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# Influence of the composition of glycerides on the solid-state behaviour and the dissolution profiles of solid lipid extrudates

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ABSTRACT

A monoacid triglyceride and a partial glyceride were extruded below their melting ranges alone and together in different mixture ratios to investigate the influence of the chemical composition of the lipid matrix on the solid-state properties and dissolution characteristics. The partial glyceride exhibits a faster release of the drug compared to the triglyceride due to its surfactant properties. The lipid mixtures show rather complex solid-state behaviour and hence unexpected dissolution characteristics. Adding 10% (w/w) partial glyceride to a triglyceride matrix led to increased incidence of the unstable α-form of the triglyceride leading to recrystallization of the stable β-form over time which causes fractal structures on the extrudate surface which decrease the dissolution rate. Adding 50% (w/w) partial glyceride to the triglyceride matrix also results in tristearin α-formation subsequently followed by recrystallization to the β-form. But as 50% of the matrix consists of the partial glyceride the dissolution rate was faster than the rate obtained by pure triglyceride or the 9 + 1 (w/w) mixture of triglyceride and partial glyceride. The results of this study help in understanding the complex solid-state behaviour of solid lipid extrudates with different composition and to manufacture suitable lipid-based oral dosage forms.



## 1. Introduction

The application of lipids as excipients for the processing of oral dosage forms is widespread in the field of pharmaceutical sciences. Due to their versatile structural appearance they offer a wide range of different possibilities for pharmaceutical formulation purposes. Furthermore, these substances are biodegradable and physiologically non-toxic. Lipids can be used to enhance solubility and permeability of drugs exhibiting poor bioavailability (Humberstone and Charman, 1997; Prabhu et al., 2005; Porter and Charman, 2001) to realize prolonged release (Hamdani et al., 2002) and to achieve taste masking (Qi et al., 2008).

Several techniques are established for processing lipid-based dosage forms and they are solvent free and do not involve drying steps. Either thermal or mechanical energy or a combination of both is used to produce the dosage form (Zhang and Schwartz, 2003; Liu et al., 2001; Chauhan et al., 2005). Generally, the production of lipid dosage forms involves melting the lipid and resolidification in combination with a solid active pharmaceutical ingredient (API) to form a coherent matrix in which the API is embedded. A relatively new approach to process lipid-based dosage forms is solid lipid extrusion (Pinto and Silverio, 2001; Breitkreutz et al., 2003; Windbergs et al., 2009). This technique uses lipids in powdered form available as pharmaceutical excipients like Dynasan® which are blended with the API and extruded through an extruder below the lipid melting temperature, thus avoiding melting of the complete lipid mass. In a further step the extrudates are either spheronized to pellets or cut into cylindrical pieces of suitable size (Reitz and Kleinebudde, 2007). The choice of manufacturing technology strongly influences the subsequent properties of the dosage form as surface structure, crystallinity, stability and reproducibility.

There are some difficulties in the processing of lipid-based dosage forms. Due to their versatile structure, they exhibit rather complex solid-state behaviour. Usually lipids exhibit three different polymorphic modifications: the thermodynamic least stable α-form, the metastable β′-form and the stable β-form (Sato, 2001; Sato et al., 1999). Each of these forms is defined by a specific packing mode of the fatty acid chains, with the stable β-form exhibiting the densest packing mode. Transformations from a less stable to a more stable form can occur. Therefore, the processing of lipid-based dosage forms is often accompanied by transformations, melting events and recrystallization. Furthermore, the processed dosage forms often show transformations during storage, which finally affect the dissolution behaviour (Choy et al., 2005). This effect in

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the literature often called "aging" is mostly due to the appearance of a metastable lipid modification during processing which eventually transforms to a more stable modification during storage (Whittam and Rosano, 1975; Sutananta et al., 1994). These effects might result in alterations of the drug release. Therefore, the solid-state behaviour of lipids during processing and its relationship to drug release and storage is quite difficult to predict.

The aim of this study is to modify the composition of a lipid matrix under controlled conditions in order to develop solid lipid extrudates with tailor-made dissolution profiles. Furthermore, the solid-state behaviour of the glycerides that are used should be understood for the production of dosage forms according to the Quality by Design approach. Based on the results of studies done on pure triglycerides (Windbergs et al., 2009) a partial glyceride was extruded alone and in different ratios with a triglyceride to evaluate the effect of the lipid matrix composition and possible interactions between either the lipids or matrix components and API. Solid-state analysis was conducted on the powders and on the extrudates using a combination of DSC, XRPD, contact angle measurements and ATR-IR spectroscopy. In addition, dissolution testing and storage experiments were performed.

## 2. Materials and methods

### 2.1. Materials

The following powdered glycerides were provided by Sasol (Witten, Germany) and were used as received: tristearin (Dynasan 118®) and glyceryl monostearate (Imwitor 491®). Tristearin is a monoacid triglyceride which is 98% pure, whereas glyceryl monostearate is a partial glyceride consisting of 96% monoglycerides. Theophylline anhydrate (BASF, Ludwigshafen, Germany) was used as a model drug in powdered form as supplied. Each of the crystal forms was verified by X-ray powder diffraction and where possible compared to the theoretical patterns provided by the Cambridge Structural Database (Cambridge Crystallographic Data Centre (CCDC), Cambridge, United Kingdom) with the associated software Mercury (v. 1.5). The ref codes for the crystal structures used were: BAPLOT01 (theophylline anhydrate) and QOYKIY (tristearin β-form). All lipid powders were in their stable β-form before processing. The particle sizes were determined with laser diffraction and the following results were obtained: tristearin $x^{50} = 27\,\mu m$, $x^{90} = 90\,\mu m$; glyceryl monostearate $x^{50} = 316\,\mu m$, $x^{90} = 556\,\mu m$; theophylline anhydrate $x^{50} = 94\,\mu m$, $x^{90} = 288\,\mu m$ taking the mean of three measurements.

### 2.2. Methods

#### 2.2.1. Extrusion

The powdered glycerides in different ratios were weighed in a 1:1 ratio with theophylline anhydrate and then blended in a laboratory mixer (LM20 Bohle, Ennigerloh, Germany) for 15 min at 25 rpm. A gravimetric dosing device (KT20 K-Tron Soder, Lenzhard, Switzerland) fed the powder mixtures into the barrel of a co-rotating twin-screw extruder (Mikro 27GL-28D, Leistritz, Nürnberg, Germany). Extrusion was performed with a constant screw speed of 30 rpm and a feeding rate of $40\,g\,min^{-1}$. The processing temperature was either 55 °C or 65 °C with both temperatures below the melting temperature of the excipients. The extruder die plate contained 23 holes of 1 mm diameter and 2.5 mm length.

#### 2.2.2. Differential scanning calorimetry (DSC)

For DSC experiments a DSC 821e calorimeter (Mettler-Toledo, Gießen, Germany) was used. The heating rate was $10\,°C\,min^{-1}$ within a temperature range of 20–300 °C. Hermetically sealed aluminium pans (40 μl) were used containing samples of approximately 5 mg each. All experiments were conducted twice.

#### 2.2.3. X-ray powder diffraction (XRPD)

A theta-theta X-ray powder diffractometer (D8 Advance, Bruker AXS GmbH, Karlsruhe, Germany) was used for XRPD analysis. The measurements were performed in symmetrical reflection mode with CuKα radiation (λ = 1.54 Å) using Göbel mirror bent multilayer optics. The angular range measured was 5–40° ($2\theta$), with a step size of 0.05° ($2\theta$) and a measuring time of 1 s per step. The samples were gently compressed in the sample holders to obtain a smooth and flat surface. All experiments were conducted in triplicate. With the same diffractometer variable temperature measurements were performed in the temperature range of 25 °C up to the melting temperatures of the individual lipids.

#### 2.2.4. Attenuated total reflectance infrared (ATR-IR) spectroscopy

For these experiments an FTIR spectrometer (Bruker FTIR Vertex 70, Bruker, Ettlingen, Germany) with an ATR accessory fitted with a single reflection diamond/ZnSe crystal plate (MIRacle ATR, PIKE Technologies, Madison, WI, USA) was used. Spectra were collected of powder or extrudate between 4000 and 650 $cm^{-1}$ at a resolution of 4 $cm^{-1}$ and using an average of 64 scans for each spectrum. All experiments were conducted in triplicate.

#### 2.2.5. Dissolution

A basket apparatus (Sotax AT7 smart, Sotax, Lörrach, Germany) in accordance with the USP29 Method 1 was used for dissolution experiments. For each vessel a sample size of 140 mg was used consisting of extrudates cut to approximately 1 cm. Experiments were performed in purified water containing 0.001% polysorbate 20 as a dissolution medium. The temperature was kept at 37 ± 0.5 °C and the stirring speed was 50 rpm. The absorption of the dissolution medium was measured using the absorption wavelength of 242 nm in 2.5 min intervals using a UV–Vis spectrometer (Lambda 40, Perkin–Elmer, Rodgau-Juegesheim, Germany) in a continuous flow-through cuvette. Each experiment was conducted in triplicate and for the dissolution curve the mean was calculated. The standard deviation of the replicates was below 2%.

#### 2.2.6. Storage

Samples were placed in open Petri dishes and exposed to accelerated constant climatic conditions (40 °C/75%RH) for 12 months in a climate chamber (KBF 240, Binder, Tuttlingen, Germany).

#### 2.2.7. Scanning electron microscopy (SEM)

SEM micrographs were recorded with a working voltage of 20 kV using a scanning electron microscope (Leo 1430VP, Leo Elektron Microscopy, Cambridge, UK). Samples were mounted on aluminium stubs using double-sided carbon tape and sputter-coated with gold for 150 s (Agar Manual Sputter Coater B7340, Agar Scientific, Stansted, UK).

#### 2.2.8. Contact angle measurements

Contact angle measurements were performed with an optical contact angle meter (Drop shape analysis system DSA100, Krüss, Hamburg, Germany). A 0.8 μl drop of distilled water was placed on the extrudate surface and the contact angle was directly determined by using the associated software (Drop shape analysis DSA1 v 1.90, Hamburg, Germany). For each sample eight measurements were performed and the mean was calculated.

## 3. Results and discussion

### 3.1. Extrusion and solid-state characterization of triglycerides

As shown in a previous paper (Windbergs et al., 2009) triglycerides provide a suitable matrix for oral dosage forms. However, a good understanding and appropriate monitoring of the solid-state formation is mandatory to obtain reliable dosage forms. The solid-state behaviour during processing and storage is quite complex and difficult to predict. The combination of friction and temperature during the extrusion process was found to influence the solid-state formation to a large extent. Tristearin, for instance, partly forms the metastable α-form at a processing temperature of 55 °C, whereas at a production temperature of 65 °C only the stable β-form is obtained. In the thermogram depicted in Fig. 1 relevant melting endotherms can be found at 70.7 °C (onset tristearin β-form) and at 50.2 °C (onset tristearin α-form) (Hagemann, 1988). Interaction with the model drug theophylline anhydrate was not observed as the endotherms in the DSC thermograms depict. Lipid as well as drug (onset melting endotherm 271.1 °C) provide sharp and clearly defined melting peaks (Chen et al., 1997).

### 3.2. Extrusion and solid-state characterization of partial glycerides

A partial glyceride was investigated with respect to its suitability as matrix material for solid lipid extrudates. For the solid-state characterization a combination of DSC, XRPD and ATR-IR spectroscopy was used to monitor solid-state changes in powders and extrudates. The partial glyceride glyceryl monostearate consists of 96% monoglycerides exhibiting a reported melting temperature of 77–83 °C for the stable β-form (Hagemann, 1988). Extrudates were obtained with processing temperatures of 50, 55, 62 and 65 °C. The smoothest extrudates were achieved at 65 °C. Fig. 2 depicts the analytical results obtained for the powder compared to extrudates produced at different temperatures. XRPD diffractograms suggest that the powder exists in the β-form as their peak positions (Fig. 2) did not change irrespective of extrusion temperatures. The stable β-form of the lipid was maintained (Yajima et al., 2002). Minor differences in peak intensity are due to orientation effects of the crystals. Therefore the lipid remains in a stable conformation after processing.

Adding 50% (w/w) theophylline anhydrate as a model drug led to interesting results. The DSC thermograms of the pure powders and the extrudate consisting of lipid and drug (50%, w/w) (Fig. 3a) show

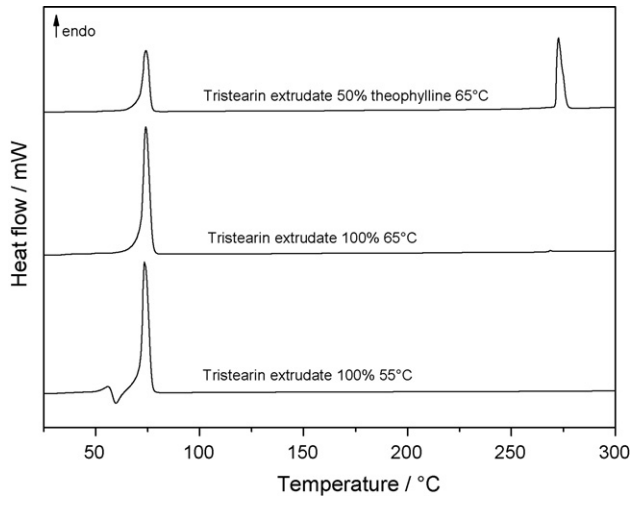


**Fig. 1.** DSC thermograms of tristearin extrudates.

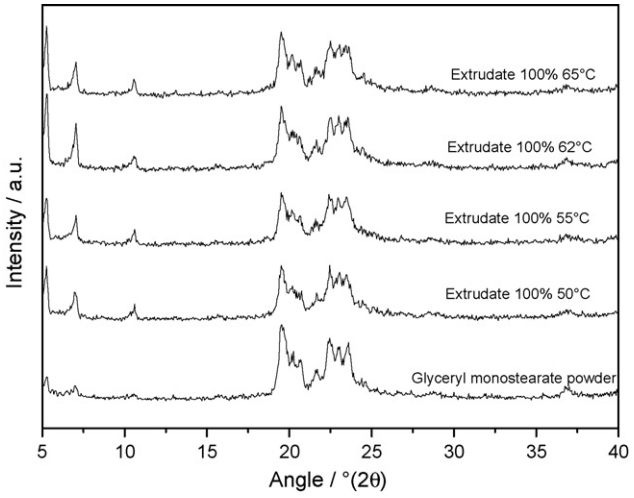


**Fig. 2.** XRPD patterns of glyceryl monostearate powders and extrudates.

a limited interaction between lipid and drug. In the thermogram depicting the results for the extrudate the lipid is characterized by its clear melting peak (onset 76 °C) whereas the drug shows a broad endotherm (onset 250 °C) instead of the sharp melting peak observed for the pure drug powder (onset 270.7 °C). Due to the surfactant properties of glyceryl monostearate the drug is able to partially dissolve into the molten lipid when the melting temperature of the lipid is exceeded during the measurement. The XRPD and ATR-IR spectra indicate that the crystalline structures of lipid and drug in the extrudate remain intact (Fig. 3b,c). In the XRPD pattern the drug in the extrudate exhibits the same peak positions (at 7.1° (2$\theta$) and 12.6° (2$\theta$)) as in the powder, and therefore one can conclude that no polymorphic changes have occurred. Furthermore, the ATR-IR spectra suggest no solid-state changes as the peaks specific to theophylline anhydrate, such as the C=O stretching (1665 and 1713 $cm^{-1}$) and CH stretching (3122 $cm^{-1}$), remain unchanged (Nolasco et al., 2006; Kobayashi, 1988). The lipid exhibits several characteristic peaks such as those due to $CH_2$ scissoring (1473 $cm^{-1}$) and C=O stretching (1735 $cm^{-1}$) (Yano and Sato, 1999).

From these results it can be summarised that extrudates could be produced in the chosen temperature range without undergoing solid-state transformations as a result of processing. The crystal structure of the drug was unchanged, but DSC thermograms were able to indicate a limited interaction between drug and lipid during the measurement.

### 3.3. Extrusion and solid-state characterization of mixtures of a triglyceride and a partial glyceride

To investigate the impact of composition of the lipid matrix structure powder mixtures of tristearin and glyceryl monostearate were prepared in two different weight ratios (9 + 1 and 5 + 5 w/w). The 9 + 1 mixture was extruded at 55 and 65 °C. As the results of the solid-state analysis at the different temperatures led to the same results the 5 + 5 (w/w) mixture was only extruded at 65 °C.

Fig. 4a depicts the DSC thermograms of the lipid powders and the extrudates of the mixture tristearin/glyceryl monostearate (9 + 1 w/w) at two different processing temperatures. As the melting peaks of the pure powders (both β-form) are quite close to each other, they only form one melting peak due to the β-form in the extruded mixture (onset 70 °C). In addition, there is a small melting peak at 50.2° in the extrudates which is due to the metastable α-form of tristearin (Hagemann, 1988). At a processing temperature of 55 °C this phenomenon can also be found for the pure tristearin extrudate (Fig. 1) as this extrusion temperature leads

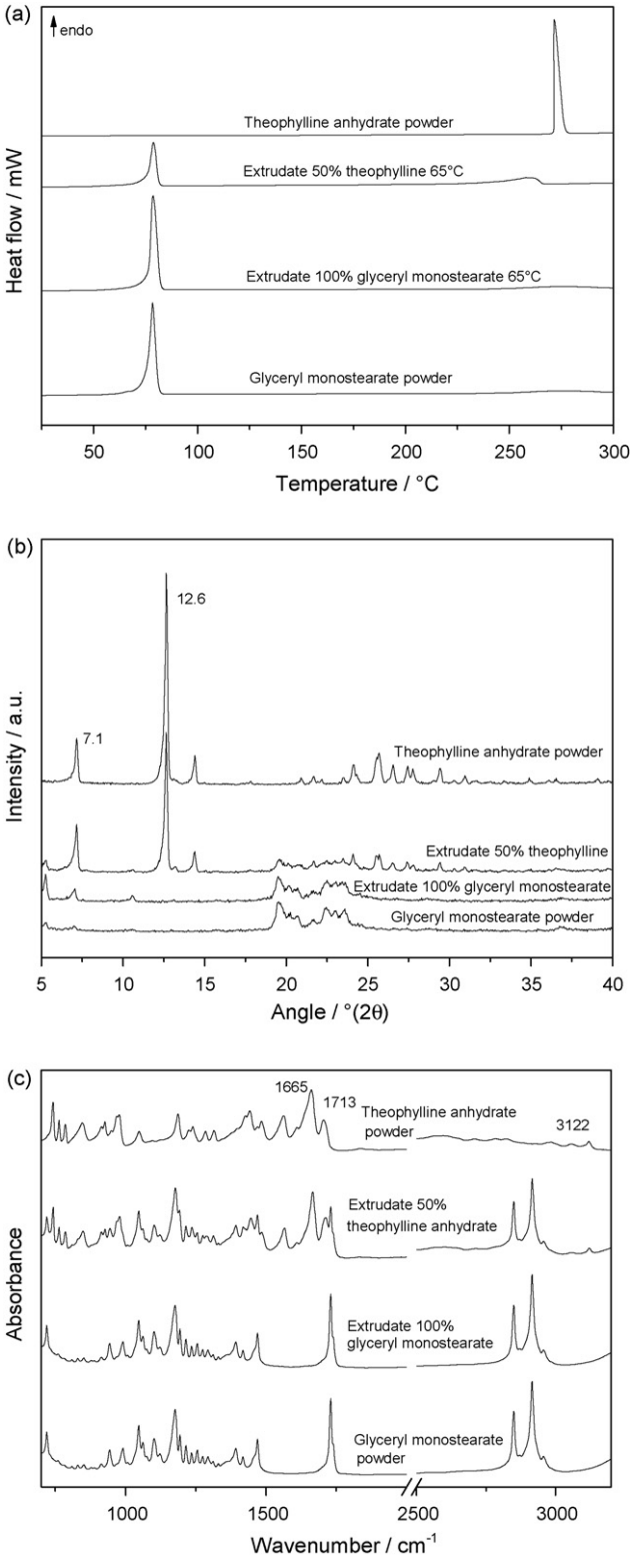


**Fig. 3.** Physical characterization of glyceryl monostearate and theophylline powder and extrudates (a) DSC thermograms, (b) XRPD patterns and (c) ATR-IR spectra.

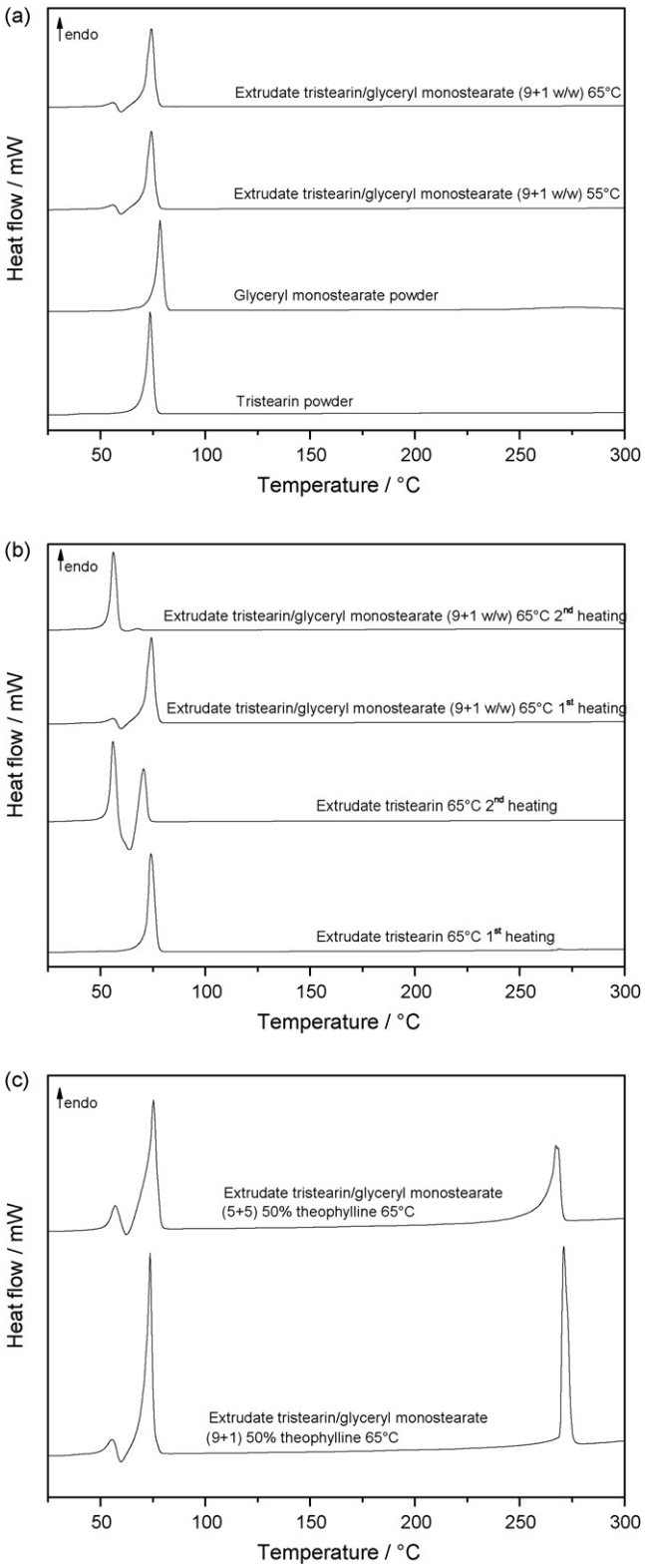


**Fig. 4.** DSC thermograms of tristearin and glyceryl monostearate (a) powders and extrudates, (b) different heating schemes and (c) mixed extrudates with drug.

to a partial solid-state transformation of tristearin (Windbergs et al., 2009). Small parts of the lipid mass melt during the extrusion process induced by a combination of friction and temperature. The temperature at which the extrudate leaves the extruder determines whether the molten parts recrystallize in the metastable α-form or directly in the stable β-form. For pure tristearin extrudates only the β-form is obtained at a processing temperature of 65 °C (Fig. 1).

When the tristearin is extruded with glyceryl monostearate, the α-form is also obtained at a processing temperature of 65 °C. Modifying the DSC measurements led to a deeper insight into these solid-state phenomena. The DSC samples were measured once (1st

heating), then stored for 24 h in ambient conditions and measured again (2nd heating). The results are shown in Fig. 4b. During the first measurement the samples melt completely, and therefore the results of the second measurements depict the thermograms of the recrystallized melts. By comparing the pure tristearin to the mixed sample it becomes quite obvious that the presence of the partial glyceride, glyceryl monostearate, hinders the formation of the tristearin β-form, which is consistent with previous findings (Garti et al., 1988). Glyceryl monostearate is able to stabilize the α-form of tristearin and prevent or delay the transformation to the stable β-form.

The chemical structure of glyceryl monostearate exhibits some compatibility with the tristearin structure and therefore it is likely that some formation of structures that combine both tristearin and glyceryl monostearate occurs, which appears to promote the formation of the α-form (Garti, 1988). In the food industry especially in the chocolate manufacturing this effect is deliberately used to prevent crystallization of cocoa butter to the stable polymorph of cocoa butter as it lacks gloss and is aesthetically unappealing (Schlichter-Aronhime and Garti, 1988). The melt of the pure tristearin extrudate recrystallizes in a mixture of α- (onset 53.5 °C) and β-forms (onset 67 °C). The two melting endotherms are connected by a recrystallization exotherm (onset 58.8 °C) which is due to the metastable β′-form. Unfortunately, melting of the β′-form cannot be detected properly as it is severely suppressed by the recrystallization to the stable β-form (Kellens et al., 1991). The second measurement of the mixed matrix sample depicts almost completely the α-form of tristearin (onset 53.5 °C). To test the observed correlation between the presence of the partial glyceride and the effect on solid-state behaviour, two mixing ratios of the lipids were compared (Fig. 5c). As can be seen from the thermogram the quantity of tristearin α-form in the extrudate and the intensity of the interaction with the drug can both be correlated to the amount of glyceryl monostearate in the mixture. The comparison of the two tristearin α-form endotherms (onset 52.8 °C) shows that even though the amount of tristearin is lower in the 5 + 5 mixture, the intensity of the α-form peak is higher than in the 9 + 1 mixture. The extent of the interaction between glyceryl monostearate and drug can be seen in the intensity of the drug melting endotherm. In the 9 + 1 mixture the peak is sharp and clear (onset 269.3 °C) whereas the peak in the 5 + 5 mixture is much broader and less defined (onset 263.7 °C) indicating the increased interaction with glyceryl monostearate.

To test the hypothesis that the tristearin α-form in the lipid mixture is only formed via the melt powder mixtures of tristearin and glyceryl monostearate (9 + 1 and 5 + 5) were prepared and diffractograms were taken while heating the samples up from 25 to 75 °C in 5 °C steps (Fig. 5a and b). There was no evidence of any solid-state changes until the sample melted completely as can be seen from the diffractograms.

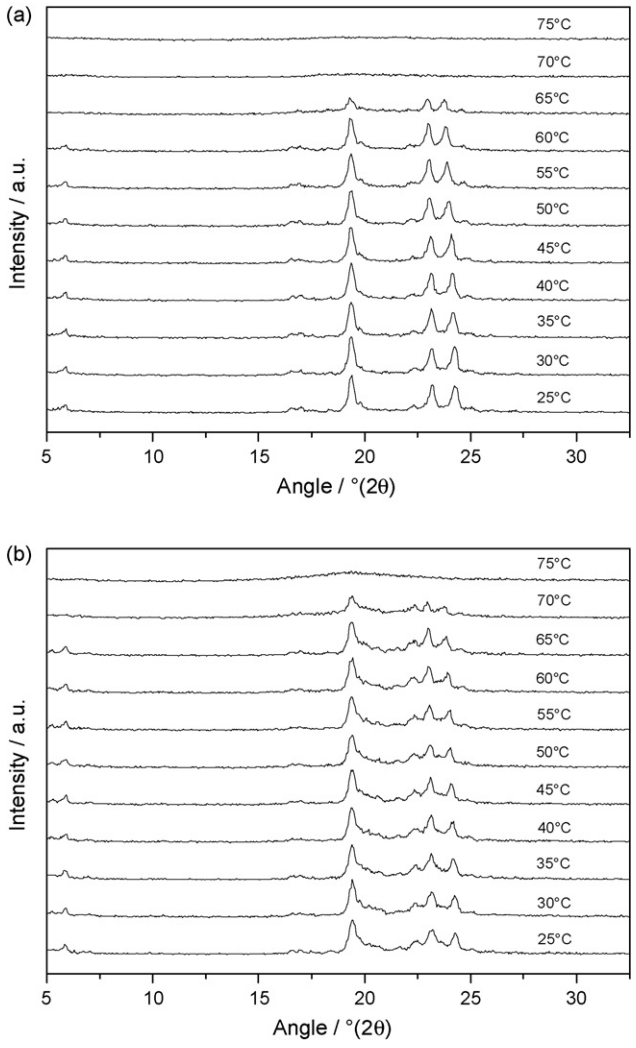


**Fig. 5.** Variable temperature XRPD patterns of physical powder mixtures (a) tristearin/glyceryl monostearate (9 + 1 w/w) and (b) tristearin/glyceryl monostearate (5 + 5 w/w).

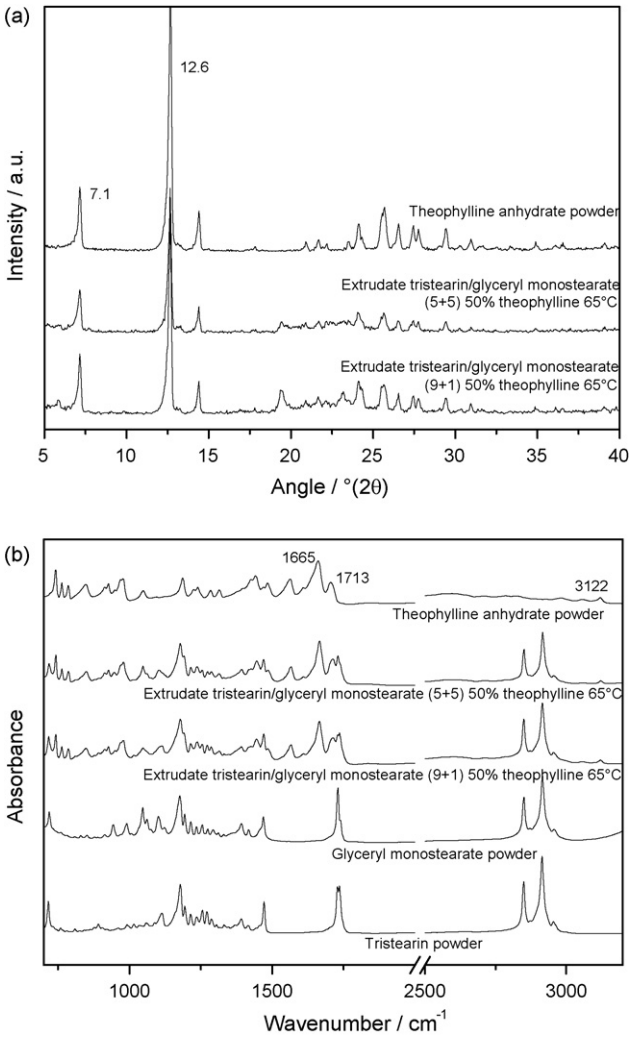


**Fig. 6.** Physicochemical characterization of powders and mixed extrudates of tristearin and glyceryl monostearate (a) XRPD patterns and (b) ATR-IR spectra.

Fig. 6 displays the results obtained with XRPD and ATR-IR measurements. For both mixing ratios of the two lipids in the extrudates the XRPD peaks for the drug and lipid are obvious (Fig. 6a). ATR-IR spectra (Fig. 6b) support the XRPD results. The crystalline structure of the lipids and the drug is maintained.

### 3.4. Surface characterization

The surface of solid lipid extrudates is very important with regard to the dissolution behaviour as the dissolution from glyceride matrices is completely diffusion controlled. Thus, the matrix stays intact and no erosion occurs. The surface of the processed extrudates was investigated using SEM and contact angle measurements.

The SEM images (Fig. 7) provide visual support for the results already obtained with solid-state analysis. The surface of extrudates containing 50% (w/w) theophylline anhydrate was investigated. The extrudates consisting of glyceryl monostearate exhibit a rather smooth surface. The contact angle of 106° is in good agreement with the SEM image (Fig. 7a) (Fang et al., 2007). Fig. 7b depicts the surface of a tristearin/glyceryl monostearate (5 + 5 w/w) extrudate. The surface is also smooth but the higher contact angle of 116° is due to the triglyceride which reduces the surfactant effect of the partial glyceride glyceryl monostearate. The extrudate consisting of tristearin (manufactured at 65 °C) exhibits a contact angle of 121° and a relatively smooth surface (Fig. 7c). As a comparison Fig. 7d depicts an extrudate consisting of tristearin and glyceryl monostearate (9 + 1 w/w) produced at 65 °C which should be expected to possess a reduced contact angle due to the surfactant properties of the partial glyceride glyceryl monostearate. But Fig. 7d depicts an extrudate surface exhibiting needle-like structures. This phenomenon, sometimes called blooming, is due to the transformation from the unstable tristearin α-form to the stable β-form (Khan and Craig, 2004). This effect is intensified at a processing temperature of 55 °C. Fig. 7e depicts the surface of the tristearin extrudates whereas Fig. 7f depicts the surface of the tristearin/glyceryl monostearate (9 + 1 w/w) mixed extrudate. The surface of both extrudates is completely covered with sharp needles possessing a contact angle of 125° in both cases. As the contact angle is a predictor of the wettability it is quite obvious that the needles at the extrudate surface strongly affect the dissolution behaviour.

### 3.5. Dissolution

As already stated the dissolution from solid lipid matrices is purely diffusion controlled. Fig. 8 depicts the dissolution characteristics of the processed batches. The surfactant properties of the pure partial glyceride matrix made of glyceryl monostearate lead to the fastest release of the drug compared to the other batches. The 50% tristearin and 50% glyceryl monostearate matrix materials exhibit a release curve between those of the pure triglyceride and pure partial glyceride. Even though the partial glyceride portion results in a pronounced recrystallization of the tristearin to the unstable α-form during extrusion which is followed by transformation to the β-form, the release of theophylline anhydrate is faster than from the pure tristearin extrudate due to the surfactant properties of the partial glyceride. By comparing the pure tristearin matrices produced at different extrusion temperatures with the tristearin (90%) and glyceryl monostearate (10%) mixture produced at the same temperatures two key factors can be identified. On the one

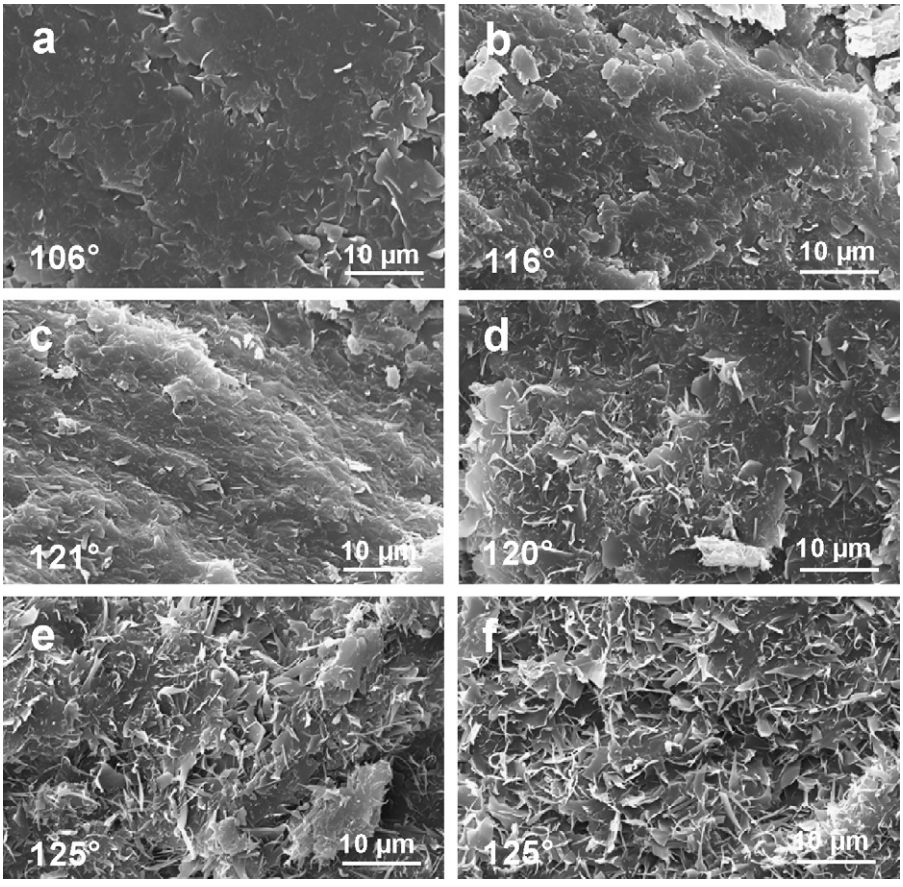


**Fig. 7.** SEM images of extrudate surfaces containing 50% theophylline anhydrate produced at different temperatures (a) glyceryl monostearate 65 °C, (b) tristearin/glyceryl monostearate (5 + 5 w/w) 65 °C, (c) tristearin 65 °C, (d) tristearin/glyceryl monostearate (9 + 1 w/w) 65 °C, (e) tristearin 55 °C and (f) tristearin/glyceryl monostearate (9 + 1 w/w) 55 °C.

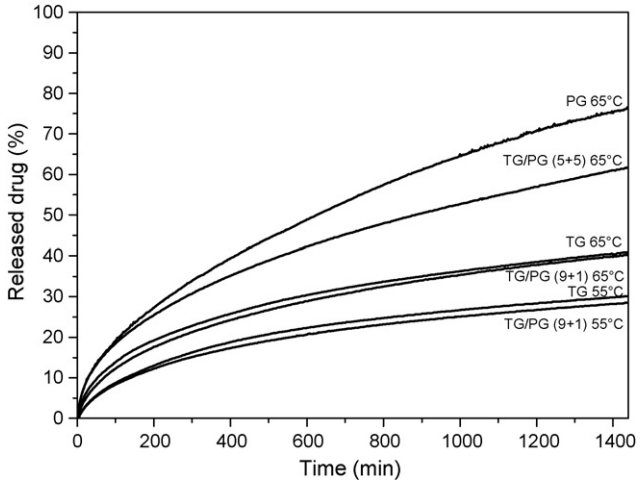


**Fig. 8.** Dissolution profiles of different lipids and their mixtures at different extrusion temperatures (TG, triglyceride tristearin; PG, partial glyceride glyceryl monostearate) ($n = 3$, SD <2% not shown).

hand the batches produced at 55 °C exhibit a significantly slower drug release than the batches produced at 65 °C. On the other hand the drug dissolution from the 9 + 1 (w/w) mixtures is slower than from the pure tristearin matrix which is unexpected on first glance regardless of extrusion temperature. The mixed matrix would be expected to show a faster release due to the surfactant properties of the partial glyceride. In this case these surfactant properties are overcome by the recrystallized β-form creating fractal structures on the surface of the extrudate that impair the wettability of the extrudate by the dissolution medium and hence reduce the release of the drug.

### 3.6. Storage stability

Storage experiments were performed in two different climate conditions (ambient condition and 40 °C at 75%RH) for 12 months. Samples were investigated using DSC. Fig. 9a depicts the thermograms for the samples stored at ambient conditions. The tristearin extrudate produced at 55 °C and the mixed extrudates 9 + 1 (w/w) produced at both extrusion temperatures both still contain a small portion of tristearin α-form. In the 5 + 5 (w/w) mixed extrudates after one year only the tristearin β-form exists, the recrystallization process from the metastable α-form to the stable β-form is already completed. The molecular mobility in this matrix compared to the 9 + 1 (w/w) matrix is increased which might facilitate the restructuring of the stable β-form. In comparison all the samples stored at 40 °C and 75%RH for one year exhibit only the stable tristearin β-form, and thus the transformation process is already completed. The results show the strong temperature dependency of the transformation from tristearin α-form to β-form.

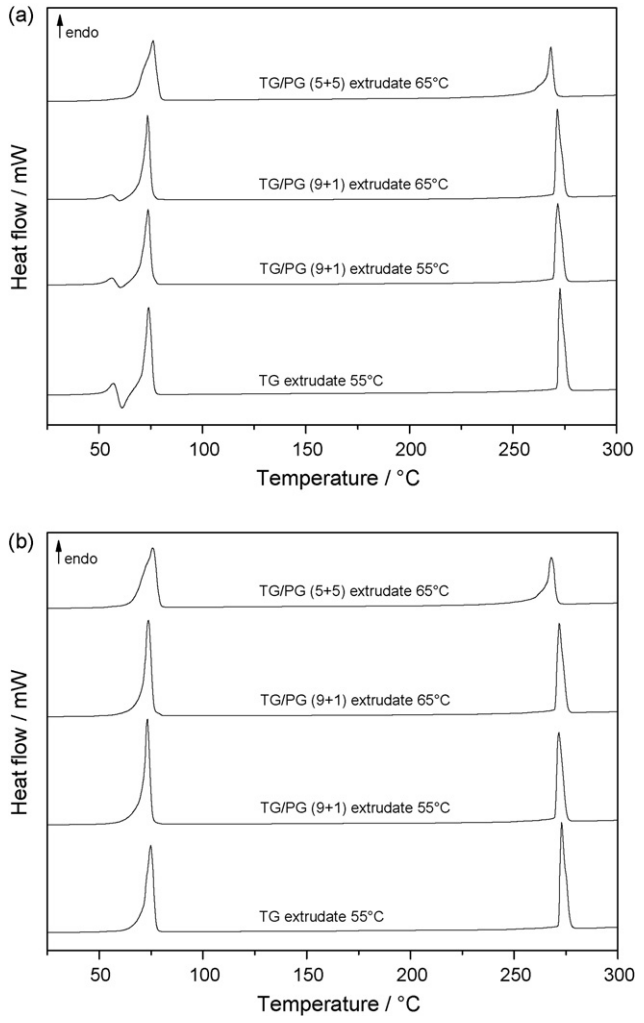


**Fig. 9.** Storage stability of solid lipid extrudates (a) one year at room conditions and (b) one year at 40 °C/75%RH.

## 4. Conclusions

The chemical composition of glycerides used for the manufacturing of solid lipid extrudates was found to have a large influence on the solid-state behaviour and dissolution profiles. Due to its surfactant properties the partial glyceride exhibits a faster release of the drug compared to the triglyceride. In different mixtures of both lipids the partial glyceride led to increased incidence of the unstable α-form of the triglyceride leading to recrystallization of the stable β-form over time which causes fractal structures on the extrudate surface deteriorating the dissolution properties. Storage experiments under accelerated and ambient conditions revealed a strong influence of temperature on the recrystallization kinetics. The results of this study help to elucidate the complex solid-state behaviour of solid lipid extrudates with different compositions which facilitates the development of suitable lipid-based oral dosage forms with desired dissolution characteristics.

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