Ultrasonic approach for viscoelastic and microstructure characterization of granular pharmaceutical tablets

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A B S T R A C T

The mechanical properties of a solid dosage, defined by its granular micro-structure and geometry, play a key role in its dissolution profile and performance. An ultrasonic method for extracting the viscoelastic material properties and granular structure of drug tablet compacts is introduced and its utility is demonstrated for tablet compacts made of microcrystalline cellulose (MCC), lactose monohydrate, and sodium starch glycinate as well as magnesium stearate as lubricant. The approach is based on the effect of viscoelasticity and internal micro-structures on the frequency-dependent attenuation of an ultrasonic wave propagating in a granular medium. The models for viscoelastic (a two-parameter Zener model) and scattering attenuation (Rayleigh model) mechanisms are employed. The material parameters including viscoelastic and scattering parameters (average Young’s modulus, stress and strain relaxation time constants, and the Rayleigh scattering material parameter) and grain size distribution with a known distribution profile are extracted by an optimization algorithm based on the least square method. The results also indicate good agreement between experimentally and computationally determined phase and group velocities in compacted samples. It is found that the effects of both attenuation mechanisms are present and the extracted grain size distribution parameters are in good agreement with the optically determined values.

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1. Introduction

It is well-established that the dissolution profile and release rate of drug tablets depend on various mechanical properties, such as hardness (Saravanan et al., 2002), inter-granular bonding, and the internal microstructure and grain size distribution of the tablet (Jounela et al., 1975; Lee, 2003; Narayan and Hancock, 2003, 2005). Techniques for accurate and rapid microstructure characterization and effective monitoring of associated meso-scale properties (‘hardness’, elasticity, and porosity) are of practical interest in pharmaceutical manufacturing. Consequently, in addition to several other approaches, acoustic techniques have been introduced and evaluated for pharmaceutical product testing and characterization applications such as tablet hardness (Lum and Duncan-Hewitt, 1996), tablet porosity and particle size fraction (Hakulinen et al., 2008), acoustic emission during compaction (Serris et al., 2002), elasticity and integrity of tablets (Ketolainen et al., 1995; Varghese and Cetinkaya, 2007; Akseli and Cetinkaya, 2008; Akseli et al., 2009; Leskinen et al., 2010; Simonaho et al., 2011), and mechanical characterization of multi-layer tablets (Akseli et al., 2010). Extracting material properties from the propagation of elastic waves is an attractive direct method due to its non-destructive/non-invasive nature and potential in real-time in-die monitoring, as well as its relatively low equipment and operational cost.

In current study, the focus is on the characterization of pharmaceutical granular materials for their microstructural and viscoelastic properties. Viscoelasticity is related to such time-dependent responses as damping, creep and stress relaxation of materials. These effects are of practical interest in solid dosages since they are formed by a rapid compaction process of polymeric materials, followed by a long relaxation time as various other processes (e.g. coating, packaging, handling, and storage) occur. Elastic wave fields propagating in a solid sample are affected by the viscoelasticity of its material (observed as a dissipation mechanism) and geometric discontinuities such as inter-granular boundaries and cracks (e.g. scattering and wave localization effects). Consequently, the frequency content and amplitude (dispersion properties) of an elastic wave pulse are modulated as it propagates in the spatially textured solid body. Thus the attenuation of the wave includes information about the dissipation
mechanisms (i.e. viscoelasticity and friction) and the nature of wave scatterers (such as grain–matrix boundaries, voids, inclusions, micro-cracks, macro-cracks, and other structural defects and irregularities) in the sample.

In many applications, the standard linear solid (Zener) model is often considered as a good approximation to model the viscoelasticity of polymeric materials (Lucke, 1956; Rippie and Danielsson, 1981). However, in a granular medium because of the scattering of the traveling wave fields from the geometric features (e.g. grains and cracks), the observed total attenuation is typically significantly stronger than the single crystal form of the same material assuming that the viscoelastic parameters remain unchanged. Especially when grain–matrix boundaries, voids, inclusions, micro-cracks, macro-cracks, and other structural defects and irregularities are present in the solid body, scattering needs to be understood and taken into consideration in the material modeling effort to accurately extract the viscoelastic parameters and also to characterize the microstructure of the drug tablet material. Scattering attenuation has been studied for a long time by considering the size and shape of the geometry features and the wavelength of the traveling wave field (Roney, 1950).

The main objective of the current study is to simultaneously extract the viscoelastic properties and scattering material parameters of pharmaceutical tablet materials from their ultrasonic attenuation profiles in a non-destructive manner. From our previous experience, we know that in such materials both mechanisms are equally relevant. An approach based on the effect of viscoelastic materials properties and scattering on the attenuation of an ultrasonic wave in a granular medium is presented. Zener’s viscoelastic material model is modified and employed along with the Rayleigh scattering regime relationship to take the viscoelastic and scattering effects into consideration, respectively, in the material model. Using the method of least squares, the material parameters including viscoelastic and scattering material parameters (namely, average Young’s modulus, stress relaxation and strain relaxation time constants, and Rayleigh scattering parameter times the number of grain per unit length) and the grain size distribution parameters (assuming a Gaussian distribution) are extracted. The phase and group velocities from the extracted dispersion relation are computationally determined employing a modified version of the Kramer–Kronig (K–K) relation (Kronig and Kramers, 1928) and compared to the experimental data. Good agreements are observed between the experimental results (namely, the obtained grain size distributions, and the attenuation and dispersion profiles) and the computationally determined ones.

2. Mathematical formulation for attenuation mechanisms

As an elastic wave pulse propagates in a dissipative granular medium, a number of attenuation mechanisms can modulate its frequency content and amplitude. The total attenuation is a result of dissipative material properties (e.g. viscoelasticity) and geometry (e.g. reflection and diffraction by grain–matrix boundaries, voids, inclusions, micro-cracks, macro-cracks, and other structural defects and irregularities). To characterize the material of interest for these mechanisms, a computational method for the extraction of the dispersion relation of the propagating wave and a material model are required. One-dimensional wave displacement field \( u(x, t) \) in the direction \( x \) can be expressed in the Fourier integral form as follows:

\[
 u(x, t) = \int_{-\infty}^{+\infty} G(\omega)e^{i\kappa(\omega)x - \omega t} d\omega \tag{1}
\]

where \( \omega \) is the angular frequency (\( \omega = 2\pi f \)), \( G(\omega) \) represents the waveform \( u(x, t) \) in spectral domain \( (\omega) \), \( \kappa(\omega) = \beta(\omega) + i\alpha(\omega) \) the (complex) dispersion relation and \( \alpha(\omega) \) and \( \beta(\omega) \) the attenuation and angular wavenumbers, respectively (Whitham, 1974). From Eq. (1), the waveforms at two locations \( x=0 \) and \( x=h \) planes are expressed as:

\[
 u(x=0, t) = \int_{-\infty}^{+\infty} G(\omega)e^{-i\omega h} d\omega \\
 u(x=h, t) = \int_{-\infty}^{+\infty} G(\omega)e^{i\kappa(\omega)h - \omega t} d\omega \tag{2}
\]

where, in the current context, \( h \) represents the thickness of the sample tablet in the propagation direction \( x \) of the elastic wave. The displacement waveforms \( u(x=0, t) \) and \( u(x=h, t) \) can be experimentally excited and acquired using a pulser/receiver unit, a transducer and a digitizing oscilloscope. The Fourier transform \( (\mathcal{F}) \) of the two expressions in Eq. (2) with respect to \( t \) yields:

\[
 \mathcal{F}(u(x=0, t)) = \sqrt{2\pi}G(\omega) \\
 \mathcal{F}(u(x=h, t)) = \sqrt{2\pi}G(\omega)e^{i\kappa(\omega)} \tag{3}
\]

and the complex wavenumber \( \kappa(\omega) \) is therefore extracted as:

\[
 \kappa(\omega) = \beta(\omega) + i\alpha(\omega) = \frac{1}{\Im} \ln \left\{ \frac{\mathcal{F}(u(x=h, t))}{\mathcal{F}(u(x=0, t))} \right\} \tag{4}
\]

By definition, from Eq. (4), the phase \( \beta(\omega) \) and group \( c_g \) velocities in the material are obtained as \( c_g(\omega) = \omega/\beta(\omega) \) and \( c_g(\omega) = d\omega/d\beta \) respectively.

In general, the nature of scattering attenuation strongly depends on the wavelength \( \lambda \) of traveling waves, which can be viewed as a characteristic length-scale of the texture and the mechanical property distribution in the material of the tablet compact. The common modeling assumptions made for the grain scattering attenuation in polycrystalline materials are as follows: (i) grain boundary discontinuity is elastic in nature, thus allowing for a continuous density distribution, (ii) individual grains are equiaxed (e.g., spherical, cubic, or cylindrical), (iii) the crystalline structure of grains is weakly anisotropic, (iv) the number of grains in the sample is high, (v) individual grains do not scatter coherently, and (vi) the scattered energy is relatively low, allowing multiple scattering effects to be neglected.

For the compacts in the sample sets in current work, a material model for dissipation and scattering is developed based on the following assumptions: (i) viscoelastic dissipation and elastic scattering are the only attenuation mechanisms present in the tablet material, (ii) the interactions between these attenuation mechanisms are de-coupled, (iii) the standard linear solid model applies to the viscoelastic behavior of the material, (iv) the scattering attenuation is governed by the Rayleigh scattering model (long wavelength), and (v) the number of particle in a table is sufficiently high, and the particle size distribution is Gaussian. According to (Morse, 1936; Roney, 1950) each grain within an attenuating material contributes to attenuation depending on the ratio of the acoustic wavelength of the propagating pulse \( (\lambda) \) to the scatterer size \( (D) \) of the material structure, namely, \( \lambda/D \). Under the assumptions listed above, three main scattering regimes have been identified (Papadakis, 1965) and are distinguished by the acoustic wavelength to mean grain diameter ratio. For \( \lambda * D \) (i.e. \( \lambda/D < 1 \)), attenuation, known as Rayleigh scattering, is represented in terms of frequency \( f \) as: \( \alpha (f, D) = c_t D^2 f^4 \) where \( c_t \) is a material constant. In the stochastic regime, \( \lambda \approx D \), that is \( \lambda/D \approx 1 \), the attenuation coefficient is given as follows: \( \alpha (f, D) = c_t D^2 f^2 \) where \( c_t \) is a material constant. As discussed in (Stanke and Kino, 1984), the low scattered energy assumption \( (vi) \) does not apply in the stochastic regime, where multiple scattering effects are significant. The third regime is characterized by an acoustic wavelength that is substantially shorter than the characteristic scatterer size (i.e., \( \lambda * D \), or
\[ \lambda (D + 1) \] referred to as the diffusion regime, independent of the frequency: \( \alpha(D) = c_D D \) where \( c_D \) is a material constant. Assumption (vi) is invalid for the diffusion regime since multiple scattering effects dominate in this regime. Based on the characteristic size of grains (and/or defect sizes), and the approximate value of the speed of sound (pressure wave) in the samples, a piezoelectric transducer with 1 MHz central frequency is employed in the experimental setup, leading to a millimeter-scale wavelength, so that the Rayleigh scattering approximation \( \lambda (D + 1) \) is applicable.

In Rayleigh scattering, the expression \( \alpha(f, D) = c_D D f^4 \) represents the scattering attenuation for a uniform grain size distribution of a granular solid medium. Considering a size distribution of scatterers (e.g., grains) for the feature size \( D \), defined by the probability density function \( (q(D)) \) where \( \int_0^\infty q(D) dD = 1 \), the contributions from all the grains of a solid body in scattering attenuation can be taken into consideration. Here we assume that Gaussian probability distribution represents \( q(D) \) for the samples granular medium, thus: \( q(D) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(D - \mu)^2}{2\sigma^2}\right) \) where \( \mu \) is the mean grain size and \( \sigma \) is its standard deviation in the sample. The total scattering attenuation in \( f = 2\pi f \) for a sample consisting of \( N_0 \) number of scatter (grains) per unit length in the direction of wave propagation is expressed as (Smith, 1982):

\[ \alpha_s(f) = c_D N_0 f^4 \int_0^\infty q(D) D^3 dD \tag{5} \]

and the total scattering attenuation coefficient for the Gaussian distribution becomes:

\[ \alpha_s(f) = \frac{c_D N_0 f^4}{\sqrt{2\pi}\sigma} \int_0^\infty D^3 \exp\left(-\frac{(D - \mu)^2}{2\sigma^2}\right) dD \tag{6} \]

Based on the K–K relation, the scattering-based attenuation \( \alpha_s \) is related to the scattering angular wavenumber \( \beta_s \), as follows:

\[ \alpha_s = \frac{\pi}{2} \beta_s^2 (\omega) \frac{d}{d\omega} \left( \frac{\omega}{\beta_s} \right) \tag{7} \]

As a linear dissipation mechanism, internal friction and/or intergranular viscoelastic coupling in granular matter is often approximated as viscoelastic damping and modeled using viscoelastic material models, in which both stress and strain relaxations are represented simultaneously. Here the following generalized one-dimensional linear viscoelastic material model is employed:

\[ \sigma_{xx} + \sum_{i=1}^n p_i \frac{\partial \varepsilon_{xx}}{\partial t^i} = E \left( \varepsilon_{xx} + \sum_{i=1}^m q_i \frac{\partial \varepsilon_{xx}}{\partial t^i} \right) \tag{8} \]

where \( \sigma_{xx} \) and \( \varepsilon_{xx} \) are stress and strain, respectively, \( E \) is the material Young’s modulus and \( p_i \) and \( q_i \) are stress and strain relaxation times, respectively, representing rate-dependent material parameters (see Moe and Rapp, 1997) for its various applications to polymeric materials. Using this material model, and the equation of longitudinal motion, \( \rho \beta^2 u \frac{\partial^2 u}{\partial t^2} = \sigma_{xx} / \rho \), along with the strain-displacement relation, \( \varepsilon_{xx} = \partial u / \partial x \), where \( u(x,t) \) and \( \rho \) are the displacement field and the average mass density of the medium material, respectively, the wave equation for this material model becomes:

\[ \frac{\partial^2 u}{\partial t^2} + \sum_{i=1}^n p_i \frac{\partial^{i+2} u}{\partial t^{i+2}} = \frac{E}{\rho} \left( \frac{\partial^2 u}{\partial x^2} + \sum_{i=1}^m q_i \frac{\partial^{i+2} u}{\partial x^{i+2}} \right) \tag{9} \]

The viscoelastic attenuation and the corresponding dispersion relation are determined considering the harmonic dispersive wave motion in the form of \( u(x,t) = U(\omega) e^{i k_s(x) x - \omega t} \) where \( k_s(\omega) = \beta_v(\omega) + i \alpha_v(\omega) \) is the viscoelastic complex wavenumber, and \( \alpha_v(\omega) \) and \( \beta_v(\omega) \) are the attenuation and dispersion terms, respectively. In current study, setting \( m = n = 1 \) in Eq. (9), a first-order standard linear viscoelastic solid is employed as the viscoelastic material model for compact materials. Rearranging after substituting harmonic dispersive wave solution into Eq. (9), the viscoelastic attenuation coefficient \( \alpha_v(\omega) \) and the wavenumber \( \beta_v(\omega) \) are determined as follows:

\[ \alpha_v^2(\omega) = \frac{\rho \omega^2}{2E} \left( \frac{1 + p_1 \omega^2}{1 + q_1 \omega^2} \right)^{1/2} - \frac{1 + p_1 q_1 \omega^2}{1 + q_1 \omega^2} \tag{10} \]

Assuming decoupled interactions with respect to the frequency-dependency of the viscoelastic and scattering attenuation mechanisms, the total attenuation in the propagating acoustic waves in the granular medium is approximated by:

\[ \alpha(\omega) = \alpha_s(\omega) + \alpha_v(\omega) \]

Adding up the total scattering attenuation coefficient for the Gaussian distribution (Eq. (6)) and the viscoelastic attenuation coefficient \( \alpha_v(\omega) \) (Eq. (10)), the total attenuation for the medium is approximated as:

\[ \alpha(\omega) = \left( \frac{\rho \omega^2}{2E} \left( \frac{1 + p_1 \omega^2}{1 + q_1 \omega^2} \right)^{1/2} - \frac{1 + p_1 q_1 \omega^2}{1 + q_1 \omega^2} \right)^{1/2} + \frac{N_0}{\sqrt{2\pi}\sigma} c_D \exp \left(-\frac{(D - \mu)^2}{2\sigma^2}\right) \int_0^\infty \frac{\omega}{\beta_s(\omega)} \frac{d\omega}{d\omega} \right) \tag{11} \]

Based on the K–K relation, the total attenuation \( \alpha(\omega) \), and the wavenumber \( \beta(\omega) \), are related by:

\[ \alpha(\omega) = \frac{\pi}{2} \beta^2(\omega) \frac{d}{d\omega} \left( \frac{\omega}{\beta(\omega)} \right) \tag{12} \]

Eq. (12) represents the nearly local generalized attenuation-wavenumber relation (O’Donnell et al., 1981). It is noteworthy that even though Eq. (12) appears highly nonlinear in \( \beta(\omega) \), its evaluation results in a linear form in \( \beta(\omega) \): \( \alpha(\omega) = \pi \left( \beta(\omega) - \omega \frac{d\beta(\omega)}{d\omega} \right) \) and it is clear that a linear modifying function added to \( \beta(\omega) \) in the form of \( a \omega + b \), where \( a \) and \( b \) are arbitrary interaction constants, plays no role in calculating the attenuation coefficient \( \alpha(\omega) \) from a given form for \( \beta(\omega) \). Thus it is concluded that the K–K relation results in a linear combination of the scattering and viscoelastic terms as well:

\[ \alpha_s(\omega) + \alpha_v(\omega) = \pi \left( (\beta_s(\omega) + \beta_v(\omega)) - \omega \left( \frac{d\beta_s(\omega)}{d\omega} + \frac{d\beta_v(\omega)}{d\omega} \right) \right) \tag{13} \]

As discussed in (Waters and Hoffmeister, 2005) in detail, the nearly local approximation to the K–K relation (Eq. (12)) involves an implicit assumption that the same behavior for the attenuation coefficient \( \alpha(\omega) \) exists outside its measurement bandwidth. Therefore determining \( \beta(\omega) \) from an experimentally extracted total attenuation relation \( \alpha(\omega) \) requires an extrapolation outside this bandwidth. In experimental studies, the measurement bandwidth is the bandwidth of the ultrasonic transducer, therefore in order to employ the nearly local approximation form of the K–K relation, the attenuation behavior is assumed to be the same in the entire spectral domain. This assumption results in deviation of the extracted dispersion term \( \beta(\omega) \) from the experimentally extracted one. Therefore the extracted term \( \beta(\omega) \) needs to be modified by adding an arbitrary function so that a good agreement is obtained with experimentally obtained wavenumbers without violating the K–K relation. The modified total wavenumber including scattering...
Table 1
(a–f) Extracted mechanical and viscoelastic material model parameters for the sample tablet sets I–VI.

<table>
<thead>
<tr>
<th>Tablet set I</th>
<th>Thickness (mm)</th>
<th>MCC to lactose ratio</th>
<th>Experimentally approximated parameters</th>
<th>Computationally extracted parameters</th>
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<tbody>
<tr>
<td>S01</td>
<td>4.07</td>
<td>1:1</td>
<td>1258.59 ± 1.74</td>
<td>131 ± 27.0</td>
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<tr>
<td>S02</td>
<td>4.00</td>
<td>1:1</td>
<td>1287.75 ± 1.62</td>
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<tr>
<td>S03</td>
<td>4.19</td>
<td>1:1</td>
<td>1260.96 ± 1.80</td>
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<tr>
<td>S04</td>
<td>4.08</td>
<td>1:1</td>
<td>1301.72 ± 1.71</td>
<td>131 ± 27.0</td>
</tr>
<tr>
<td>S05</td>
<td>4.09</td>
<td>1:1</td>
<td>1265.99 ± 1.62</td>
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<tr>
<td>S01</td>
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<td>1:1</td>
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</tr>
<tr>
<td>S02</td>
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<td>1:1</td>
<td>1198.17 ± 1.15</td>
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<td>1187.90 ± 1.10</td>
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<td>1269.29 ± 1.17</td>
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<td>2:1</td>
<td>1315.85 ± 1.48</td>
<td>163 ± 27.9</td>
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and viscoelastic dispersion terms is expressed as additive effects:

\[ \beta(\omega) = \beta_1(\omega) + \beta_2^m(\omega) = \beta_1(\omega) + \beta_2(\omega) + A(\omega; \omega_{\text{min}}, \omega_{\text{max}}) \]

(14)

where \( \beta_2^m(\omega) \) is the modified scattering wavenumber and \( A(\omega; \omega_{\text{min}}, \omega_{\text{max}}) \) is a frequency-dependent function to be determined equating the wavenumber calculated using Eq. (12) to the experimentally obtained dispersion data. Ideally, \( A(\omega; \omega_{\text{min}}, \omega_{\text{max}}) \) is a linear function in \( \omega \) since a linear modifying function cancels out in Eq. (12) and, consequently, the original form of the K–K relation is guaranteed to stay satisfied in the entire spectrum.

3. Materials and methods

In the reported experiments, a sample set of 30 compacts made of microcrystalline cellulose (MCC; Avicel PH102 grade, FMC Biopolymer, Philadelphia, PA 19103), lactose monohydrate (FastFlo grade, ForeMost Farms, Baraboo, WI 53913-8115), and sodium starch glycolate (Glycolys grade, Roquette America Inc, Geneva, IL 60134) as well as magnesium stearate (vegetable grade, Malinckrodt, Hazelwood, MO 63042) as lubricant are employed. Experiments are performed using six five-tablet sample sets (Sample Sets I–VI) with varying mass densities and mixing ratios (see Table 1a–f for the complete geometric and material properties). The sample tablets are compacted from two types of mixtures: (i) Powder I containing MCC (64%, w/w) and lactose monohydrate (32%, w/w) with 3% sodium starch glycolate and 1% magnesium stearate (MCC/Lactose ratio is 2:1) and (ii) Powder II: MCC (48%, w/w) and lactose monohydrate (48%, w/w) with 3% sodium starch glycolate and 1% magnesium stearate (MCC/Lactose ratio is 1:1). These formulations produced by blending the excipients in a twin-shell mixer are common in many immediate release pharmaceutical tablets. By analyzing the morphology of micro-structures using an optical microscope (BH2-MJLT, Olympus, Center Valley, PA), it is determined that the characteristic grain size in the compacts ranges approximately between 10 and 300 μm. In size characterization, the boundaries of features are distinguished and, due to the arbitrary shapes of the features, a statistical approach is employed for determining the mean characteristic length-scale of each feature (see Fig. 1a as a representative of Sample Set IV). As in the experiments, the wavelength of ultrasonic waves are long compared to

![Image](https://via.placeholder.com/150)

Fig. 1. (a) Optical microscope image of a representative tablet of Sample Set IV at 5× magnification, (b) statistical method to determine the characteristic length scale distribution (thick and black lines represent the characteristic length scales used for calculating the grain size distribution).

![Diagram](https://via.placeholder.com/150)

Fig. 2. Connectivity diagram of the experimental instruments supporting both Setup A and Setup B.)
the grain sizes, the grain shape is a secondary effect in the current analysis. For compacts in each sample set, several images at various layers in a compact are captured and analyzed for obtaining accurate grain size distributions and the optically obtained grain size distribution is reasonably close to the Gaussian normal distribution (the inset of Fig. 1b).

In the reported experiments, a pitch-catch experimental set-up (Setup A) was utilized to transmit ultrasonic wave pulses in a sample compact for characterizing the viscoelastic and microstructure properties of the compact materials (Fig. 2). In calibrating the set-up without a sample, Setup B is used. Each setup consists of an ultrasonic pulser/receiver unit (Panametrics 5077PR), a pair of piezoelectric transducers (Panametrics A103 S) with the central frequency of 1 MHz, the bandwidth of 0.53–1.52 MHz and the element diameter of 15 mm, a steel calibration piece (KB-Aerotech, Lewistown, PA) utilized as a delay line, a networked digitizing oscilloscope (Tektronix TDS3052), and a computer with software for data acquisition and signal processing analysis. The delay line is adequately wide in the direction perpendicular to the wave propagation so that the effects of side walls reflections are minimized. A couplant gel (UltraGel II, Sonotech Inc., Bellingham, WA)

**Fig. 3.** The normalized temporal waveforms acquired by Setup A for five samples of Sample Set I (thin solid, thin dashed, thin dotted, thin dot-dashed and thick dashed lines) and Setup B (thick solid line).

**Fig. 4.** The normalized spectral waveforms acquired by Setup A for five samples of Sample Set I (thin solid, thin dashed, thin dotted, thin dot-dashed and thick dashed lines) and Setup B (thick solid line). The bandwidth of the employed transducer (0.53–1.52 MHz) is indicated by the gray box.
is employed to ensure the effective transmission of the acoustic pulses through each interface. A thin enamel (acrylic) is spray-coated on the surface of each sample compact to prevent it from being damaged by repeated use, as well as by moisture and glycerin contained in the couplant gel. For each compact, a standard 24-h dry time was instituted prior to the experiments. The effects of the couplant gel and enamel coating on wave transmission are negligible due to the minimal thickness of the gel layer and enamel coat (50–100 μm) compared to the tablets thickness (3.93–4.69 mm), and the minimum wavelength of the excitation acoustic pulse. A digital caliper (CD-6 in CS Absolute Digimatic Caliper, Mitutoyo Inc., Aurora, IL) was used to measure the dimensions of the tablets and a digital scale (A1205-L, Mettler-Toledo Inc., Columbus, OH) was employed to determine the compact mass. See (Varghese and Cetinkaya, 2007; Akseli and Cetinkaya, 2008; Akseli et al., 2009, 2010) for the details of the experimental study, as the experimental set-up utilized in the current study is similar to those used in these previous studies.

In Setup A, an electrical pulse is generated by the pulser/receiver unit connected to Transducer 1, launching an elastic (strain) wave pulse into the delay line and sample, and the transmitted pulse is ultimately received by Transducer 2. In Setup B, the elastic wave pulse launched into the delay line from Transducer 1 is passed through the delay line, and is finally captured by Transducer 2. In each setup, the acoustic pulse acquired at Transducer 2 is converted back to an electrical signal, which is then received by the pulser/receiver unit as an analog signal and saved as a digital waveform by the digitizing oscilloscope. A computer with signal processing software is used to process and analyze the waveforms.

In all experiments reported in current work, the pulser/receiver unit was set to a pulse repetition frequency (PRF) of 100 Hz, a pulser voltage of 400 V, and the high-pass filter (HPF) at “Out” and low-pass filter (LPF) at “Full Bandwidth” settings to allow the entire frequency spectrum of the transducers to pass through the tablets. The transducer frequency of the pulser/receiver is set on 1 MHz. The statistically determined grain size distribution for each tablet from the optical images is employed to verify the computational results and to eliminate possible erroneous multiple solutions in the mathematical inversion procedure (see Table 1a–f).

4. Extracting the materials properties and inversion process

An inversion procedure is developed and employed for extracting the material properties of interests from the acquired ultrasonic waveforms \( A_i(t) \) and \( B_i(t) \) in Setups A and B sampled by the digitizing oscilloscope. The waveforms were transformed into the frequency domain using a Fast Fourier Transform (FFT) routine. For the tablets of each Sample Set, waveforms in both temporal and spectral domains were normalized with respect to their maximum amplitudes and compared to each other as shown in Figs. 3 and 4, respectively for Sample Set I. Utilizing Eq. (4), the frequency-dependent attenuation \( \alpha(f) \) and wavenumber \( \beta(f) \) for each tablet are determined by

\[
\kappa(f) = \beta(f) + i\alpha(f) = \frac{1}{ih} \ln \left( \frac{A_i(f)}{B_i(f)} \right) \tag{15}
\]

Fig. 5. Experimentally obtained total attenuation curves \( \alpha(f) \) for Sample Sets I–VI in the transducer bandwidth (0.53–1.52 MHz) (a–f).
The procedure for extracting the parameters of the viscoelastic material and Rayleigh scattering models and the grain size distribution is described as follows. In current method, the unknown material parameter set of interest \(X = \{ E, p_1, q_1, N_0 \text{gr}, \mu, \sigma \}\) is extracted by minimizing the sum of squared errors function
\[
S(X) = \sum_{n=1}^{N} [\alpha(f_n) - \alpha(X; f)]^2
\]
between the computational attenuation \(\alpha(X; f)\) expressed in Eq. (11) and experimental attenuation \(\alpha(f)\) (extracted using Eq. (15)). Experimental attenuation profiles \(\alpha(f)\) are sampled into \(n = 100\) equally spaced data points with a frequency step size of \(\Delta f = 10\text{kHz}\) in the spectral bandwidth of the transducer (0.53–1.52 MHz). Therefore the error function \(S(X)\) is the sum of squared errors for all \(n\) data points. Considering the attenuation expression \(\alpha(X; f)\) in Eq. (11), the error function \(S(X)\) is nonlinear in the viscoelastic properties and grain-size distribution parameters and thus cannot be minimized using a linear technique (such as the Simplex method). Unlike the minimization of a linear error function, the minimization of a nonlinear error function such as \(S(X)\) could converge to several possible local minima. Therefore multiple solutions are obtained for the unknown model parameter set \(X\) considering several plausible initial estimates for the unknown model parameters during minimization of the error function \(S(X)\). In order to avoid the local minima and locate the global minimum of the error function \(S(X)\), a global optimization method known as Differential Evaluation (DE; Storn and Price, 1997) is employed for the current minimization task. DE optimization algorithm is a stochastic optimization approach and is quite effective in nonlinear constraint optimization problems with more local minima (Abbas et al., 2001; Karaboga and Oktedem, 2004). DE method has high convergence rate and often locates the true global minimum regardless of the initial guesses. In current work, its implementation in Mathematica software (Wolfram Research, Champaign, IL) is utilized. The name of the Mathematica Function is NonlinearModelFit. In current computational effort, the extracted material parameter set \(X\) for each initial guess is back-substituted into Eq. (11) and the attenuation profile \(\alpha(X; f)\) is calculated. By comparing calculated attenuation profiles \(\alpha(X; f)\) for each material parameter set \(X\) to the corresponding experimental attenuation curves \(\alpha(f)\), the solution is validated by visually. A comparison for a tablet of Sample Set I is presented in Fig. 7.

5. Results and discussions

The viscoelastic material model and grain size distribution parameters \(X = \{ E, p_1, q_1, N_0 \text{gr}, \mu, \sigma \}\) extracted based on the DE global optimization method for each tablet are listed in Table 1a–f for Sample Sets I to VI, respectively. The computational attenuation profiles \(\alpha(X; f)\) obtained by substituting the parameters reported in Table 1 into Eq. (11) are found to be in good agreement with the experimentally obtained attenuation profiles \(\alpha(f)\) in the bandwidth of transducers (see Fig. 7 for an example comparison). Based on the time-of-flight in a sample from the waveform comparisons from the Setup A and B measurements (see Fig. 3 for Sample Set I), approximations for the average Young’s modulus of tablets in the sample sets can be determined with \(c_L = \sqrt{E/\rho}\) in which \(c_L\) is the speed of sound (pressure wave) in the sample material. The computationally extracted Young’s modulus \(E\) in the material parameter sets \(X\) (Table 1) and the Young’s modulus \(E\) calculated from the approximate speed of pressure wave are in a good agreement. The measurements for MCC PH102 material (Welch et al., 2005) report a relaxation time of 15.45 μs, which is in the same range as those reported in Table 1a–f. The characteristic grain size distribution where \(A(f)\) and \(B(f)\) are the acquired spectral waveforms from Setups A and B, respectively. For Sample Set I–VI, the attenuation profiles \(\alpha(f)\) are depicted in Fig. 5a–f (with a gray box indicating the transducer bandwidth), respectively. As shown in Fig. 6, the phase and group velocities for tablet materials are also calculated for a sample tablet in Sample Set I.

The characterization process requires the extraction of the materials parameters (namely, Young’s Modulus \(E\), stress relaxation time \(p_1\) and strain relaxation time \(q_1\), and Rayleigh scattering constant times the number of grains per unit length \((N_0 \times c_r)\) and the grain size distribution (the mean grain size \(\mu\) and standard deviation \(\sigma\) parameters of the Gaussian probability distribution) from the experimental total attenuation curve \(\alpha(f))\).

![Fig. 6. Comparisons of the experimental phase velocity \(c_p(f)\) (thick dotted line) and group velocity \(c_g(f)\) (thick dashed line) and computational phase (thick solid line) and group (thick solid line) velocities for one sample of Sample Set I with the marked transducer bandwidth (0.53–1.52 MHz).](image-url)
extracted from the computational analysis (reported in Table 1a–f) is also in good agreement with those from the optical microscope images (see Fig. 1a and b). By substituting extracted mechanical and geometrical parameters in Table 1a–f into Eqs. (6) and (10), the contributions of scattering and viscoelastic attenuation mechanisms on the total attenuation experienced in the tablets are determined, as depicted in Fig. 8 for the Sample Set I. It is observed that viscoelastic attenuation is more dominant than the scattering attenuation in the bandwidth of the transducer. Therefore it can be concluded when the scattering attenuation lies in the Rayleigh regime, the viscoelastic attenuation is the dominant attenuation mechanism. From the extracted material parameters of the scattering and viscoelastic material models, the computational phase and group velocities are determined. Good agreement between the computational and experimental phase and group velocities are observed as shown in Fig. 6 for a tablet from Sample Set I, considering the modified wavenumber function $\beta_{\text{ms}}^2(\omega)$ corresponding to scattering attenuation. The frequency-dependent modifying functions $A(f; f_{\text{min}}, f_{\text{max}})$ are nearly linear, as depicted and compared for each tablet of Sample Set I in Fig. 9. As discussed in Section 2 in detail, adding a linear function to the wavenumber expression $\beta(\omega)$ in the K–K relation (Eq. (12)) has no effect in the relationship, indicating the K–K relation is not violated in the computational approach taking in current
is demonstrated. Employing an optimization technique, a set of material parameters including average Young's modulus (E), stress relaxation (p₁) and strain relaxation (q₁) times and Rayleigh material parameter (c₁) multiplied with the average of grains (N₀ c₁) and grain size distribution parameters including the mean grain size (μₐ) and standard deviation (σ) of grain distribution were extracted for each tablet in the sample sets. It is observed that the extracted grain size distributions are in good agreement with the optically determined grain size distributions. The contributions of viscoelastic and scattering attenuation are determined and compared applying extracted material parameters to the linear viscoelastic attenuation and Rayleigh scattering attenuation models, respectively. Comparing the contributions of scattering attenuation and internal friction in the total attenuation profile, it is found that viscoelastic attenuation is more dominant than that from wave scattering in the transducer bandwidth.

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Fig. 9. Arbitrary modifying function A(f; f_min, f_max) for samples in Sample Set I.


