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# Process induced degradation of carbamazepine during hot melt extrusion.

Sarbamangala Bose[a]*, Anant Paradkar[b], Adrian Kelly[c], Harika Magam[d]

[abcd]Univeristy of Bradford, Richmond Rd, Bradford BD7 1DP, United Kingdom

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*Corresponding author.
Tel.: +44 7466 286 137
E-mail:
s.bose2@bradford.ac.uk

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SUMMARY

The aim of this study was to evaluate hot melt extrudates of carbamazepine (CBZ) for presence of process induced degradation product iminostilbene (IMB) and quantifying using high performance liquid chromatography (HPLC). CBZ was used as model drug. Hot-melt extrusion (HME) was performed to prepare solid dispersions. Different grades of compatible polymers were used. Drug loading, processing temperature and screw rotations per minute (RPM) showed significant effect on degradation of CBZ The extrudates were characterized by differential scanning calorimetry (DSC), X-ray diffraction (XRD), Fourier transform infrared (FTIR) studies. DSC and XRD data confirmed formation of amorphous solid dispersions of CBZ. HPLC was performed to quantify percentage amount of CBZ and IMB. Process induced degradation was significantly varied depending on polymer grade and (w/w) percentage combinations. In addition, processing temperature and RPM had direct effect on percentage of IMB formation.



## INTRODUCTION

The objective of this study was to evaluate hot melt extrudates of carbamazepine (CBZ) for presence of process induced degradation product iminostilbene (IMB) and quantifying using high performance liquid chromatography (HPLC).

CBZ, a Biopharmaceutics Classification System (BCS) class II active pharmaceutical ingredient (API) with multiple polymorphs was used as model drug. Hot-melt extrusion (HME) was performed to prepare solid dispersions (Djuris *et al.*, 2013; Alshetaili *et al.*, 2020)

## MATERIALS AND METHODS

Different grades of Hydroxypropyl-Methylcellulose-Acetate-Succinate (HPMCAS) supplied by ShinEtsu, Poly (vinyl alcohol) (PVA) supplied by Mistubshi Chemical Corporation and Polyethylene glycol 2000 (PEG) sourced from Alfa-Aesar and Carbamazepine supplied by Salvavidas Pharmaceuticals Pvt Ltd. were used.

***Table 1.*** *W/W % combination of API and Polymer*

| **Carbamazepine** | **10%** | **20%** |
|---|---|---|
| HPMC -AS- MF | 90% | 80% |
| HPMC -AS- MG | 90% | 80% |
| PVA EG 05P | 90% | 80% |
| PVA -EG30PW | 90% | 80% |

***Table 2.*** *W/W % combination of API, Polymer and plasticiser.*

| **Carbamazepine** | **5%** | **10%** | **20%** |
|---|---|---|---|
| HPMC -AS- MF | 75% | 70% | 60% |
| HPMC -AS- MG | 75% | 70% | 60% |
| PVA EG 05P | 75% | 70% | 60% |
| PVA -EG30PW | 75% | 70% | 60% |
| PEG 2000 | 20% | 20% | 20% |

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PEG was used as plasticizer to lower processing temperature during HME. The (w/w) percentage combination of API and polymer used for HME are summarised in Table 1. Table 2 summarises the weight-by-weight percentage combination where PEG was used as plasticiser.

The extrudates were characterized by differential scanning calorimetry (DSC), X-ray diffraction (XRD), Fourier transform infrared (FTIR) studies. HPLC was performed to quantify percentage amount of CBZ and IMB (Džodić *et al.*, 2010). HPLC analyses were done using a Waters e-2695 HPLC system. C18 Column, 5µm particles size with dimensions of 4.6× 250 mm along with solvent system comprising of A: acetonitrile acidified with 0.1 % v/v formic acid and B: deionised water acidified with 0.1 % v/v formic acid was used. Injection volume: 10µL; Flow rate: 1.2 mL/min. Wavelengths: 285 nm, 253 nm, 219 nm Linearity range: 10 - 60µg/mL.

## RESULTS AND DISCUSSION

DSC and XRD data confirmed formation of amorphous solid dispersions of CBZ in the polymeric blends of HPMCAS, PVA and PEG. HPLC was performed to quantify percentage amount of CBZ and IMB.

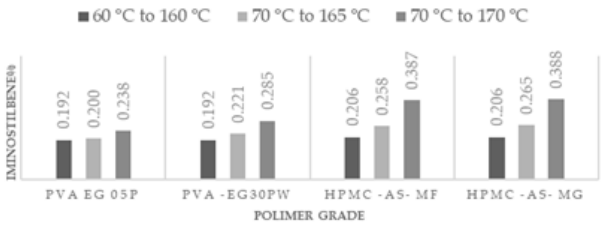


***Fig. 1.*** *Effect of temperature on process degradation.*

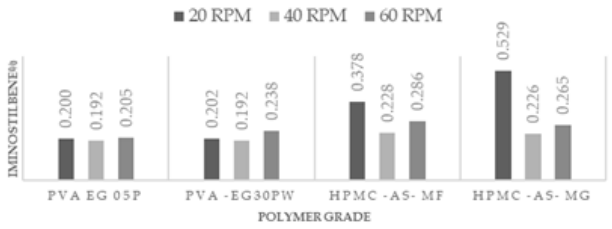


***Fig. 2.*** *Effect of RPM on process induced degradation.*

Processing temperature (Fig. 1) and screw rotations per minute (RPM) (Fig. 2) and drug loading (Fig. 3) showed significant effect on degradation of CBZ in all tested ratios of HPMCAS and PVA.

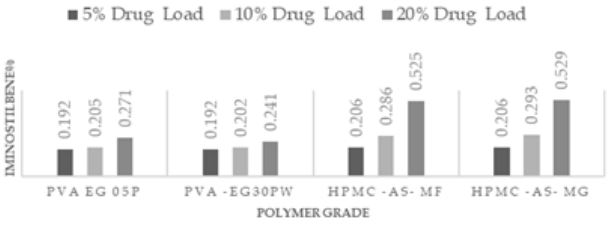


***Fig. 3.*** *Effect of drug loading on degradation.*

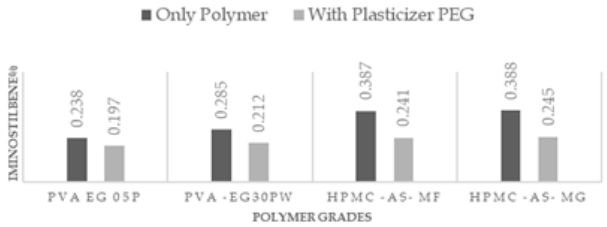


***Fig. 4.*** *Effect of plasticiser on degradation.*

PEG was used as plasticizer to lower processing temperature (Fig.4). CBZ was completely miscible in the polymeric blends to 20% drug loading.

## CONCLUSIONS

Process induced degradation was significantly low in PVA compared to HPMCAS, further lower with 20% (w/w) PEG. In addition, processing temperature and RPM had direct effect on percentage of IMB formation.

## ACKNOWLEDGEMENTS

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