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# Modification of Ibuprofen Drug Release from Poly(ethylene glycol) Layered Silicate Nanocomposites Prepared by Hot-Melt Extrusion

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**ABSTRACT:** Composites of the poorly water soluble drug ibuprofen, a nonsteroidal anti-inflammatory commonly used for pain relief, with layered silicates (nanoclays) and a poly(ethylene glycol) (PEG) were prepared by hot melt extrusion. A highly intercalated and partially exfoliated morphology was determined using wide-angle x-ray diffraction, field emission scanning electron microscopy, and high-resolution transmission electron microscopy. The crystalline content of PEG was significantly reduced, as shown by differential scanning calorimetry studies, as a consequence of the large surface area of clay platelets physically hindering polymer chain dynamics and, in the case of montmorillonite, by tethering of PEG via hydrogen bonding. Addition of layered silicate retarded the release of ibuprofen from the PEG matrix, even though the crystalline content of PEG was reduced. This study therefore indicates that drug release in solid dispersion systems may be modified or indeed tailored by the inclusion of layered silicates. © 2013 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40284.

**KEYWORDS:** nanoparticles; nanowires and nanocrystals; drug delivery systems; biomedical applications; biomaterials

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## INTRODUCTION

There are significant challenges to overcome in the processing of poorly water-soluble active pharmaceutical ingredients as not only may their solubility influence bioavailability but in addition their solid state properties may influence the way in which they may be manufactured and formulated.[1] Different methods have been employed to overcome these difficulties that have included the use of medicinal grade polymers such as poly(ethylene glycol) (PEG) and more recently starch as meltable polymer excipients.[2–5] These polymers may improve the solubility and dissolution profile of the drugs while also facilitating preparation as commercially viable and scalable products.[3] In this investigation we study the use of hot melt extruded nanocomposites as a means of preparing low melting point, poorly soluble drugs. The model drug chosen for this study was ibuprofen, ((*RS*)-2-(4-(2-methylpropyl) phenyl) propanoic acid), a nonsteroidal anti-inflammatory with a relatively low melting temperature (77°C), which is poorly soluble in water, difficult to compact and has a soapy bitter taste, hence it is an ideal "difficult" candidate with which to study alternative processing methods.[6] Ibuprofen exists as a racemate with a dimeric crystalline unit cell structure, although it is only the (S+) enantiomer that is pharmaceutically active. This is further complicated by the solvent-dependence of the crystal habit and the possible generation of amorphous material on processing.[6–11] The melt processable polymer chosen for this study was PEG 20000 as it is a nontoxic, semicrystalline polymer with a low melting point below that of ibuprofen.[2,3] Newa et al. studied the drug release profiles of ibuprofen from PEG 6000 and PEG 20000 prepared through a simple melting solid dispersion technique [rather than via hot melt extrusion (HME) as used here] and was able to demonstrate favorable dissolution behavior from the solid disperse systems.[3,4]

HME is a technique gaining increasing interest within the pharmaceutical field as a means to prepare active drug formulations. A recent review by Repka et al. highlighted the advantages of HME over traditional pharmaceutical batch processes, including solvent free formulations, an important environmental consideration, continuous processing, the ability to process in the form of a solid dispersion or a solid suspension, fewer processing steps and requires no compression.[6] Several drugs have been successfully manufactured using HME including the HIV drug Kaletra Meltrex ®.[13] By using the same pharmaceutically active ingredients but changing the processing medium from a soft gel

Additional Supporting Information may be found in the online version of this article.

**Table I.** Thermal Properties of PEG, Ibuprofen (I), Cloisite 20A (M), Somasif MEE100 (S), and Composite Materials

| Composite name | $T_c$ (°C) | $T_m$ (°C) | $\Delta H_c$ (J/g) | $\Delta H_m$ (J/g) | $X_c$ (%) |
|---|---|---|---|---|---|
| PEG | 41.8 | 68.7 | −182.0 | 161.4 | 81.9 |
| PEGI5 | 39.2 | 65.9 | −153.8 | 153.0 | 73.9 |
| PEGM5 | 37.4 | 64.7 | −162.4 | 154.9 | 74,8 |
| PEGI5M1 | 35.7 | 62.2 | −148.3 | 144.4 | 69.0 |
| PEGI5M3 | 35.1 | 62.9 | −131.8 | 113.0 | 52.8 |
| PEGI5M5 | 37.4 | 62.6 | −135.6 | 133.6 | 61.1 |
| PEGS5 | 40.5 | 68.2 | −181.8 | 168.2 | 81.2 |
| PEGI5S1 | 34.9 | 62.2 | −147.3 | 143.4 | 68.5 |
| PEGI5S3 | 34.9 | 63.4 | −145.0 | 140.0 | 65.4 |
| PEGI5S5 | 33.6 | 62.6 | −136.8 | 133.0 | 60.8 |

The numbers after each letter refer to the % composition.

to a molten polymer and using HME to produce a hard tablet formulation, fewer doses were required and the product did not require refrigeration.[13]

The HME approach was further developed in this study to form a solid suspension by processing composites of a PEG with ibuprofen and a layered silicate (nanoclay) using HME at a temperature below the melting temperature of ibuprofen.[14] This methodology provides additional functionality as the very high aspect ratio and surface area of layered silicates (up to 1000 $m^2/g$) are also exploited to provide a tortuous path for ibuprofen diffusion and release. Ternary mixtures of polymer, drug, and nanoclay (a multiplatelet structure) and the issue of effective dispersion and distribution of these platelets in a biopolymer matrix is an area of recent interest,[15–20] and could provide a route to produce tablet formulations in a continuous process. More specifically, our previous studies have indicated that the inclusion of nanoclays may alter both the mechanical (and hence processing) and dissolution properties of dispersions via distribution of the silicate layers through the polymer matrix, thereby forming a suspension of nanolayers.[15–17] This inclusion may profoundly alter performance, although to date the predictability of the interaction and associated structural properties is poorly understood. In this study we look to correlate the composition, processing, and performance properties of a model ternary system using a drug with known associated formulation challenges and two nanoclay systems (a surfactant modified montmorillonite and a partially synthetic fluoromica) with PEG 20,000 used as the base polymer carrier.

## EXPERIMENTAL

### Materials

PEGEG Polyglykol 20000S was supplied by Clariant (Horsforth,UK), ibuprofen (I): (USP purity>99 %) was purchased from Voigt Global Distribution (Kansas City, USA) and Cloisite 20A (referred to as M) was purchased from Southern Clay Products (Gonzales, USA), and is a natural montmorillonite modified with a dimethyl, dihydrogenated tallow (i.e. ~65% C18; ~30% C16; ~5% C14), quaternary ammonium surfactant. Somasif MEE100 (referred to as S) was supplied by CBC (Tokyo, Japan) and is a partially synthetic layered silicate, a fluoromica modified with *bis* (2-hydroxylethyl methyl dodecylammonium chloride).

### Composite and Test Specimen Preparation

PEG, ibuprofen, and the layered silicate (either M or S) were melt compounded in a Collin Zk25 twin screw extruder with six heater zones set to 55°C, 60°C, 60°C, 60°C, 60°C, and 60°C from feed section to the die, respectively, and a screw speed of 60 rpm. The extrudate was air cooled by a gun blowing air onto the extrudate just after the die entrance and further cooled along a customized conveyor belt, (Collin CR 136/350)). The composition and codes for the composites prepared are listed in Table I. Test specimens for drug release studies were prepared by compression moulding disks (diameter 18 mm; height 1.2 mm).

### Characterization of Materials

Wide angle X-ray diffraction (XRD) patterns were recorded using a PANanalytical X'Pert Pro MPD XRD (Almelo, The Netherlands) instrument using Cu-$K_\alpha$ radiation ($\lambda = 1.54$ Å) generated at 45 kV and 40 mA. The samples were scanned at 0.63°/min in the range of $2\theta = 1$–$40^o$ and a step size of 0.02°. The surface morphology of all samples was examined using a JEOL JSM-6500F Field Emission Scanning Electron Microscope (FE-SEM) at 10 keV. Two types of samples were prepared for analysis by SEM, cryo-fractured and "surface"and all were sputtered with a thin layer of gold prior to imaging. Samples for examination using high-resolution transmission electron microscopy (HRTEM) were obtained using a Reichert-Jung Ultracut E (FC-4E cryo-unit) ultramicrotome with a glass knife at −117°C and collected onto 400 mesh copper grids. Images were obtained using a FEI Tecnai F20 field emission HRTEM (Philips) at 200 keV. Nonisothermal crystallization, melting, and dissolution experiments were conducted on thin slices (~1 mm) of polymer sandwiched between microscope glass slides and placed on a hot stage (Mettler Toledo FP90) attached to a LSL Leica-Toleda PP polarizing microscope equipped with a video camera system. The samples were heated at 5 K/min. to 80°C then cooled at 5 K/min to room temperature. The images in Supporting Information Figure S1 shows the loss of ibuprofen crystalline phase after melting, confirming the ibuprofen

was in the solid state when mixed with molten PEG at 60°C. Differential scanning calorimetry (Perkin-Elemer high speed Diamond DSC) was used to measure the thermal properties of the unfilled PEG, ibuprofen and extrudates (~5 mg) of the composite materials using a heating and cooling rate of 10 K/min. between 20°C and 100°C. The crystalline content ($X_c$ %) of all materials was calculated using an enthalpy value of 197 J/g for a theoretically 100% crystalline PEG and corrected for blend composition.

### *In Vitro* Drug Release

Dissolution studies were performed using a Copley DIS 8000 USP standard dissolution apparatus with paddle stirrer (Nottingham, UK). The dissolution medium (900 mL of phosphate buffer pH 7.2) was maintained at 37°C ± 0.5°C and stirred at 50 rpm. The samples of a known weight (average 350–400 mg) were added to the buffer solution and at predetermined intervals (5, 10. 15, 20, 25, 30, 60, 90, 120, 180 and 240 min), 5 mL of sample was withdrawn (5 mL syringe Terumo syringe without needle) and replaced with the same volume of fresh dissolution medium at 37°C ± 0.5°C to maintain constant volume. The samples were filtered with a Millipore (Watford, UK) 0.45-m Millex syringe driven filter unit, placed into clean numbered sample vials and analyzed by UV spectroscopy using a Hitachi U2000 UV Spectrophotometer at 243 nm using 10 mm silica cells (VWR International, Lutterworth UK Model 307 370002). Each sample had a uniform amount of ibuprofen added (5 wt %) to enable comparison across all samples. A set of standard solutions of ibuprofen were made in the buffer solution and a calibration curve was constructed from the UV spectrum at 243 nm. The percentage ibuprofen release was calculated from the amount of ibuprofen released divided by the theoretical amount for 100% release of 5 wt % ibuprofen in the solution. The results reported are an average of four measurements ± standard deviation.

## RESULTS AND DISCUSSION

Composites of PEG with 5 wt % ibuprofen (I) and 1, 3, and 5 wt % of either a naturally derived montmorillonite (M) or partially synthetic fluoromica (S) were prepared using a twin-screw extruder as outlined in the experimental section using the formulations listed in Table I. The extent of dispersion of both ibuprofen and the respective layered silicate (M or S) and the morphology of the nanocomposites were investigated using a combination of wide-angle X-ray diffraction (WAXD), FE-SEM and HRTEM.

Figure 1(a,b) show the WAXD patterns for PEG, I, S, and M and the respective nanocomposites. The *d*-spacings for the $d_{001}$ basal plane reflection were determined using Bragg's equation:

$$n\lambda = 2d\sin\theta \quad (1)$$

where n is an integer ($n = 1$), $\lambda$ is the wavelength of the incident X-ray beam ($\lambda = 1.5406$ Å), $\theta$ is the angle of incidence of the X-ray beam, and $d$ is the interatomic distance between silicate layers. The $d_{001}$ spacing for M itself was measured at 2.54 nm which on addition of 5 wt % M to PEG increased to 4.23 nm, suggesting a highly intercalated structure whereby the polymer chains diffuse in to the intergallery spacing, contributing to

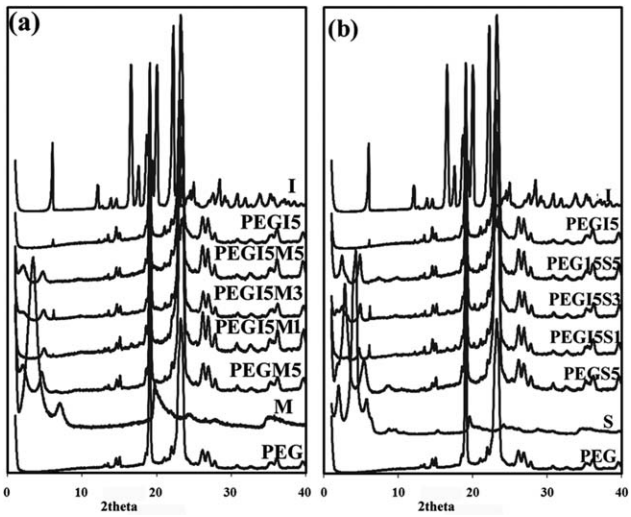


**Figure 1.** WAXD patterns for composites of PEG and ibuprofen with (a) montmorillonite (M) and (b) fluoromica (S).

delamination of the clay platelets. Application of shear during melt mixing also contributes to delamination of the layered silicate stucture again allowing PEG chains to diffuse between silicate layers. Addition of 5 wt % ibuprofen to PEGM composites made no difference to the increase in basal spacing obtained on addition of 3 wt % (PEGI5M3) and 5 wt % (PEGI5M5) M, and there was no $d_{001}$ peak detected for the PEGI5M1 sample, the latter associated with the limits of detection. For S itself, the $d_{001}$ spacing was determined to be 2.05 nm which again increased but to 3.12 nm on addition of 5 wt % S to PEG, hence once again evidence was seen for intercalation of the polymer chains in the intergallery spacing of the layered silicate S. However, in contrast to the PEGM composites, addition of 5 wt % ibuprofen to PEGS, irrespective of the loading of S, yielded an increase in $d_{001}$ spacing. Interestingly the hydrophilic PEG chains were less effective at entering the intergallery spacing of the hydrophilic S clay relative to the hydrophobic M clay.[21] The differences in expansion of the galleries of the two nanoclays used may be attributed to the different conformations and arrangements of the surfactants on the layered silicates, and thus the initial size of the intergallery spacing, in addition to the larger aspect ratio of the fluoromica (S) ~600,[22] compared to montmorillonite (M) ~280.[23] A further consideration is the anchoring of PEG oxygen atoms with clay platelets induced by $Na^+$ cations.[24]

Ibuprofen is present in a small concentration of 5 wt %, although diffraction peaks were nevertheless observed which confirmed the presence of crystalline ibuprofen by WAXD for both PEGM and PEGS systems. If amorphous ibuprofen had been formed as a consequence of the heat and shear applied during melt processing of the nanocomposites then a broad amorphous peak at ~17° $2\theta$ would be expected.[8] Indeed, Zhu et al. reported that the crystalization rate of ibuprofen was enhanced by the additional heterogenous nucleation sites in crystalline PEG, although their ibuprofen concentration was 20 wt % and hence not directly comparable with the present study.[25] It is the structure of ibuprofen which influences its low

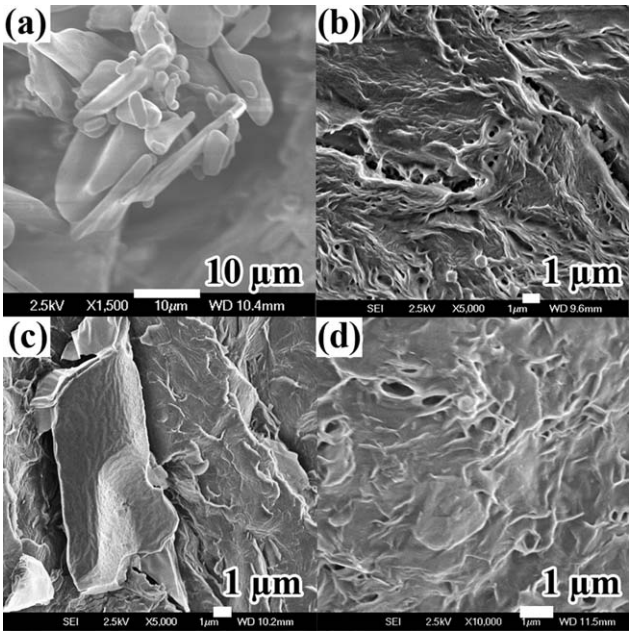


**Figure 2.** FE-SEM images of (a) ibuprofen (scale bar 10 μm) and fractured surfaces of (b) PEG (scale bar 1 μm), (c) PEGI5 (scale bar 1 μm), and (d) PEGI5S5 (scale bar 1 μm).

melting point and poor water solubility because of the aromatic ring having a butyl side chain and an ionizable carboxyl group attached. When the crystal structure is disrupted it is weak hydrogen bonds breaking which affects the packing arrangement of the crystal planes in the raecmic ibuprofen mixture. Romero et al. proposed that the crystal packing in ibuprofen forms preferentially in a plane in which the intermolecular distances between are affected when stress is applied tangentially such that crystal habit is changed but not internal structure.[26]

The morphology of the composite materials was examined using FE-SEM (Figure 2). The crystalline form of ibuprofen can be clearly seen in (a) and the porous surface of neat PEG in (b). However, on addition of both M (c) and S (d) to PEG the platelet structure of both are clearly evident, resulting in a less porous PEG surface. The morphology at higher magnification was examined by HRTEM (Figure 3). By way of example, in Figure 3(a) the long thin strands of ibuprofen crystals can be observed for PEGI5S5. The entrapment of the ibuprofen molecules by the clay platelets is suggested from the HR-TEM image shown in Figure 3(b), where the ibuprofen appears encased by clay platelets. Figure 3(c) shows a large crystal of ibuprofen marked with an X, approximately 500 nm in diameter for the PEGI5S3 composite. Further evidence is also provided from HR-TEM studies for a highly intercalated, partially exfoliated composite morphology, as many sub-20nm thick groups of clay platelets of M, typically of length 60–200 nm were readily observed [area encircled in Figure 3(d)].

The thermal and crystallization behavior of PEG after addition of ibuprofen and both nanoclays (M and S) was studied using DSC, (Figure 4). The enthalpies of melting and crystallization ($\Delta H_m$ and $\Delta H_c$), onset of melting and crystallization, temperature of melting ($T_m$), crystallisation temperature ($T_c$), and crystalline content ($X_c$ %) for all materials were determined and are listed in Table I. Typically, the melting point ($T_m$,°C) of PEG decreased by ~2°C on addition of 5 wt % ibuprofen (I) and by 4°C when M was added, again at the 5 wt % loading level. However, $T_m$ for PEG was unchanged on the addition of S (within experimental error). Interestingly, the $T_m$ of PEG decreased by ~6°C when both I and either M or S was added. The temperature of crystallisation ($T_c$,°C) of PEG decreased by approximately 3°C on addition of I only, by ~ 4°C when M was added, but $T_c$ was unaltered on addition of S. When both I and M or S was added to PEG, the decrese in $T_c$ was between 4°C and 6°C. Moreover, the crystalline content ($X_c$ %) of PEG decreased from ~82% to ~74% on addition of I or M alone alone, but was unchanged when S was added. Interestingly, this effect was not observed when 3 wt % M was added, perhaps as a consequence of the increased concentration of M being less well dispersed, thus rendering less effective surface area available for nucleating PEG crystallization. However, when both I and either M or S were blended with PEG, the crystalline content fell from ~82% down to 53% and 61%, a 35% and 25% reduction, respectively. The significant changes in $X_c$ after melt blending PEG with ibuprofen (I) and M and further supports the evidence from HRTEM and WAXD that an intercalated composite morphology predominates for the ternary systems. Furthermore, the mobility of the PEG chains is constrained by the clay platelets, (both $X_c$ and $T_c$ decreased), thus hindering PEG crystallization. A decrease in PEG crystalline phase on addition of I and M or S will alter PEG dissolution and directly counteract any barrier effect anticipated on addition of layered silicate.

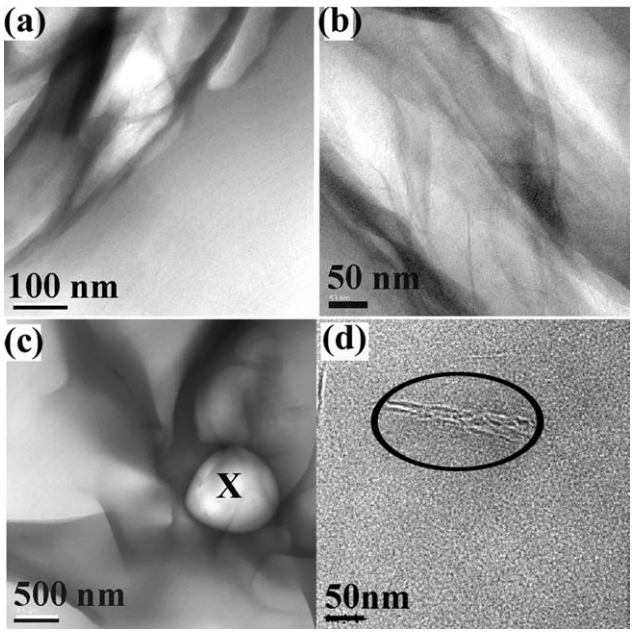


**Figure 3.** Bright field HRTEM images of PEGI5S5 showing (a) ibuprofen surrounded by platelets of S dispersed in a PEG matrix (scale bar 100 nm), (b) ibuprofen with the platelets twisted around the I crystal (scale bar 50 nm), (c) PEGI5S3 (scale bar 500 nm) where X indicates the ibuprofen crystal, and(d) sub-20nm group of platelets of M in the PEG matrix (scale bar 50 nm).

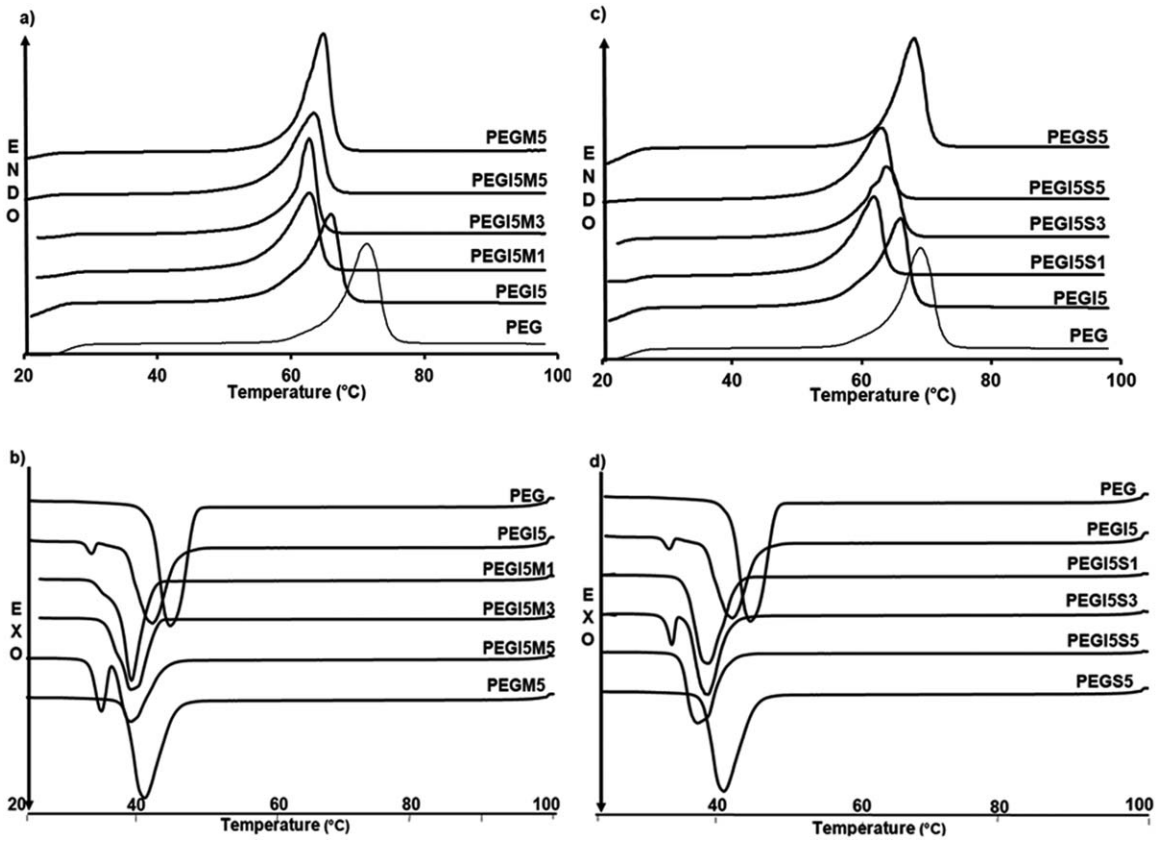


**Figure 4.** DSC melting endotherms (a) and (c), and crystallization exotherms, (b) and (d) for composites of PEG and ibuprofen with M and S, respectively.

Concomitant with the reduction in the $X_c$ of PEG on addition of I, the spherulite size of the PEG was significantly altered. Figure 5 shows images captured during video recording of PEG (a) and PEGI5 (b) on cooling, demonstrating the addition of ibuprofen to PEG results in spherulites with larger diameters. On average the diameters increased from 75 μm to about 300 μm, illustrating the effect ibuprofen has on the crystallization behavior of PEG. The broadening, and in some instances, most notably for the PEGI5M5 sample, the splitting of the crystallization peak of PEG in the DSC curves further supports the hypothesis that addition of M and S alters PEG crystallization by interupting chain folding.[27] In a recent study by Zhu et.al addition of 20 wt % ibuprofen resulted in a slowing of the spherulite growth rate of PEG (molecular wt 3350), which the authors attributed to hydrogen bonding between ibuprofen and PEG.[25] Interestingly, the size of the ibuprofen crystals after PEG dissolution is smaller than that prior to the experiment confriming the poor water solubility of ibuprofen, see photographs in Figure 5(c,d).

The *in-vitro* dissolution and drug release kinetics of ibuprofen from PEG with and without nanoclay was investigated. Figure 6 shows the percentage ibuprofen release as a function of time. There are three distinct steps in drug release from a matrix; liquid penetration into the matrix, dissolution of the drug and diffusion, the latter is not relevant in this system. Within the first 15 min the release rate is altered by the presence of M or S, the effect more pronounced for S and with increasing concentration

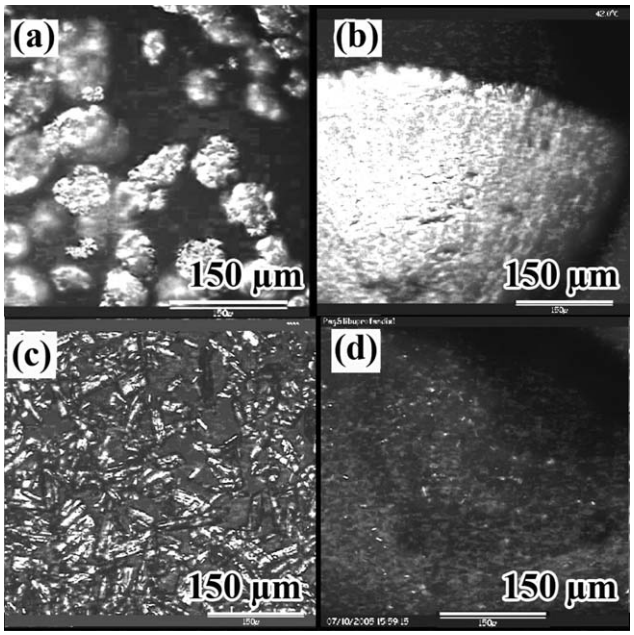


**Figure 5.** Optical micrographs captured taken from hot stage microscopy videos of the onset of crystallization for (a) PEG (scale bar 150 μm), (b) PEGI5 (scale bar 150 μm), and optical micrographs of (c) ibuprofen crystals, and (d) ibuprofen crystals released from a PEGI5 to a water solution.

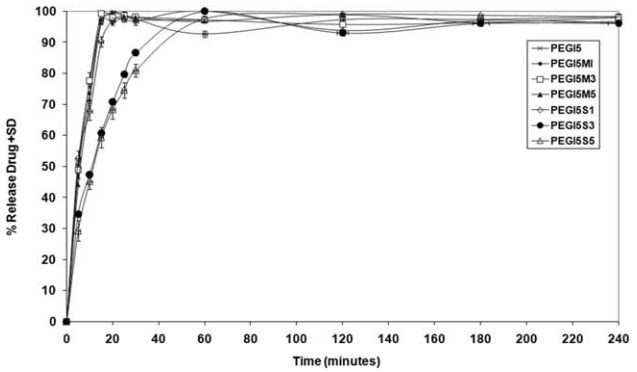


**Figure 6.** Drug release profiles for ibuprofen loaded PEG nanocomposites.

of S in the composite, behavior associated with the larger effective surface area of S relative to M (600 compared to 280). Thus, liquid penetration and the dissolution behavior of ibuprofen are retarded. The time for 50%, 80%, and 100% release of ibuprofen from each formulation was measured and the diffusion coefficients determined using classical Fickian diffusion theory, see Table II. In effect, the drug release rate has been manipulated by altering the dissolving rate of the polymer.[28]

Furthermore, to aid the standardization of the dissolution experiments the composite materials were compression moulded into disks having uniform dimensions. Equation (2) can be used to describe the diffusion controlled release behavior of drugs which have an assumed diffusion coefficient ($D$) for one-dimensional diffusion:

$$\frac{M_t}{M_\infty} = 1 - \frac{8}{\pi^2}\sum_{n=0}^{\infty}\frac{1}{(n+1)^2}\exp\left\{-\frac{(2n+1)^2 D\pi^2}{l^2}t\right\} \qquad (2)$$

where $M$ is defined as the mass of drug released at time $t$, $M_\infty$ is the mass of drug released as time approaches infinity, and $l$ is the thickness of test sample. Taking the first term from the summation series eq. (1) can be reduced to the following equation:

$$\ln\left(1\frac{M_t}{M_\infty}\right) = \ln\frac{8}{\pi^2} - \frac{D\pi^2}{l^2}t \qquad (3)$$

From a linear regression of eq. (3) a plot of $\ln(1 - M_t/M_\infty)$ against $t$ can be constructed and $D$ determined from the slope of the line ($D\pi^2/l^2$), see Figure 6. One of the assumptions made in calculating the diffusion coefficients is that sink conditions are maintained, (i.e. saturation solubility is at least three times more than the drug concentration in the dissolution medium as outlined in USP (US Pharmacopeia, 2005). By using 900 mL of dissolution medium and standard USP apparatus this condition has been fulfilled. The time taken for 50%, 80%, and 100% ibuprofen release from PEG increased on addition of either M or S. The most significant increase from 15 to 60 min was with the synthetic fluoromica (S) with increasing addition of S from 1 wt % (20 min) to 3 wt % (60 min) to 5 wt % (60 min). The same dissolution and drug release experiment was peformed on non-uniform as extuded samples, see Supporting Information Figure S2 and Table S1. Overall, the time for 100% release was less than that achieved for the uniform compression moulded samples, ~25 and 30 min for the 5wt % M and S loaded PEG, respectively.

## CONCLUSIONS

In summary, a series of ibuprofen loaded PEG layered silicate nanocomposites were readily prepared using melt mixing in an extruder, characterized and the drug release profile and diffusion coefficients for ibuprofen release determined. Ibuprofen maintained its crystalline form after processing by hot-melt extrusion (HME) but the crystalline content of the PEG was reduced on addition of ibuprofen. When both drug and either M or S was blended with PEG, the crystalline content decreased significantly, by up to 35%. The greatest retardation in drug release occurred when the synthetic fluoromica (S) was added to PEG, because of the larger effective surface area of the S platelets compared to those of M.

Ibuprofen was chosen as a model drug to demonstrate the possibilities of tailoring the release properties of a poorly water soluble drug when added to PEG using HME. This is important as many new pharmaceutically active ingredients developed are poorly water soluble and difficult to process conventionally. In this study, we have demonstrated that by tailoring processing conditions and nanocomposite composition, retardation of drug release of a poorly water soluble drug can be realized by using a small concentration of layered silicates. However, before the dissolution of poorly water soluble drugs like ibuprofen can be

**Table II.** Diffusion Coefficients for Ibuprofen Release Kinetics

| Sample | Time 50% release (min | Time 80% release (min) | Time 100% release (min) | Diffusion coefficients $10^{-5}$ $cm^2s^{-1}$ |
|---|---|---|---|---|
| Ibuprofen powder | 2.75 ± 0.1 | 4.4 ± 0.1 | 5.6 ± 0.1 | - |
| PEGI5-D | 4.6 ± 0.1 | 10 ± 0.1 | 15 ± 0.3 | 3.5 ± 0.1 |
| PEGI5M1-D | 5.0 ± 0.1 | 11 ± 0.1 | 15 ± 0.3 | 3.2 ± 0.1 |
| PEGI5M3-D | 4.8 ± 0.1 | 11.5 ± 0.1 | 15 ± 0.3 | 3.5 ± 0.2 |
| PEGI5M5-D | 5.75 ± 0.1 | 11.5 ± 0.3 | 15 ± 0.3 | 3.0 ± 0.1 |
| PEGI5S1-D | 5.0 ± 0.1 | 12.8 ± 0.1 | 20 ± 0.3 | 2.9 ± 0.1 |
| PEGI5S3-D | 12.5 ± 0.1 | 25 ± 0.1 | 60 ± 0.3 | 1.6 ± 0.1 |
| PEGI5S5-D | 12.5 ± 0.1 | 30 ± 0.1 | 60 ± 0.3 | 1.5 ± 0.1 |

D is disc sample

significantly retarded or controlled by nanoclay addition the role of surfactant modifier, clay platelet size and clay dispersion in the PEG matrix must be better understood.

## ACKNOWLEDGMENTS

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