British Journal of Pharmacy
https://doi.org/10.5920/bjpharm.2017.24

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 8th APS International PharmSci 2017

The Use of XRPD and ATR-FTIR in the Screening of Three Component Co-amorphous Systems Created via a Melt- Quench Method

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ARTICLE INFO

Received: 17/03/2017
Revised: 19/06/2017
Accepted: 07/08/2017
Published: 11/07/2018

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KEYWORDS: Co-amorphous; DSC; TGA; XRD; ATR-FTIR

SUMMARY

Multiple three-component co-amorphous systems have been created via a melt-quench method. This has been confirmed by a single glass transition in the individual DSC traces and then reinforced by X-ray diffraction data, which show an absence of crystalline material.

ATR-FTIR has also been used to show a change in bonding vibrations between the physical mixtures and co-amorphous samples. The change in bonding vibrations indicates different molecular interactions within the co-amorphous materials.

INTRODUCTION

Melt-quench methods have been shown to reliably create amorphous and co-amorphous materials (Beneš et al., 2017). A co-amorphous system can be identified using DSC, in which one glass transition indicates that the components are miscible and interacting. Solid-state characterisation techniques can be used to further confirm the successful creation of a co-amorphous material.

Three-component co-amorphous systems are of interest as by mediating the amounts of each component it may be possible to manipulate the overall properties of the material, such as stability and dissolution rate. X-ray diffraction (XRD) allows the confirmation of the creation of an amorphous material and the determination of crystalline content if present. Infrared spectroscopy can be used to observe the bonding vibrations present within a sample. This can be used to confirm the creation of an amorphous material by comparison to the physical mixture of the pure compounds (Beneš et al., 2017). It can also give information on the molecular interactions within the amorphous material but this can be harder to elucidate and may not be representative of the bulk.

MATERIALS AND METHODS

Thermo-gravimetric analysis (TGA) was carried out using a Q5000 IR TGA (TA Instruments, UK). Mass loss was recorded between ambient temperature (20°C) and 300°C, heating at 10°C/min, under nitrogen (25 ml/min). Differential scanning calorimetry (DSC) was conducted using a Q2000 DSC (TA Instruments, UK) in hermetically sealed Tzero aluminium pans. Samples were heated to 180°C at 10°C/min and cooled at 20°C/min.

Piroxicam (PXC), indomethacin (IND), acetaminophen (AC) and clotrimazole (CTMZ) were chosen as DSC data showed the formation of amorphous material after quenching the melt. Benzamide and caffeine were used as DSC showed that both returned to crystalline forms after

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quenching the melt. Each mixture was heated using an aluminium pan until melted; this was then mixed to create a homogenous distribution of components. The sample was then cooled using liquid nitrogen ensuring an amorphous phase was created.

X-ray diffraction XRD was used to determine whether any crystalline material was present within the prepared samples. The instrument used was a D8 Advance X-ray Diffractometer (Bruker, Germany, CuKα radiation, 2-40° 2θ. Infrared spectroscopy was carried out using a Perkin Elmer Spectrum Two with ATR attachment, 4000-650 cm^{-1}.

RESULTS AND DISCUSSION

DSC results showed that a 1-1 molar ratio of PXC and IND created a co-amorphous material with a glass transition (Tg) of 57.6℃. The DSC traces for all three-component mixtures showed single glass transitions, indicating co- amorphous systems. The introduction of a third component caused a lowering of Tg in all samples, such as acetaminophen which lowered the Tg to 44.1℃.

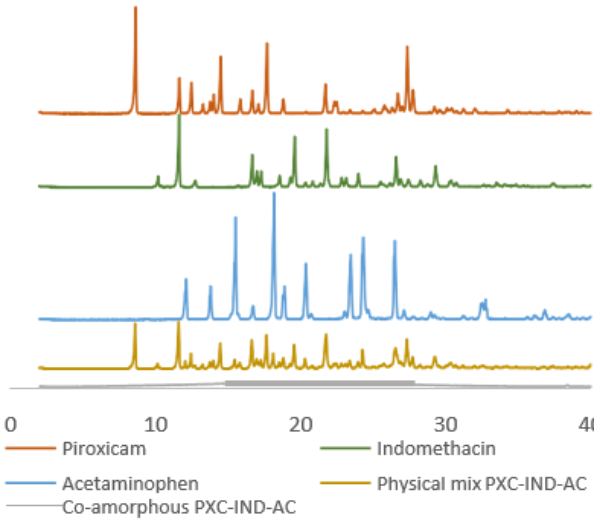

Fig.1. *A comparison of the PXC-IND XRD diffractograms.*

The XRD diffractograms clearly show that a highly amorphous material was created (Fig.1). Any crystalline material present is < 1% and is likely to be due to the production method used to create large quantities as no crystalline material was detected in the DSC trace. Comparing the ATR-FTIR spectra for the pure compounds, physical mixture and co-amorphous it can be seen that the co-amorphous has different bonding vibrations suggesting differing interactions (Fig.2.).

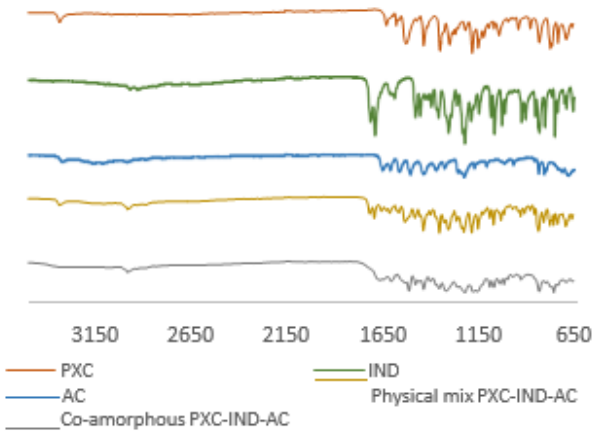

Fig.2. A comparison of the PXC-IND ATR-FTIR spectra.

Table 1. *The temperatures at which mass was lost during TGA and the glass transition temperatures (Tg).*

Chemicals	Start of mass loss in TGA (℃)	(Tg) (℃)
PXC-IND	186	57.6
PXC-IND-AC	187	44.1
PXC-IND-CAF	180	40.2
PXC-IND-CTMZ	184	43.1
PXC-IND-BZD	176	25.6

[a] Tg – Glass transition, Tc – Crystallisation, Tm – Melting

CONCLUSIONS

DSC and XRD have been used collaboratively to confirm the creation of multiple three-component co-amorphous systems using a melt quench method. The DSC traces confirmed this by containing only one glass transition, which shows the components are miscible and interacting.

XRD showed that all co-amorphous systems were >99% amorphous. As the production method for the large quantities of amorphous material is not as easily controlled as the small quantities in the DSC pan, it expected that this is the cause for the very small amounts of crystallinity.

The ATR-FTIR data indicate a clear change in bonding vibrations, which shows that the molecules within the amorphous system are interacting differently to those within the physical mixture.

REFERENCE

Beneš M., et al., 2017. Journal of Drug Delivery Science and Technology, 38:125–34.