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Measurements of non-uniform water content in hydroxypropyl-methyl-cellulose based matrices via texture analysis

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ABSTRACT

The use of hydrogels in the preparation of controlled release pharmaceutical forms is extensively diffused. The main feature of these polymers is their ability to swell forming a gel layer when they enter in contact with fluids. Once the gel layer is formed, the drug contained in the matrix can easily diffuse ensuring a controlled release from the tablet. Measurement of water content within a hydrating matrix based on hydrogels is a key topic in the study of pharmaceutical solid dosage forms. The aim of this work is to evaluate the water content of swollen matrices composed by HPMC and theophylline both in axial and in radial direction, as a function of time, using a texture analysis. A relationship between water content and slope of the force–penetration curves has been obtained using a simplified system in which the water uptake is allowed only in radial direction, obtaining thus partially hydrated matrices with the water content varying only along the radial direction. Once the relationship has been validated, it has been applied in a more complex system in which the polymer swelling takes place in both axial and radial direction. Thus, using the texture analysis it has been possible to determine the water in each position within the hydrated matrices.

1. Introduction

Understanding and development of controlled drug delivery systems represents one of the research topics in the pharmaceutical field. In particular, modified release matrix tablets are widely used as one of the most successful oral drug delivery systems. In fact, selection of the appropriate polymer allows to easily prepare matrix tablets able to reproduce the desired release pattern. Use of cellulose derivative, such as HydroxyPropyl MethylCellulose (HPMC), in the preparation of pharmaceutical solid dosage forms is extensively diffused. When this polymer contacts with water, water diffusion through the matrix causes the polymer to swell, as the drug contained in the polymer matrix begins to diffuse in the hydrated hydrogel and it is released in the dissolution medium. When the external polymer layers became extremely hydrated and, thus, subjected to disentanglement and erosion, they start to dissolve in the physiological fluids. Drug release from such polymeric matrix is therefore achieved by diffusion, swelling, erosion, or a combination of all those phenomena.

To the purpose of studying and understanding the mechanisms involved, firstly the swelling process during the water uptake, and then the gel layer formation in the drug diffusion from the tablet, several methods have been used. A method based on image analysis, in which the water mass fraction in a simplified system (the water uptake is allowed only from radial direction, the so called "radial" system) is related to the normalized light intensity profiles has been developed (Chirico, Dalmoro, Lamberti, Russo, & Titomanlio, 2007) and subsequently refined (Barba, d'Amore, Chirico, Lamberti, & Titomanlio, 2009c). A more complete approach to determine the water content for each section of the matrix swollen in the radial direction has been then proposed using gravimetric analysis (Barba, d'Amore, Cascone, et al., 2009) on the same system. Optical image analysis has been adopted to study the dynamic swelling behavior of the HPMC based matrix tablet also by previous researches (Gao & Meury, 1996). This method has been applied to determine the polymer concentration across the gel founding a relationship between the intensity of light scattering and the polymer content. The swelling of hydrating HPMC tablets has been studied also by NMR microscopy (Rajabi-Siahboomi, Bowtell, Mansfield, Henderson, Davies, & Melia, 1994), which is a non-invasive technique. Hydration at the edges of the tablet occurred to a greater extent than in the center of the table surfaces, giving rise to a convex shaped hydrated layer. The same

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authors evaluated the spatial distribution of self-diffusion coefficient founding that the water mobility varies across the gel layer of HPMC (Rajabi-Siahboomi, Bowtell, Mansfield, Davies, & Melia, 1996).

A recent approach in pharmaceutical research and development consists in the study of the correlation between drug release and polymer hydration via texture analysis. A characterization of modified release matrix tablet for different compositions of tablets has been carried on (Li & Gu, 2007). The authors found that drug dissolution from modified matrix tablets was dependent upon drug solubility, hydrogel formation and matrix excipient proportion in the preparation. Moreover, a linear multiple regression was established among drug dissolution, polymer ratio, hydrogel formation and drug solubility (Li, Hardy, & Gu, 2008). In general, variation in the textural and physic-mechanical properties could be associated with changes in gel layer and glassy core (Yang, Johnson, & Fassihi, 1998). In this case, pure polymer has been used to avoid the influence of additives on the gel layer formation and growth. The force-displacement profile is qualitatively indicative of the polymer concentration profile within the swollen region. With this technique, the gel layer thickness could be evaluated during the time. The dynamic of gel layer growth was found to be similar both in axial and radial dimensions and the water penetration front was found to depend on the square power of time. Of course, using the texture analysis, it is possible to identify many variations in the analysis. In particular, a probe able to measure dimensional changes in the swollen layer and in the core of hydrophilic matrices in real time has been developed (Nazzal, Nazzal, & El-Malah, 2007). Both erosion and swelling fronts were measured for the same tablet every hour for 12 h. The probe measures the thicknesses of both the swollen region and the glassy core in the same position in contact with the dissolution medium. A combination of different approaches and techniques could be useful to understand the complex phenomenon of swelling. Thus, four different methods were applied to study swelling of the tablets: determination of the expansion factor, texture analysis, visual swelling observation of dye containing tablets (sandwiched between Plexiglas®) discs and photomicroscopy (Zuleger, Fassihi, & Lippold, 2002). Although these methods are not singularly able to determine all the phenomena involved, their combination allows the investigation of dimensional changes, swelling velocity, thickness, appearance and strength of the gel layer, and of the front movements. The authors found a good agreement in the results obtained by the different techniques. Another approach consists in the evaluation of the water concentration profiles inside the gel layer from magnetic resonance microimaging data used in combination with a texture analysis (Kaunisto et al., 2010). This method has been used to study the swelling, diffusion, and erosion phenomena related to the dissolution process. A mathematical model has been then presented to describe swelling and dissolution of a polyethylene oxide tablet.

The water content has been determined as a function of the matrix radius for cylindrical matrices made of pure HPMC or HPMC plus a model drug, by texture analysis for each dissolution time analyzed in the radial system (Lamberti et al., 2013). Obviously, the water content is an increasing function of the matrix radius, since the hydration proceeds from the extern (high radius) toward the matrix's core (low radius). The work of penetration was successfully related to the hydrogel water content assayed by a gravimetric technique. Moreover, a fitting model was proposed to correlate the two variables explored (water content and work of penetration). However the relationship can be used only for systems where the water content does not change along the thickness (such as the radial systems). In more complex systems (as the ones for which the solvent can penetrate through the full surface of the tablet), the water content also varies along the thickness. On the other side, the work of penetration is an average value along the axial distance, therefore just a partial (average) information could be obtained on the water content.

1.1. Aim of the work

Purpose of the work is to find the relation holding between the force measurements obtained by texture analysis and the water content, both in the gel layer and in the glassy-core, for matrices composed of HPMC and theophylline (as a model drug), subjected to both axial and radial swelling after several immersion times.

2. Materials and methods

2.1. Materials

Powders of Hydroxy-Propyl-MethylCellulose (HPMC, Methocel K15 M, Colorcon, Varese, Italy) and theophylline (TP, Sigma–Aldrich, Milan, Italy, CAS 58-55-9) have been used to produce hydrogel tablets. Deionized water, HCl (37% w/w, purchased from Sigma–Aldrich, cas number 7647-01-0) and sodium phosphate tribasic dodecahydrate (purchased from Sigma–Aldrich, cas number 10101-89-0) have been used for the dissolution media preparation.

2.2. Tablet preparation

Both HPMC and TP powders have been mixed (25% TP, 75% HPMC w/w) and compressed in cylindrical tablets (radius 6.5 mm and thickness about 1 mm) using a tableting machine (Specac PN3000, equipped with flat-faced punches, diameter 13 mm and with a Carver Press), implementing a loading force of 50 kN, kept for 5 min. Each tablet for the radial tests was found to weight about 350 ± 5 mg, for the semi-overall tests (see next section) was found to weight about 175 ± 5 mg.

2.3. Dissolution methods

Different media have been used to reproduce the gastrointestinal environments during the dissolution step. Therefore, during the first 2 h of dissolution, a solution at pH 1 has been used to reproduce the acidic environment of the stomach. The solution has been prepared using 6.25 mL of HCl diluted with deionized water to 750 mL. After 2 h, which represents the average residence time into the stomach, the solution has been neutralized to pH 6.8 to simulate the almost neutral intestinal environment. The neutralization has been realized adding to the previous solution 250 mL of deionized water containing 19 g of Sodium Phosphate Tribasic Dodecahydrate. The medium during all the tests has been kept at 37 °C and at constant rotation speed of 100 rpm.

To allow only lateral uptake of water for the radial dissolutions (the "radial" test) the matrices have been confined between two glass slides, keeping the total thickness constant (2 mm). This systems have then been kept immersed into a USP II apparatus (AT7Smart, Sotax, Allschwil, Switzerland) for a predetermined time. In this way the tablet preserved its thickness and swells only radially due to the effect of water penetration. After the immersion time, the systems have been withdrawn from the bath and the superior slide has been carefully removed. The matrices have been then subjected to mechanical analysis. In the radial experiments, the dissolution times considered were 24, 48, 72, and 96 h.

The second system used, named "semi-overall system" consisted of a matrix with half of the weight of the previous one. This tablet (of 1 mm thickness) has been glued on a glass slab paying attention to overlap the centers of the tablet and of the glass slab. Only a very small center-part of the tablet has been glued to the glass slide, in order to allow the free swelling of the tablet

also very close to the glass slide. The resultant system, composed by the tablet and the glass, has been then immersed in the USP apparatus for a predetermined time. After the immersion time, the system has been withdrawn and subjected to mechanical analysis. The behavior of such a system was considered to mimic an half part of a 2 mm overall system: the glass slide, in fact, could be seen as the symmetry plane orthogonal to the *z*-axis (the cylinder axis) of the whole tablet. In this case the swollen matrix changes not only its radius, but also its thickness due to both the hydration and erosion effect. These phenomena are more evident as the dissolution time increases. In the semi-overall experiments the dissolution times considered were 3, 4.5, 5, 6, 7, and 8 h.

2.4. Mechanical tests

After the immersion times, indentation tests using a texture analyzer (TA.XT Plus Stable Micro System Godalming, UK) have been performed for both the systems. To perform the tests, a needle probe (P/2N) and a 5 kg loading cell have been used and the swollen matrix has been penetrated radially at several distances from the center. To guarantee the accuracy of the holes position, a micro-translator device has been designed, built and used in connection with the instrument. The velocity of the indentation test has been kept constant at 0.03 mm/s, and the instrument measures the force necessary to penetrate into the swollen matrix. Data acquisition starts when the probe touches the sample (this means that the sample offers a not negligible force to penetration) and it ends when the probe reaches 90% of the total sample thickness (which is previously evaluated by a proper instrument calibration). A recording rate of 100 point/s has been set. For sake of representation clarity, figures in this paper reports points skipped every 400. To ensure reproducibility of the experimental data, every test has been performed in triplicate. Results are given as average values.

3. Results and discussions

3.1. Radial dissolution

The matrices used in the work have been penetrated at different radii. For each point of penetration, the force required for penetration has been measured. Results obtained in a test are plotted as in Fig. 1, where the experimental data have been reported as full gray squares. The force values are reported vs. the depth of penetration. The origin of this axis (identified as *s*) corresponds to the lowest detectable penetration force: actually it does not corresponds to the surface of the tablet, but rather to the position where the water content is low enough – roughly 90% – to cause a sufficient hardness of the hydrogel to give rise to a detectable force, with the instrument adopted; anyway this position was taken as a measure of the tablet thickness (which was function of the radius) and the measurements were ended when the probe had penetrated of 90% of the total thickness of the tablet (defined as above described). In the radial experiments, the total thickness is the same for all the experiments, thus the penetration axis has the same length; furthermore, in the radial experiments the matrix, for a given radius, has been hydrated at the same level, i.e. the water concentration is uniform along the axial *z*-direction. The example reported in Fig. 1 shows a typical behavior, it is worth to point out that the relationship between the force applied and the penetration inside the matrix is linear, therefore, the experimental data have been nicely fitted by a line. The fitting has been repeated for each force curve in the tablets for different radii and for each immersion time. In Fig. 1 the slope of the curve is emphasized. The slope *dF*/*ds*, in fact, is a measure of the penetration resistance: the higher the slope of the line, the higher the force required to penetrate into the tablet. Thus, when the inner

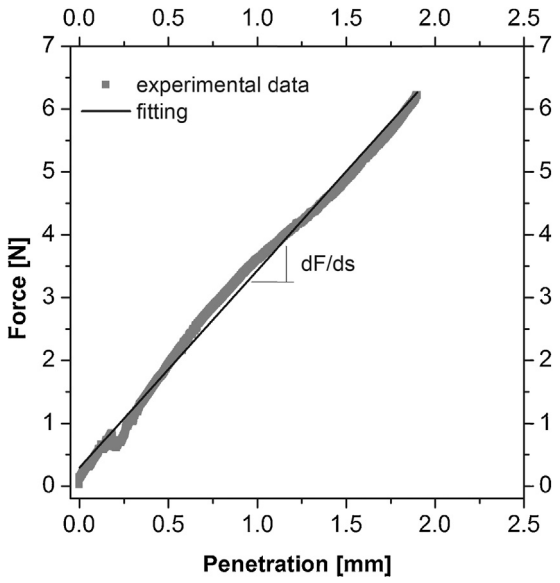

Fig. 1. Force vs. penetration distance for a radial system after 24 h of immersion. In the graph the experimental data (full squares) are fitted with a linear regression (line). The slope of the line (*dF*/*ds*) is emphasized.

radius of the matrix (less hydrated, then more hard) is penetrated, the force required at the same penetration distance is larger; when the outer radius of the matrix (more hydrated, then more soft) is penetrated, the force is smaller. As a result, it can be said that the slope of the force–penetration graph is correlated to the water content: in particular, the higher the water content, the lower the slope of the curve. Constance of the slope during the whole penetration is likely due to the uniformity of the water content in a tablet section in the simplified radial system.

Once the force–penetration curves have been evaluated for different radii and for each immersion time, slopes of the lines fitting the experimental data have been calculated, and correlated to the water content, that has in turn been evaluated by a gravimetric analysis (original data and details on gravimetric methods are reported in (Lamberti et al., 2013) and in references therein). The experimental data of water content at different radii of the matrix are reported in Fig. 2 vs. the slope *dF*/*ds* for all the tests carried out (different radii for different immersion times). The experimental data, reported as open symbols in a semi-logarithmic scale, show a linear trend, and therefore they can be easily fitted by the following equation:

$$W = a \cdot log_{10}\left(\frac{dF}{ds}\right) + b \quad (1)$$

where the regression parameters are $a = -24.37 \pm 0.66$, and $b = 33.97 \pm 0.89$, the Pearson's correlation coefficient being $R^2 = 0.986$. In Fig. 2 the fitting has been reported as a continuous line. The range of confidence for the correlation given by Eq. (1) is due to the limits in the force measurement. High levels of water give raise to undetectable forces (too low), whereas low levels of water can cause rupture in the specimen during the test. Then, the upper limit of the obtained correlation is 90% of water content (higher hydration produce a force of penetration hardly detectable) whereas the lower limit is 20% of water content. Using the empirical correlation obtained, the slope of the curve force–penetration (measured in mechanical tests), and the content of water in each section can be easily correlated, without the use of the gravimetric analysis which is more time and work-consuming.

The experimental method presented, and the fitting procedure, deserves a couple of observations:

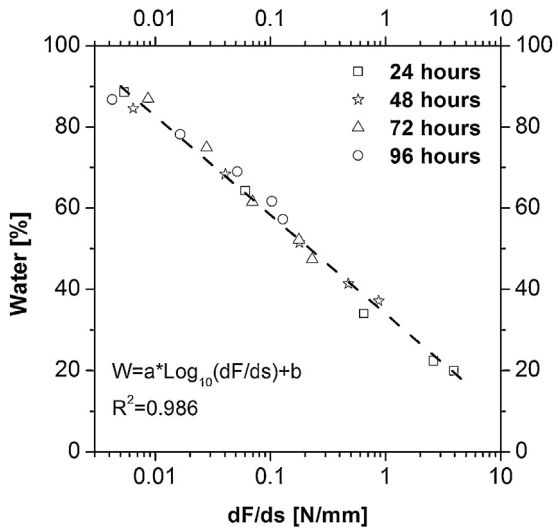

Fig. 2. Water content vs. the slope of the force–penetration curve (logarithmic scale). Open symbols are the experimental data for different times, the curve is the data fitting. The equation and R^2 are reported in the graph. The parameters are $a = -24.37 \pm 0.66$, and $b = 33.97 \pm 0.89$.

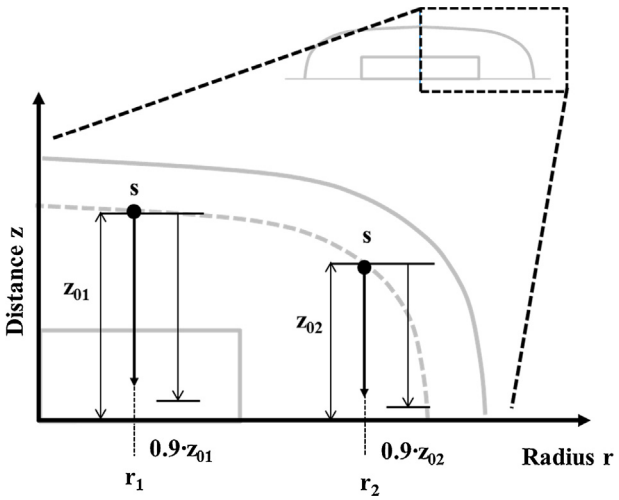

Fig. 3. Representation of a swollen overall tablet after the dissolution time on the left. On the right a zoom of a quarter of the tablet. Defining z_{01} and z_{02} two different thicknesses of the tablet (the point where the water content is below the threshold limit of 90%) corresponding to two value of radius (r_1 and r_2), the penetration axis (s) is added to the graph, as well as the values of penetration stop (0.9 z_{01} and 0.9 z_{02} respectively).

1. The parameters in Eq. (1), in principle, could be material dependent, i.e. they should be different working with a different hydrogel. In our experience (Barba, d'Amore, Cascone, et al., 2009; Barba, d'Amore, Chirico, Lamberti, & Titomanlio, 2009c; Chirico, 2008; Chirico, Dalmoro, Lamberti, Russo, & Titomanlio, 2007), working with the same polymer HPMC K15 M, there is not too much dependence of the swelling and erosion rate from the drug content. Therefore, similar values are expected working with matrices with different initial drug ratio. Anyway, the application of the technique presented in this work on different systems is object of further analysis.
2. The data in Fig. 2 suggested a linear fitting, which is given by Eq. (1). However, the dependency of a material parameter such as an elastic modulus, which should be proportional to dF/ds, from the water content (which influences the polymeric network free volume) has been postulated as a decreasing exponential by Fujita (Fujita, 1961), and it has been largely adopted in the drug release modeling from polymer networks (Barba, d'Amore, Chirico, Lamberti, & Titomanlio, 2009b; Lamberti, Galdi, & Barba, 2011; Siepmann, Kranz, Bodmeier, & Peppas, 1999). It is worth to note that Eq. (1) is fully coherent with a Fujita-type equation relating the dF/ds and the water content. Actually, it could be written in agreement with the Fujita structure:

$$\frac{dF}{ds} = \left(\frac{dF}{ds}\right)_0 \exp\left[-\frac{b}{a \cdot \log_{10}(e)}\left(1 - \frac{W}{b}\right)\right] \quad (2)$$

(dF/ds) is not a further optimization parameter, being known defining b as the water content at which the force derivative is unity. The fact that Eq. (1) can be rewritten as a Fujita-type equation (Eq. (2)) means that Eq. (1), even if obtained by fitting, has a good theoretical basis.

3.2. Semi-overall dissolution

The relation between water content and force–penetration diagram, once calibrated on the basis of experimental data of radial dissolution, can be easily applied, replacing the gravimetric analysis, to predict the water content in a swollen matrix.

In the semi-overall test (a tablet with thickness a half of a full tablet was glued to a glass slab which mimics the cylinder symmetry plane, then hydration was allowed through all the exposed surface) the water diffuses into the matrix from both the axial and the radial direction; as a results, the final shape of the tablet (after hydration) of the matrix is shown in Fig. 3. Analyzing what happens when the matrix is penetrated by the probe in one position, i.e. the radius r_1 in Fig. 3, it can be seen that, starting from the height z_{01} of the matrix the probe encounters an external gel layer which is very easy to penetrate. Note that z_{01} is the origin of the penetration axis s, defined as the point where the resistance force becomes detectable, being the locus of these points reported as the dashed line in the graph, corresponding to a water content roughly equal to 90%. As the probe approaches the matrix center, it detects harder layers up to the final position which is indicated as 0.9 z_{01}. It has to be outlined that, if another penetration is done at another radius, the starting height (z_{02} corresponding to the radius r_2 in Fig. 3) is not the same value of the previous one, because the matrix, subjected to swelling and erosion, varies its shape in height and radius. However, if the penetration axis is considered, the penetration distance equally starts from 0 to its maximum value.

The mechanical tests previously described have been performed on semi-overall swollen matrices. The force–penetration curves obtained in this case are shown in Fig. 4. In this graph the experimental data are reported as symbols, the exponential fitting of data are reported as lines. As can be seen, the curves in the semi-overall case are not linear. This is likely so because the force necessary to penetrate the external matrix layers is very low and increases in the inner layers. The difference with the radial test has its origin in the hydration of the matrix which is not homogeneous in the axial direction, differently from the previous system studied.

The different composition of the tablet thus reflects the shape of the force–penetration curves: in fact, at the beginning the force registered is very low (Fig. 4), then approaching the matrix center the force registered increases continuously up at the end of the run and the slope of force vs. displacement curve increases with the sensor penetration. This behavior is characteristic of all the curves; the force magnitude varies depending on the radius where the penetration is carried on, since the hydration of the matrix occurs also along the radial direction, thus leaving the matrix center the water content is higher, that means that the force necessary to penetrate the matrix is lower (as can be seen in Fig. 4, matching the curves at various radii values). The experimental data are very well fitted by simple exponential curves. Actually, the exponential function

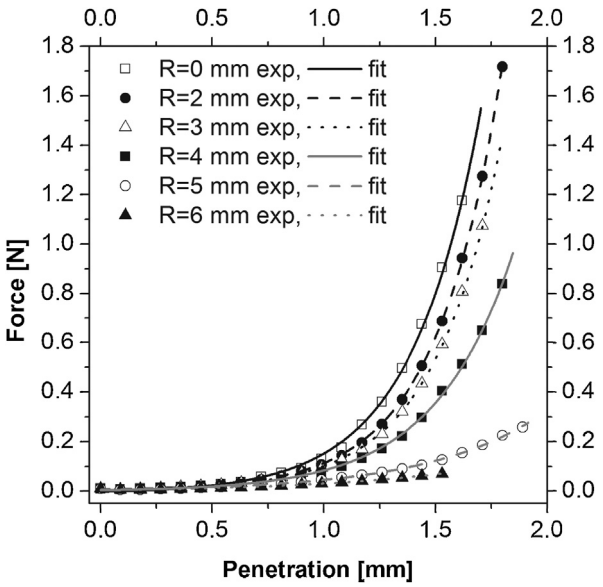

Fig. 4. Force vs. penetration distance for a semi-overall tablet after 180 min of immersion. The symbols are the experimental data (it is shown one experimental data point over 400 sampled data) at different radii of the tablet, the curves are exponential fittings.

was the best choice (in term of accuracy of fitting and of limited number of fitting parameters), out of several curves tested for the fitting. Since the penetration test is just a measurement tool, the shape of the curves F vs. s is strictly related to the shape of the profile of the water content along the axial direction, because of Eq. (1). As a matter of fact, an exponential shape in Fig. 4 just imply that the axial water content profile will be linear. The procedure has been carried out for all the curves for each immersion time analyzed to obtain continuous curve which could describe the force profile vs. penetration. It is thus easy to obtain dF/ds which is, in this case, a function of the penetration distance rather than a single value for each test. Using Eq. (1) is possible to predict the axial water content of the matrix for all the positions studied. The results obtained for a matrix after 180 min of immersion are shown in Fig. 5. The water content starts, for each penetration, from a high value, which corresponds to the high water content in the gel layer, and then decreases approaching the glass slide (which means the

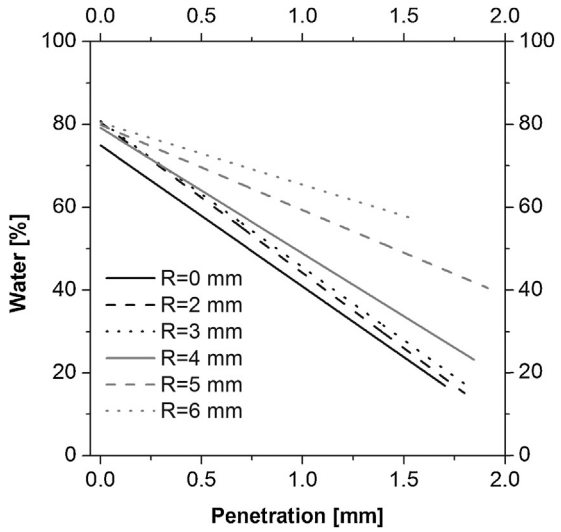

Fig. 5. Water content vs. distance of penetration in a semi-overall tablet at different radii after an hydration time of 180 min.

maximum penetration distance). Even if a decrease of water content with the axial position is expected, since the hydration proceeds from the external toward the matrix core, there is no reason to a priori postulate a linear trend of water content with the axial position. Quite the reverse, if the main transport mechanism would be (Fickian) diffusion, the concentration profile would be shaped as a sigmoidal curve, rather than a straight line. It should be stated that the transport process in hydrating polymer matrices is not a "simple" Fickian diffusion. A complex framework of phenomena takes place: the diffusivity is not constant but it increases with the hydration; the swelling phenomenon plays a significant role, since it induces movements of the network, which can be viewed as an additional convective term for the drug and the water; even if with minor effects, the drug solubility and the polymer erosion can play a role (for the present system, these are really secondary effects). In our opinion, the shape of water content profiles are mainly due to the diffusion with a variable diffusivity coefficient and to the translation due to the swelling phenomenon. Data describing the water content in the matrix are scarcely available in literature and their experimental values could be obtained only with complex devices and techniques. However, the linear dependence has been observed before, for example by means of MRI analysis on hydrating matrices (see Fig. 5 in (Kaunisto, Abrahmsen-Alami, Borgquist, Larsson, Nilsson, & Axelsson, 2010). On the other hand, in the present work a simple relation between the force/displacement derivative vs. the water content, based on mechanical data quite easy to be obtained, has been proposed, that could be used in a large range of water concentration values describing the water content almost through the whole tablet. It is worth noticing that the linear behavior of water concentration with axial position (penetration distance) is a direct consequence of the exponential shape of the force–penetration graph, since in this way the force derivative is described by an exponential, and applying Eq. (1) – which includes a logarithm – the water content has to be a linear function. However, there is not in this calculation procedure any shortcut which coerces the result to be a linear function, since the fitting of the force–penetration data with a function different from the exponential would give a water-penetration curve different from the linear graph. But, as stated before, the exponential fitting was the best choice for the experimental data in Fig. 4.

The measurement of water content in the axial direction can be repeated for each penetration point for all the hydration times considered. Thus, a contour plot representing the water content of the tablet after dissolution can be done and compared with the snapshot of a real tablet. The comparisons are shown in Fig. 6 for several hydration times. As can be seen, for each tablet the first step was to identify its boundary after the swelling process. Then, for each image on left is the real tablet photo, whereas on right is the contour plot overlapped with the same tablet dimensions Areas containing the same water amount are colored with the same filling and, in general, the water content decreases approaching the glass slide of the tablet. It can be noted that there are zones where it is not possible to evaluate the water content, due to both a water content higher than the limit imposed by the obtained relationship applicability (relationship between the force/displacement derivative and the water content), and the hydration in the more external zones, so high that the force opposed by the gel to the penetration is negligible and not easily detectable by the instrument. Shape of the contour plot, and iso-water areas reflect the real tablet shape. After 180 min of immersion the tablet radius is not changed as much with respect to its original value. On the contrary, the tablet thickness has increased three times. This latter is an evidence that the axial swelling is faster than the radial one. Increasing the dissolution time, the tablet shape is deformed by swelling so that both radius and thickness become larger and larger. When dissolution time increases (i.e. 420–480 min) the tablet changes its dimensions

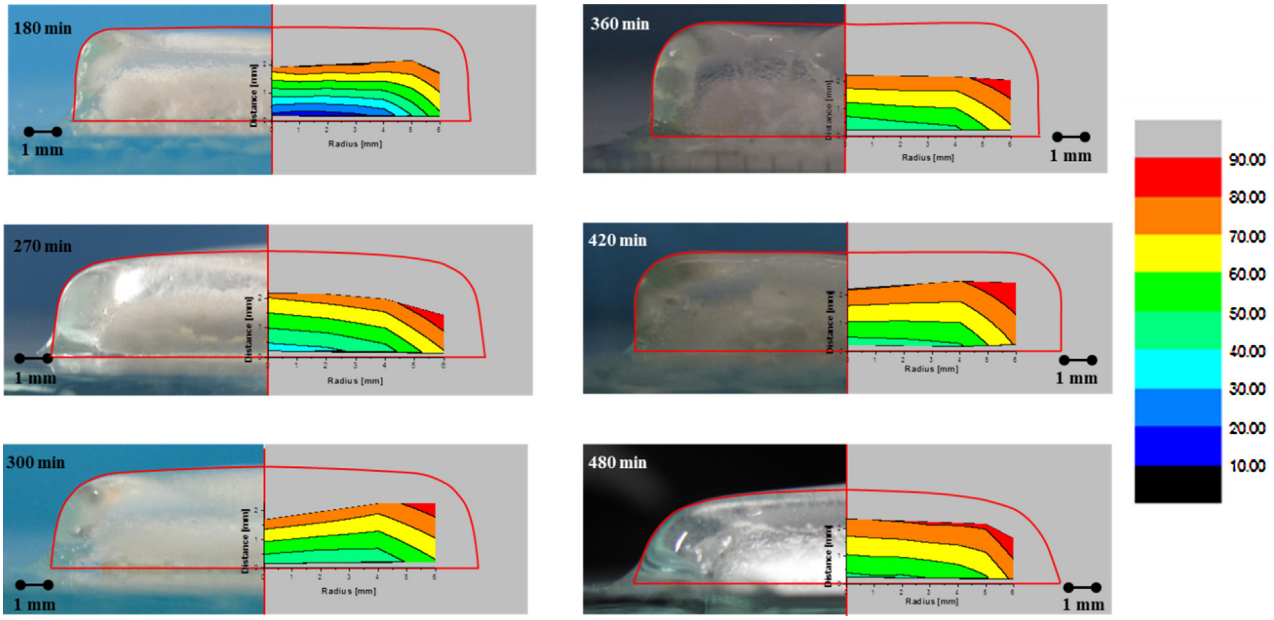

Fig. 6. Tablets after the hydration for each hydration time considered. On the left of each image, the matrix is reported and its boundaries are emphasized. On the right of each image, the contour plot representing the water content in the matrix is overlying the tablet. The percentage of water corresponding to a color filling is unique for all the contour plots and the legend is reported on the right of the figure. (For interpretation of the references to color in figure legend, the reader is referred to the web version of the article.)

and its shape due to the swelling and to the erosion phenomena, the last being more relevant. Evaluating the water content in each tablet, it was seen that after 180 min, the inner areas of the tablet are still relatively dried, with a water content less than 20%. The tablet is more hydrated in the external areas. After 270 min, the water content increase in the tablet, the inner part reaches an hydration of 40%; after 360 min the hydration is of 50%; the maximum is reached after 480 min of dissolution, where the tablet center is composed by 60% water. Of course, the higher the radius of the hydrated tablet, the higher the water content in the tablet.

4. Conclusions

The measurement of water content within an hydrogels-based hydrating matrix is an interesting goal for the study of pharmaceutical solid dosage forms. Several methods are available, but all of them are work- or time-consuming and/or require complex analytical devices. In this work, a simple and fast method has been proposed to correlate the water content in a matrix to the force–penetration distance diagrams obtained by a texture analysis. For a simplified system in which the water up-take is only allowed through the lateral surface, the water content was assayed via a gravimetric method, and the force–penetration as function of the matrix radius was measured by a texture analyzer. Then, the two measurements successfully correlated, and a fitting equation has been also proposed and tuned. Once the relationship has been validated, it has been applied in a more complex system in which the swelling of the polymer takes place both in axial and in radial direction, and the water content has been evaluated. The water profiles along the axial direction have been found to follow a linear trend.

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