European Journal of Pharmaceutics and Biopharmaceutics 79 (2011) 458–463

Contents lists available at ScienceDirect

European Journal of Pharmaceutics and Biopharmaceutics

journal homepage: www.elsevier.com/locate/ejpb

Research paper

Dynamic mechanical thermal analysis of hypromellose 2910 free films

Marco Cespi [a], Giulia Bonacucina [a], Giovanna Mencarelli [a], Luca Casettari [b], Giovanni Filippo Palmieri [a,*]

[a] University of Camerino, School of Pharmacy, Camerino (MC), Italy
[b] University of Urbino, Department of Biomolecular Sciences, Urbino (PU), Italy

ARTICLE INFO

Article history:
Received 10 February 2011
Accepted in revised form 23 May 2011
Available online 30 May 2011

Keywords:
Hypromellose (HPMC)
Dynamic mechanical thermal analysis
DMA TDMA
Glass transition
Activation energy
Coating films

ABSTRACT

It is common practice to coat oral solid dosage forms with polymeric materials for controlled release purposes or for practical and aesthetic reasons. Good knowledge of thermo-mechanical film properties or their variation as a function of polymer grade, type and amount of additives or preparation method is of prime importance in developing solid dosage forms. This work focused on the dynamic mechanical thermal characteristics of free films of hypromellose 2910 (also known as HPMC), prepared using three grades of this polymer from two different manufacturers, in order to assess whether polymer chain length or origin affects the mechanical or thermo-mechanical properties of the final films. Hypromellose free films were obtained by casting their aqueous solutions prepared at a specific concentrations in order to obtain the same viscosity for each. The films were stored at room temperature until dried and then examined using a dynamic mechanical analyser. The results of the frequency scans showed no significant differences in the mechanical moduli E' and E'' of the different samples when analysed at room temperature; however, the grade of the polymer affected material transitions during the heating process. Glass transition temperature, apparent activation energy and fragility parameters depended on polymer chain length, while the material brand showed little impact on film performance.

1. Introduction

Most of the oral solid dosage forms currently available on the market are coated with polymeric materials, making the coating procedure a crucial step in the manufacturing process. Coating films are used for several purposes, such as modifying release, affording gastroprotection, protecting tablets from environmental agents, masking unpleasant taste or just enhancing product aesthetics.

The physical and mechanical properties of polymeric films are fundamental for their performance. The release properties and the integrity of the final dosage forms during packaging, storing and shipping are all issues strongly influenced by the physical and mechanical features of the polymeric coating.

There are many papers in the literature on the mechanical properties of free films and their relation to polymer type [1–4], quantity and quality of additives [1,2,5–8], preparation methods or drying techniques [1,4,9]. Most of the papers deal with measuring the mechanical properties using the tensile tester and classical tests such as indentation, stress-strain, puncturing or transient mechanical tests (creep or stress relaxation). A detailed description of these kinds of tests for free film characterisation is offered in reviews by Aulton [10] and Felton et al. [11].

A very powerful alternative to traditional methods is dynamic mechanical thermal analysis (TDMA or DMA). This technique applies an oscillating stimulus (load or deformation) to a sample and analyses the response of the material. From the raw data, mechanical parameters such as storage modulus (E'), loss modulus (E'') and damping (the tangent of the phase angle tan d) can be determined and used to characterise the material properties. DMA can work scanning temperature, the amplitude or frequency of the stimulus or simply its extent [12]. Although DMA is an essential approach in many scientific areas involving materials characterisation, it is still largely underused in the pharmaceutical field. Up to now, DMA has been used in the analysis of film viscoelasticity and temperature-induced transitions [13–16], in the characterisation of the mechanical properties of pellets [17,18] or in the measurement of glass transition temperatures of powdered materials [19,20].

Hypromellose (formerly known as hydroxypropylmethylcellulose, HPMC) 2910 represents one of the more widespread polymer in pharmaceutical film coating, used mainly for aesthetic and protective reasons. Despite its wide use in the last 20–30 years as a polymer coating, there is still a lack of information concerning the film properties compared to those of the powder form.

Thus, aim of this work is to perform a complete thermo-dynamic-mechanical analysis of hypromellose 2910 free films, taking into account several grades available by the two main world manufacturers.

A deep knowledge of films mechanical and thermal properties, together with its variation according to the polymer length, is

* Corresponding author. University of Camerino, School of Pharmacy, Via S. Agostino 1, I-62032 Camerino (MC), Italy. Tel.: 737 402289; fax: 737 637345.
E-mail address: gianfilippo.palmieri@unicam.it (G.F. Palmieri).

0939-6411/$ - see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.ejpb.2011.05.008

crucial in order to better formulate coating system used for solid oral dosage forms or any other products requiring the use of this polymeric films.

2. Materials and methods

2.1. Materials

Three different grades of hypromellose 2910 were selected in order to cover the entire range of viscosity types (or molecular weight) available from the two major suppliers. Methocel E6 premium LV, Methocel E15 premium LV and Methocel E50 premium LV (Colorcon, Dartford England) were supplied by Colorcon S.r.l. (Gallarate, Italy), while Pharmacoat 606, Pharamacoat 615 and Metolose 60 SH 50 (Shin-Etsu Chemical Co., LTD, Tokyo, Japan) were supplied by Seppic Italia Srl (Milan, Italy). The physico-chemical properties of the polymers are summarised in Table 1.

2.2. Preparation of polymer solutions

All the hypromellose solutions were prepared using the 'hot/cold' technique [23], by dispersing the polymer in one-third of the required amount of hot water (80 °C), then adding the remaining amount of cold water, under magnetic stirring until a clear viscous solution was obtained. All the solutions were left at 5 °C for at least 24 h before being analysed.

Solutions were prepared in the concentration range 2–10% w/w for each hypromellose viscosity type.

2.3. Flow curves of the solutions

Flow curves were determined with a controlled stress rheometer (StressTech, Reologica) using steel cone–plate geometry (C40/4). Shear stress was increased from 0.01 to 50 Pa and the corresponding shear rate measured, at a constant temperature of 20 °C.

Each sample was analysed in triplicate.

2.4. Preparation of the free films

Free films were obtained by casting aqueous hypromellose solutions at a suitable concentration (determined by viscosity analysis). For each viscosity grade, a different amount of solution was cast on a glass surface, in order to obtain a dry polymeric disc of equal weight and thickness (280 μm ± 5%). The discs were dried on a glass surface at ambient conditions until no decrease of weight was recorded. Once the discs were dried, they were removed from the glass surface and cut into regular rectangular samples (9.5 × 20 mm) using a guillotine cutter specifically modified for this purpose.

2.5. Thermogravimetric analysis of free films

The real water content of samples was determined by thermogravimetric analysis using an STA 6000 (Perkin Elmer, USA). For each viscosity and brand type, approximately 5–20 mg of samples were placed in aluminium crucibles and the weight loss analysed from 25 to 250 °C at a rate of 10 °C/min under nitrogen atmosphere.

2.6. Dynamic mechanical analysis of free films

The thermo-mechanical properties of the free films were analysed using a DMA 8000 (Perkin Elmer, USA) equipped with a closed furnace. All the tests were performed in bending mode, using dual cantilever geometry. All the free films were analysed using the following tests:

- Strain sweep: This test determines the linear viscoelastic region (LVR) of the samples, and therefore provides information for choosing the strain value to use in the other tests. The test was performed at 25 °C and at a constant frequency of 1 Hz, increasing the deformation amplitude from 1 to 100 μm.
- Frequency sweep: The test highlights the time-dependent behaviour of the samples under study. This analysis was performed at constant temperature (25 °C) by applying a fixed deformation amplitude (within the LVR) and increasing the frequency from 0.1 to 100 Hz.
- Temperature sweep: This test allows the study of the temperature-dependent behaviour of the samples and the analysis of possible temperature-dependent transitions such as melting, glass transitions (Tg or $T\alpha$) or sub-Tg transitions ($T\beta$ and $T\gamma$) [24]. The tests were carried out by applying a constant deformation amplitude (within the LVR) and increasing the temperature from 25 to 200 °C at a scanning rate of 3 °C/min. All the tests were performed in multifrequency mode (1, 2.5, 5 and 10 Hz), in order to highlight the time dependency of the transitions.

All the samples were analysed in triplicate.

3. Results and discussion

3.1. Viscosity of polymer solutions

The shear stress/shear rate curves obtained by the rheometer were analysed by the well-known power law equation:

$$\sigma = k\dot{\gamma}^n \quad (1)$$

where σ is the shear stress, $\dot{\gamma}$ the shear rate, k the consistency index and n the power law index.

The power law equation is an easy rheological model able to describe the flow of Newtonian and many non-Newtonian systems. The consistency index k, also called power law viscosity, is related to the system viscosity, while the power law index n is related to

Table 1
Physico-chemical properties of the polymers used in the work. Data are collected by the manufacturers' notes [21,22].

Polymer	Manufacturer	Degree of substitution (% W/W)		Labelled viscosity[a] (mPa s)
		Methoxy	Hydroxypropyl	
METHOCEL E6	Colorcon	28–30	7–12	6
METHOCEL E15	Colorcon	28–30	7–12	15
METHOCEL E50	Colorcon	28–30	7–12	50
PHARMACOAT 606	Shin-Etsu	28–30	7–12	6
PHARMACOAT 615	Shin-Etsu	28–30	7–12	15
METOLOSE 60SH50	Shin-Etsu	28–30	7–12	50

[a] The viscosity of the polymers is referred to the viscosity of 2% water dispersions at 20 °C.