was dispersed in warm distilled water (up to 50°C). All formulations were then transferred into amber ointment jars, evacuated to remove incorporated air and stored at 4°C for at least 24 h prior to further analysis.

Preparation of binary polymeric formulations

Binary polymeric formulations were prepared, containing 10, 15 or 20% (w/w) of P407 with C934P or GELA. C934P (0.10, 0.15, 0.20 or 0.25%, w/w) or GELA (0.5, 0.75 or 1.0%, w/w) was initially dispersed in distilled water with a mechanical stirrer. Following complete dissolution, P407 was added to this gel and the mixture was stored at 48°C for 12h to ensure complete wetting. Formulations were then stirred to ensure complete mixing of the two components and those containing C934P were neutralized with TEA. All preparations were stored at 4°C for 24h, transferred into amber ointment jars, evacuated to remove incorporated air and then stored at 4°C for at least 24h prior to further analysis.

Preparation of formulations containing propolis

Binary polymeric formulations were prepared as described above. At 20°C, PE was slowly added to the formulations to 4% (w/w), the amount normally used, by dropwise addition, with magnetic stirring, for 30 min (Bruschi et al., 2007). All samples were then transferred into amber ointment jars, evacuated to remove incorporated air and stored at 4°C for at least 24h prior to further analysis.

Determination of formulation pH

The pH each formulation was determined with a pH meter (Gehaka, São Paulo, Brazil), calibrated with buffer solutions (pH 4.0 and 6.86). Three replicates of each formulation were tested to estimate the inherent variability of the determination.

Determination of gelation temperature of formulations

Gelation temperatures were measured as previously described by Bruschi et al. (2007). A 20mL transparent vial containing a magnetic bar and 10g of each polymer system was placed on a low-temperature thermostat plate. A thermometer was immersed in the mixture, which was heated at a constant rate with constant magnetic stirring. When the magnetic bar stopped moving, due to gelation of the sol, the temperature displayed on the thermometer was taken as the gelation temperature or sol/gel transition temperature ($T_{sol/gel}$) (Choi et al., 1999).

Rheological characterisation of formulations

The rheological analysis of formulations was performed at 20°C in a ViscoStar – Plus R controlled shear rate rotating viscometer (Fungilab, Barcelona, Spain), equipped with spindle R4 or R5, according to the consistency of each formulation (Bruschi et al., 2007). Samples were carefully applied to the cup, ensuring that formulation shearing was minimized, and allowed to equilibrate for at least 5min prior to analysis. In continuous shear analysis (viscosity), upward and downward flow curves for each formulation were recorded over shear rates ranged from 0.3 to 200 rpm. Shearing rate was increased over a period of 150s, held at the upper limit for 10s, and then decreased over a period of 150s. In each case, the continuous shear properties of at least three replicates were determined.

Assessment of mucoadhesive strength of formulations

The mucoadhesive strength of each formulation under study was estimated by measuring the force required to detach it from a mucin disc, with a TA-XTplus Texture Analyser (Stable Micro Systems, Surrey, United Kingdom) in tension mode (Bruschi et al., 2007). Mucin discs were prepared by compressing a known weight of crude porcine mucin (250 mg) in a ring press with a 13mm diameter die and a defined compression force (10 tonnes), applied for 30s. All mucin discs used in the experiment were shown to have uniform weight and height. These discs were then attached horizontally to the lower end of the cylindrical probe (length 5cm, diameter 1cm), using double-sided adhesive tape. Prior to mucoadhesion testing, the mucin disc was hydrated by immersion in a 5% solution of mucin for 30s. Excess surface liquid was removed by gentle blotting. At a temperature of 37°C, samples of each formulation, previously packed into shallow cylindrical vessels, were placed under the analytical probe which was then lowered until the mucin disc was in contact with the surface of the sample. Without delay, a downward force of 0.1 N was applied for a predefined time (30s) to ensure intimate contact between the mucin disc and the sample. The probe was then moved upwards at a constant speed of 1.0 mm s^{-1} and the force required to detach the mucin disc from the surface of each formulation was determined from the resulting force-time plot. All measurements were performed on at least five replicates.

RESULTS

Characterisation of the PE

Propolis extract dry residue (DR) constituted 15.70 ± 0.19% of the original weight of propolis / extract, with 1.21% relative standard deviation (RSD). Content of total flavonoids was 1.26 ± 0.02%, with 1.59% RSD (Table 1).

Table 1. Characteristics of propolis extract (PE)

Parameters	Result ± s	RSD (%)
Dry residue (%, w/w)	15.70 ± 0.19	1.21
PH	4.89 ± 0.04	0.82
Relative density (g/mL)	0.8541 ± 0.0006	0.06
Content of total flavonoids (%, w/w)	1.26 ± 0.02	1.59

s: standard deviation; RSD: relative standard deviation

Determination of pH

The pH results for monopolymeric formulations are shown in Table 2. They accord with the literature (Rowe et al., 2001). However, the pH of the binary polymeric formulations was corrected to 7.0, for compatibility with the buccal mucosa (Bruschi & De Freitas, 2005).

Table 2. Observed pH of monopolymeric formulations

Formulations		pH		
Polymer	Concentration (%, w/w)	Result	s	RSD (%)
C934P	0.10	3.5	0.1000	2.85
	0.15	3.5	0.1000	2.85
	0.20	3.5	0.1000	2.85
	0.25	3.5	0.1000	2.85
GELA	0.50	5.5	0.1000	1.81
	0.75	5.3	0.2000	3.77
	1.0	51	0.1000	1.96
P407	10	5.7	0.2000	3.50
	15	5.9	0.1000	1.69
	20	6.1	0.1000	1.63

s: standard deviation; RSD: relative standard deviation

Determination of gelation temperature

The formulations described in this study were easy to prepare and variation of the contents of P407, C934P or GELA in the structure of these products provided them with a wide range of consistency, as observed. Moreover, in view of the thermosensitive properties of P407, the binary formulations were subjected to determination of $T_{sol/gel}$. Only the formulations containing 15% P407 and 0.20% C934P or 1.0% GELA displayed a $T_{sol/gel}$ suitable for application to the buccal mucosa, between 29 and 30°C. In fact, all formulations containing 10% P407 failed to gel at all (Table 3).

Rheological characterisation

The flow properties of monopolymeric formulations were determined at 20°C and rheograms were plotted of viscosity (Pa.s) versus velocity rate (rpm), showing a nonlinear response. All the monopolymeric formulations containing C934P exhibited shear-thinning behaviour (pseudoplastic flow) with thixotropy. It was also observed that viscosity increased with increasing C934P concentration (Figure 1).

Table 3. Gelation temperature ($T_{sol/gel}$) of the binary polymeric formulations

Formulations		$T_{sol/gel}$		
Polymers	Concentration (%, w/w)	Result	s	RSD (%)
P407/C934P	10/0.10	NG	-	-
	10/0.15	NG	-	-
	10/0.20	NG	-	-
	10/0.25	NG	-	-
	15/0.10	31.23	0.2517	0.81
	15/0.15	30.33	1.0408	3.43
	15/0.20	29.00	0.8660	2.99
	15/0.25	28.17	1.5275	5.42
	20/0.10	23.33	1.1547	4.95
	20/0.15	21.83	0.2887	1.32
	20/0.20	19.33	0.5774	2.99
	20/0.25	16.00	0.0000	0
P407/GELA	10/0.50	NG	-	-
	10/0.75	NG	-	-
	10/1.00	NG	-	-
	15/0.50	37.67	1.5275	4.06
	15/0.75	33.00	1.0000	3.03
	15/1.00	30.00	1.0000	3.33
	20/0.50	20.33	0.5774	2.84
	20/0.75	23.00	1.0000	4.35
	20/1.00	22.00	1.0000	4.55

s: standard deviation; RSD: relative standard deviation; NG: no gelation

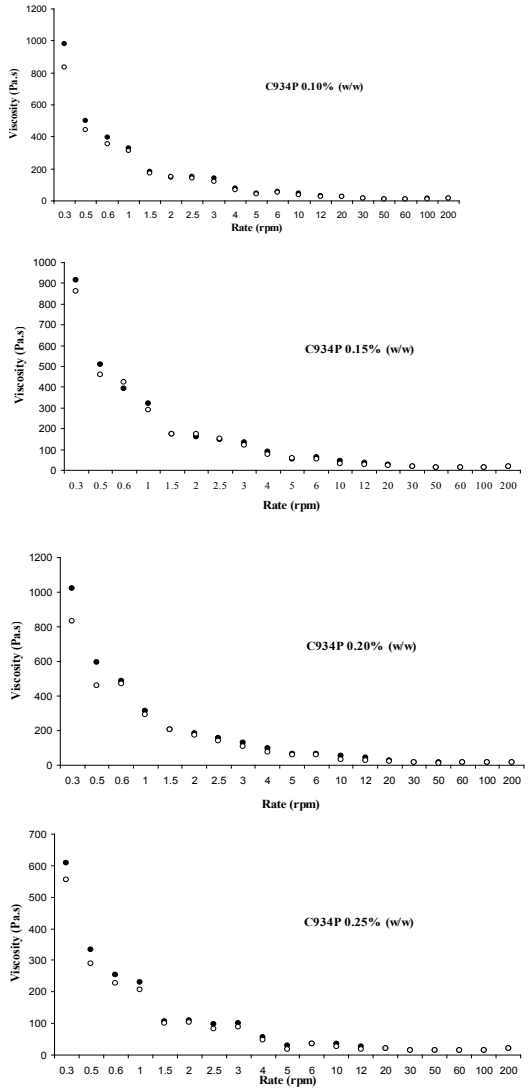

Figure 1. Flow rheograms of monopolymeric formulations containing C934P at 20°C. Filled symbols show the upcurve and empty symbols the downcurve. Standard deviations have been omitted for clarity; however, in all cases the coefficient of variation of at least 3 replicate tests was less than 5%.

GELA-monopolymeric formulations exhibited similar rheological properties to C934P-monopolymeric formulations, namely pseudoplastic flow and thixotropy (Figure 2). However, in this case, the thixotropy area tends to decrease with increasing GELA concentration. It was also observed that increasing the concentration of GELA by 0.25% increased the final viscosity by more than 100%.

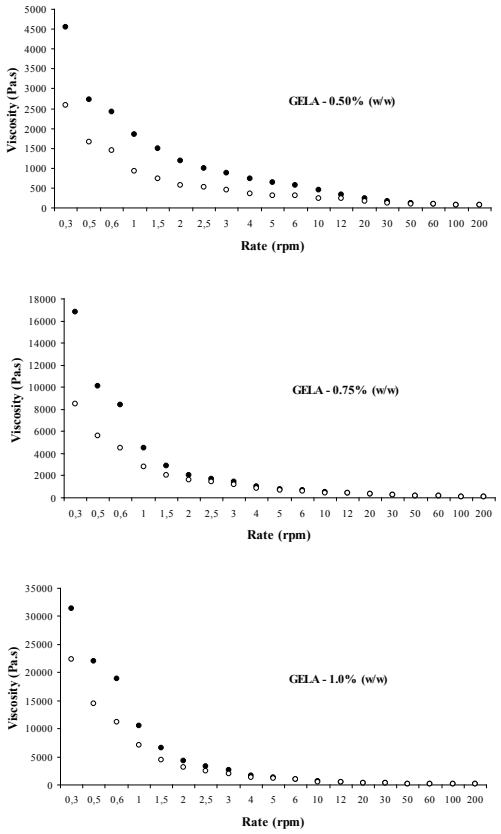

Figure 2. Flow rheograms of monopolymeric formulations containing GELA at 20°C. Filled symbols show the upcurve and empty symbols the downcurve. Standard deviations have been omitted for clarity; however, in all cases the coefficient of variation of at least 3 replicate tests was less than 5%.

P407-monopolymeric formulations exhibited pseudoplastic flow and rheopexy (Figure 3). The rheopexy area tended to increase as the P407 concentraion increased.

Similar results were obtained for binary polymeric formulations containing P407 with C934P or GELA, which exhibited pseudoplastic flow. The flow properties of binary polymeric formulations, with and without PE, are displayed graphically in Figures 4 and 5.

Assessment of mucoadhesive strength

The mucoadhesive properties of the binary polymeric formulations P407/C934P 15/0.20% (w/w) and P407/GELA 15/1.0% (w/w), with and without propolis, were examined by a tensile test in which a partially hydrated mucin disc was employed as the model substrate. As the strength of the cohesive bonds within these formulations was lower than the semisolid–mucin adhesive bonds, direct measurement of their mucoadhesion could not be performed.

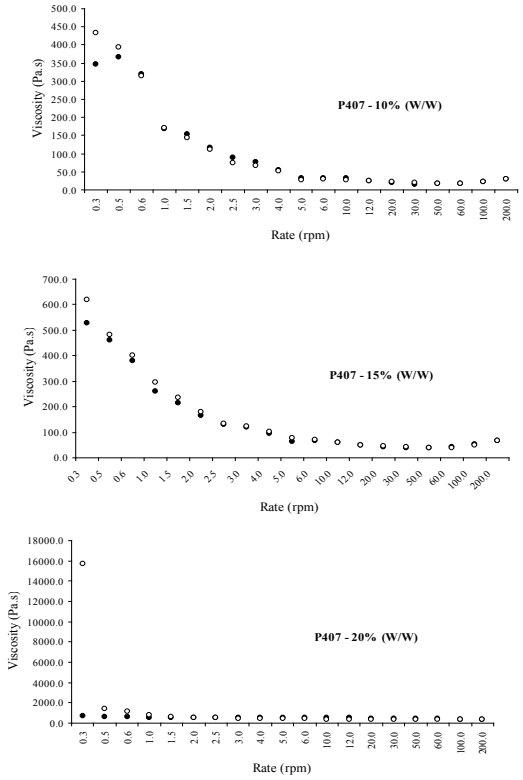

Figure 3. Flow rheograms of monopolymeric formulations containing P407 at 20°C. Filled symbols show the upcurve and empty symbols the downcurve. Standard deviations have been omitted for clarity; however, in all cases the coefficient of variation of at least 3 replicate tests was less than 5%.

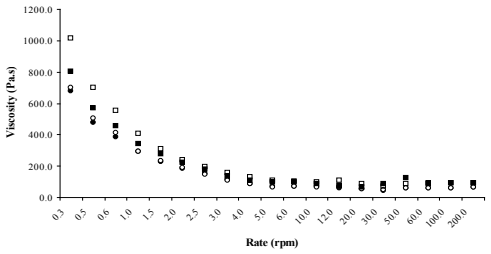

Figure 4. Flow rheograms of binary polymeric formulations P407/GELA (15/1.0%, w/w) at 20ºC, without (□) and with (○) propolis extract. Filled symbols show the upcurve and open symbol the downcurve. Standard deviations have been omitted for clarity; however, in all cases the coefficient of variation of at least 3 replicate tests was less than 5%.

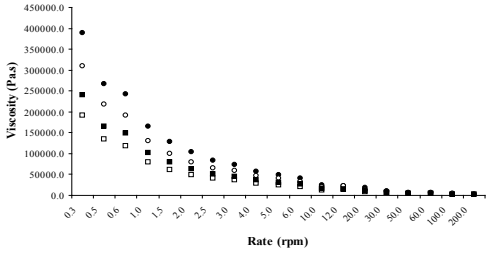

Figure 5. Flow rheograms of binary polymeric formulations P407/C934P (15/0.20%, w/w) at 20ºC, without (□) and with (○) propolis extract. Filled symbols show the upcurve and open symbol the downcurve. Standard deviations have been omitted for clarity; however, in all cases the coefficient of variation of at least 3 replicate tests was less than 5%.

DISCUSSION

The application of antimicrobial or anti-inflammatory agents is very important in the treatment of oral cavity disorders, in particular neoplasia, periodontal diseases, bacterial and fungal infections, aphthae and stomatitis (Bruschi & Freitas, 2005; Jones et al., 2009). Thus, ethanolic extract of propolis has been much used against these disorders (Burdock, 1998; Bruschi et al., 2008). Formulations designed for delivery to the oral mucosa should eliminate the inflammation and/or prevent the colonization of the site with pathogenic microorganisms (Bruschi & Freitas, 2005). Thus, the ideal candidate formulation for the controlled delivery of an agent to the oral mucosa should exhibit a variety of characteristics. These include ease of application and retention in the mucosa, controlled (prolonged) drug release, ease of manufacture and eventual clearance from the periodontal pocket by product biodegradation and/or dissolution. While there have been several reports of controlled drug delivery systems for the treatment of oral diseases (Ali et al., 2002; Vivien-Castionia et al., 2000; Bruschi & Freitas, 2005), few of those containing propolis have an ideal product profile (Bruschi et al., 2007; 2008). Moreover, thermoresponsive mucoadhesive systems facilitate the application and improve the intimacy of contact and retention time of the formulation in the oral mucosa (Gu et al., 1988; Smart, 2005). Therefore, this study reports the formulation of semisolid devices based on a combination of poloxamer 407, a thermoresponsive polymer, with Carbopol 934P or gelatin (highly mucoadhesive polymers). Crucially, the concentrations of binary-mixture components were chosen for their capacity to undergo gelation at the buccal temperature, safety, lack of irritancy, and biodegradation/dissolution (Jones et al., 2009). Furthermore, propolis is safe to use and has shown activity against oral pathogens (Burdock, 1988; Bruschi et al., 2006).

The flavonoids constitute a very important class of polyphenols, widely present in propolis (Bruschi et al., 2006), to which are attributed most of propolis' biological activities (Burdock et al, 1998). The evaluation of PE showed it to be of good quality, indicating that the extract could be used in the development of mucoadhesive formulations (Bruschi et al., 2002).

Monopolymeric and binary polymeric formulations were prepared without problems or difficulties. The formulations were then subjected to physicochemical characterisation. Only those containing 15% P407 and 0.20% C934P or 1.0% GELA yielded homogeneously dispersed preparations with $T_{sol/gel}$ between 29 and 30°C. This temperature interval is suitable for application of the sol formulation, as it undergoes gelation near the temperature of oral mucosa (Bruschi & Freitas, 2005). Thus, only P407/C934P containing 15/0.20% and P407/GELA containing 15/1.0% were tested further.

The flow properties of monopolymeric and binary polymeric formulations, at 20°C, are displayed graphically in Figures 1 to 5. In the development of topical formulations for the oral cavity, these properties determine the ease of administration and the (time-dependent) recovery of the product following administration (Bruschi et al., 2007). In continuous shear rheometry, P407

monopolymeric formulations exhibited shear-thinning behaviour (pseudoplastic flow) with rheopexy. Despite the controlled temperature of rheological analysis, a fractional increase of temperature may have occurred, increasing the interactions between P407 chains and increasing the viscosity on the downcurve (return) (Kabanov et al., 2002). Binary polymeric systems, both with and without PE, exhibited shear-thinning behaviour (pseudoplastic flow). Moreover, the formulation P407/C934P (15/0.20%), with and without PE, exhibited low degrees of thixotropy. These nonlinear responses to shear stresses exhibited by the formulations resulted from structural changes caused by shearing. Probably, the formulations consisted primarily of highly entangled long-chain polymer molecules in a relaxed state. On exposure to a shear stress, the polymer chains disentangled and became aligned along the direction of shear, releasing the solvent that had been previously trapped in the molecular coils. As a result, subsequent shearing occurred more readily and the apparent viscosity was decreased (Bruschi et al., 2007). Shear thinning is a desirable property in formulations intended for application to the oral mucosa (Bruschi & Freitas, 2005). For example, during spreading, at high rates of shear, the material will flow readily, facilitating successful clinical administration. However, under the conditions of low shear experienced subsequently in the oral mucosa, the material will adopt the higher consistency that it possessed before administration. As the pre-administration temperature of the binary systems will be up to 25°C and the oral cavity temperature is between 34 and 37°C (Bruschi & Freitas, 2005; Bruschi et al., 2007), the recovery of the original rheological properties of formulations will take place together with the gelation of the system. The viscosities observed at 20°C for the binary formulations with and without PE indicate that restoration of the relaxed molecular configuration resulted in a greater apparent viscosity and required only a short time after removal of the shearing stress. Moreover, binary formulations containing C934P exhibited higher viscosities than those containing GELA, indicating a greater interaction between P407 and C934P, as previously described (Jones et al., 2009). Furthermore, the low degree of thixotropy of P407/C934P formulations (with or without PE) also indicates a short time for restoration of the relaxed molecular configuration. These attributes are desirable in formulations designed for delivery to the oral mucosa, as they enhance retention within this environment (Bruschi et al., 2007).

The mucoadhesive properties of these systems could not be assessed. Fragments of formulation were found to remain adhered to the mucin disc at some places, due to cohesive failure of the sample and of the sample/mucin interface. These results were more evident for binary formulations containing GELA. It is known that C934P and GELA exhibit great mucoadhesiveness (Matsuda et al., 1999; Bruschi & Freitas, 2005; Jones et al., 2009). Bruschi et al. (2007) tested the mucoadhesive properties of binary polymeric formulations containing P407 and C934P. They reported that only formulations containing 0.25% (w/w) of C934P were suitable to undergo this test and the vertical detachment force needed to break the mucoadhesive bond of the formulation was significantly decreased by the addition of PE. Therefore, this test was deemed to be unsuccessful.

This paper reports the development and characterisation of semisolid systems designed for delivery of propolis in the oral cavity. The pH, gelation temperature, rheological and mucoadhesive properties of these systems were studied and shown to be beneficial for easy application of the candidate formulations. These results indicate that it is possible to select formulations with suitable properties for topical administration in the oral cavity.

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RESUMO

Desenvolvimento e caracterização de sistemas semi-sólidos para liberação de própolis na cavidade bucal

Formulações farmacêuticas contendo poloxamer 407 (P407), Carbopol 934P (C934P) ou gelatina (GELA), e extrato de própolis (EP) foram desenvolvidos para o tratamento de doenças da mucosa oral. EP foi produzido e sua qualidade foi avaliada quanto ao resíduo seco e ao teor de flavonóides totais. Formulações monopoliméricas e poliméricas binárias foram produzidas e a temperatura de gelificação ($T_{sol/gel}$), o pH, a reologia, assim como a mucoadesão das mesmas foram avaliados. O EP apresentou boa qualidade, as preparações foram fáceis de produzir e apresentaram uma ampla variação de consistência. A maioria das preparações apresentou comportamento de resposta térmica e apenas as formulações contendo 15% P407 e 0,20% C934P ou 1,0% GELA apresentaram $T_{sol/gel}$ adequada para a administração na mucosa oral. Formulações monopoliméricas, contendo C934P ou GELA, e binárias exibiram comportamento de fluxo pseudoplástico e baixo grau de tixotropia. Formulações monopoliméricas de P407 exibiram fluxo pseudoplástico e reopexia. As propriedades mucoadesivas dos sistemas não puderam ser avaliadas. Fragmentos de formulações foram encontrados aderidos em alguns lugares do disco de mucina devido à falha de coesão das amostras e da interface amostra/mucina. Os resultados obtidos com essas formulações indicam a utilidade das mesmas no tratamento de doenças da mucosa oral.

Palavras-chave: Própolis. Mucoadesão. Poloxamer 407. Carbopol 934P. Gelatina.

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