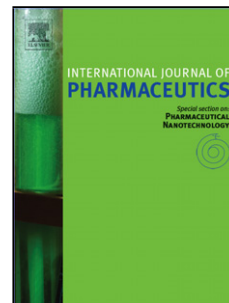


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Author: Prince Bawuah Mousumi Chakraborty Tuomas
Ervasti J.Axel Zeitler Jarkko Ketolainen Patrick A.C. Gane
Kai-Erik Peiponen



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A structure parameter for porous pharmaceutical tablets obtained with the aid of Wiener bounds for effective permittivity and terahertz time-delay measurement

Prince Bawuah^{1*}, Mousumi Chakraborty¹, Tuomas Ervasti², J. Axel Zeitler³, Jarkko Ketolainen², Patrick A. C. Gane^{4,5}, Kai-Erik Peiponen¹

¹Institute of Photonics, University of Eastern Finland, P.O. Box 111, FI-80101 Joensuu, Finland

²School of Pharmacy, Promis Centre, University of Eastern Finland, P. O. Box 1617, FI-70211, Kuopio, Finland

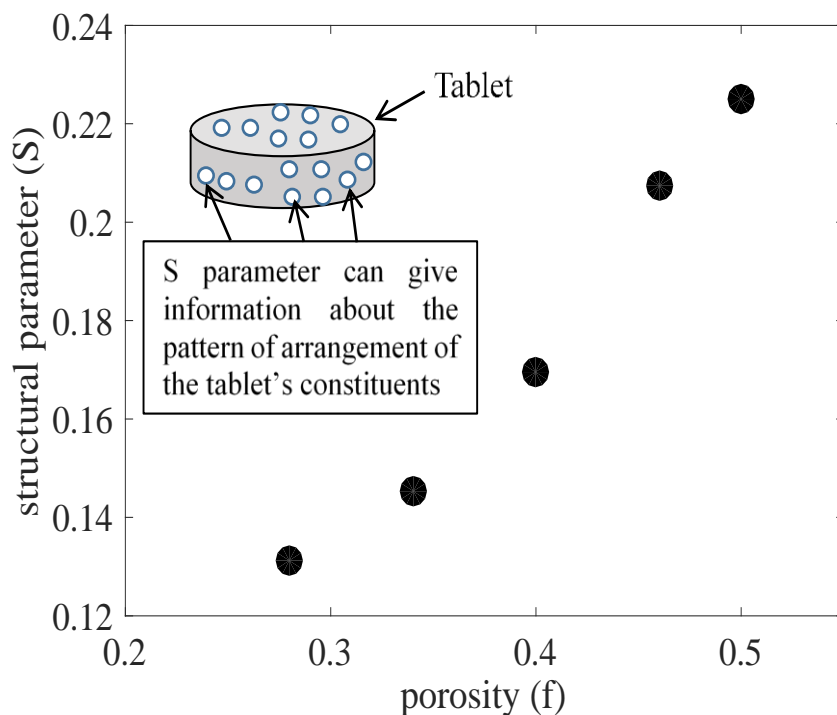
³Department of Chemical Engineering and Biotechnology, University of Cambridge, Cambridge CB2 3RA, United Kingdom

⁴School of Chemical Technology, Department of Forest Products Technology, Aalto University, FI-00076 Aalto, Helsinki, Finland

⁵Omya International AG, CH-4665 Oftringen, Switzerland

* Corresponding Author: Prince Bawuah
Email Address: prince.bawuah@uef.fi
Tel: +358442374671

Graphical abstract

**Abstract**

A structure parameter that can be used to predict the pattern of arrangement of porous inclusions in pharmaceutical tablets is introduced. By utilizing the effective refractive index of a pharmaceutical tablet obtained from terahertz time-domain measurements, we have shown that there exists a promising correlation between the calculated structural parameter and the porosity of training sets of pharmaceutical tablets, having well-defined characterization. Knowing of the structural arrangement, i.e. combined constituent skeletal-pore elements in series, parallel or mixed within porous media, could serve as a basis for understanding the ingress and permeation of liquids in such media. In the realm of pharmaceutical applications, such knowledge of the structural arrangement of air voids within a medicinal tablet could enable correlation with mechanical strength and dissolution behaviour in aqueous systems.

KEYWORDS: Pharmaceutical tablet, microcrystalline cellulose, indomethacin, terahertz, microstructures, effective medium

1. Introduction

Prediction of transport properties of porous media, such as heat conductivity, fluid uptake and permeation, disintegration etc., is of key importance in order to enable design and control of the functional properties of porous products. Typical porous products having topologically connected porosity include, for example, paper, ceramics and pharmaceutical tablets. Additionally, bone, teeth, soil and plant materials are typical examples of functional porous media present in nature. Depending on the physical quantity of interest, namely heat conduction, elasticity, liquid or gas flow inside the porous medium, and optical properties like light transmission, different measurement techniques are applied to extract information concerning these quantities. If we consider a porous medium from the viewpoint of electromagnetic wave interaction with said medium, under the assumption that the effective medium approximation (EMA) (Bruggeman, 1935; Maxwell Garnett, 1904) is valid, prediction of the magnitude of the porosity is possible from measured optical spectra. In such a case, the scattering of light is assumed negligible, and the electric permittivity of the constituents of the two or multi-phase porous medium, such as a nanocomposite, are known (Aspnes, 1982; Boyd and Sipe, 1994; Zeng et al., 1988). The effective medium model, apart from being useful in photonics and the applications thereof, has also been used to extract the thermal properties of porous media. Actually, similar EMA models can be shown to be valid for various different physical properties of porous media as described in the review article of Hale (Hale, 1976).

One shortcoming of EMA models is that assumptions are usually made on the shape of pores embedded in the medium. For example, spherical voids are assumed in the frame of the models of Maxwell Garnett and Bruggeman (Bruggeman, 1935; Maxwell Garnett, 1904). The concept of a spherical inclusion can be reasonable because of the fact that a sphere presents usually a minimum interfacial energy preferred by nature. However, artificial porous effective media can show complex structures that cannot be described with the aid of a simple spherical model of a void. Fortunately, there is a rather general EMA model that provides upper and lower limits for the electric permittivity of porous insulators, namely Wiener bounds (Wiener, 1912). These bounds, apart from assuming a negligible scattering of an electromagnetic wave, place no restriction or assumption on the shape of the constituents of a multi-phase porous medium. In

the case of two-phase composites, tighter parameter estimates than those of Wiener bounds have been presented in the literature in the example of a light absorbing effective medium (Bergman, 1980; Milton, 1980). Furthermore, the theory related to Wiener bounds of three or multi-phase composites have been developed further (Peiponen and Gornov, 2006).

In the case of pharmaceutical tablets, they are compressed from a powder mixture, which includes excipients and one or more active pharmaceutical ingredient(s) (API). Microcrystalline cellulose (MCC), used in this study, is one of the most popular excipients to be found in pharmaceutical tablets, known for its properties of binding and water absorption, in turn providing simultaneous swelling and enhanced break-up of the tablet. Instead of the typical case of using the concept of a polyethylene (PE) pellet as a matrix in THz measurements, we report here, rather, on the evaluation of a structural parameter for three-phase real pharmaceutical compacts, namely MCC plus air (pores) plus indomethacin, used commonly in painkillers, as API. THz waves have a relatively long wavelength, which can be considered as an advantage when studying porous media due to low to negligible levels of scattering of the incident wave. The presence or absence of THz scattering from a porous tablet can be detected and analysed using the methods introduced in (Silfsten et al., 2011; Tuononen et al., 2010). The applicability of the THz measurement techniques has been shown to be valid in industrial conditions that correspond to the production of pharmaceutical tablets (Shen, 2011; Zeitler and Shen, 2013). Our goal is to develop a simple and fast measurement method, which is based on a single THz pulse detection, which would yield simultaneously information on various parameters of pharmaceutical tablets, such as the structural parameter, which is based on utilization of Wiener bounds, as suggested in this article.

Recently, we have been studying effective refractive index of MCC pharmaceutical compacts with a priori known properties such as height, diameter, weight, surface roughness and porosity by detection of THz time delay from such samples (Bawuah et al., 2014b; Chakraborty et al., 2016). These and other samples, we have used as training sets to learn the correlation between the effective refractive index and porosity of the tablets (Bawuah et al., 2014b), and also porosity dependent elastic properties such as the Young's modulus of elasticity which is related to the effective refractive index of the porous tablet (Bawuah and Peiponen, 2016; Peiponen et al., 2015). In the latter case we have suggested that a mechanical property of the porous tablet can be predicted by THz sensing. Hence, this sensing method provides a non-destructive method to gain information on the elasticity of porous media. We expect that information on

the structural parameter of this study can play an important role in the description of the different arrangement of microstructures inside pharmaceutical tablets by THz sensing.

2. Theory

We start with the Wiener bounds for the effective permittivity of a porous effective medium. These are obtained by considering the one-to-one homomorphic equivalence to having different dielectrics in parallel and series connection inside a capacitor, and dealing with the total capacitance of a plate capacitor. From the expression of the total capacitance, one can solve the effective permittivity of the dielectric medium. Wiener bounds describe the two extreme cases where all the different constituents are either in parallel or in series connection (Aspnes, 1982). Hence, in the case of a finite number of constituents, the upper (denoted by subscript U) and lower (subscript L) Wiener bounds are as follows:

$$\varepsilon_U = f_1\varepsilon_1 + f_2\varepsilon_2 + \dots + f_J\varepsilon_J = \sum_{j=1}^J f_j\varepsilon_j \quad (1)$$

and

$$\frac{1}{\varepsilon_L} = \frac{f_1}{\varepsilon_1} + \frac{f_2}{\varepsilon_2} + \dots + \frac{f_J}{\varepsilon_J} = \sum_{j=1}^J \frac{f_j}{\varepsilon_j}, \quad (2)$$

where f_j is the fill fraction and ε_j is the relative permittivity (in the general case a complex number) of the component j . Obviously, it holds that

$$\sum_{j=1}^J f_j = 1. \quad (3)$$

In the case of air voids, the fractional air volume that occupies the pores (i.e. the porosity) is obtained from the volume ratio V_{air}/V_{total} , which can be taken to correspond to, for instance, f_1 . For air, we assume that its relative permittivity is unity, and hence the refractive index of air is also assumed to have the value 1 in the THz spectral range 0.1 - 1.5 THz of this study. It is well known that the bounds given in Eqs. (1) and (2) are not tight, and much tighter bounds, e.g. in the case of a two-phase system have been derived with the aid of the calculus of variations (Hashin and Shtrikman, 1962) and utilized to characterize properties of pharmaceutical compacts (Bawuah & Peiponen, 2016). As we already mentioned, the advantage of Eqs. (1) & (2) is that no assumption is made concerning the shape of the structures of the porous medium. Furthermore, the true value of the effective permittivity is always

between ε_L and ε_U . In reality, part of the randomly distributed structures of the porous medium can be considered to have a share in parallel and the rest in series connection. Using such a model for the share, the effective heat conductivity, for example, can be calculated as shown in (Krischer and Kast, 1978). We utilize such a share as a structure parameter, S , using the concept of relative permittivity and Wiener bounds, and deal with an inverse problem in comparison with the method of (Krischer and Kast, 1978), namely we get experimental information on the effective THz refractive index of a porous medium as a function of porosity and, therefrom, calculate S . The appealing feature with using the structure parameter S is that it holds for multi-phase systems. Following the definition given in (Krischer and Kast, 1978) for heat conductivity, we apply it to the relative permittivity as follows:

$$\varepsilon_{eff} = \frac{1}{\frac{1-S}{\varepsilon_U} + \frac{S}{\varepsilon_L}}. \quad (4)$$

According to the definition in Eq. (4), S is always a real number between zero and one. In Eq. (4) it is assumed that once the totals for parallel and serial effective permittivity are given, they can be effectively stuck together (concatenated) end-to-end, i.e. a region of parallel construction itself put in series with a serial grouping. This is the case since a further “in parallel” makes no sense. This type of lumped parameter expression has been shown to be useful in the description of heat conductivity in porous medium (Gerstner et al., 2008).

Next, we assume that absorption of THz radiation by the porous medium is negligible because THz wave absorption of indomethacin is weak in the THz frequency range (Shen, 2011; Shibata et al., 2015). Thus, the assumption is valid for the present relatively thick samples of the current study because the THz pulse time delay could be measured in the transmission measurement mode. In the case of strong THz wave absorption, one may face the problem of lack of signal in the transmission measurement geometry. Then one may try to find an appropriate THz spectral window for transmission measurement. In the absence of, or low, absorption of THz waves in an insulator, we have the well-known relation between real relative permittivity and refractive index of a medium, namely $\varepsilon = n^2$. By applying this relation in Eq. (4), and solving for S , we get

$$S = \frac{1}{n_U^2 - n_L^2} \left[\frac{n_U^2 n_L^2}{n_{eff}^2} - n_L^2 \right], \quad (5)$$

where n_{eff} , is the effective refractive index of the porous medium that has been obtained from THz pulse time delay data. In the calculation of n_U and n_L we use the information on the dependence of effective refractive index on the porosity of the tablet sample.

The effective refractive index of a pharmaceutical tablet was calculated from the equation of optical path length, given by

$$(n_{\text{eff}}(f) - 1)H = c\Delta t \quad (6)$$

where, f is the porosity and H is the height (thickness) of the tablet, c is the light velocity in vacuum and Δt is the measured THz pulse time-delay.

In the case of a three-phase tablet containing MCC, API and air, n_U and n_L were calculated from the formulas

$$n_U = \sqrt{f_{\text{air}} + f_{\text{MCC}}n_{\text{MCC}}^2 + f_{\text{API}}n_{\text{API}}^2} \quad (7)$$

and

$$n_L = \frac{1}{\sqrt{f_{\text{air}} + \frac{f_{\text{MCC}}}{n_{\text{MCC}}^2} + \frac{f_{\text{API}}}{n_{\text{API}}^2}}}, \quad (8)$$

3. Materials and methods

Here, we report on data for two flat-faced pharmaceutical tablet sets labelled as “1” and “2”. Indomethacin (Hangzhou Dayangchem Co. Ltd., Hangzhou, China), in its crystalline gamma polymorph, was used as the API in the tablet sets. The tablets were compressed incorporating MCC as an excipient (Avicell PH101, FMC BioPolymer, Philadelphia, USA). Avicell PH101 has a nominal particle size of 50 μm and a true density of 1.55 gcm^{-3} . The tablets were compacted with a compaction simulator (PuuMan, Kuopio, Finland). With the compaction simulator, it is possible to adjust and control the value of porosity and height of the tablet by making use of the adjustable simulator parameters in respect to the choice of options in respect to different compression cycles of the lower and the upper punches, and also the magnitude of the compression force. The properties of the resulting tablet sets 1 and 2 are presented in Tables 1 and 2, respectively. In the case of set 1, the nominal porosity of the tablets is held the same, namely 0.36, and the weight percentage (wt%) of the API is changing from 0 up to 15 wt%. In the case of set 2, both porosity and API concentration are variables (see Table 2). The values given in Tables 1 and 2 are average values of five tablets belonging to a given tablet number. In other words, in set 1 the actual number of tablet samples is 40, and in set 2 the sample

number is 25. For each tablet set, the statistical errors in the calculations made for the nominal porosities are as follows: diameter ± 0.008 mm, height ± 0.005 mm (standard deviation of the sample mean), weight ± 0.01 mg (readability of the scale) and porosity ± 0.2 % (calculated using the error propagation law).

The THz pulse time delay measurement was based on the well-known optical concept of using a femtosecond pulsed laser to generate THz radiation. The time-delay (Δt) was obtained from the measurement of the time-of-flight difference of THz pulses with and without the sample (the latter case forming the reference), all made under nitrogen atmosphere (the THz refractive index of nitrogen being 1). The THz measurements of sets 1 and 2 were carried out with the home-built time-domain THz spectrometer at the University of Cambridge, UK. The measurement error of the effective refractive index is ± 0.002 (Ervasti et al., 2012).

4. Results and discussion

Before dealing with the structural parameter S of sets 1 and 2, we first wish to show S in the case of the tablet set “B”, which effective refractive index was studied in (Ervasti et al., 2012). The target nominal porosity of MCC tablets in the set was 30 % but the height of the tablet was a variable. The case of set B is instructive and has partly motivated us to study S of the tablet sets 1 and 2, which contain in addition to MCC also API. In the case of set B, we have obtained an estimate for the magnitude of the refractive index of MCC of the grade used by (Ervasti *et al.*, 2012) using two different, and independent, methods. The methods used for the refractive index estimate were the Bruggeman effective medium model (Bawuah et al., 2014a), and the zero porosity approximation (Bawuah et al., 2014b). Both methods gave almost the same value for n_{MCC} . Here we use the value $n_{\text{MCC}} = 1.400$, obtained from the Bruggeman model. In Fig. 1 is illustrated the S for the set B. The interesting observation is that for a relatively narrow porosity range S can vary relatively widely. It is possible to speculate what happens if the refractive index estimate of MCC is erroneous. Even if the refractive index of MCC would be erroneous (that is to say there would be a systematic error in S), we would nonetheless get a variation of S , as shown in Fig. 1. This is because in the calculation of S , always the same refractive index value n_{MCC} is used. In Fig. 1, as an example, two values of S with constant porosity of 30.1 % are highlighted. The difference of the two S values is relatively big, namely more than 6 %, which is due to the slightly different magnitudes of the effective refractive index of these two samples (the error of estimation of S is ca. ± 0.015). This fact, and observation that the rest of the data points form a scatter plot, as shown in Fig. 1, suggest that

S does not correlate with porosity across the whole range of samples. Hence, all the studied 21 tablets are “individuals” if S is used as a measure. We could draw similar conclusions as above about a scatter plot and almost the same magnitudes and range of variation of S (data not shown here) of another set of thirteen MCC tablets of the study (Ervasti *et al.*, 2012), but having a broader porosity range from 23.2 % to 40.1 % and nominally constant height. Naturally, pharmaceutical tablets containing API are interesting regarding the behaviour of the structural parameter, and we will deal next with such a case.

In the case of S of sets 1 and 2 we need information on the magnitude of n_{MCC} and n_{API} when we exploit Eqs. (7) and (8) in the calculation of S . These refractive indices were obtained using the data in Table 1 and the zero porosity extrapolation technique. The extrapolation is made using a linear fitting of effective index with respect to MCC and API content. In the absence of API, from Table 1, we get $n_{\text{eff, MCC}}(f = 0.36) = 1.543$ (i.e. a tablet containing MCC and air only). In addition, we know that $n_{\text{eff}}(f=1) = n_{\text{air}} = 1$ (air as an anchor point). Then extrapolation using the two refractive index values give an estimate $n_{\text{eff, MCC}}(f = 0) = n_{\text{MCC}} = 1.847$ (i.e. a tablet containing MCC only). In (Bawuah et al., 2014b), we have previously used this type of linear extrapolation technique for MCC - only compacts in a relatively wide porosity range. The higher n_{MCC} value for sets 1 and 2 than for MCC of data for set B is most probably due to the different grade and purity of the MCC.

Next, we let the API concentration be extrapolated to 100 %. Thus, using the data from Table 1, we get the value $n_{\text{eff, API}}(f = 0.36) = 1.392$ (i.e. a tablet containing API and air only). In addition, we use the anchor point, namely $n_{\text{eff}}(f = 1) = 1$ (air). Using these two refractive index values, we fit a line and obtain an estimate $n_{\text{eff, API}}(f = 0) = n_{\text{API}} = 1.613$ (i.e. a tablet containing API only). Since the porosity of all tablet samples is a priori known, we can calculate the fill fraction of MCC using the height, diameter, weight of the tablet and known amount, in wt% (data given in Tables 1 and 2), using the true density of MCC, namely 1.55 gcm^{-3} . Then, after application of Eq. (3) for a three-component system, we can solve the fill fraction of the API.

Before proceeding with the description of S for the sample sets 1 and 2, we wish to remark that we analysed also the possible frequency-dependency of the effective refractive index of all tablets of sets 1 and 2, because, in the presence of dispersion of the THz wave, re-shaping of the THz pulse might cause an error in the calculation of the effective refractive index of the tablet when using Eq. (6). In all cases a plateau-type effective refractive index was obtained

(results to be presented elsewhere), and hence the effective refractive index was a constant in the range 0.1- 1.5 THz. Thus, we conclude that the utilization of Eq. (6) is reasonable.

The calculated structural parameter S of sets 1 and 2 is shown in Figs 2 & 3.

Since the porosity of the samples of set 1 is a constant, we have plotted S as a function of n_{eff} in Fig. 2. It is evident from Fig. 2 that the sample numbers 1 and 4 through 7 have, practically speaking, the same value of S , which is equal to ca. 0.18, whereas tablet number 3 has the highest and tablet number 8 the lowest value, respectively. If we compare the magnitude and change of S , in Figs. 1-3, it is obvious that for the narrow porosity range shown in Fig. 1, S has a relatively wide range of variation from ca. 0.22 to 0.36. Figs. 2 and 3 show relatively regular behaviour of the structural parameter, and value of S of set 1 is between ca. 0.17- 0.19, and of set 2 ca. 0.13- 0.23. The range of variation of S is relatively narrow and less “chaotic” in the case of set 1, as shown in Fig. 2, than in the case of set B, as illustrated in Fig. 1. A comparison of Figs. 1 and 2 suggests that the presence of API has brought more “order” in the tablets regarding the behaviour of S . The way of compression of tablets of set B was different from that of the sets 1 and 2, which may explain also the behaviour of the S parameter shown in Figs. 1-3. Practically, MCC is known to be a poorly flowing, easily aggregated powder with a somewhat sticky particle surface especially when moist. Uneven compaction of 100 % MCC is, therefore, not surprising at relatively low tableting pressure. If these properties of material and compaction lead to such variation, then S could serve, at least as a qualitative measure, to parameterise tablets regarding the arrangement of microstructures, since the magnitude of S is the measure of upper and lower bounds of effective refractive index of constituents in the series. Suggested ranking by S can have importance in powder technology in general. If the target of a tablet would be to have a constant S , then tablets 1 and 4 through 7 in set 1 (target porosity 36 %) fulfil such a demand.

Next, we consider the values of S of the tablet set 2. In this case, the porosity of the tablet has been varied significantly, whereas the change of API concentration is small, a situation that might occur during pharmaceutical tablet production. In Fig. 3, we show S as a function of the porosity for the set 2. It is evident from Fig. 3 that when the porosity of the tablet is decreasing (the effective refractive index is increasing) the structural parameter S is changing monotonically for these samples. From Fig. 3 it can be observed that there is a relatively large change of S as a function of the porosity of the tablet. The behaviour of S shown in Fig. 3 suggests that the parallel connection of constituents of the tablet is increasing as the porosity is

decreasing within a relatively wide porosity range of 28 - 50 %. Nevertheless, comparison of the data of Figs. 1 and 3 shows that the structural parameter S for set 2 takes lower values than for set B. Probably API has also an important role in series/parallel arrangement of the microstructures in the case of set 2. However, more studies are needed to be conducted to comprehend fully the role played by the API in ensuring the orderliness in the particle arrangement during the compaction.

Additionally, the less variation of S observed in both sets 1 and 2 other than in set B, as well as the strong correlation observed between S and porosity of set 2 samples, can be attributed to the small particle size (ca. 50 μm) of the MCC grade of these new sets compared with that of the set B (ca. 180 μm). Small particle size means large surface area, which leads to relatively strong particle-particle surface and contact interactions during the compaction process, and, hence, yields tablets with relatively ordered particle arrangements.

The parallel and series connections of constituents of the pharmaceutical tablet can be understood to be the porous matrix “skeleton” of solid materials, in this case MCC and API, and from a network of pores that can be connected by air channels. Liquid penetration into the pore network plays a crucial role in the disintegration of the tablet, and, in the case of water, its dissolution. We suggest that S could have importance in predicting the disintegration properties of the tablet in relation to the specific excipient used, but this needs further studies to be confirmed in practice. In general, an important issue in the case of a porous medium is, for example, fluid flow in the medium. The dynamics of fluid flow depends, for instance on the connectivity of the air pores by channels (Jiang et al., 2011; Ridgway and Gane, 2002; Roberts et al., 1997). In other words, fluid flow depends on the topology of the porous medium. The S parameter has obviously importance as an interdisciplinary scientific factor regarding the study of connectivity and topology of porous structures, for example, pharmaceutical tablets. The promising results and observations made from the correlation between the S parameter, and the effective refractive index of the training sets of pharmaceutical tablets, has shown that the S parameter could serve potentially as the basis for understanding ingress of liquids into and permeation through a porous medium. This is considered to be possible because the S parameter can give information about the pattern of arrangement (i.e. either parallel, series or a mix of both series and parallel) of the constituents of a porous medium. As shown above, in cases where the porous structure is transparent or semi-transparent to THz radiation and develops only weak/insignificant THz scattering, we can retrieve information regarding the S parameter. Thus, in the field of pharmacy, in principle this S parameter could serve as a novel

quality parameter for predicting the tablet dissolution rate from (Kraemer et al., 2012; Kumar et al., 2011) and, for that matter, the bioavailability of a pharmaceutical API measured directly from a dry tablet. In addition, the S parameter could give valuable information on the content uniformity of a pharmaceutical tablet. Content uniformity is one of the critical quality attributes (CQA) of pharmaceutical tableting, and it is the desire of pharmacists to seek non-destructive techniques of testing this CQA. These predictive properties will be tested in future work.

5. Conclusions

This article introduces and theoretically ascertains a structural parameter, S , which, when combined with a THz pulse time-delay measurement made on porous pharmaceutical tablets of known dimension and physical bulk properties, can offer valuable information on how the various constituents of the composite medium are arranged in a porous matrix. The pattern of arrangement of the constituents is assumed to be in parallel, series or a mix of both patterns. The S descriptor is a useful structural parameter because no pre-assumption is made on the morphology of the constituents. In addition, due to the definition of S , the number of constituents can be high and complex; hence, this model is suggested to be generally valid in those cases where the scattering of the THz wave is weak.

To test for the applicability of the S parameter, we used the effective refractive index of prepared training sets of pharmaceutical tablets obtained from the measured THz pulse delay data in the spectral range of 0.1 – 1.5 THz. These sets of pharmaceutical tablets with a priori known parameters are three-phase media, which are comprised of mixtures of MCC, air and API (indomethacin). Significant differences in the S parameter between tablets could be observed, and S can be used to rank tablets according to parallel and series share of the constituents, such as excipient(s) and API.

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Figure captions

Fig.1. Structural parameter S for 21 MCC pharmaceutical compacts. The porosity of the tablet is in the range from 27.5 to 32.0 %. Two tablets with the same porosity 30.1 % are highlighted by arrows.

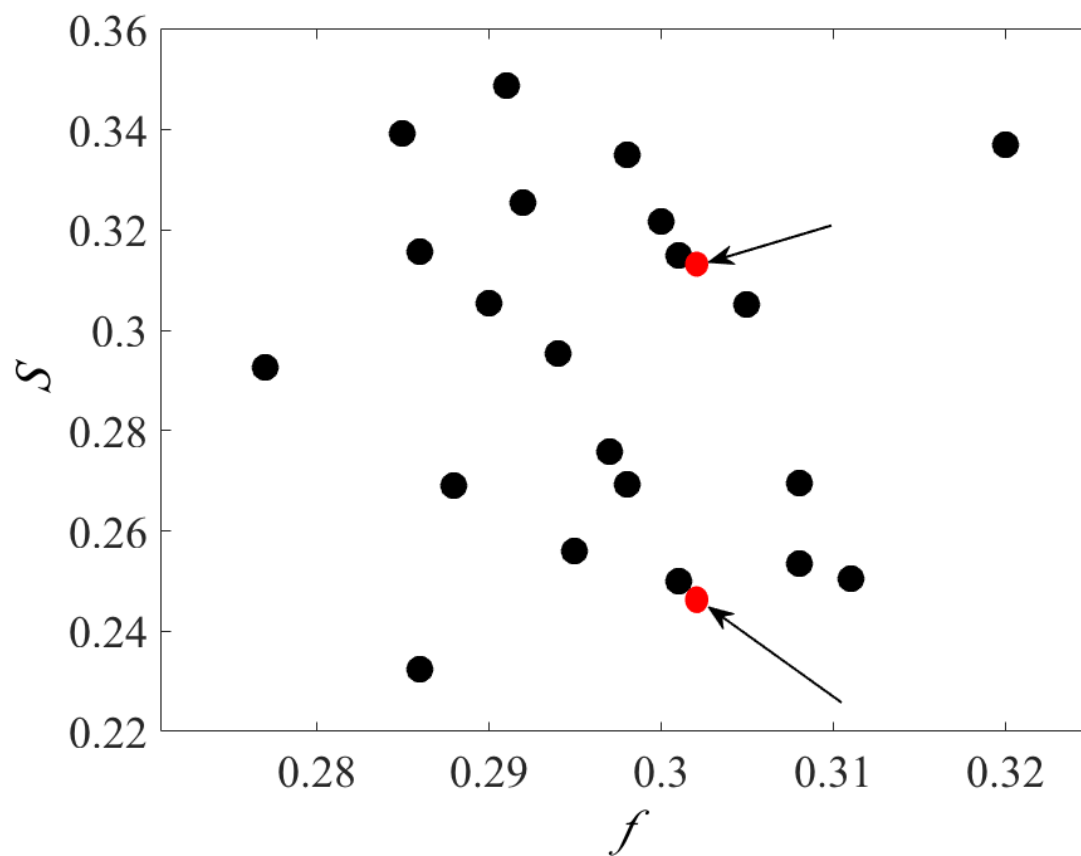


Fig.2. Structural parameter S of eight pharmaceutical tablets as a function of effective refractive index. The tablets have nominally constant porosity 36 % and constant height, but API wt% is a variable. The numbers indicate the tablets in the order of increasing API wt%.

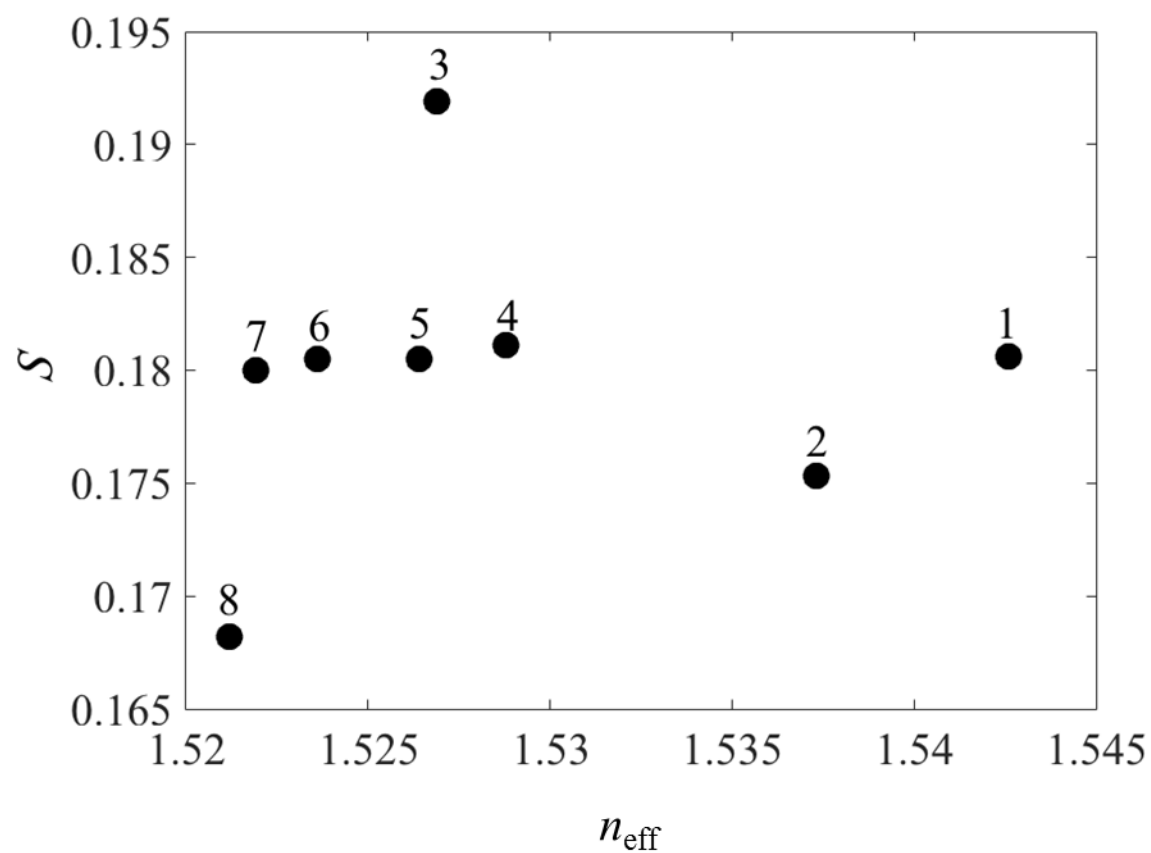


Fig. 3. Structural parameter S of five pharmaceutical tablets as a function of porosity. API wt% and height of the tablets are different.

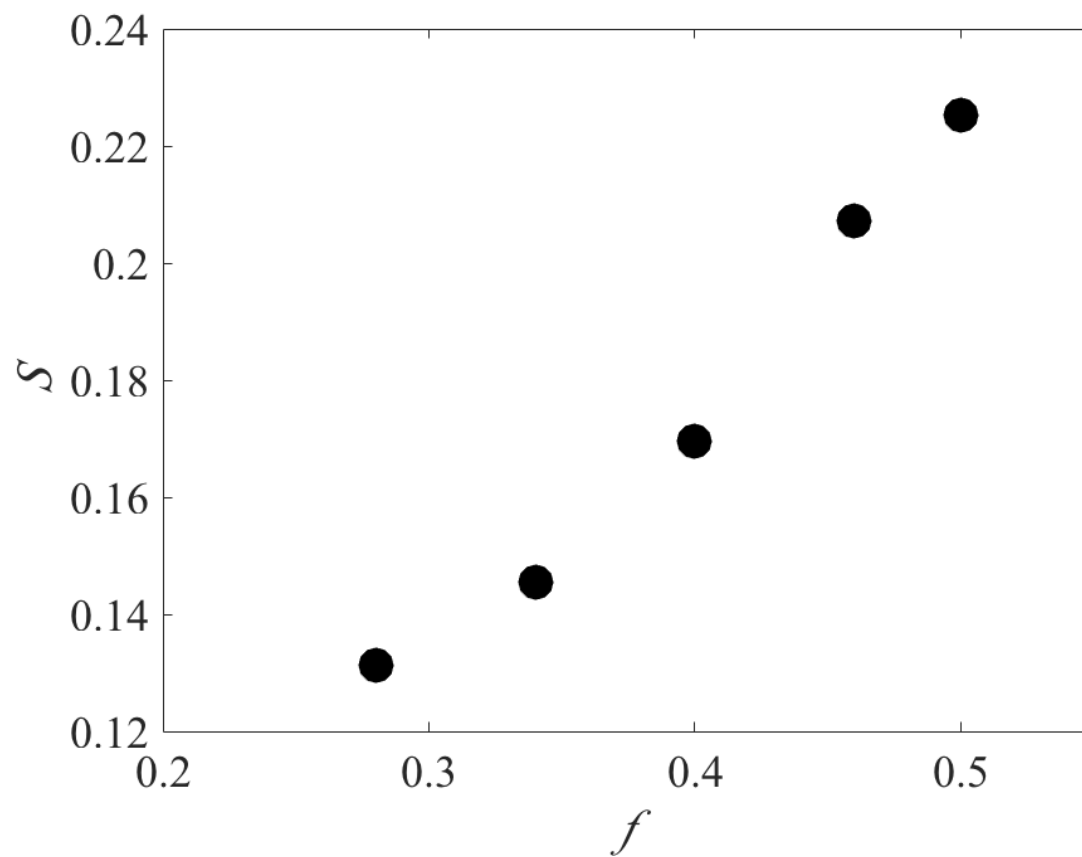


Table 1: Data of tablet set 1. The values of the diameter (d), height (H), weight (W), porosity (f), effective refractive index (n_{eff}) and API wt% (x) for eight pharmaceutical tablets. The porosity of the tablets was calculated by forming a ratio between the tablet density and the true density of MCC and indomethacin. The tablet density was calculated from the measured weight and dimensions of the tablet.

Sample number	d (mm)	H (mm)	W (mg)	f (%)	n_{eff}	x (wt %)
1	13.104	3.034	410.55	36	1.543	0.00
2	13.079	3.023	403.13	36	1.537	3.75
3	13.103	3.025	403.04	36	1.527	7.50
4	13.101	3.001	401.90	36	1.529	8.75
5	13.097	3.016	401.15	36	1.526	10.00
6	13.099	3.036	400.56	36	1.524	11.25
7	13.096	3.034	399.82	36	1.522	12.50
8	13.110	3.039	400.20	36	1.521	15.00

Table 2: Data of tablet set 2. The values of the diameter (d), height (H), weight (W), porosity (f), effective refractive index (n_{eff}) and API wt% (x) for five pharmaceutical tablets.

Sample number	d (mm)	H (mm)	W (mg)	f (%)	n_{eff}	x (wt%)
1	13.076	3.955	404.02	50	1.405	11.00
2	13.075	3.642	403.64	46	1.441	10.50
3	13.094	3.273	405.67	40	1.498	10.00
4	13.093	2.971	404.23	34	1.551	9.50
5	13.081	2.734	406.20	28	1.602	9.00