POSTER 74

Non-destructive Estimation of Particle Size in Powder Compacts

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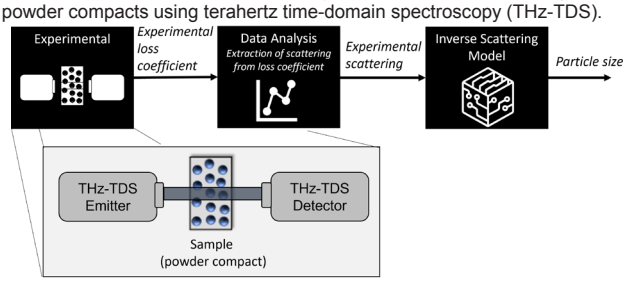
Objectives

To develop a model to non-destructively estimate particle size changes in powder compacts using terahertz time-domain spectroscopy (THz-TDS).

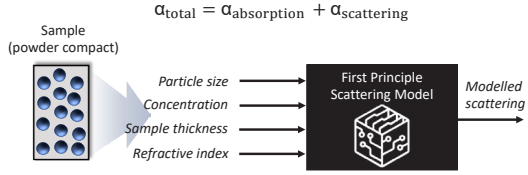


Introduction

As solid oral dosage forms are the widest accepted vector of drug delivery with > 60% of the market share [1], the properties that affect the performance of such drugs has been extensively researched. One such property is the particle size of both the active pharmaceutical ingredient (API) and excipients. Variations in particle size are known to have an adverse effect on dissolution outcomes in compacts, with smaller particles dissolving and being absorbed faster [2]. Changes in particle size can occur through various manufacturing processes such as fragmentation during compaction, among others [3].

THz-TDS enables the measurement of the refractive index and loss coefficient of a formulation/tablet [4]. The loss coefficient is the sum of the absorption contribution of the formulation and the scattering contribution driven by particle size and shape.

$$\alpha_{\text{total}} = \alpha_{\text{absorption}} + \alpha_{\text{scattering}}$$



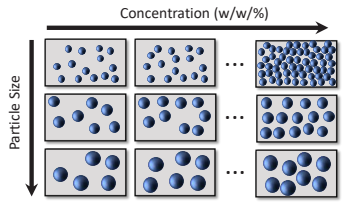
The Christiansen model [5] can be applied to estimate the scattering contributions in compacts given significant material knowledge such as the particle size (Δ), sample thickness (d), frequency (ω) and refractive index of the various components (n_{API} & n_{Blend}). Along with these material properties, this model also requires knowledge of the area of the wavefront covered by scattering objects (K) which is commonly fitted from experimental data [5].

$$\alpha_{\text{scattering}} = K^2 \frac{\omega^2}{2c^2} (n_{\text{API}} - n_{\text{blend}})^2 d\Delta$$

Using specially fabricated compacts containing borosilicate glass microspheres suspended in a polytetrafluoroethylene (PTFE) matrix [6], we present a model that enables the estimation of particle size using THz-TDS.

Experimental Design

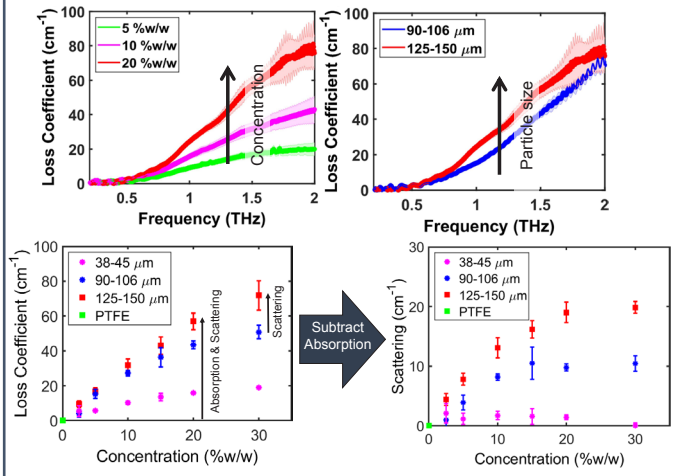
- Samples consisted of borosilicate glass microspheres suspended in a PTFE matrix to minimise sample porosity and the effect of particle shape on the scattering extraction.
- Materials: Borosilicate glass beads with 3 particle sizes: 38 - 45 µm, 90 – 106 µm and 125 - 150 µm.
- Six concentration levels: 2.5, 5, 10, 15, 20 & 30% w/w.
- Samples were compacted at 400 MPa using a compaction simulator (HB50, Huxley-Bertram).
- THz analysis was performed with a commercial THz-TDS system (Terapulse Lx, TeraView).



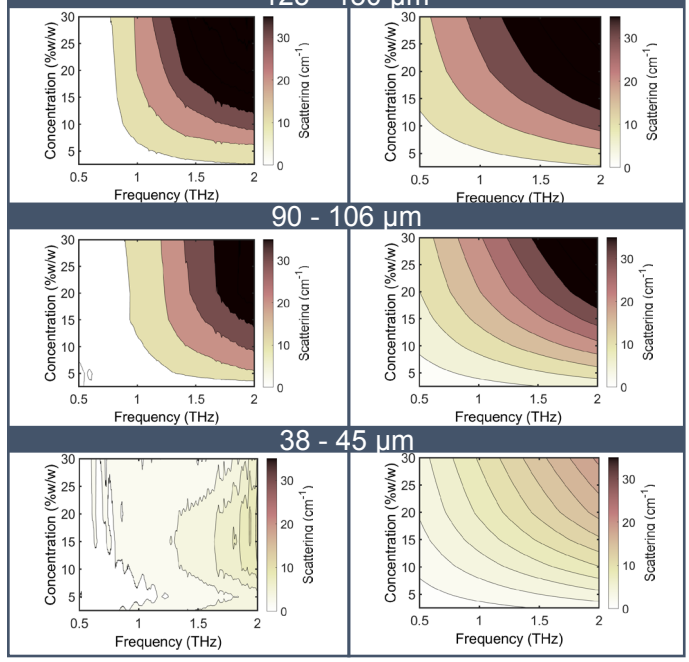
Results

Extraction of Terahertz Scattering

- Extraction of THz scattering requires the absorption contributions of the formulation.
- Estimation of the scattering contributions from the glass beads from the estimated absorption contributions and the extracted loss coefficient.



Experimental vs Model



Discussion

- Scattering contributions maximise at a given concentration dependent on the particle size and concentration.
- The first principles model is accurate in predicting scattering from particle size changes.
- Further validation is required on the inverse scattering model to predict particle size of complex pharmaceutical samples.

References

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Acknowledgments

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