Build-up Caps to be Used in In-vivo Thermoluminescence Dosimetry

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ABSTRACT: Thermoluminescence dosimeters (TLDs) are widely used for quality assurance in radiation therapy. To avoid steep dose gradients, such measurements are usually made at either the depth of maximum dose D_{max} or at the exit skin surface, to assess in vivo the entrance and exit doses respectively. The build-up caps to be used have, among others, to induce minimal perturbation to the treatment field and the registered dose to be as close as possible to that to be assessed in order to reduce the size of the possible errors of the measurement. The aim of the present study was to assess the influence on the TL signal of the geometrical characteristics of cylindrical caps made of various materials at various photon fields. Cylindrical caps of various sizes made of plexiglas, aluminum, copper and stainless steel were constructed to accommodate four 3.1x3.1x0.9 mm LiF: Mg, Ti TLDs per cap. The relationships between the doses registered by the TLDs and the entrance and exit doses measured in phantoms with ionization chambers in 6 and 15 MV fields, were determined. The deviations from the dose registered by the TLDs and those measured by ionization chambers, increased with increasing material density. The ratio of the measured dose to the expected dose was equal to ±2.5%. The signal increased with build-up cap atomic number. On the other hand, build-up caps made up of Cu were found to be optimum for high-energy photon fields and caps made up of Plexiglas for low energy fields.

KEYWORDS: TLD, Radiation therapy, Thermoluminescence

INTRODUCTION

The uses of thermoluminescent dosimeters (TLDs) for in vivo dosimetry during radiotherapy have been proved to be a valuable technique for quality assurance [1-3]. The TLDs were used to verify the photon beam output with high accuracy is well documented in literature that suggests it for mailed dosimetry with high precision of approximately ±3% [1-3]. Entrance and exit dose can be performed using TLDs inserted in a build-up cap made of high(Z) material with a wall thickness equivalent to the depth of dose maximum to guarantee that the detector is measuring under electron equilibrium conditions [1-6]. The signal from TLD is strongly affected by the build up cap material, and thus the linearity and hence the accuracy of the detector. Furthermore, the perturbation of the build up cap, which may make a limitation for the daily use for the patients and the scatter radiation from build up cap might affect the skin sparing effect [1]. TLDs should be commissioned prior to use for different physical parameters in order to obtain correction factors. These factors include: linearity, fading, energy dependence and reproducibility. The supralinearity of the TL response on ionization density continues to be major subjects of importance. Recently some published studies [1-5], used the TLDs in build up caps in different materials. Some studies used powder [2,3] and others used TLD chips [1,4,5] with variable type of caps materials.

Although, the potential advantages of powder over other types of TLD (because it has the highest sensitivity)
the convenience, and the ability to vary the shape or thickness of the dosimeter for specific applications, but it is inconvenience in handling, requires dispensing system, poor spatial resolution and microbalance to determine accurately the amount of the material used for a particular purpose. Therefore, the chips, rods or other solid forms are preferable [7].

The purposes of this study were to

i. determine the feasibility and evaluate the effect of different buildup-caps materials (Copper, Aluminum, stainless steel and Plexiglas) on the onset of supralinearity of the entire dosimeters.

ii. Evaluate the perturbation of variable materials for 6 MV and 15 MV.

iii. Study the effect of different geometrical setting (source surface distance (SSD) and field size).

**MATERIALS and METHODS**

**Dosimeter:** TLD-100 produced by Harshaw (Bicron-NE, Solon, Ohio, USA) of dimensions 3.1 x 3.1 x 0.89 mm³ was used. A batch of 100 TLD chips with sensitivity within 2% was used divided equally into two groups on the basis of the energy applied (6 MV and 15 MV). Prior to the measurements, each TLD group were calibrated in correspondence to specific energy and standard geometry (SSD=100 cm, and field size 10x10 cm²). The calibration was performed using the same radiation source for both energies against an ionisation chamber (IC) model M30001-PTW-Freiburg, Germany. The chamber was calibrated at the National Standard Laboratory, Greek Atomic Energy Commission (EEAE). The annealing cycle of 400 °C for 1 hour and 100 °C for 2 hours was used in annealing oven (TLDO, PTW). Post irradiation annealing was carried out for 10 minutes at 100 °C. The mean minimum detection limits (3 standard deviations from zero reading) were determined to be 15 µGy. The TLD system used was a manual TLD reader (Harshaw 3500, Solon, USA). The read out for TLD-100 was at a 100 °C preheat temperature and the signal was acquired from 100°C to 280 °C for TLD-100 with heating rate of 10 °C/s.

**Build up cap design:** Four cylindrical build-up caps of various sizes made of Plexiglas, aluminum, copper and stainless steel were constructed for both energies to accommodate four TLD chips per cap (Figure 1, a and b). The caps dimension and physical construction are demonstrated in the Figure1 and Table 1. The inner pocket, 14 mm in diameter were constructed to accommodate four 3.1x3.1x 0.89 mm³ TLDs per cap, but those made of Plexiglas of 10 mm pockets that may accommodate up to three TLDs.

The caps were constructed with wall thickness equivalent to depth of maximum dose (1.6 cm and 2.7 cm of water for 6 MV and 15 MV, respectively). Prior to be used, all build up caps were calibrated for the same dose, the difference in the dose was less than 0.2%. Because insufficient build-up caps lead to larger correction factors to be applied this will influence the accuracy of the dose due to lack of electronic equilibrium [2,6]. The build caps were manufactured in a private workshop in Larissa, Greece, while the Plexiglas one is manufactured by Kalef-Ezra et al [1], University of Loaninna, Greece.
Table 1. Physical data of build up caps (all dimensions in mm).

<table>
<thead>
<tr>
<th>Material</th>
<th>Atomic Number</th>
<th>Density (g/cm³)</th>
<th>6 MV</th>
<th>15 MV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diameter</td>
<td>Wall Thickness</td>
<td>Height</td>
<td>Diameter</td>
</tr>
<tr>
<td>Copper</td>
<td>29.0</td>
<td>18.0</td>
<td>1.8</td>
<td>7.0</td>
</tr>
<tr>
<td>Aluminium</td>
<td>13.0</td>
<td>25.0</td>
<td>5.7</td>
<td>12.0</td>
</tr>
<tr>
<td>Stainless steel</td>
<td>25.6</td>
<td>18.0</td>
<td>2.3</td>
<td>7.5</td>
</tr>
<tr>
<td>Plexiglas*</td>
<td>6.25</td>
<td>30</td>
<td>10.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Stainless steel</td>
<td>12.0</td>
<td>10</td>
<td>11.9</td>
<td>20.0</td>
</tr>
</tbody>
</table>

* The build up cap used for both energies

Experimental set up: Build up cap was placed in the centre of surface of Plexiglas phantom with dimensions of 30 x 30 x 12 cm³. Figure 1.c. Two Philips Linear accelerators SL-75 and SL-18 were used in this work installed in the University Hospital of Larissa.

The standard irradiation setting is: SSD 100 cm, field size 10X10 cm². Each TLD was identified by its position in the cap, while each cap has specific number. Each point is an average of the reading of 12 TLDs. The build up cap was positioned with its long axis perpendicular to the central axis of the beam. The data was corrected for background radiation and by element correction coefficient. The applied dose values ranged between 0.25 cGy to 10 Gy for supralinearity effect, while a dose of 0.5 Gy was used to detect the effect of SSD and field size.
Figure 1. (a) and (b) Comparison of different build up caps materials in size and dimensions. (c) Build up caps TLD calibration setup, PMMA phantom, linear accelerator and ion chamber dose measurement device.

**Dose perturbation and in vivo dose measurement:** Dose perturbation was determined using radiographic film (Kodak-X Omat) at D\text{max} of Plexiglas phantom using standard irradiation conditions. The profile was obtained using film densitometer (VIDAR system corporation, USA). The different build-up caps have been calibrated to measure entrance dose. In vivo entrance and exit dose measurements were carried out for patients with simple fields for 15 patients (Prostate, stomach and head and neck cancer) to assess the appropriateness of the build up caps. The range of dose is found to be within ±2.5%.

**RESULTS AND DISCUSSION**
The TLD signal for different build up caps materials are shown in figure 2 (a & b) as a function of radiation dose. The figure shows linear function with the dose. The variation of the signal is due to the variation in the material density and atomic number \[^{[11]}\], i.e. copper signal is approximately double the signal from the Plexiglas signal. This variation ranged from 1.5% in low doses till 2.5% for the highest dose. The TL signals for the same dose values are highly different in different energies; this might be due to pair production interaction in high energies, while Compton scatter is dominant in low energies. Therefore for a better accuracy, each TLD should be calibrated to measure the dose for specific build up cap. The signals obtained from different geometrical settings also show no variations. As expected, the signal decreased with the increase of the field size and with decrease of SSD. Therefore, perturbation is the only factor that affects the selection for specific material for a build up cap. The dose perturbation of all build up caps is presented in Table 1 (waiting the film densitometer). It was found that there was generally very good agreement between all the materials used for measurements. Although differences of 3% are seen, some of these differences are likely to be due to real variations in build up cap thickness and manufacturing or beam output. From figure 1 c , it is clearly that there was no sign that the onset of the dose supra-linearity will change in different materials.

The linear relationship between the corresponding signal and the absorbed dose is one of the main advantages of TLDs, although, the signal has three levels; sublinearity, linearity and supralinearity. The linearity to dose depends on the dosimeter and TLD reader. The onset supralinear occurs because the dosimeter is saturated at 100 Gy. Supralinear behaviour of TLD-100 depends on the chemical composition of the material. In particular the concentration of titanium affects positively the onset of supralinear behaviour \[^{[8]}\].
Our results of patient’s measurements showed a deviation of ±1% less than stated deviation (±2.5%) from tissue equivalent materials. Therefore, copper and steel are more suitable for in vivo dosimetry for small fields, while aluminium and Plexiglas can be used for large fields with a better accuracy but higher perturbation. Although, Loncol et al \cite{5} used build up cap with three different materials (Perspex, Paraffin and stainless steel). However, no significant difference was shown. Moreover, these build up caps can be used for wide therapeutic energies with new setting of correction factors, i.e. from cobalt-60 till 18 MV.

CONCLUSIONS

In conclusion, the use of high atomic number (Z) material build up caps resulted in relatively high TL signal, although it does not affect the incidence of supra-linearity or the accuracy of the dose. Build-up caps made of Cu were found to be optimum for high-energy photon fields and caps made of Plexiglas are suitable for low energy fields. Copper has higher
atomic number, electron density and lower dimension with a reasonable accuracy. Tissue equivalent material and low Z material has better results, but the size of the build up cap is not suitable for small field and high energies.

REFERENCES
Effect of Different Parameters on Diclofenac Sustained Release Tablets

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ABSTRACT: In the present study different parameters influence the design and development of sustained release (SR) matrix tablets of diclofenac sodium were investigated. The aim was to increase therapeutic efficacy, reduce frequency of administration, and improve patient compliance. Sustained release matrix tablets of diclofenac sodium, were developed by using different drug: gum ratios, using Xanthan gum as matrix former, microcrystalline cellulose as diluent and Polyethylene Glycol (PEG 6000) as release modifier. Formulated tablets were evaluated for friability, hardness, thickness and their relation to the amount of gum:drug ratio and drug release. The drug release was evaluated in different pH, rotation speed and stirrer. All the formulations showed compliance with pharmacopoeial standards. Formulation consisting of drug:Gum ratio of 1:0.12 showed sustained release of drug for 12 hours with 89.67% release. The release pattern exhibited zero order kinetics. Thus, Xanthan Gum can be used as an effective matrix former.

KEYWORDS: Xanthan gum, Hydrophilic, matrix, Sustained release, Diclofenac sodium

INTRODUCTION

Increased complications and expense involved in marketing of new drug entities has focused greater attention on development of sustained release (SR) or controlled release (CR) drug delivery systems. Although the matrix system is the most innumerable method used in the development of controlled release (CR) formulations, there are a lot of parameters which control the release of the drug from it. Beside, long-term therapy for chronic disease conditions, multiple administration is inconvenient to the patients. Therefore, improving drug delivery system by maintenance of a steady drug plasma concentration is the aim of many studies to improve therapeutic efficiency by sustain release the drug. The use of polymers in controlling the release of drugs has become an important tool in the formulation of pharmaceutical dosage forms. Also the matrix tablets are easy to prepare and they are cost effective and exhibit predictable release behavior. In fact, a matrix is defined as a well-mixed composite of one or more drugs with a gelling agent i.e. hydrophilic polymer such as Xanthan Gum. Xanthan gum is a high molecular weight extracellular polysaccharide, produced on commercial scale by the viscous fermentation of gram negative bacterium Xanthomonas campesteris. Its high gelling capacity is of particular interest in the field of controlled release. On coming in contact with aqueous medium it hydrates at solid-liquid interface and form vicious layer which retards the release of the drug. It is used in thickening, suspending and emulsifying water based systems and fabrication of matrices. The appropriate drug/gelling agent ratio can play a role in prolonging and controlling the release of drug that is dissolved or dispersed. Diclofenac sodium is a most widely used NSAID, useful in the treatment of inflammation and pain.
of rheumatic disorders\textsuperscript{11}. It is characterized by rapid systemic clearance and thus warrants the use of SR formulation\textsuperscript{12}. Few SR formulations of diclofenac sodium (100 mg) are also available commercially.

The aim of the present study was to investigate the effect of the following parameters in sustaining the release of sodium diclofenac: drug/gum ratio, physical properties of the formulations such as friability, hardness and thickness, inclusion of some additives in the formulation such as microcrystalline cellulose (MCC) as diluent and Polyethylene Glycol (PEG) as release modifier, swelling index and different dissolution conditions such as change in pH, rotation speed and stirrer. Drug release from Xanthan matrix usually is preceded by polymer erosion or hydration, or a combination of both processes, depending on the drug/diluent ratio\textsuperscript{12}. That is why the release kinetics and mechanism of drug release were also investigated by using various release kinetics model equations.

**MATERIALS and METHODS**

**Materials:**

The study was conducted in Julphar Company, research unit, Ras Elkeimah, UAE 2007. Diclofenac sodium (DS), the pharmacopoeial grade of Xanthan gum (XG), viscosity of 1% an aqueous solution is 1350 cps at 25°, particle size less than 14.28 µm) was obtained from Julphar Co., Polyethylene glycol (PEG) was obtained from Rhone-Poulenc, Paris, France; diclofenac sodium from Yung Zip Chemicals, Taiwan, ROC; microcrystalline cellulose (MCC) Avicel PH101\textsuperscript{®} from FMC Corporation, Philadelphia, PA; and magnesium stearate from Shanghai Medicines and Health Products, Shanghai, China. All chemicals used were of analytical grade, and procured from commercial source.

**Methods**

**Preparation of SR matrix tablets:** SR matrix tablets of diclofenac sodium were prepared by using different drug:gum ratios viz. 1:0.12, 1:0.16, 1:20, 1:0.24, 1:0.28, as per the formula given in Table 1. Xanthan Gum (XG) was used as matrix-forming material, while microcrystalline cellulose (MCC) was used as diluent. Magnesium stearate was incorporated as lubricant. All ingredients were passed through a #100 sieve, weighed, and blended. The lubricated formulations were compressed by a direct compression technique, using 8 mm flat faced punches.

<table>
<thead>
<tr>
<th>Table 1: Composition of Diclofenac Sodium SR Matrix Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredients (mg)</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Diclofenac Sodium IP</td>
</tr>
<tr>
<td>Xanthan gum</td>
</tr>
<tr>
<td>Microcrystalline Cellulose</td>
</tr>
<tr>
<td>PEG</td>
</tr>
<tr>
<td>Magnesium stearate</td>
</tr>
<tr>
<td>Total Weight</td>
</tr>
<tr>
<td>Drug /Gum ratio</td>
</tr>
</tbody>
</table>

**Preparation of modified tablets by incorporation of PEG 6000:** Formulation F6 was modified by incorporating 12 mg of PEG 6000, to develop new formula F6 (Table -1), to observe the effect of PEG 6000 on drug release. Firstly, a physical mixture of drug and PEG 6000 was heated to temperature of a 70° C, till it was converted into a fluid state. It was
allowed to cool, and was then dried at room temperature. This mixture was then blended with XG, diluted with MCC, and finally the lubricated formulation was compressed directly with 8 mm flat faced punch, and evaluated.

**Estimation of diclofenac:**
Diclofenac content of the tablets was estimated by UV spectrophotometric method based on the measurement of absorbance at 276 nm in phosphate buffer of pH 6.8. The method was validated for linearity, precision and accuracy. The method obeyed Beer’s Law in the concentration range 0-10 μg/ml. When a standard drug solution was assayed repeatedly (n=6), the mean error (accuracy) and relative standard deviation (precision) were found to be 0.6 and 0.8%, respectively.

**Evaluation of physical properties:**
All the batches were evaluated for weight variation, hardness, friability, thickness and drug content as per USP XXIV monograph. The weight variation was determined by taking 20 tablets using an electronic balance. Tablet hardness was determined for 10 tablets using a Monsanto tablet hardness tester. Friability was determined by testing 10 tablets in a friability tester for 4 minutes at 25 rpm. Thickness was measured and SD was determined.

**In vitro drug release study:** In vitro drug release was studied using USP I apparatus, with 900 ml of dissolution medium maintained at 37±1° for 12 h, at 50 rpm. 0.1 N HCl pH 1.2 was used as a dissolution medium for the first 2 h, followed by pH 6.8 phosphate buffer for further 10 h. 5ml of sample was withdrawn after every hour and was replaced by an equal volume of fresh dissolution medium of the same pH. Collected samples were analyzed spectrophotometrically at 276 nm; cumulative percent drug release was calculated. The study was performed in triplicate. Formulation F1 was used to investigate the effect of dissolution variables including pH (1.2, 6.8), rotation speed (50,100 rpm), stirrers (paddle, basket) on drug release.

**ANALYSIS OF RELEASE DATA**
**Mathematical modelling:** The release profile of the drug obtained was analysed using different kinetic models such as zero order, first order, Higuchi, Korsmeyer- Peppas equation is used in order to evaluate the release mechanism from the matrices.

**Swelling Index:** The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation F1, F3 and F5 was studied. One tablet from each formulation was kept in a Petri dish containing phosphate buffer pH 6.8. At the end of 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 2 h, weights of the tablet were noted, and the process was continued till the end of 12 h. % weight gain by the tablet was calculated by formula;

$$S.I = \frac{X_t - X_0}{X_0} \times 100$$

where, S.I = swelling index, $X_t$ = weight of tablet at time ‘t’ and $X_0$ = weight of tablet at time t = 0.

**Accelerated stability studies:**
Stability study was carried out to observe the effect of temperature and relative humidity on optimized formulations (F1-F6), by keeping at 4° (in refrigerator), room temperature (28°), and at 45°, at RH 75±5%. In air tight high density polyethylene (HDP) bottles for three months. Physical evaluation and in vitro drug release was carried out after every 1 month.

**RESULTS and DISCUSSION**
**Evaluation of physical properties:** Hardness of the formulated tablets was in the range of 6-7 kg/sq.cm and the
percent weight loss in the friability test was found to be less than 0.4%, in all the formulated tablets. The content of diclofenac in all the matrix tablets was within 100±5% of the labelled amount. As such all the formulated matrix tablets prepared were of good quality with regard to hardness, friability and drug content (Table 2). All the formulations met the pharmacopoeial requirement range and all values were well within acceptable limits.

Table 2: Physical properties of Diclofinac Sodium SR Matrix Tablets

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Hardness (Kg/cm²)</th>
<th>Friability (%)</th>
<th>Thickness (mm)± SD</th>
<th>Batch code</th>
<th>Average weight (mg)± SD</th>
<th>% Drug Content mg± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>5.50±1.10</td>
<td>0.20</td>
<td>4.59±0.02</td>
<td>201 ± 3.43</td>
<td>100.1216</td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>5.50±1.50</td>
<td>0.27</td>
<td>4.48±0.04</td>
<td>204±2.44</td>
<td>99.1534</td>
<td></td>
</tr>
<tr>
<td>F3</td>
<td>5.45±1.35</td>
<td>0.33</td>
<td>4.41±0.07</td>
<td>209±2.36</td>
<td>99.5632</td>
<td></td>
</tr>
<tr>
<td>F4</td>
<td>5.40±1.27</td>
<td>0.36</td>
<td>4.51±0.07</td>
<td>208±4.52</td>
<td>100.02563</td>
<td></td>
</tr>
<tr>
<td>F5</td>
<td>5.45±1.10</td>
<td>0.40</td>
<td>4.46±0.04</td>
<td>209±4.01</td>
<td>99.2345</td>
<td></td>
</tr>
<tr>
<td>F6</td>
<td>3.00±0.20</td>
<td>0.50</td>
<td>4.41±0.06</td>
<td>208±3.52</td>
<td>100.4562</td>
<td></td>
</tr>
</tbody>
</table>

Effect of dissolution variables on drug release: Dissolution studies were conducted at two pH conditions acidic pH 0.1 N HCl and pH 6.8 buffer and the effect of pH and time was studied in all formulations. It showed that the tablet dissolved in alkaline medium as compared to acidic pH (Figure 1). From this it could be concluded that all the batches showed pH dissolution dependent. The increase in the percentage release may be due to decrease in the amount of polymer as hydration is a function of amount of polymer present.

Concerning the rotation speed, a slight positive influence was observed, as stirring speed was increased, the thickness of hydrated gelatinous layer surrounding the intact tablet core decreases, resulting in slight increase in the rate of drug release from matrix tablet (Figure 2). Our results were in disagreement with that obtained by Vazquez, and et al. who reported a positive influence of rotation speed drug release.

Regarding the effect of using different stirrers, there was no significant difference observed between basket method and paddle method at the same experimental conditions (P >0.05), when data was analyzed using student 't' test (Figure 3). That finding is in agreement with Efentakis M.

The incorporation of PEG 6000 (6% of weight of tablet) in formulation F6, the release were sustained observed in 12 h (Figure 1). Thus, there was no significant increase in drug release. This may be attributed to the little amount of PEG. Sankar, was reported that incorporation of drugs into a water soluble carrier such as PEG has frequently improved drug dissolution rate and bioavailability.

Swelling Studies: The swelling index was calculated with respect to time (Figure 4). The swelling index increased with time, because weight gain by tablet was increased proportionally with rate of hydration up to 3 h. Later on, it decreased gradually due to the dissolution of outermost gelled layer of tablet into dissolution medium. The relationship between swelling index gum concentration and drug release decrease was observed. It was observed that as gum concentration increased, swelling index increased and the cumulative percent drug release decreases. The reason attributed to the slow erosion of the gelled layer from the tablets containing higher amount of xanthan gum.

The pattern of drug release from hydrophilic polymeric matrices involves solvent penetration, hydration and swelling of the polymer, diffusion of the dissolved drug in the matrix, and
erosion of the gel layer. Initially, the diffusion coefficient of drug in the dehydrated polymer matrix was low; it increased significantly as the polymer matrix imbibes more and more water and forms a gel, as time progressed (Fig. 4). That is attributed to the hydration rate of the polymer matrix, and thereby the gel formation which depends significantly on polymer proportion, viscosity, and to a lesser degree on polymer particle size.

In order to investigate the release mechanism, the data were fitted to models representing zero-order, first-order and Higuchi’s square root of time (Table-3). It had been found that all the fabricated tablets followed Higuchi release kinetics. The diffusion was non-Fickian mechanism, which indicates the drug release through diffusion and relaxation, that was similar to study reported by Sankar, et al.

Accelerated stability studies:
Accelerated stability conditions did not appear to have any effect on the rate of drug release. All formulations were stable physically and chemically within the limits.

CONCLUSIONS
Diclofenac sodium release from different gum concentrations formulations studied was generally linear. Accelerated stability conditions did not appear to have any effect on the rate of drug release. However, pH of the dissolution medium had a significant effect on the release while the rotation speed, the apparatus method and additives have little effects on drug release from xanthan gum matrices. These parameters should be properly controlled to avoid variations in rate of drug release among production of matrix sustained release tablets.

<table>
<thead>
<tr>
<th>Function</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero order</td>
<td>% diss = Kt</td>
</tr>
<tr>
<td>First order</td>
<td>% diss = 100 (1 - e-kt)</td>
</tr>
<tr>
<td>Higuchi</td>
<td>% diss = Kt 0.5</td>
</tr>
<tr>
<td>Korsmeyer- Peppas</td>
<td>Q = Kpt</td>
</tr>
</tbody>
</table>

Figure 1
Figure 2
Figure 3
Figure 4
Table 4: Drug release kinetics from different matrix tablets (using Higuchi, zero order and first order release)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Higuchi model</th>
<th>Zero order release</th>
<th>First order release</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( K )</td>
<td>( r^2 )</td>
<td>( K )</td>
</tr>
<tr>
<td>F1</td>
<td>26.77</td>
<td>0.9831</td>
<td>8.6982</td>
</tr>
<tr>
<td>F2</td>
<td>24.49</td>
<td>0.9822</td>
<td>7.916</td>
</tr>
<tr>
<td>F3</td>
<td>23.07</td>
<td>0.9827</td>
<td>7.4919</td>
</tr>
<tr>
<td>F4</td>
<td>22.08</td>
<td>0.9848</td>
<td>7.155</td>
</tr>
<tr>
<td>F5</td>
<td>21.04</td>
<td>0.9858</td>
<td>6.8239</td>
</tr>
<tr>
<td>F6</td>
<td>19.568</td>
<td>0.9776</td>
<td>6.4581</td>
</tr>
</tbody>
</table>

Table 5: Determination of drug release mechanism using Peppas exponential model equation.

<table>
<thead>
<tr>
<th>Formulations</th>
<th>( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.6741</td>
</tr>
<tr>
<td>F2</td>
<td>0.6652</td>
</tr>
<tr>
<td>F3</td>
<td>0.6223</td>
</tr>
<tr>
<td>F4</td>
<td>0.6277</td>
</tr>
<tr>
<td>F5</td>
<td>0.6215</td>
</tr>
<tr>
<td>F6</td>
<td>0.6985</td>
</tr>
</tbody>
</table>

REFERENCES


