Journal of Pharmaceutical and Biomedical Analysis 112 (2015) 85–88

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

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

Short communication

Evaluation of the swelling behaviour of iota-carrageenan in monolithic matrix tablets

András Kelemen[a], Gyula Buchholcz[b], Tamás Sovány[c], Klára Pintye-Hódi[c,*]

[a] Department of Applied Informatics, University of Szeged, Boldogasszony sgt. 6, H-6725 Szeged, Hungary
[b] Central Clinical Pharmacy, University of Debrecen, Nagyerdei krt 98, H-4032 Debrecen, Hungary
[c] Department of Pharmaceutical Technology, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary

ARTICLE INFO

Article history:
Received 9 February 2015
Received in revised form 14 April 2015
Accepted 17 April 2015
Available online 24 April 2015

Keywords:
Monolithic matrix tablet
Biodegradable polymer
Biomaterials
Iota-carrageenan
Swelling force meter
Swelling kinetics

ABSTRACT

The swelling properties of monolithic matrix tablets containing iota-carrageenan were studied at different pH values, with measurements of the swelling force and characterization of the profile of the swelling curve. The swelling force meter was linked to a PC by an RS232 cable and the measured data were evaluated with self-developed software. The monitor displayed the swelling force vs. time curve with the important parameters, which could be fitted with an Analysis menu. In the case of iota-carrageenan matrix tablets, it was concluded that the pH and the pressure did not influence the swelling process, and the first section of the swelling curve could be fitted by the Korsmeyer–Peppas equation.

1. Introduction

In the past decade, swellable matrices have become a popular solid dosage form for controlled release drug delivery systems. For both conventional tablets and swellable matrices, the rate of disintegration determines the drug release profile, and the swelling force is proportional to the rate of disintegration. Study of the swelling behaviour of swellable matrices therefore plays an important role in the prediction of the drug release profile. Different methods have been applied to study the swellability or water uptake of polymers [1–6].

We earlier developed a swelling force meter with appropriate software for evaluation of the swelling behaviour of conventional tablets which contain disintegrants (e.g. corn starch or different types of modified starches). These excipients cause the rapid disintegration of the tablets. The mechanism of disintegration is influenced by different factors, among them the water uptake and the swelling force playing important roles. This swelling force meter and its software may be applied for the measurement of swelling force and also calculation of the kinetics of swelling [7]. In the most common cases, the swelling kinetics of these disintegrants can be described by RRSBW (Rosin–Rammler–Sperling–Bennett–Weibull, or simply Weibull) distribution (Eq. 1):

$$M(t) = M_\infty(1 - e^{-(t-T)^\beta/a}) \quad (1)$$

where $M(t)$ is the swelling force as a function of time t, M_∞ is the maximum value of the swelling force, T is a lag time, a is a scale parameter that describes the time dependence, and β describes the shape of the swelling force curve. This empirical distribution was adopted in dissolution studies by Langenbucher [8] and was extensively used more than 30 years ago. However, the swelling behaviour of matrix systems follows other kinetics. Various mathematical models (e.g. those of Noyes–Whitney, Korsmeyer–Peppas, Higuchi, etc.) are used in the literature to describe the profile of drug release from matrices. The Korsmeyer–Peppas or power law model (Eq. 2) is commonly used:

$$\frac{M(t)}{M_\infty} = kt^n \quad (2)$$

where $M(t)$ is the accumulated mass of drug released at time t, M_∞ is the maximum amount of drug released, n is a shape parameter and k is a release rate constant [9,10].

The matrix tablets did not disintegrate, but in the case of a swellable matrix the swelling force plays an important role in the dissolution process. For determination of the swelling force of

* Corresponding author. Tel.: +36 62 545 576; fax: +36 62 545 571.
E-mail address: klara.hodi@pharm.u-szeged.hu (K. Pintye-Hódi).

http://dx.doi.org/10.1016/j.jpba.2015.04.025
0731-7085/

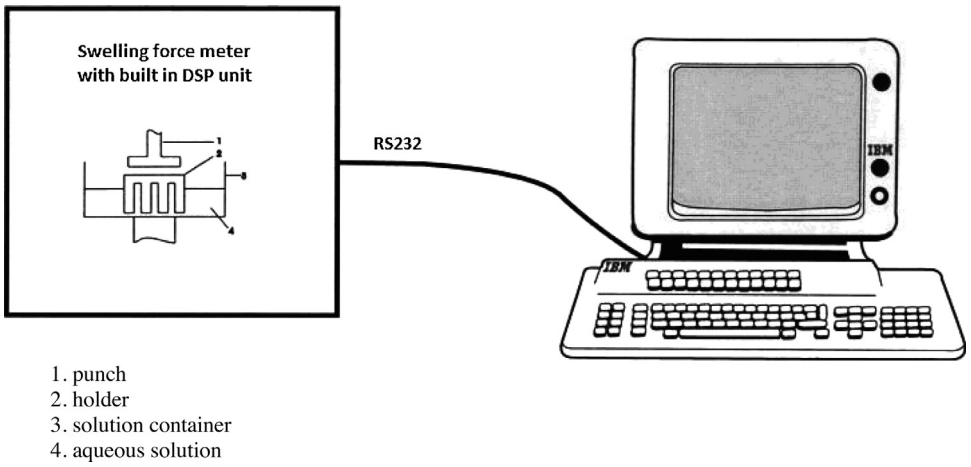

Fig. 1. Experimental set-up of the swelling force meter [7].

matrix tablets, the development of new software was necessary. It is well known from the literature that matrix dissolution can be described by the Korsmeyer–Peppas model [9,11].

In the present study, therefore, we focus on use of the Korsmeyer–Peppas model to describe the swelling behaviour of swellable matrices with the aid of the new software.

2. Solvent uptake study

When a tablet comes into contact with an aqueous solution, the solution penetrates into the tablet and fills the porous gaps at the start of the liquid uptake process. Simultaneously with this process, the solution penetrates into the disintegrants. This transfer process is based on Fick's second law of diffusion in cylindrical coordinates:

$$\frac{\partial c}{\partial t} = \left(\frac{1}{r}\frac{\partial}{\partial r}\left(rD\frac{\partial c}{\partial r}\right) + \frac{1}{r}\frac{\partial}{\partial \theta}\left(\frac{1}{r}D\frac{\partial c}{\partial \theta}\right) + \frac{\partial}{\partial z}\left(rD\frac{\partial c}{\partial z}\right)\right) \quad (3)$$

where t is time, c and D are the concentration and diffusion coefficient of the aqueous solution, r denotes the radial coordinate, z is the axial coordinate, and Θ is the angle perpendicular to both axes.

3. Materials and methods

3.1. Material

Iota-Carrageenan (Gelcarin GP 379) (FMC BioPolymer, Philadelphia, USA) was used as swellable matrix material.

3.2. Methods

Swelling force was measured with equipment developed in our laboratory (see below). Tablets were prepared at different pressures (see below) and their swelling was tested in hydrochloric acid of pH 1.2 and in phosphate buffer of pH 4.5. The temperature applied was 37 °C and the duration of measurements was 30 min. Five parallels were measured.

3.3. Tableting

Tablets were prepared with a Korsch EK0 eccentric tableting machine equipped with strain gauges and a displacement transducer. The strain gauges were calibrated with a Wazau HM-HN-30kN-D cell (Kaliber Ltd., Budapest, Hungary), which allowed measurement of the compression forces on the upper and lower punches. The displacement transducer (Micropulse, BTL5-A11-M0050-P-532, Balluff, Neuhausen/Filder, Germany) was fitted over the upper punch. The applied compression force was 5, 10 or 15 kN.

3.4. Swelling

The measurement is performed with a Sartorius microbalance with electronic compensation, which is built into the equipment with the DAQ hardware. The built-in DAQ unit is based on a PIC16F871-I/P microcontroller. The Sartorius balance and the temperature sensor are connected to the ADC channel 0 and channel 1, respectively. The equipment is linked to a PC via an RS232 cable as shown in Fig. 1.

The tablet-holder is a copper cylinder 10 mm in diameter with slits in the side, into which a copper punch with the same diameter is fitted. The tablet is placed in the holder, the equipment heats the aqueous solution to the desired temperature, the liquid is injected and measurements are started.

The aqueous solution penetrates into the tablet through the slits. The force that builds up inside the comprimate as it absorbs the liquid is transmitted vertically and is detected by the built-in Sartorius balance. During the measurement, the embedded software uses the timer interrupt for the DAQ from the ADC channels. [8]

3.5. Data analysis

Software was developed for data acquisition, evaluation and demonstration of the swelling process. The monitor displays the swelling force vs. time curve with the important parameters (the swelling force and the characteristic swelling time ($t_{63.2\%}$)). An Analysis menu facilitates fitting of the swelling curve.

4. Results and discussion

In earlier work in which the swelling properties and swelling forces of different disintegrants were tested, it was concluded that in the case of disintegrating tablets the swelling curve can be fitted by the RRSBW equation (Eq. 1), and the swelling process can be characterized by the RRSBW model [7,8].

In the present work, we studied the swelling properties of matrix tablets. Matrix tablets may contain swellable, non-swellable or erodable polymers [12]. In the case of swellable matrix tablets, the swellability is an important factor influencing the process of release of the API. When oral tablets pass into the stomach, their swelling or disintegration generally influences the dissolution of the API from the tablet. However, matrix tablets do not disintegrate.