The Application of SIFT-MS for examining the Degradation of Polymers

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Aims

- To utilise SIFT-MS to examine volatile compounds produced during the heating and shearing of materials used to produce amorphous solid dispersions via Hot-Melt Extrusion

Introduction

Polymers are a main component in the production of amorphous solid dispersions via Hot-Melt Extrusion therefore, it is important to understand as much as possible about the thermal properties of these materials. Heating these materials produces volatile compounds and potential impurities that could affect the success of the amorphous formulation. Thermogravimetric Analysis (TGA) is a common technique for analysing the thermal stability of materials based on the mass lost upon heating. Selective-ion-flow-tube-Mass-Spectrometry (SIFT-MS) is a technique than can identify these volatile compounds and at what temperature they are produced (Langford *et al*, 2019). This can potentially confirm an ideal processing temperature for a polymer to avoid degradation products in the final amorphous drug.

Figure 1: SIFT-MS Equipment (Fully mobile)

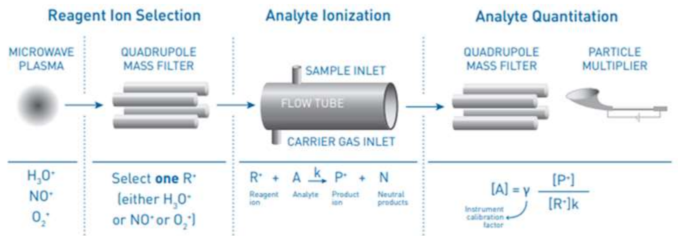

Figure 2: Operational Schematic of SIFT-MS adapted with permission from Syft Technologies

SIFT Ionization Reactions

Proton Transfer $H_2O.H^+ + A \longrightarrow A.H^+ + H_2O$

Electron Transfer Ion-A + Molecule-B ⟶ Ion-B + Molecule-A

Hydride Abstraction $NO^+ + A\text{-}H \longrightarrow A^+ + HNO$

TGA-SIFT-MS Equipment Setup

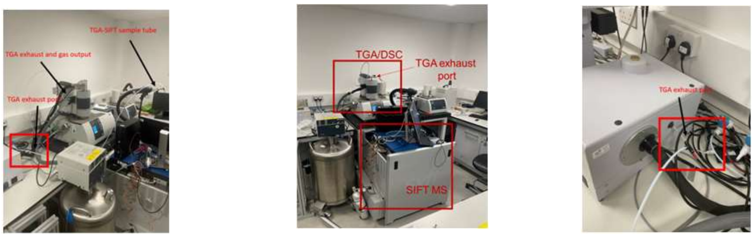

Figure 3: Equipment setup for the SIFT connected directly to the TGA exhaust

Methodology

PVA was chosen as a proof-of-concept material – a simple hydrocarbon with only C, H and O atoms. Processing temperatures for this in Hot-Melt Extrusion (HME) do not go beyond 200^{o}C therefore a range of 20-200^{o}C was chosen to investigate. With the sample tube of the SIFT connected directly to the exhaust of the TGA as showing in Figure 3. This allows for real-time analysis of volatile compounds produced during each temperature run of the TGA.

Results

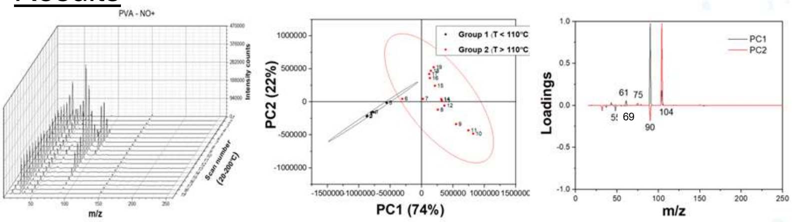

Figure 4: Spectrum for NO$^+$ reagent ion along with PCA plot to confirm main peaks

ID/m/z	BP/^{o}C	Risk
Acetic Acid (90)	118	Acidic and could contaminate API during processing and a known heating degradation product of PVA
Methanol 62	64.7	Toxic and irritant and used in the production of PVA (residual solvent)
Methyl Acetate (104)	56.9	Toxic and irritant and commonly produced together with PVA and collected for its own use
Ethylene Glycol (61)	197.3	A common plasticizer and potential ingredient within PVA
Acetic Anhydride (90)	139.5	Highly corrosive solvent potentially produced during manufacture of PVA
Butenal (69)	104	Known degradation product of PVA

Table 1: A list of identified compounds based on m/z with the potential risk they pose to an ASD

Discussion

A spectrum for each reagent ion is produced (H_3O^+, NO^+ and O_2^+) with Figure 3 showing an NO^+ spectrum along with a PCA plot to confirm the main peaks within the system and where in the temperature range they appear. This allows for the identification of compounds based on the presence of the mass to charge ratio (m/z) for that peak. Table 1 outlines a selection of potential degradation products based on functional groups present in PVA and evaluated using Labsyft software. Figure 5 shows the concentration of the compounds at a particular temperature. These compounds correlate with Taghizadeh *et al*, 2015 who examined thermal degradation of PVA using FTIR combined with TGA.

Future Plans

Future plans include examining more polymers used in HME (Figure 8) and connecting the SIFT-MS directly to an extruder to examine how the combination of elevated temperatures and mechanical shear affects the degradation. For example the presence of different compounds or an increase in the concentration of current analytes produced with the extra mechanical energy. Figure 7 shows some early data showing this correlation.

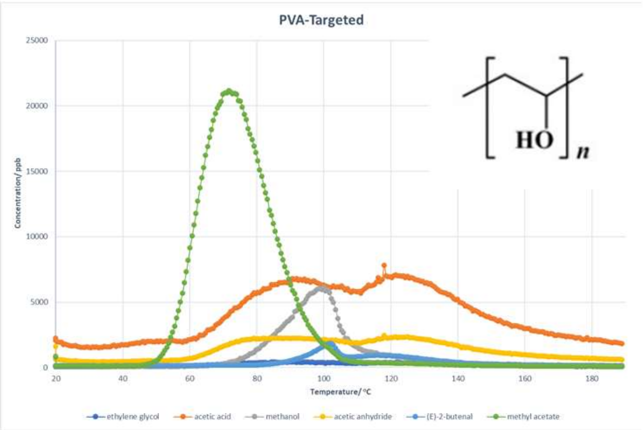

Figure 5: Quantification method for SIFT-MS with identified compounds

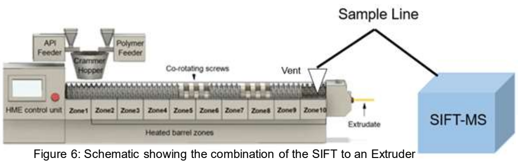

Figure 6: Schematic showing the combination of the SIFT to an Extruder

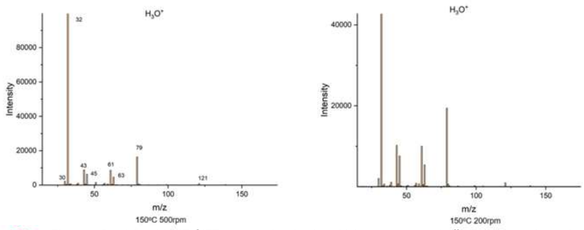

Figure 7: Provisional HME-SIFT spectra showing how higher screw speed affects the intensity and therefore concentrations of the analytes

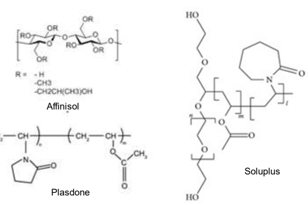

Figure 8: Common HME polymers to be investigated using this method

References

- Taghizadeh, M. T., Yeganeh, N., & Rezaei, M. (2015). The investigation of thermal decomposition pathway and products of poly(vinyl alcohol) by TG-FTIR. *Journal of Applied Polymer Science*, *132*(25). DOI: 10.1002/APP.42117

- Langford, V. S., Padayachee, D., McEwan, M. J., & Barringer, S. A. (2019). Comprehensive odorant analysis for on-line applications using selected ion flow tube mass spectrometry (SIFT-MS). *Flavour and Fragrance Journal*, *34*(6), 393–410. DOI10.1002/FFJ.3516

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