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Drug tablet thickness estimations using air-coupled acoustics

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Abstract

A non-contact/non-destructive acoustic technique for predicting the coating layer thickness of a drug tablet is presented. Quality of tablet coatings can play a major role in the effectiveness of drug delivery. Many pharmaceutical tablets consist of a tablet core and a coated outer cover. Variations in the tablet coating can be indicative of various process problems and, therefore, is of a concern for quality assurance. In the current non-contact measurement system, an air-coupled excitation and laser interferometric detection for predicting the coating layer thickness of a drug tablet is introduced. Drug tablets with different coating thicknesses are vibrated via an acoustic field generated by an air-coupled transducer in a frequency range sufficiently high to excite their several vibrational modes. The tablet surface vibrational responses are acquired at a number of measurement points by a laser interferometer in a non-contact manner. An iterative computational procedure, based on the FE method and Newton's method, was developed and demonstrated to extract the coating layer thicknesses of the tablets from a subset of the measured resonance frequencies.

Keywords: Tablet coating thickness; Thickness measurements; Drug tablet coating; Acoustic process monitoring; Process Analytical Technology; PAT

1. Introduction

Many modern commercial drug tablets consist of two basic structural parts: the core and coating layer(s). The core of a typical drug tablet contains a mixture of one or more active pharmaceutical ingredient(s) (APIs) with a number of *inactive* fillers named *excipients*, containing diluents, binders and lubricants. As a result, a tablet can be considered as a mechanical delivery device consisting of bonded functional and structural parts (*e.g.* core and coating layers). Tablet coats, forming a control barrier to the release of the active ingredients and govern the sustained release of the drug, are functional parts of the tablets. Tablet coats can serve a wide range of purposes, such as to control release of active ingredients in the body, to avoid irritation of oesophagus and stomach, to provide a barrier to unpleasant taste or odor, and to protect the stomach from high concentrations of active ingredients, to improve drug effectiveness and stability and to regulate and/or extend dosing interval. For instance, functional coatings, such as enteric coats, designed to protect the tablet core from the acidic environment of the stomach, resulting in drug release in the higher pH environment of the small intestines. Coats can protect the ingredients from degradation and, therefore, extend shelf life by minimizing the effect of ambient humidity and tablet water content storage, which are often caused by ambient temperature variations, environmental gases and light exposure. In addition, tablet coats contribute to the consumer acceptability and the product identity of tablets.

Non-uniformity and/or surface or sub-surface defects of the tablet coatings could compromise the desired dose delivery and bioavailability of the drug tablet as well as its shelf life and physical stability. As these dosage forms can contain an entire day's worth of drug, problematic coats could subject the patient to hyper-therapeutic levels of drug. Evaluating the properties of coating layers, such as thickness and uniformity, is therefore imperative for demonstrating adequate manufacturing process controls and quality, and for ensuring optimal performance of the final product. The criticality of the coating performance is often paramount and its careful control is essential to the tablet production process (Mathiowitz, 1999; Varghese and Cetinkaya, 2007).

In recent years, along with various other pharmaceutical production processes, the monitoring of drug tablet manufacturing has attracted regulatory attention as part of an effort to better understand and quantify the performance of associated pro-

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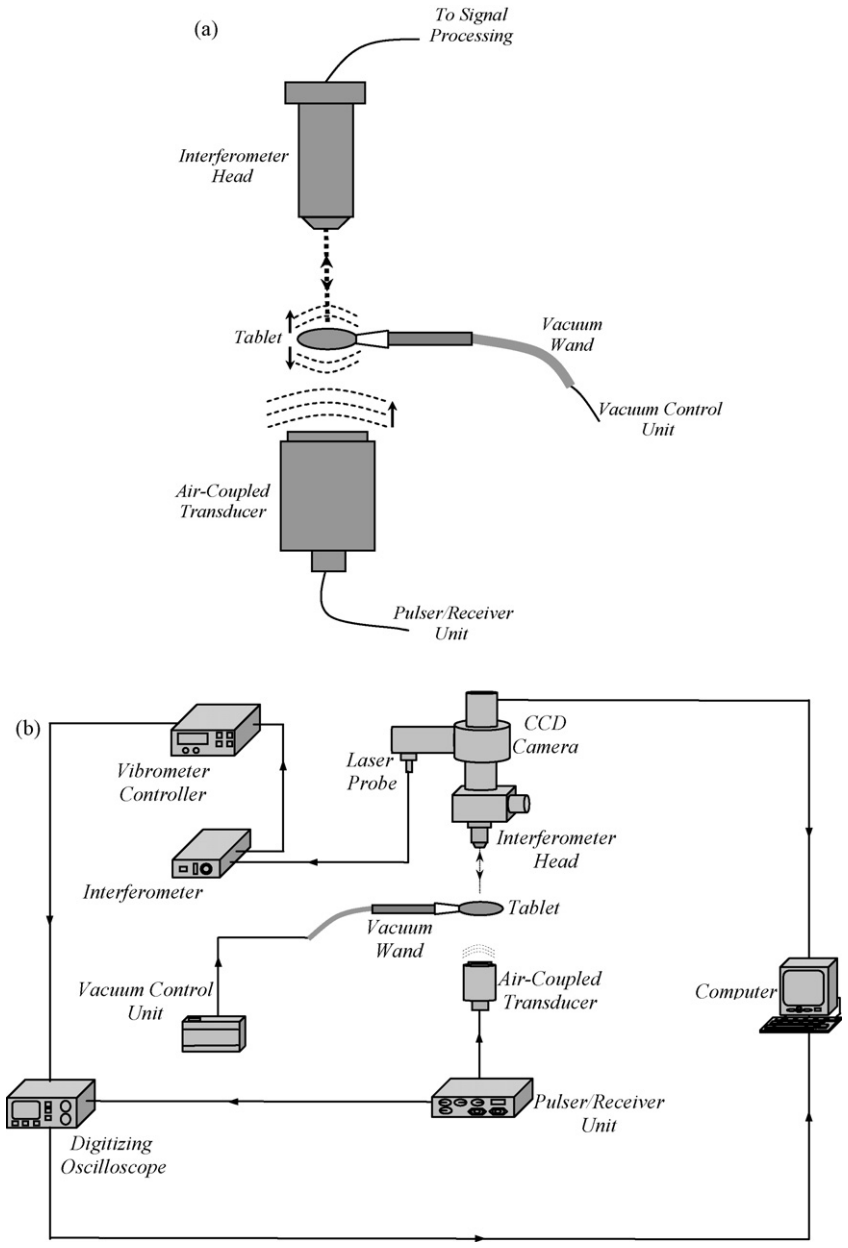

Fig. 1. Schematics of the tablet mounting apparatus with the vacuum wand configuration (a) and the instrumentation diagram of the experimental setup (b).

duction units. The Food and Drug Administration (FDA) has initiated a program entitled the Process Analytical Technology (PAT) to address various aspects of manufacturing issues in the pharmaceutical industry. The PAT initiative is intended to *improve consistency and predictability of drug action by improving quality and uniformity of pharmaceutical materials* (Hussain et al., 2004).

In the pharmaceutical industry, for coating thickness measurements and characterization, various techniques, such as the propagation of short pulses of electromagnetic radiation (*e.g.* Terahertz pulsed spectroscopy) (Fitzgerald et al., 2005), laser induced breakdown spectroscopy (LIBS) (Mowery et al., 2002), X-ray fluorescence method (Behncke, 1984), and Fourier transform infrared (FTIR) spectroscopy (Felton, 2003), have been introduced and discussed in the pharmaceutical research literature. A number of contact ultrasonic measurement techniques for micro-scale layered structures made of attenuative materials similar to tablet coats, such as polymers and biological tissues, have also been proposed. In the Terahertz pulsed method ($1\ \text{THz} = 10^{12}$ Hz), ultra-short pulses of electromagnetic radiation at lower frequencies than infrared are launched into the multilayered coats, and the reflections from interfaces between coats are detected and used for the determination of coating thicknesses. However, the size and cost of the current implementation of this technique somewhat limits its applications. Laser induced breakdown spectroscopy, X-ray fluorescence method and Fourier transform infrared spectroscopy, which are indirect measurement approaches, are either expensive or incapable of rapid measurements for tablet coating thicknesses. In contact pulse/echo acoustic measurements, short ultrasonic pulses are

generated by a piezoelectric transducer to transmit through the layers. Signal-processing the reflected acoustic field from the layer interfaces, either the resonance frequencies of the layered coat structure are obtained and related to the thicknesses of the layers (Li and Cetinkaya, 2006), or the time-of-flight in each layer and corresponding layer thicknesses are determined, provided that the speed of sound in each layer material is available through a calibration process. In the contact ultrasonic measurements, the use of a couplant gel required for maximizing the transmission of ultrasonic energy between the transducer and the test specimen often cause permanent damage to sensitive materials such as tablet coats and core. A detailed review of various monitoring techniques for tablet defects is reported in (Cetinkaya et al., 2006).

In current study, based on air-coupled acoustics and the finite element method, a non-contact/non-destructive technique for predicting the thickness of a drug tablet coating layer is presented. Compared to the measurement techniques discussed above, the main advantages of the proposed approach include its non-contact/non-destructive nature, relatively reasonable cost compared to other measurement techniques, and suitability for rapid (microsecond-scale time scale) on-line monitoring applications.

2. Materials and methods

2.1. Experimental procedure for determining tablet resonance frequencies

The experimental set-up utilized for the current study consists of three major components: (i) air-coupled acoustic excitation source, (ii) non-contact interferometric out-of-plane displacement measurement system, and (iii) tablet/transport/handling system. The set-up incorporates a square pulser/receiver (Panametrics 5077PR), an air-coupled transducer (QMI AS120Ti), a vibrometer controller (Polytec OFV3001), a laser Doppler vibrometer (Polytec OFV511), and a digitizing oscilloscope (Tektronix TDS3052), as well as a vacuum handling apparatus consisting of a vacuum wand and a vacuum pump with a suction pressure of −30 kPa (FVW-110 Duovac). The experimental setup utilized for non-contact coating thickness determination of drug tablets and tablet mounting apparatus with a vacuum wand are well established as depicted in Figs. 1 and 2. The pulser/receiver unit excites an air-coupled transducer with a square pulse at a central frequency of 120 kHz (Fig. 1a and b).

Fig. 2. Image of the bottom excitation configuration of the experimental set-up. The interferometer laser beam is visible on the top of the tablets.

Tablets used in this study (referred to as P-tablets) are excited by an acoustic field generated by the air-coupled transducer in a frequency range sufficiently high to excite several vibrational modes of the tablet (Fig. 1a and b). The tablet transient responses (out-of-plane displacements) are acquired at a set of measurement points by the interferometer in non-contact manner over a bandwidth of 50 kHz–30 MHz, including a displacement decoder with (specified) sub-nanometer resolution in the range of ±75 nm. The diameter of the probe laser beam is specified as small as sub-micron. The responses are digitized in the oscilloscope for further FFT-based signal processing to determine the resonance frequencies of the tablet. In the test set-up, the air-coupled transducer is placed under the sample P-tablet (Fig. 3) at the focal distance of the transducer (specified as 2.35 mm) (Fig. 2). The tablet is placed such a way that the central point of its bottom coincides with the focal point of the transducer for maximum tablet-acoustic field interactions and, consequently, maximum tablet vibrations. The bandwidth of the air-coupled transducer (QMI AS120Ti) used for the set of experiments reported in this study is 105–150 kHz. The characteristic dimensions and masses of the P-tablets are listed in Table 1. The laser interferometer embedded into the optical microscope is directly focused at a point on the tablet surface through the objective lens of the microscope. The P-tablet is placed under the objective at a distance of approximately 6.5 mm. The pulser/receiver unit used in this study delivers a 200 V square pulse to the transmitting air-coupled transducer and provides a synchronizing pulse to trigger the digital oscilloscope (Fig. 1b). The acquired waveforms are digitized and averaged by the oscilloscope and uploaded to a computer. In the current study, eight coated tablets with two tablets per each coating levels (102.3 μm (100%), 76.7 μm (75%), 51.5 μm (50%), and 25.5 μm (25%)) (Fig. 4) were employed to obtain their resonance frequencies in a certain range of frequency. Resonance frequencies of tablets with four different coat thicknesses (δ_{coat}) are obtained by using Fast

Table 1
Dimensions and mass of the coated P-tablets employed in the experiments

Coating layer thickness	Tablet no.	Dimension (mm)			Mass (mg)
		Width	Length	Thickness	
102.3 μm (100%)	1	5.79	11.45	3.33	205.4
	2	5.78	11.47	3.35	209.1
76.7 μm (75%)	1	5.71	11.36	3.31	203.3
	2	5.72	11.34	3.31	202.2
51.1 μm (50%)	1	5.69	11.26	3.26	196.0
	2	5.67	11.25	3.25	196.5
25.5 μm (25%)	1	5.64	11.23	3.21	190.4
	2	5.63	11.23	3.22	191.4

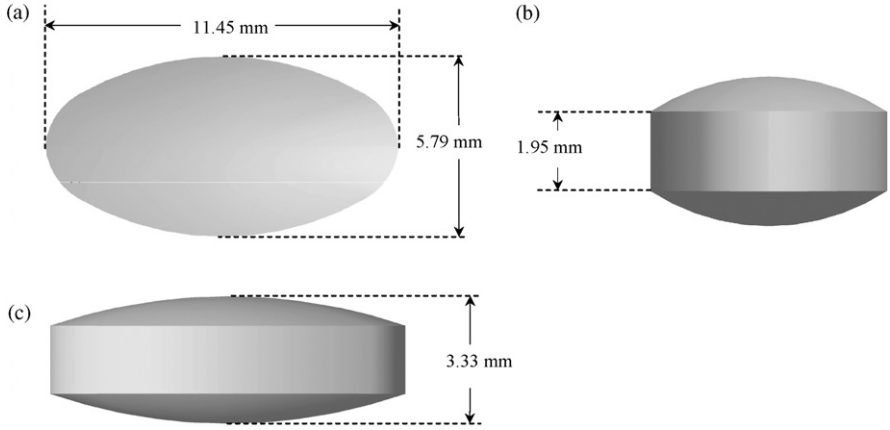

Fig. 3. The dimensions of a 100% coated P-tablet (Tablet No. 1) with its top (a), front (b) and side (c) views.

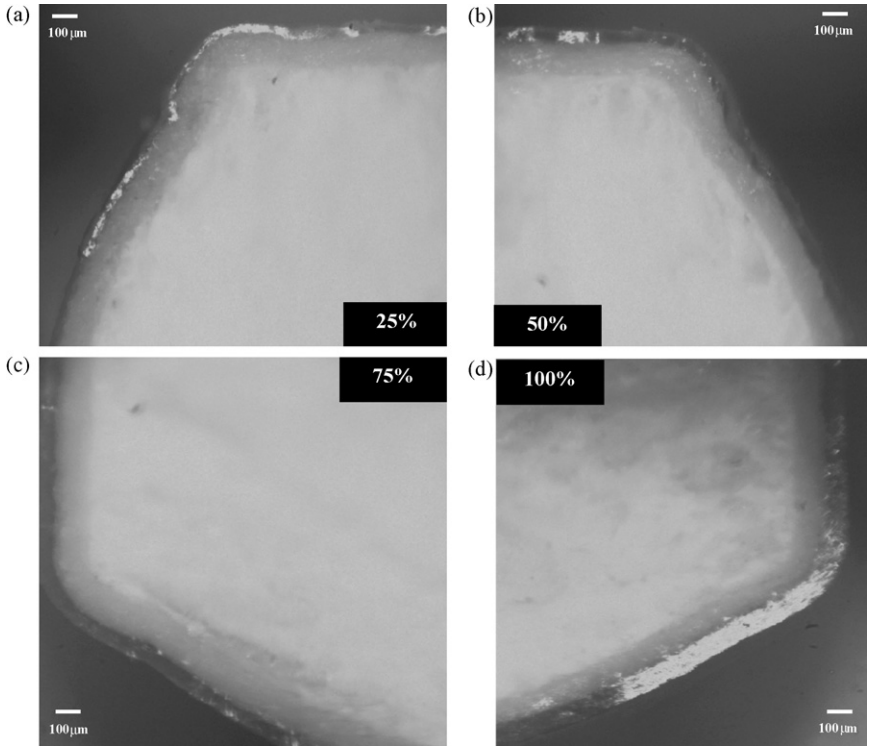

Fig. 4. Microscope images of the P-tablets at 100× with four different coating layer thicknesses: 25% coating – $\delta = 25.5$ μm (a), 50% coating – $\delta = 51.1$ μm (b), 75% coating – $\delta = 76.7$ μm (c), and 100% coating – $\delta = 102.3$ μm (d).

Fourier Transform (FFT) algorithm from the acquired digital waveforms (Fig. 5).

2.2. Computational procedure for extracting tablet coating thicknesses

Vibrational spectral properties of a tablet are related to its mechanical properties such as Young's modulus (E_{core}, E_{coat}), Poisson's ratio (ν_{core}, ν_{coat}) and mass density (ρ_{core}, ρ_{coat}) of the core and the coating layer as well as its geometry (*e.g.* shape and dimensions of the core and the coating layer). Using a finite element (FE) algorithm, such as the Lanczos method, the modal properties of the tablet (*e.g.* a set of resonance frequencies and corresponding mode shapes) can be obtained provided that these mechanical properties and the geometry of the tablet are available. Generally, these properties are not readily available from the properties of the starting tablet materials due to the complexity of the compaction and other manufacturing process steps. The extraction of δ_{coat} of a tablet from its measured resonance frequencies requires the development and use of an iterative computational procedure such as Newton's method as well as a method to compute its resonance frequencies for a given geometry and a set of material properties. In the finite element study conducted to compute resonance frequencies of the tablets with different levels of δ_{coat}, three-dimensional meshes for the coated tablets are developed as

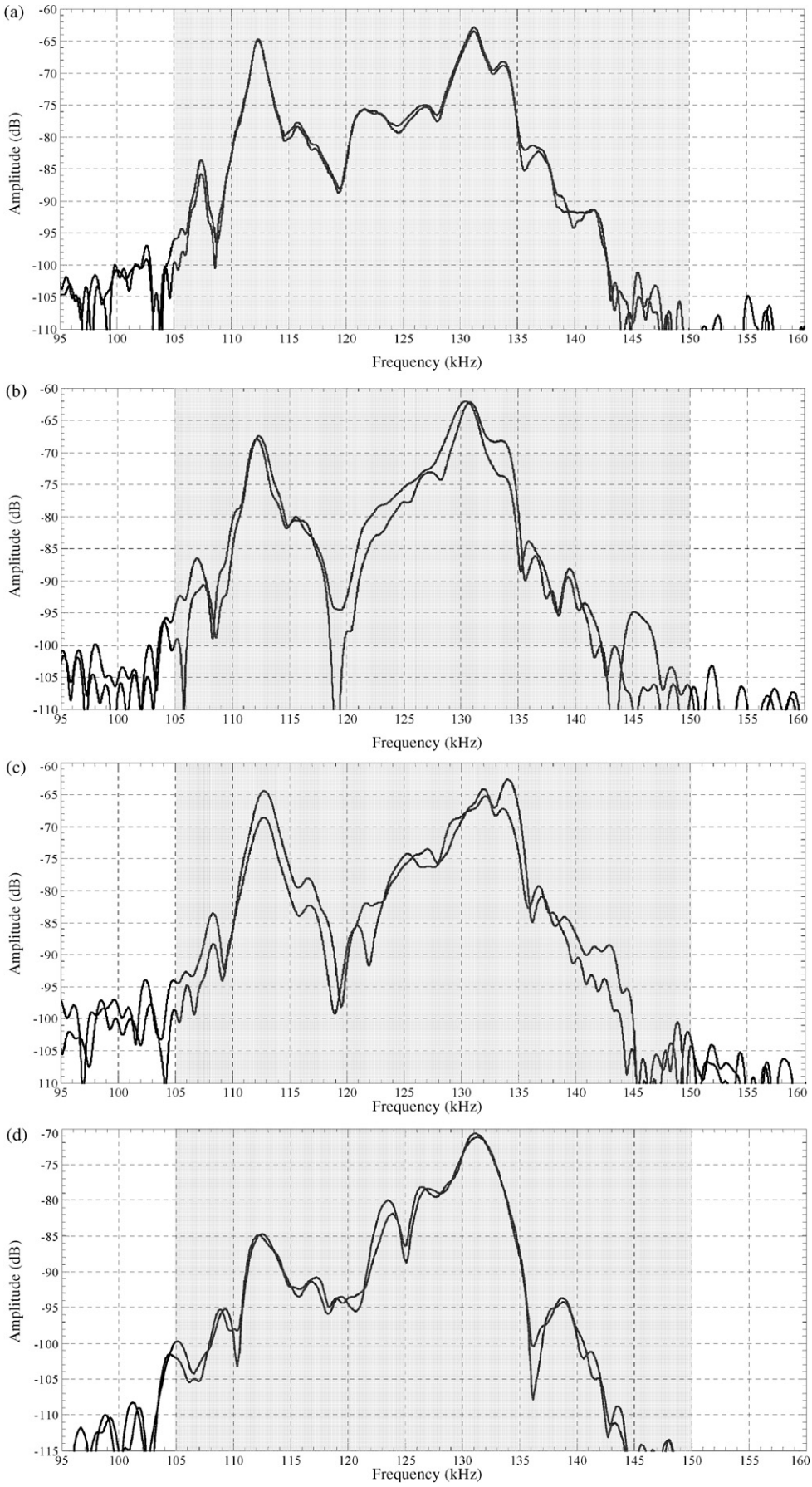

Fig. 5. Frequency responses of four different coating layer thicknesses (two tablets for each coating levels): (a) as 25%, (b) as 50%, (c) as 75%, (d) as 100%.

Table 2
Summary of the numerical iteration results of the P-tablets

Parameters	100% Coated tablet (102.3 μm)			75% Coated tablet (76.7 μm)		
	$\bar{p}_k^*$	$\bar{p}_k^e$	Convergence (%): $\bar{p}_k^* - \bar{p}_k^e$	$\bar{p}_k^*$	$\bar{p}_k^e$	Convergence (%): $\bar{p}_k^* - \bar{p}_k^e$
E_{core} (MPa)	3177.864	2600.777	22.189	3177.864	2634.427	20.628
ρ_{core} (kg/m^3)	1602.915	1313.598	22.024	1602.916	1330.663	20.459
ν_{core}	0.396	0.333	18.918	0.396	0.324	22.222
E_{coat} (MPa)	3627.780	3041.857	19.262	3627.780	2956.952	22.686
ρ_{coat} (kg/m^3)	876.876	742.404	18.113	876.876	722.400	21.383
ν_{coat}	0.458	0.428	7.009	0.458	0.371	23.450
δ (μm)	122.762	99.968	22.801	92.072	75.525	21.909
Parameters	50% Coated tablet (51.1 μm)			25% Coated tablet (25.5 μm)		
	$\bar{p}_k^*$	$\bar{p}_k^e$	Convergence (%): $\bar{p}_k^* - \bar{p}_k^e$	$\bar{p}_k^*$	$\bar{p}_k^e$	Convergence (%): $\bar{p}_k^* - \bar{p}_k^e$
E_{core} (MPa)	3177.864	2632.345	20.723	3177.864	2628.384	20.905
ρ_{core} (kg/m^3)	1602.915	1327.235	20.771	1602.915	1325.577	20.922
ν_{core}	0.396	0.332	19.277	0.396	0.330	20.000
E_{coat} (MPa)	3627.780	3019.346	20.151	3627.780	3029.347	19.754
ρ_{coat} (kg/m^3)	876.876	725.345	20.890	876.876	722.346	21.392
ν_{coat}	0.458	0.382	19.895	0.458	0.382	19.895
δ (μm)	61.380	51.435	19.335	30.690	25.598	19.892

$\bar{p}_k^*$ is the vector of starting parameters for the iterative computational procedure. $\bar{p}_k^e$ is the extracted parameter vectors of the tablets with four different δ_{coat} (102.3 μm, 76.7 μm, 51.5 μm, 25.5 μm) upon completion of iterative procedure for $\bar{p}_k^*$.

homogenous and isotropic elastic solid consisting of a core and a coating layer. Some level of inhomogeneity and anisotropy can be present in pressed tablets for numerical predictions of the tablet resonance frequencies. However, in the current study, the resonance frequency predictions of the tablets are assumed to be unaffected by inhomogeneity and anisotropy of the tablet material. The dimensions of the coated P-tablet with δ_{coat} of 102.3 μm (100% coated tablet) used in the FE analysis are depicted in Fig. 3. Four-node linear tetrahedron elements are used in the mesh generation for the coated tablets. The number of elements, number of nodes, and degrees of freedom for four coated tablets are between 62,635–62,191, 14,357–14,008, and 43,071–42,220, respectively. The characteristic element size for the tablet meshes is specified as 300 μm. The Lanczos eigenvalue solver implemented to compute the resonance frequencies of the modeled tablet in the frequency range of 40–200 kHz for

Table 3
Summary of the resonance frequencies of the P-tablets

100% Coated tablet (102.3 μm)					75% Coated tablet (76.7 μm)				
Modes	$\bar{f}_k^*$	$\bar{f}_{100}^e$	$\bar{f}_{v_{100}}^e$	Convergence (%): $\bar{f}_{v_{100}}^e - \bar{f}_{100}^e$	Modes	$\bar{f}_k^*$	$\bar{f}_{75}^e$	$\bar{f}_{v_{75}}^e$	Convergence (%): $\bar{f}_{v_{75}}^e - \bar{f}_{75}^e$
8	107,223	108,754	109,137	0.352	8	106,865	108,798	108,180	−0.568
9	111,894	112,303	112,181	−0.108	9	110,670	111,341	112,901	1.401
10	119,868	119,257	119,114	−0.119	10	120,845	121,571	121,774	0.166
13	122,071	123,535	123,870	0.271	14	130,442	132,918	132,127	−0.595
14	130,964	131,651	131,655	0.003	15	132,348	134,695	134,118	−0.428
16	138,092	141,174	141,133	−0.029	16	138,903	141,781	141,224	−0.392
17	140,394	142,682	143,100	0.295	17	140,418	142,212	142,323	0.078
50% Coated tablet (51.1 μm)					25% Coated tablet (25.5 μm)				
Modes	$\bar{f}_k^*$	$\bar{f}_{50}^e$	$\bar{f}_{v_{50}}^e$	Convergence (%): $\bar{f}_{v_{50}}^e - \bar{f}_{50}^e$	Modes	$\bar{f}_k^*$	$\bar{f}_{25}^e$	$\bar{f}_{v_{25}}^e$	Convergence (%): $\bar{f}_{v_{25}}^e - \bar{f}_{25}^e$
8	105,645	106,697	107,314	0.578	8	106,331	106,857	107,131	0.256
9	110,324	111,013	112,003	0.891	9	110,149	111,289	112,125	0.751
10	119,312	120,956	120,030	−0.765	10	119,249	120,973	121,524	0.455
14	130,416	130,721	130,915	0.148	14	130,455	131,047	131,113	0.050
15	132,451	133,412	133,624	0.158	15	132,788	133,231	133,812	0.436
16	138,924	140,557	140,956	0.283	16	138,973	140,887	141,095	0.147
17	140,497	142,085	142,123	0.026	17	140,521	141,614	141,726	0.079

$\bar{f}_k^*$ and $\bar{f}_{100}^e$, $\bar{f}_{75}^e$, $\bar{f}_{50}^e$, $\bar{f}_{25}^e$ are the FE resonance frequency vectors corresponding to $\bar{p}_k^*$ and $\bar{p}_k^e$, respectively. $\bar{f}_{v_{100}}^e$, $\bar{f}_{v_{75}}^e$, $\bar{f}_{v_{50}}^e$, $\bar{f}_{v_{25}}^e$ are the experimental resonance frequency vectors directly measured with the vacuum wand for different δ_{coat} (102.3 μm, 76.7 μm, 51.5 μm, 25.5 μm).

initially estimated material properties and coating layer thicknesses.

In order to extract the coating layer thickness (δ_{coat}) of the P-tablets from their resonance frequencies, an iterative procedure based on Newton's method and the finite element method has been developed. It was observed that shifts in resonance frequencies are nearly linear with small changes in the coating thickness, and no intersection of modes occurs within ±20% variation of the initial (estimate) coating thicknesses. If modes traverse as a result of material property and thickness variations in iterations, the correspondence between the mode shapes and resonance frequencies will change and each resonance frequency and corresponding mode shape must be verified before continuing the inversion process.

In extracting the δ_{coat}, a set of initial (estimate) values for the mechanical property and δ_{coat} vector ($\bar{p}_k^*$) is chosen (Table 2) and the corresponding resonance frequency vector $\bar{f}_k^*$ is calculated via the FE method as reported in Table 3. The reason for choosing a wide range for initial (estimate) values is to demonstrate the algorithm converges even if the initial estimates are considerably off from their actual values. Each iteration step denoted by index k and each parameter (E_{core}, ρ_{core}, ν_{core}, E_{coat}, ρ_{coat}, ν_{coat}, δ_{coat}) in the vector $\bar{p}_k^*$ and the vibrational mode numbers obtained from FE are denoted by indices i and j, respectively. Consistent seven modes calculated from FE ($j = 1, 2, \ldots, 7$) for $\bar{p}_k^*$ are compared to the experimentally obtained resonance frequencies vector $\bar{f}_v^e$ for the four types of coating levels, *i. e.* $\bar{f}_{v100}^e$, $\bar{f}_{v75}^e$, $\bar{f}_{v50}^e$, $\bar{f}_{v25}^e$ (Table 3) for the P-tablets with the four values of δ_{coat} (102.3 μm, 76.7 μm, 51.5 μm, 25.5 μm) were selected for iterative calculations. In calculating the sensitivity coefficient (derivatives), the i-th component of $\bar{p}_k^*$ is perturbed by a factor of $(1 + \varepsilon)$ and the resulting seven perturbed mechanical property and δ_{coat} vectors denoted by $\bar{p}_i$ ($i = 1, 2, \ldots, 7$) are calculated. A typical value for ε is taken as $\varepsilon = 0.005$. The FE model is run for each $\bar{p}_i$ to determine the corresponding seven resonance frequency vectors $\bar{f}_i'$ and to calculate their shifts $\Delta\bar{f}_i = \bar{f}_i' - \bar{f}^*$ due to their perturbations. Using the first term in Taylor's expansion (Newton's method), the sensitivity coefficient vector $\{s\}$ is approximated for $i = 1, 2, \ldots, 7$ by:

$$\Delta\bar{f}_i \cong \{s\}^T\{\Delta p\} \tag{1}$$

where

$$\{\Delta p\} = \{\ \Delta E_{core} \quad \Delta\rho_{core} \quad \Delta\upsilon_{core} \quad \Delta E_{coat} \quad \Delta\rho_{coat} \quad \Delta\nu_{coat} \quad \Delta T_{coat}\ \}^T,$$

$$\{s\} = \left\{ \frac{\partial f_j}{\partial E_{core}} \quad \frac{\partial f_j}{\partial\rho_{core}} \quad \frac{\partial f_j}{\partial\nu_{core}} \quad \frac{\partial f_j}{\partial E_{coat}} \quad \frac{\partial f_j}{\partial\rho_{coat}} \quad \frac{\partial f_j}{\partial\nu_{coat}} \quad \frac{\partial f_j}{\partial T_{coat}} \right\}^T,$$

$$\Delta\bar{f}_i = \bar{f}_i' - \bar{f}^*,$$

$$\Delta p = \bar{p}_i - \bar{p}^*,$$

j is the mode number, and $\{s\}$ the sensitivity coefficient (derivatives) vector. After running the FE model and applying Eq. (1) for $i = 1, 2, \ldots, 7$ to calculate the sensitivity coefficients for $j = 1, 2, \ldots, 7$, the sensitivity tangent matrix $[S_\varepsilon]_k$ is constructed for the selected seven vibrational modes as

$$[S_\varepsilon]_{k_{j,i}} = \frac{\partial\bar{f}_j}{\partial\bar{p}_i}$$

Then the change in mechanical property and δ_{coat} vector due to the shift $\{\Delta\bar{f}_k\}$ in the selected set of resonance frequencies can be approximated by

$$\{\Delta\bar{p}\}_k = [S_\varepsilon]_k^{-1}\{\Delta\bar{f}_k\} \tag{2}$$

where $\Delta\bar{f}_k = \bar{f}_v^e - \bar{f}_k^*$, and $\{\Delta\bar{p}\}_k$ the change in mechanical properties and δ_{coat} after the execution of an iteration step with a perturbation of $\bar{p}_k^e = \bar{p}_k^* + \Delta\bar{p}_k$.

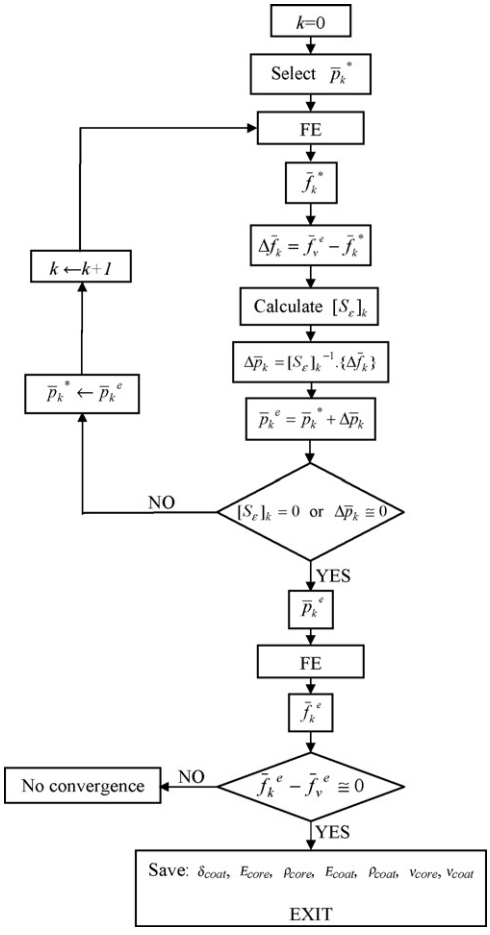

Fig. 6. Flow chart for the iterative process for extracting the δ_{coat} and the mechanical properties of a coated tablet.

3. Results and discussion

In current study, a number of iterations are required to approximate reasonable values for E_{core}, E_{coat}, ν_{core}, ν_{coat}, ρ_{core}, ρ_{coat}

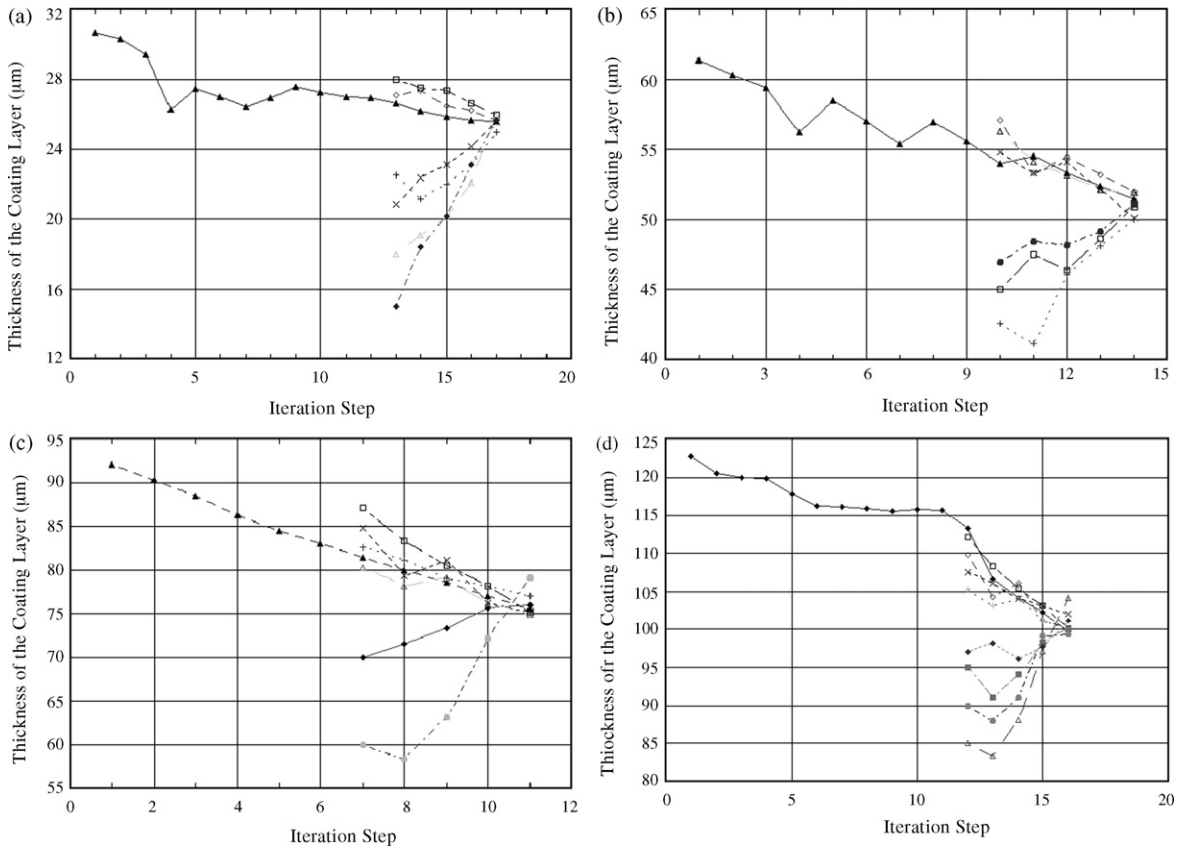

Fig. 7. Convergence of δ_{coat} of the (a) as 25% (25.5 μm), (b) as 50% (51.1 μm), (c) as 75% (76.7 μm), and (d) as 100% (102.3 μm) coated P-tablets during the numerical iterations.

and δ_{coat}. In the iterations, once $\{\Delta\bar{p}\}_k$ values converge to zero or singularity in the sensitivity tangent matrix $[S_\varepsilon]_k$ is observed, the iteration cycle is terminated. The values of $\bar{p}_k^*$ used in the last iteration correspond to the experimental δ_{coat} and mechanical property vector $\bar{p}_k^e$ of the core and coating of the tablet since $\Delta\bar{p}_k \cong 0$. The numerical values for $\bar{p}_k^*$ and $\bar{p}_k^e$ for the four P-tablets are listed in Table 2. A flow chart for this iterative process is depicted in Fig. 6.

After extracting δ_{coat} and the mechanical properties for each tablet, the FE method was employed to determine the corresponding resonance frequencies $\bar{f}_{100}^e$, $\bar{f}_{75}^e$, $\bar{f}_{50}^e$, $\bar{f}_{25}^e$ for comparison purposes (see Table 3 for the numerical values of the resonance frequencies). Due to tablet to tablet variations as listed in Table 1, after the completion of the iterative procedure minor differences are observed in δ_{coat} and resonance frequencies among two P-tablets with the same specified coating thicknesses. Within ±20% variations of the δ_{coat} changes in resonance frequencies of the 100%, 75%, 50%, 25% coated tablets are calculated approximately in the range of ±1.3%, ±0.9%, ±1.5%, ±1.2%, respectively. The average percentage errors between the experimental resonance frequencies ($\bar{f}_{v100}^e$, $\bar{f}_{v75}^e$, $\bar{f}_{v50}^e$, $\bar{f}_{v25}^e$) and the FE calculated resonance frequencies ($\bar{f}_{100}^e$, $\bar{f}_{75}^e$, $\bar{f}_{50}^e$, $\bar{f}_{25}^e$) corresponding to $\bar{p}_k^e$ are within ±0.4%, ±1.4%, ±0.9%, ±0.8%, respectively (Table 3).

Convergence of the δ_{coat} of 25%, 50%, 75%, 100% coated tablets in the iterative cycle is demonstrated in Fig. 7. Also for verification purposes, local values were selected and convergences of each δ_{coat} were tested and confirmed, as depicted in Fig. 7. It is determined that between modes 8 to 17 the sensitivity of resonance frequencies of 100% coated tablet to changes in δ_{coat} and mechanical properties in a descending order are as follows E_{core}, δ_{coat}, ρ_{core}, E_{coat}, ρ_{coat}, ν_{core} and ν_{coat} (Fig. 8).

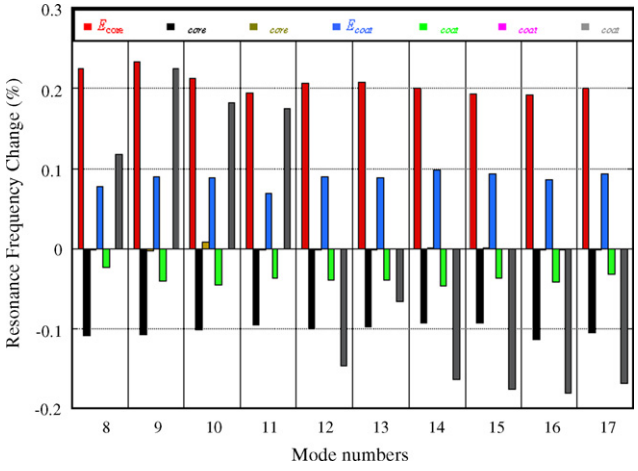

Fig. 8. Normalized sensitivities of the resonance frequencies of 100% coated P-tablet (Tablet No. 1) to the changes in δ_{coat}, E_{core}, ρ_{core}, ν_{core}, E_{coat}, ρ_{coat}, ν_{coat} for the modes 8–17.

4. Conclusions and remarks

In the present study, a non-contact/non-destructive acoustic technique for estimating the drug tablet coating thickness is introduced. The approach is based on air-coupled excitation of a tablet and laser interferometric detection of tablet surface vibrations. An evaluation platform that was previously developed for determination of the mechanical properties of a tablet has been expanded for predicting its coating layer thicknesses. A computational procedure based on the FE analysis and Newton's method for extracting the thickness of a coating layer from a set of measured vibrational resonance frequencies of the tablet is developed and implemented. The effectiveness of the procedure for predicting the thickness of a coating layer of tablets from a set of experimentally obtained resonance frequencies is demonstrated using tablets with various levels of coatings. It is reported that computationally extracted tablet coating thicknesses for four different coating levels are in good agreement with the destructively measured coating thicknesses. Acquired experimental resonance frequencies agree quantitatively well with the FE-based resonance frequency predictions corresponding to these extracted thicknesses and mechanical properties. In addition, analysis revealed that resonance frequencies of a coated tablet in the transducer bandwidth are the most sensitive to changes in E_{core} and δ_{coat} and the least sensitive to changes in ν_{core} and ν_{coat}. This observation holds for the resonance frequency range (105–150 kHz) considered in this study. One conclusion is that, in this frequency range, it is easier to measure the Young's modulus of the core and the thickness of the coat than the Poisson's ratios of core and coat since resonance frequencies are less sensitive to the Poisson's ratios of the materials. It is reasonable to expect that one can find mode shapes and, consequently, frequency ranges (transducer bandwidths) in which the locations of the resonance frequencies are more sensitive to the Poisson's ratios of the materials. This knowledge can play an important role in PAT applications since it could allow to the user identify the frequency range (transducer bandwidth) of interest for a particular application.

In order to apply the proposed technique to tablets with multiple coatings layers, prior to the analysis, the number of layers must be known to decide how many resonance frequencies are to be determined to extract the thickness of each sublayer. However, if the acoustic properties of the sublayer materials are similar, it may be difficult to distinguish thin sublayers from each other.

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