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International Journal of Pharmaceutics 342 (2007) 18–25
INTERNATIONAL JOURNAL OF PHARMACEUTICS
www.elsevier.com/locate/ijpharm

Correlation between drug dissolution and polymer hydration: A study using texture analysis

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Received 30 January 2007; received in revised form 9 April 2007; accepted 23 April 2007
Available online 5 May 2007

Abstract

Texture analysis is a new approach in pharmaceutical research and development; this study evaluated the correlation between drug dissolution and polymer hydration from a modified release matrix tablet of pseudoephedrine hydrochloride using a texture analyzer. A series of matrix tablets of pseudoephedrine was designed and prepared. Modified drug release was achieved by combined use of matrix excipients Polyox® WSR301 (PEO) and Compritol® 888ATO (GB). Dissolution profiles of the tablets were assessed using USP Method II. Polymer swelling behaviors during dissolution were measured using a texture analyzer. Increase in proportion of PEO and GB in the formulation reduced drug dissolution within the first 90 min. However, drug release was complete in 6 h due to high aqueous solubility of pseudoephedrine. Linear correlations were observed among drug dissolution, polymer content and parameters of texture analysis including hydrogel thickness and AUC_{TA} for formulations that contained hydrophilic PEO. The study demonstrated a unique application of a texture analyzer in characterization of modified release matrix tablets.

Keywords: Modified release matrix tablet; Texture analyzer; Drug dissolution; Polymer hydration; Pseudoephedrine

1. Introduction

Modified release matrix tablet has been extensively used as one of the most successful oral drug delivery systems by the pharmaceutical industry. By selecting appropriate matrix polymers and using direct compression tableting process, it is possible to produce quality matrix tablets that possess satisfactory processing properties and reproducible drug release profiles. In addition, large-scale industrial production of matrix tablets is normally less expensive than that of the other drug delivery systems, in which more sophisticated and complex equipment and procedures are required.

Hydrophilic polymers such as polyethylene oxide (PEO) and hydroxypropyl methylcellusose (HPMC) are dominant matrix excipients for most modified release tablet preparations (Apicella et al., 1993; Choi et al., 2003; Kim, 1998; Razaghi and Schwartz, 2002). Once in contact with a liquid, these polymers would hydrate and swell, forming a hydrogel layer that regulates further penetration of the liquid into tablet matrix and dissolution of the drug from within (Colombo et al., 2000). Drug release from such a polymeric matrix is therefore achieved by diffusion, erosion, or a combination of both (Lee and Peppas, 1987; Narasimhan and Peppas, 1997).

Changes in the thickness of a hydrogel layer over the contact time consist of three stages, i.e., initial increase due to polymer swelling, maintenance of constant gel layer between swelling and dissolution front, and reduction in gel layer due to depletion of the glassy core. Drug release in zero-order kinetics can be achieved as long as a constant gel layer thickness is maintained. Mathematical models have been established to describe behaviors of polymer swelling and drug release from hydrophilic matrix tablets and to simulate the effect of device geometry on drug release patterns. Siepmann and Peppas (2000) and Siepmann et al. (1998) used the power of “sequential layer” model to describe drug release from HPMC matrix tablets. The model was applicable to a wide range of polymers, drug candidates, release media and tablet compositions, and useful in understanding the effects of tablet designs such as tablet radius, height and size on the resultant drug release characteristics.

Numerous methods are available to determine polymer swelling behaviors of a hydrophilic matrix tablet; optical microscopy has been extensively used to observe movement of

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doi:10.1016/j.ijpharm.2007.04.024

water at the interface of polymer gel and glassy core (Colombo et al., 2000). Other sophisticated instrumentation, including NMR imaging (Rajabi-Siahboomi et al., 1994), confocal laser scanning microscopy (CLSM) (Cutts et al., 1996), cryogenic scanning electron microscopy (Cryo-SEM) (Melia et al., 1994) and light scattering imaging (LSI) (Gao and Meury, 1996), have also been used as non-invasive techniques to characterize polymer hydration of different modified release matrix tablets. While these methods are able to illustrate water mobility across hydrogel layer and transport of drug molecules within the tablet matrix, they are often time-consuming and expensive in instrument operation.

Texture analyzer is a versatile research and development instrument that has been widely used in the food industry. By using different probes and assessment criteria, it is possible for food scientists to monitor or demonstrate the texture quality and palpability of different foods. The pharmaceutical applications of a texture analyzer for quality control purposes have significantly increased for the past several years. It has been used to optimize adhesiveness and cohesiveness of water-in-oil emulsions (Lemaitre-Aghazarian et al., 2004), test tablet disintegration from fast-dissolving preparations (El-Arini and Clas, 2002), and evaluate mucoadhesive properties of various polymers (Cilurzo et al., 2005). The operation of a texture analyzer, on the other hand, is relatively simple, versatile and cost-effective; it is possible to use the same instrument for multiple measurements by changing either testing probes or measurement parameters.

In this study, we used a texture analyzer to evaluate the formation of hydrogel layer from a series of modified release matrix tablets of pseudoephedrine. The correlation among drug release rate, polymer content in tablet and gel layer formation of both hydrophilic matrix polymer and water-insoluble lipid-based excipient was attempted. The primary objectives of the study were to explore the applicability of texture analysis and to devise simplified mathematical interpretation in formulation evaluation and optimization.

2. Materials and methods

2.1. Materials

The pharmaceutical excipients used in the study were received as gifts from various sources. They were Polyox® WSR301 (PEO, polyethelene oxide, Union Carbide Corporation, Danbury, CT, USA), Compritol® 888ATO (GB, glyceryl behenate NF, Gattefossé s.a., Lyon, France), and Prosolv® HD90 (MC, silicified microcrystalline cellulose, The Dow Chemical Company, Midland, MI, USA). Pseudoephedrine hydrochloride USP and PVP K30 USP (polyvinylpyrrolidone) were purchased from Medisca Pharmaceutique Inc. (Montreal, Que., Canada) and Spectrum Chemical Manufacturing Corp. (Gardena, CA, USA), respectively.

Other chemicals used in the HPLC analysis of pseudoephedrine were commercially purchased from Fisher Scientific (Fair Lawn, NJ, USA); they included concentrated acetic acid, sodium acetate trihydrate, acetonitrile and methanol. All chemicals and reagents used were either HPLC grade or AC grade. Deionized water was obtained from a Millipore® Milli-Q System (Bedford, MA, USA).

2.2. Tableting

Ten modified release matrix tablet formulations were prepared; each formula contained a fixed dose (120 mg) of pseudoephedrine hydrochloride as the active ingredient. Proportions of hydrophilic PEO (10–50% tablet weight) and lipid-based GB (10–25% tablet weight) were variable among the formulations, while PVP K30 was maintained at a constant proportion of 5%. The total tablet weight of the preparations was 300 mg, which was achieved with the additional use of tablet excipient MC. The compositions of each matrix tablet formulation are listed in Table 1.

The matrix tablets were prepared by direct compression of the powder mixtures using a Manesty® single-punch tablet press (Liverpool, UK). A set of 7/16 punches and die was used for the tableting, and the compression pressure was maintained at 50 kg for all tablet formulations. The tablet hardness was also monitored during tableting with an Erweka® tablet hardness tester (Düsseldorf, Germany).

2.3. Drug dissolution

Dissolution test was carried out on a VanKel® 600 Dissolution Apparatus (Palo Alto, CA, USA) using USP Apparatus II. The dissolution medium was 900 mL of deionized water. The dissolution temperature was maintained at 37 ± 0.5 °C and the rotation speed was set at 50 rpm. Samples were collected from the dissolution medium at 0.5, 1, 1.5, 2, 4 and 6 h. Each sample volume removed was replenished with an equal volume of fresh pre-heated dissolution medium. Six replicates were tested for each batch of the tablet formulations. Dissolution samples were

Table 1
Compositions of modified release matrix tablets of pseudoephedrine

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Pseudoephedrine HCl	120	120	120	120	120	120	120	120	120	120
Polyox® WSR301	30	45	60	75	90	150	15	15	15	15
Compritol® 888ATO	9	9	9	9	9	9	30	45	60	75
PVP K30	15	15	15	15	15	15	15	15	15	15
Prosolv® HD90	126	111	96	81	66	6	120	105	90	75
Total tablet weight	300	300	300	300	300	300	300	300	300	300

filtered and diluted to appropriate concentrations with deionized water for drug analysis.

Concentrations of pseudoephedrine were measured using an HPLC assay developed in our laboratory (Gu et al., 2005). In brief, a Waters® HPLC system (Milford, MA, USA) comprised of a 600S Controller, a 616 Solvent Delivery Pump, a 717 Autosampler, and a 996 Photodiode Array Detector was used together with a C_{18} Nova-Pak® column (4 μm, 3.9 mm × 150 mm). The mobile phase was composed of acetate buffer (pH 4.0):acetonitrile:methanol (45:47:8, v/v/v) and was delivered at a flow rate of 0.8 mL/min. The detection wavelength was set at 214 nm. Under these chromatographic conditions, pseudoephedrine was eluted from the column at approximately 2.0 min. The detection limit was 10 ng for pseudoephedrine and the linear range of the assay was 50–1000 ng. No interference was found from any tablet excipients or additives.

2.4. Polymer swelling testing

To prepare samples for texture analysis, each modified release matrix tablet was snapped into a cylindrical polyethylene cap that had an internal diameter equal to the diameter of the prepared tablets. Samples prepared in this matter would allow water penetration from only one surface of the tablet matrix and produce gel swelling in one direction, which facilitated the characterization with a texture analyzer. These tablet samples were then placed in 900 mL of deionized water, and subjected to the same dissolution testing as previously described. Samples were collected at 0.5, 1, 1.5, 2, 4 and 6 h for texture analysis; six replicates were tested for each time interval.

The hydrogel layer thickness was determined on a TA.XT.Plus Texture Analyzer (Texture Technologies Corp., Scardale, NY, USA). A flat-end, round cylindrical stainless steel probe (Ø 2 mm × L 30 mm) was used to measure the distance that the probe traveled in the gel layer. The probe initially traveled at a rate of 2.0 mm/s until the surface of the tablet was detected at 0.7 g of the force, at which point the probe penetrated the swollen hydrogel layer at a speed of 0.2 mm/s. Once the probe detected 500 g of the force, which was determined as the unswollen matrix layer, the probe would withdraw automatically out of the gel layer at a rate of 0.2 mm/s (Yang et al., 1998). Data were collected and processed by Texture Expert software.

2.5. Data analysis

The empirical Peppas–Ritger dissolution equation (Ritger and Peppas, 1987a,b) was used to profile drug release characterization of the prepared matrix tablet formulations. Relationship between drug diffusion from the matrix tablet and dissolution time was analyzed through the following equations,

$$\frac{M_t}{M_\infty} = K \cdot t^n \tag{1}$$

$$\log\left[\frac{M_t}{M_\infty}\right] = \log k + n \log t \tag{2}$$

where M_t/M_∞ is the fraction of drug release, k a release rate constant, n the diffusional release exponent indicative of drug release mechanism, and t the dissolution time. Dissolution data of the study ($M_t/M_\infty \leq 0.6$) was correlated linearly using Eq. (2).

The time required for 50% of the drug dose to be released ($DT_{50\%}$, h) and dissolution efficiency (DE, %) of the formulations were also obtained to compare differences in drug release rate and extent among the prepared formulas (Khan, 1975; Efentakis and Koutlis, 2001). $DT_{50\%}$ was obtained directly from the dissolution time curves; dissolution efficiency was calculated using the following equation,

$$\mathrm{DE}\,(\%) = \frac{\mathrm{AUC}_{(\mathrm{dissolution},0-6\,\mathrm{h})}}{100\% \times 6\,\mathrm{h}} \times 100 \tag{3}$$

The Texture Expert software recorded several pre-determined parameters of the texture analysis, including the force (F) that the probe felt, the distance (D) that the probe traveled within the gel layer and the area under the curve ($\mathrm{AUC_{TA}}$) of the measurement.

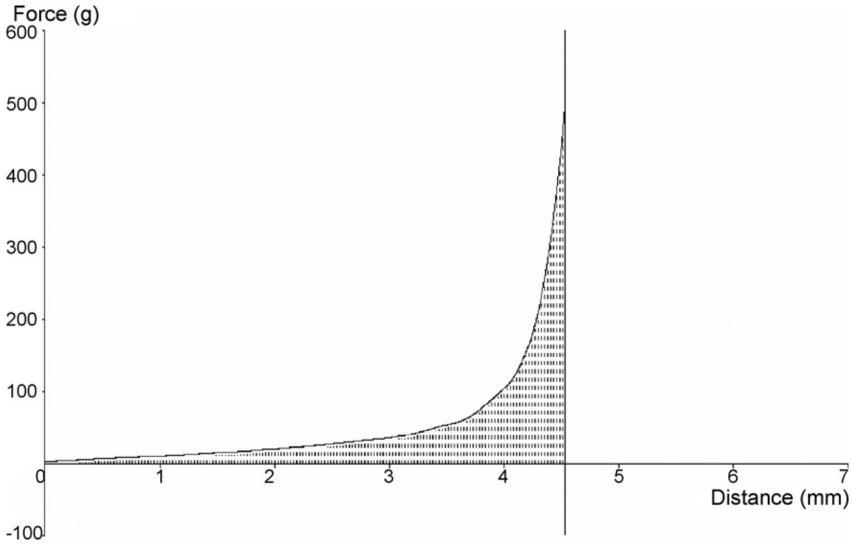

Fig. 1. A typical graph of the texture analyzer (force vs. probe travel distance, $\mathrm{AUC_{TA}}$).

A typical curve of the measurement is shown in Fig. 1. Relationship between polymer hydration and drug dissolution was attempted by mathematically correlating among texture analysis parameters, drug release rate and PEO proportion in the formulations using JMP Statistical Program (Version 4.0.2, SAS Institute, Cary, NC, USA). Both linear regression and multiple regression modeling were used; the mathematical expressions included as follows:

Linear regression:

$$Y = a + bX \quad (4)$$

Multiple regression:

$$Y = a + bX_1 + cX_2 \quad (5)$$

Best curve fitting of the correlation was determined based on the outcomes of the data analysis, and the mathematical equations were obtained. In addition, data were compared for statistical significance using Student's *t*-test; differences were considered statistically significant at $p \leq 0.05$.

3. Results and discussion

Polyethylene oxide polymers and lipid-based excipients have been widely used in the development of various tablet formulations. When in contact with water, hydrophilic polyethylene oxide polymers allow gradual hydration of the tablet matrix, leading to modified dissolution and diffusion of the active ingredients from within the swelling matrix. Lipid-based excipients are water-insoluble materials. When incorporated appropriately in a tablet preparation, they not only supplement essential tableting properties, but also aid in modified drug release through slow matrix erosion. Combined use of PEO and GB in this study enabled the preparation of modified release matrix tablets with satisfactory flowing properties and direct compressibility of the mixtures. In addition, changing proportion of the two excipients did not compromise tablet quality and tableting characteristics. Among the 10 tablet formulas tested in the study, PEO ranged between 10 and 50% (Formulas 1–6) of the total tablet weight while GB was incorporated between 10 and 25% (Formulas 7–10) of the total tablet weight. The other two excipients present in all study samples, PVP and MC, were believed to contribute minimally to hydrogel formation and drug release regulation. They were used primarily as tablet fillers to achieve required identical tablet weight.

Pseudoephedrine hydrochloride is readily soluble in the water. Its aqueous solubility was measured at 565.3 ± 0.3 mg/mL (25 °C, mean ± S.E.M., $n = 6$) in our laboratory. Selecting this water-soluble compound as a model drug for this study served various purposes. The high aqueous solubility of pseudoephedrine would not detrimentally influence the assessment of gel layer formation with a texture analyzer; the required drug dose in the tablet preparation and subsequently the tablet weight and size would facilitate easy handling of the measurements and ensure the accuracy and reproducibility of the data. In addition, experimental protocol using this model compound would lead to further studies where model candidates with lower solubility profiles could be tested and compared for characterization of drug release and polymer hydration. Formulation design was relatively simple and straightforward; all 10 formulas produced quality tablet preparations using direct compression.

The rate of pseudoephedrine dissolution from the tablets decreased as the proportion of PEO or GB increased (dissolution curves not shown). For Formulas 1–6, where the proportion of hydrophilic PEO varied between 10 and 50% of the total tablet weight, drug release was linearly suppressed with the increase of polymer percentages. Dissolution was however complete in all formulations within 6 h of the dissolution testing. When PEO took 50% of the tablet weight, drug dissolution was significantly reduced between 2 and 5 h, indicating a much slower water penetration into the tablet core as well as a longer drug diffusion from the resultant exterior hydrogel layer. For Formulas 7–10, in which the amount of lipid-based GB varied, changes in excipient proportion did not distinctly reflect in the drug dissolution. This might have been attributed to the presence of an erodible excipient that contributed little to the formation of hydrogel layer by PEO hydration. The amount of PEO in these 4 preparations was maintained at 5% of the tablet weight, which was considerably lower than those used in Formulas 1–6. This would result in less hydration of the tablet matrix, subsequently creating gel layer of thinner thickness on the exterior and allowing faster drug diffusion and dissolution. Comparing two batches of the tablet preparations made of different matrix excipients, there was no significant difference in initial and final drug dissolution percentages. This was more likely attributed to the selection of a soluble model drug, as pseudoephedrine was completely soluble in the dissolution medium.

Table 2 lists dissolution parameters of the preparations obtained from various empirical equations. Dissolution parameters in Formulas 1–6 were well correlative of changes in proportion of PEO present in the tablet matrix. Hydrophilic polymer produced a hydrogel layer upon in contact with water; drug dissolution observed a combination of diffusion and dissolution, with predominant in drug diffusion. For tablet formulations 7–10, dissolution parameters followed a pattern between 10 and 20% of GB. However, high percentage of lipid-based excipient at 25% would result in more matrix erosion than polymer hydration, subsequently facilitating more drug diffusion and dissolution. According to Peppas–Ritger Equation, the value of diffusional release exponent *n* dictates drug dissolution mechanism. Drug release in zero-order, non-Fickian (anomalous) diffusion and Fickian diffusion is represented by $0.89 < n < 1.0$, $0.45 < n < 0.89$ and $n = 0.45$, respectively. The *n* values from the test formulations ranged 0.463–0.563, indicating a non-Fickian drug diffusion mechanism. In addition, dissolution curves of the preparations demonstrated good linearity ($r^2 > 0.99$), suggesting a first-order drug dissolution kinetics for all test formulations.

The formation of hydrogel on the surface of a matrix tablet generally undergoes a transition phase, i.e., from a dry (glassy) stage where the drug and the hydrophilic polymer are in a solid and compressed preparation to a wet (rubbery) stage where drug diffusion takes place after penetrating water solubilizes the tablet

Table 2
In vitro drug release and dissolution parameters

Formulation code	PEO/GB content (%)	Diffusional exponent (*n*)	Release rate constant (*k*)	Correlation coefficient (r^2)	$DT_{50\%}$ (h)	DE (%)
F1	10/3	0.471	0.509	0.998	0.92	73.76
F2	15/3	0.501	0.499	0.999	1.00	74.35
F3	20/3	0.530	0.480	0.997	1.14	73.93
F4	25/3	0.537	0.442	0.999	1.27	68.77
F5	30/3	0.563	0.425	0.999	1.38	67.85
F6	50/3	0.496	0.398	0.996	1.65	64.05
F7	5/10	0.579	0.560	0.999	0.86	77.76
F8	5/15	0.463	0.532	0.999	0.90	73.96
F9	5/20	0.550	0.498	0.999	1.07	73.16
F10	5/25	0.476	0.528	0.999	0.89	75.49

matrix (Colombo et al., 2000). For tablet formulations that contain swellable polymers, transition between the glassy state to the rubbery state tends to complete at a relatively fast speed, as the polymers easily absorb water and swell significantly once in contact with a liquid. As the result, the formation of hydrogel may exhibit variations, dependent on the type and amount of polymers used in the tablet core. Fig. 2 shows the changes in gel thickness over the time for Formulas 1–6 recorded with a texture analyzer. No significant difference was observed in the formation of the gel layer among the 6 tablet preparations at 30 min, suggesting a fast and identical pattern in establishing the rubbery stage independent of the amount of PEO present in the tablets. After 30 min, however, gel thickness started to differentiate among the formulas, which was corresponding to varying polymer contents in the tablets. Higher percentage of PEO created thicker hydrogel on the matrix surface, which clearly resulted from the swelling ability of PEO in the preparations. Fig. 3 demonstrates similar gel thickness–time profiles for Formulas 7–10. The use of lipid-based GB in the formulations did not contribute to the formulation of hydrogel layer. On the contrary, the low proportion of GB at 10% produced the highest value in gel thickness among the 4 formulas initially. At later hydration stages (4 and 6 h), however, no difference in gel thickness was observed among the preparation; this might have been attributed to gradual erosion of tablet matrix over the time. Among the 10 formulas tested, only Formula 6 (50% PEO) produced a significantly greater hydrogel thickness; the other 9 formulations created comparable gel thickness at the end of the testing.

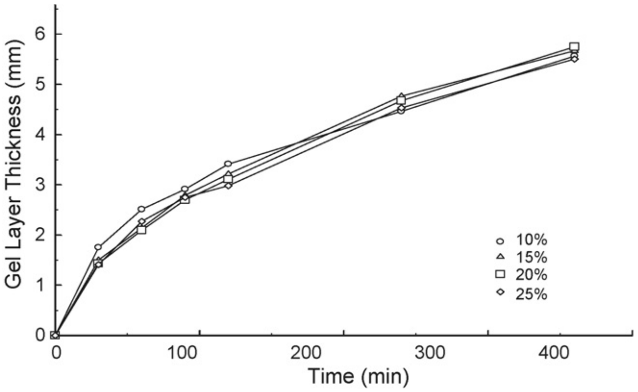

Fig. 3. Gel layer thickness–time plots of Formulas 7–10.

To characterize hydrogel formation of the test preparations, relationship between gel thickness, AUC_{TA} and proportion of both PEO and GB was correlated using linear regression processing. Linearity ($r^2 \geq 0.99$) was established between AUC_{TA} and time (Fig. 4) as well as between gel layer thickness and PEO proportion (Fig. 5) for Formulas 1–6. Different from direct measurement of hydrogel thickness, AUC_{TA} was a secondary parameter of the texture analysis that took into account both the probe force and the probe travel distance. This linear relationship was probably more correlative of characteristics of

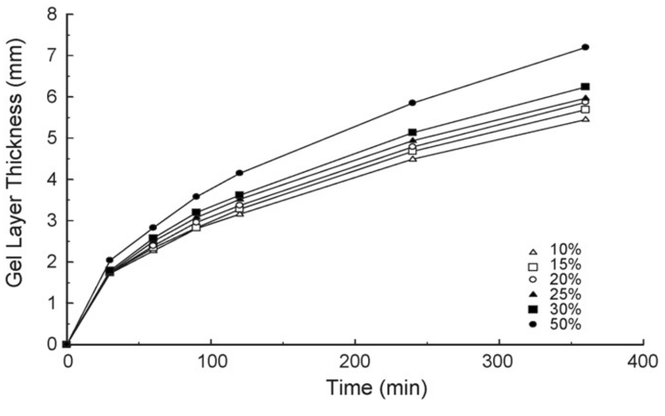

Fig. 2. Gel layer thickness–time plots of Formulas 1–6.

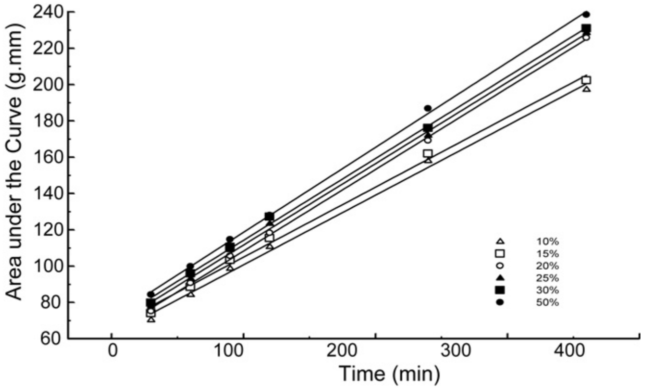

Fig. 4. Linear correlation plots between AUC_{TA} and time for Formulas 1–6 ($r^2 \geq 0.99$).

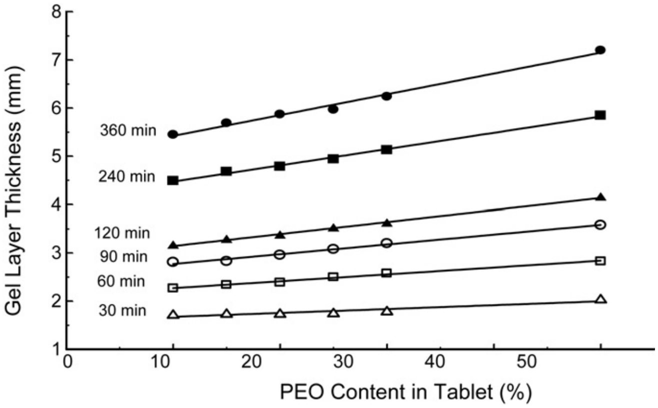

Fig. 5. Linear correlation plots between gel layer thickness and PEO content at different sampling times for Formulas 1–6 ($r^2 \geq 0.99$).

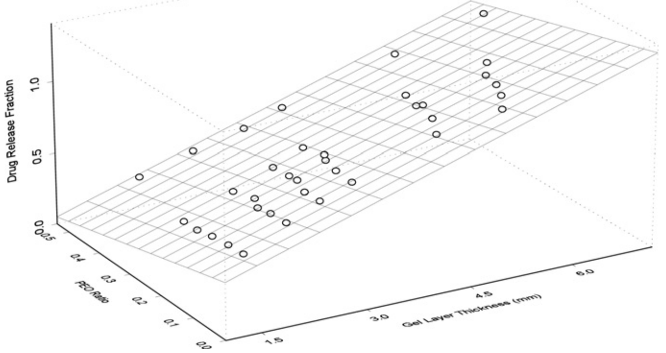

Fig. 7. Multiple regression plot of drug dissolution, PEO content and gel layer thickness for Formulas 1–6 ($r^2 = 0.97$).

polymer hydration during dissolution process. The linear relationship between polymer content and gel layer thickness would also be a satisfactory indicator for formulators to develop new matrix tablets with similar hydrophilic polymers. Specifically, the slopes of all six regression lines were within a close range, indicating similar hydration characteristics of PEO in the preparations. To expedite experimental outcome, a formulator could use data collected from a 60-min experiment to reliably extrapolate values of longer study designs. Fig. 6 shows the relationship between gel layer thickness and GB content in Formulas 7–10. Because only 5% PEO was incorporated in these preparations and GB contributed little to hydrogel formation, the correlation followed a polynomial (non-linear) pattern. In addition, the curve shapes changed over the time, suggesting geometric alterations of the tablets due to matrix erosion. Neither was linearity found between AUC_{TA} and dissolution time for these four preparations. It would therefore be difficult for formulators applying data collected from texture analysis to prediction of hydration profiles of those preparations that do not form sufficient hydrogel layer; other testing parameters might have to be selected instead during dosage design in order to achieve reproducible experimental results.

To further explore relationship among tablet formulation, drug dissolution and texture analysis, a multiple regression model was employed to directly correlate changes of drug dissolution as a function of gel layer hydration and polymer content in the preparation. Linear relationship was observed among drug dissolution, PEO content and gel layer thickness or AUC_{TA} for Formulas 1–6. The equation obtained from the mathematical fitting was Z (drug dissolution) $= 0.242 + 0.154 \times X$ (gel layer thickness) $- 0.639 \times Y$ (PEO ratio) ($r^2 = 0.97$, Fig. 7) and Z (drug dissolution) $= 0.136 + 0.004 \times X$ (AUC_{TA}) $- 0.301 \times Y$ (PEO ratio) ($r^2 = 0.92$, Fig. 8), respectively. This three-dimensional configuration defined a plane of linear fit for drug dissolution property as the function of both texture analysis parameters and polymer content present in the tablet preparations. Changing content of hydrophilic polymer incorporated in a tablet formulation would lead to variations in hydration of the tablet core, which would consequently contribute to modification of drug dissolution. Nevertheless, these three parameters can be easily correlated one another through a simple mathematical equation. This approach provides a practical and straightforward methodology to formulation scientists in tablet modification and optimization, because all three variables are directly measurable during formulation development and assessment. Similarly, no satisfactory linear fitting was achievable for Formulas 7–10, due mainly to the present of lipid-based excipient GB in these preparations.

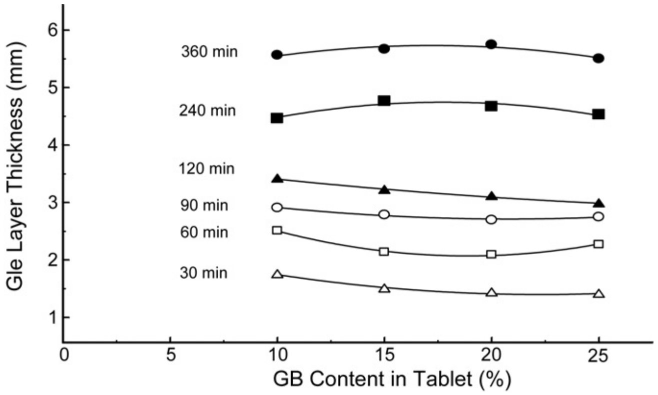

Fig. 6. Polynomial correlation plots between gel layer thickness and GB content at different sampling times for Formulas 7–10.

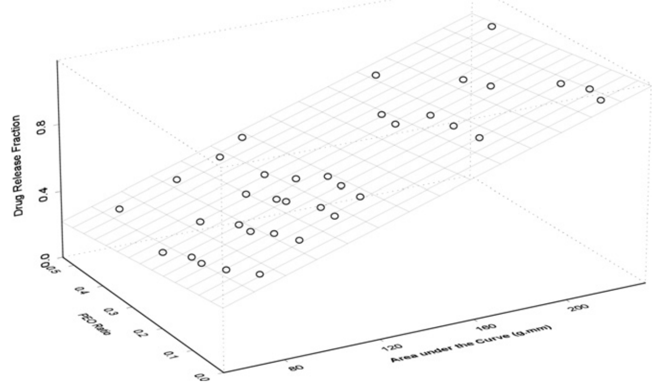

Fig. 8. Multiple regression plot of drug dissolution, PEO content and AUC_{TA} for Formulas 1–6 ($r^2 = 0.92$).

Drug solubility and polymer property undoubtedly play important roles in diffusion and dissolution of a modified release matrix tablet, which may consequently influence the applicability of certain experimentation. Due to high aqueous solubility of pseudoephedrine, it appeared that initial drug release was not influenced by the proportion of PEO in the tablet. Neither total drug release percentages were affected by PEO amount in the tablets, as its hydrophilicity enabled complete diffusion of the drug molecules after a 6-h period. The experiment of texture analysis described above was designed in a specific manner to allow for unidirectional polymer hydration in order to simplify the texture measurements. This would not be representative of actual dissolution scenario, in which dissolution medium permeates into the tablet matrix from all directions and drug diffusion also takes place similarly. It was anticipated from the results that all other surfaces of the tablet matrix would exhibit identical hydrogel swelling properties when in contact with a dissolution medium; reliable correlation could still be established among these test parameters.

Profiles of polymer hydration from a modified release matrix tablet can be determined using various study protocols; different test parameters are collected and processed to quantify stages of hydration over the time. Previous methods employed complex equations to mathematically describe the process of polymer hydration and drug dissolution. Some of the calculations used derived secondary parameters while the others required advanced mathematical background, which somehow limited the applicability of these methods in routine formulation development. By correlating directly measurable parameters from both drug dissolution and texture analysis described in this study, it is possible for formulation scientists to examine influences of hydrophilic polymers such as PEO on drug release modifications using a simple and straightforward mathematical expression. In comparison to other sophisticated instruments that are used for the measurement of polymer hydration, texture analysis is capable of offering a very easy yet reliable approach to characterize drug release and polymer swelling. This would provide additional operation tools to formulation scientists, allowing them to select optimal and easy-to-adapt methodology for dosage form development and assessment. The practical method demonstrated a unique and beneficial approach of the texture analyzer in formulation design and evaluation.

4. Conclusion

Drug dissolution from modified release matrix tablets of pseudoephedrine hydrochloride was dependent upon drug solubility, hydrogel formation and matrix excipient proportion in the preparation. Delayed drug release was largely attributed to the presence of hydrophilic polymer PEO, through the formation of hydrogel layer on the surface of the tablet. Lipid-based excipient GB did not effectively contribute to hydrogel formation, even though it aided in modified drug release by slow matrix erosion. Various mathematical correlations were explored; a linear multiple regression was established among parameters of texture analysis and drug dissolution, which would be beneficial in dosage form design and development. Texture analysis is a new and simple methodology added to pharmaceutical research and development; this study demonstrated a unique and versatile aspect of texture analysis for pharmaceutical applications.

Acknowledgements

The authors acknowledge research support from Canadian Foundation for Innovation (CFI), graduate studentship (HL) from University of Manitoba and mathematical consultation from Dr. Xikui Wang of Department of Statistics. The generous supply of tablet excipients from Dow Chemical Company, Gattefossé s.a., and Union Carbride Corporation is also acknowledged.

References

Apicella, A., Cappello, B., Del Nobile, M.A., La Rotonda, M.I., Mensitieri, G., Nicolais, L., 1993. Poly(ethylene oxide) (PEO) and different molecular weight PEO blends monolithic devices for drug release. Biomaterials 14, 83–90.

Choi, S.U., Lee, J., Choi, Y.W., 2003. Development of a directly compressible poly(ethylene oxide) matrix for the sustained-release of dihydrocodeine bitartrate. Drug Dev. Ind. Pharm. 29, 1045–1052.

Cilurzo, F., Selmin, F., Minghetti, P., Montanari, L., 2005. The effects of bivalent inorganic salts on the mucoadhesive performance of a polymethylmethacrylate sodium salt. Int. J. Pharm. 301, 62–70.

Colombo, P., Bettini, R., Santi, P., Peppas, N.A., 2000. Swellable matrices for controlled drug delivery: gel-layer behaviour, mechanisms and optimal performance. Pharm. Sci. Technol. Today 3, 198–204.

Cutts, L.S., Hibberd, S., Adler, J., Davis, M.C., Melia, C.D., 1996. Characterizing drug release process within controlled release dosage form using the confocal laser scanning microscope. J. Control. Rel. 42, 115–124.

Efentakis, M., Koutlis, A., 2001. Release of furosemide from multiple-unit and single-unit preparations containing different viscosity grades of sodium alginate. Pharm. Dev. Technol. 6, 91–98.

El-Arini, S.K., Clas, S., 2002. Evaluation of disintegration testing of different fast dissolving tablets using the texture analyzer. Pharm. Dev. Technol. 7, 361–371.

Gao, P., Meury, R.H., 1996. Swelling of hydroxypropylmenthycellulose matrix tablets. 1. Characterization of swelling using a novel optical imaging method. J. Pharm. Sci. 85, 726–731.

Gu, X., Li, H., MacNair, K.R., Simons, F.E.R., Simons, K.J., 2005. Simultaneous analysis of the H_1-antihistamine acrivastine and the decongestant pseudoephedrine hydrochloride by high-performance liquid chromatography. J. Pharm. Biomed. Anal. 37, 663–667.

Khan, K.A., 1975. The concept of dissolution efficiency. J. Pharm. Pharmacol. 27, 48–49.

Kim, C.J., 1998. Effects of drug solubility, drug loading, and polymer molecular weight on drug release from Polyox® tablets. Drug Dev. Ind. Pharm. 24, 645–651.

Lee, P.I., Peppas, N.A., 1987. Prediction of polymer dissolution in swellable controlled-release systems. J. Control. Rel. 6, 207–215.

Lemaitre-Aghazarian, V., Piccerelle, P., Reynier, J.P., Joachim, J., Phan-Tan-Luu, R., Sergent, M., 2004. Texture optimization of water-in-oil emulsions. Pharm. Dev. Technol. 9, 125–134.

Melia, C.D., Hodsdon, A.C., Davis, M.C., Mitchell, J.R., 1994. Polymer concentration profiles of surface gel layer of xanthan, alginate and HPMC matrix systems. In: Proceed Int'l Symp. Control. Rel. Bioact. Mater., vol. 21, pp. 724–725.

Narasimhan, B., Peppas, N.A., 1997. Molecular analysis of drug delivery systems controlled by dissolution of the polymer carrier. J. Pharm. Sci. 86, 297–304.

Rajabi-Siahboomi, A.R., Bowtell, R.W., Mansfield, P., Henderson, A., Davis, M.C., Melia, C.D., 1994. Structure and behaviour in hydrophilic matrix sustained release dosage forms: 2. NMR imaging studies of dimensional change in the gel layer and core of HPMC matrices undergoing hydration. J. Control. Rel. 31, 122–128.

Razaghi, A.M., Schwartz, J.B., 2002. Investigation of cyclobenzaprine hydrochloride release from oral osmotic delivery systems containing a water-swellable polymer. Drug Dev. Ind. Pharm. 28, 631–639.

Ritger, P.L., Peppas, N.A., 1987a. A simple equation for description of solute release I. Fickian and non-Ficlian release from non-swellable devices in the form of slabs, spheres, cylinders or disc. J. Control. Rel. 5, 23–36.

Ritger, P.L., Peppas, N.A., 1987b. A simple equation for description of solute release II. Fickian and anomalous release from swellable devices. J. Control. Rel. 5, 37–42.

Siepmann, J., Peppas, N.A., 2000. Hydrophilic matrices for controlled drug delivery: an improved mathematical model to predict the resulting drug release kinetics (the "sequential layer" model. Pharm. Res. 17, 1290–1298.

Siepmann, J., Podual, K., Sriwongjanya, M., Peppas, N.A., Bodmeier, R., 1998. A new model describing the swelling and drug release kinetics from hydroxypropyl methylcellulose tablets. J. Pharm. Sci. 88, 65–72.

Yang, L., Johnson, B., Fassihi, R., 1998. Determination of continuous changes in the gel layer of poly(ethylene oxide) and HPMC tablets undergoing hydration: a texture analysis study. Pharm. Res. 15, 1902–1906.