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International Journal of Pharmaceutics 330 (2007) 195–198
INTERNATIONAL JOURNAL OF PHARMACEUTICS
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Note

A novel texture-probe for the simultaneous and real-time measurement of swelling and erosion rates of matrix tablets

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Received 15 May 2006; received in revised form 2 August 2006; accepted 29 August 2006
Available online 6 September 2006

Abstract

In this note, a novel probe fitted to a texture analyzer was described. This probe has the ability to simultaneously measure, in real-time, dimensional changes in the swollen layer and the glassy core of hydrophilic matrices when exposed to aqueous dissolution media. The utility of this probe was demonstrated on directly compressed tablets containing polymer blends, a water soluble additive, and theophylline as a model drug. Both the erosion and swelling fronts were measured for the same tablet every hour for 12 h. The probe provided accurate thickness data of the swollen region and the glassy core, and was able to demonstrate the swelling and subsequent erosion of the tablet with time. With this method, it is possible to simultaneously measure the swelling rate of the rubbery region and the erosion rate of the glassy core without operator intervention, which provides many advantages over the conventional approaches frequently reported in the literature.

Keywords: Hydrophilic matrix; Erosion; Swelling; Dissolution; Texture analysis

Modified release tablet dosage forms based on hydrophilic matrices offer many advantages over conventional dosage forms (Velasco et al., 1993; Sako et al., 2002). They are widely used to control drug release due to their low cost, broad FDA acceptance and favorable in vivo performance (Durig and Fassihi, 2002; Williams et al., 2002). When hydrophilic matrices are exposed to aqueous media, two moving fronts are observed; inward erosion of the non-hydrated glassy core, and the outward swelling of the hydrated polymer and its subsequent inward erosion with time. A schematic representation of the moving fronts of a matrix tablet at time t is given in Fig. 1.

Polymer hydration and swelling play an important role in controlling the rate of drug release from hydrophilic matrices (Alderman, 1984; Bowstra and Junginger, 1993). Therefore, swelling rate and/or change in the thickness of the matrix (tablet) when exposed to the dissolution medium has been frequently reported and cited in the literature. Two methods are commonly used to generate these data. In the first method a tablet is sandwiched between two Plexiglas plates and placed in a dissolution medium. Radial expansion of the constrained plates is then used as an indirect measure of polymer swelling rate (Colombo et al., 1999; Bettini et al., 2001). In the second method a tablet is placed in the dissolution medium. At a given time interval the swollen tablet is removed from the vessel. The thickness of the swollen layer is then measured by a penetration probe fitted to a texture analyzer (Jamazad et al., 2005). The first method is useful as a qualitative and/or indirect method for estimating the swelling tendency of the polymer; however, it fails to provide useful information on the influence of fluid dynamics or the erosion-rate of the glassy core. While the second method provides more precise swelling and erosion data of the outer layer, it does not provide information on the erosion of the glassy core. Furthermore, the destructive nature of the method necessitates the use of a fresh sample at each time point in order to provide much desired time-dependent swelling kinetics, which renders the method both time and labor intensive.

To overcome these drawbacks we developed a novel non-destructive probe which could be adapted to a standard texture analysis instrument. With this probe it is possible to simultaneously measure, in real-time, the swelling and subsequently erosion rates of the tablet's rubbery region and the erosion rate of the tablet's glassy core. A schematic representation of the

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doi:10.1016/j.ijpharm.2006.08.045

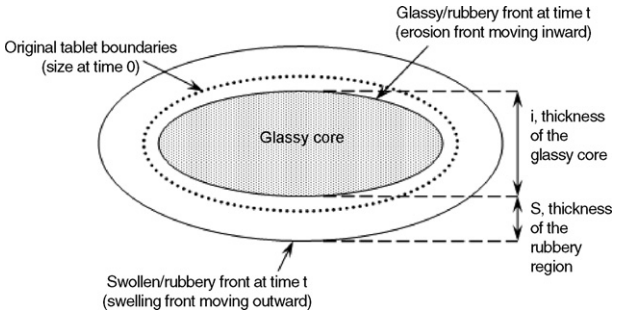

Fig. 1. Schematic representation of the moving fronts in a partially swollen matrix tablet after exposure to an aqueous medium.

probe is shown in Fig. 2. The probe consists of a body through which two supports can freely move. These supports are attached to a circular light plastic plate, which contains a central hole (2 mm diameter) that can expose a non-movable penetration probe when the plate is pushed upward. During analysis, the body of the probe and the circular plastic plate move downward towards the tablet at a rate of 0.5 mm/s. During this movement the plate is held stationary in its position by its weight. The resistance of the dissolution medium to the movement of the plate; however, is not sufficient to trigger the load cell. When the plate reaches a surface, such as the surface of the tablet (at time 0) or the swollen region (at time t), it is forced to stop or to move upwards, as the swollen region continues to expand. This forces the plate-supports to slide through the down-moving body of the probe and trigger the load cell to start recording the resistance force. As the body of the probe continues its downward movement, the penetration probe will pass through the hole in the plate and into the swollen region until it reaches the surface of the tablet (at zero time) or the tablet's glassy core (at time t). The probe will stop and retract to its original position when a maximal nondestructive resistance force of 150 g is reached. This procedure is then automatically repeated multiple times at preset time intervals, which would allow real-time measurement of the change in thickness of the swollen region and the robbery core with time. To demonstrate the utility of this method, a tablet manufactured by direct compression from a blend of Polyox® (MW 6×10^5), Carbopol®, lactose, and theophylline

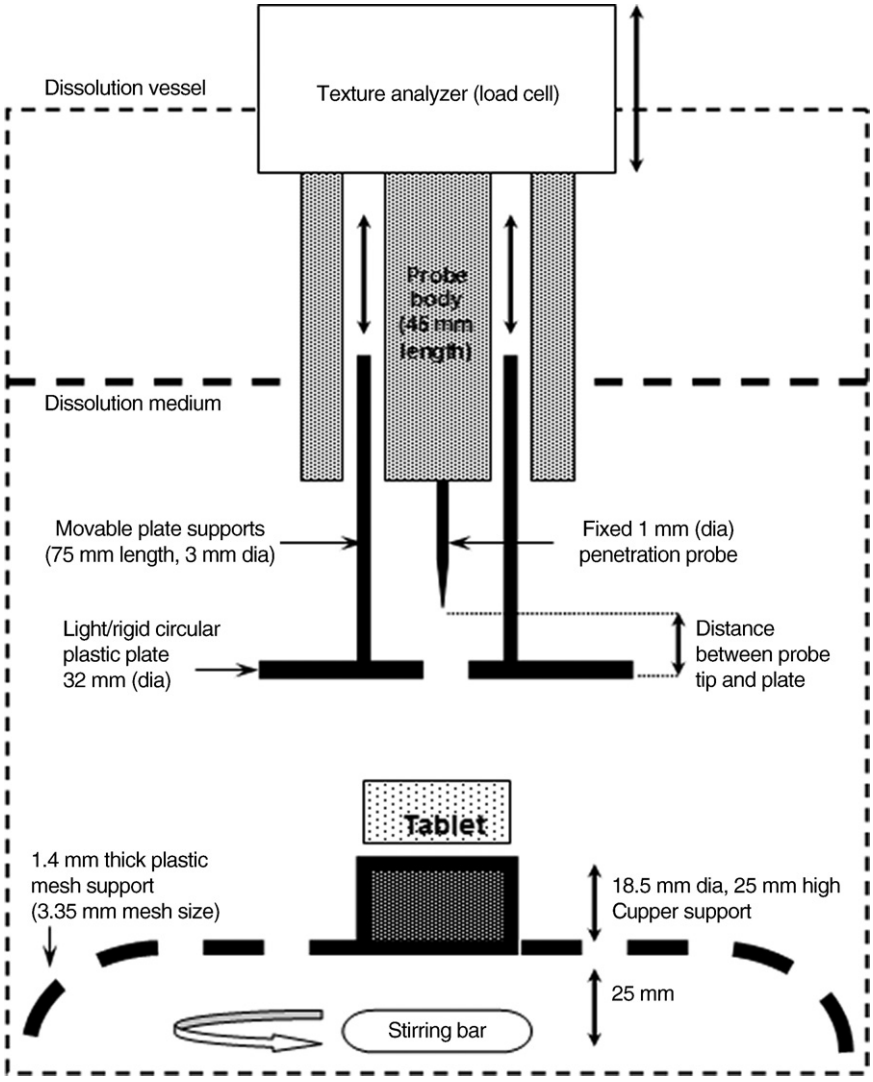

Fig. 2. Schematic representation of the experimental assembly and the novel probe.

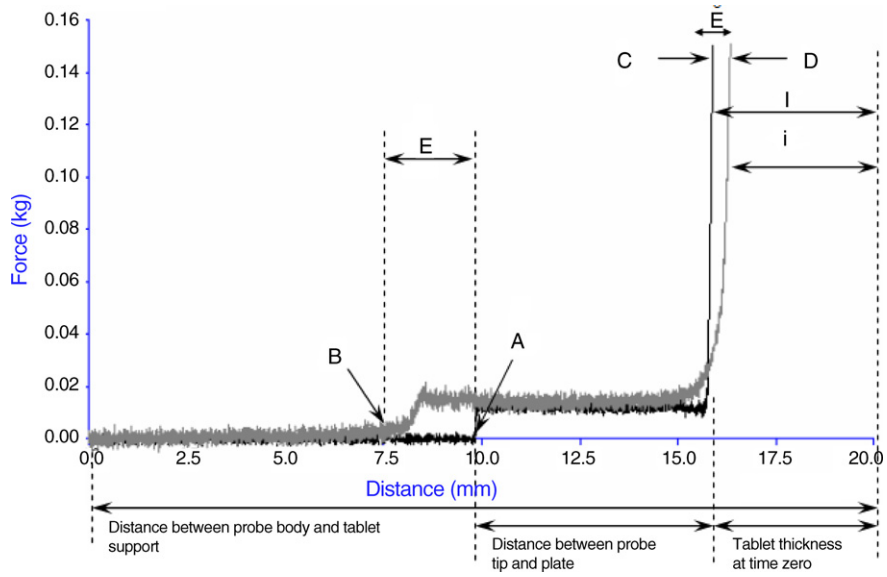

Fig. 3. Representative texture profiles of a matrix tablet at time 0 (black profile) and after 1 h (gray profile).

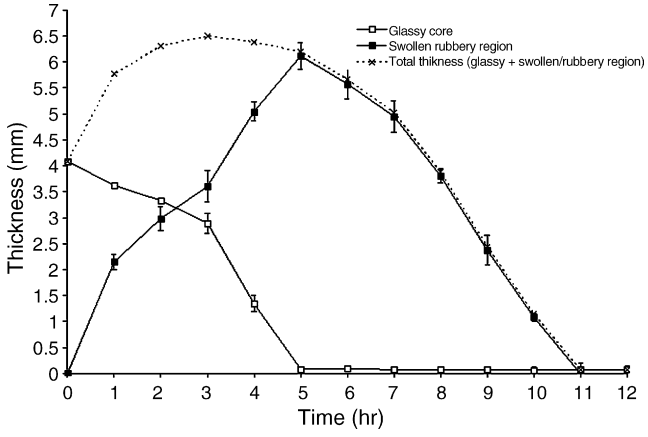

Fig. 4. Relationship between the thickness of the glassy core and the swollen rubbery region with time.

was placed in a vessel containing 900 mL of phosphate buffer at pH 7.4. The texture analyzer (TA.XTPlus, Texture Technologies Corp., Scarsdale, NY/Stable Micro Systems, Godalming, Surrey, UK) was programmed to move the probe and collect the data every 1 h for up to 12 h. The texture profiles at zero time and after 1 h are given in Fig. 3. Points A (black profile) and B (gray profile) represent the distance at which the circular plate reached the surface of the tablet (time 0) or the surface of the swollen region (after 1 h), respectively. Points C and D represent the distance at which the penetration probe reached the surface of the tablet at time 0 or after 1 h, respectively. Since the tablet is positioned on a solid support, only the surface exposed to the dissolution medium will swell/hydrate. Therefore, the thickness of the swollen/rubbery region (S) in one direction (Fig. 1) at any given time (t) can be estimated from the following equation:

$$S = E_{(\text{time zero}-\text{time } t)} + \breve{E}_{(\text{time zero}-\text{time } t)},$$

where $E = |B - A|$ and $\breve{E} = |D - C|$.

The thickness of the tablet's glassy core can be estimated from the following relationship:

$\bar{I} = I - \breve{E}$, where I is the thickness of the tablet at zero time.

Fig. 4 shows the change in the thicknesses of the glassy core and the swollen rubbery region over 12 h using the procedure described above for the same tablet (El-Malah et al., 2006). As seen from the plot the thickness of the glassy core decreased as the swelling and thickness of the rubbery region progressed. The glassy core was completely eroded after 5 h whereas the swollen region reached a maximal thickness of 6 mm after 5 h, after which it started to erode. As shown in the plots, this novel probe was successfully employed to monitor dimensional changes of both the external rubbery region and the internal glassy core for the same sample without operator intervention. The authors believe that this or similar probe assemblies could be used to provide better understanding of the drug release mechanisms and their correlation to polymer swelling and erosion.

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