Journal of Pharmaceutical and Biomedical Analysis 249 (2024) 116372

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.journals.elsevier.com/journal-of-pharmaceutical-and-biomedical-analysis

Short communication

Quantification of API content in pharmaceutical tablets within milliseconds by time-stretch near-infrared transmission spectroscopy

Koji Nakayama [a,1,*], Junki Sahara [b,1], Masaya Fujimoto [a], Yasufumi Yagisawa [a], Keiko Kobata [b], Hiroyuki Kawagoe [b], Aya Ikarashi [b], Takuma Yokoyama [b], Tomoaki Sakamoto [c]

[a] Production Division, Manufacturing Technology Department, Towa Pharmaceutical Co., Ltd., 3-8 Matsuo, Kadoma, Osaka 571-0044, Japan
[b] New Technology Development Department, R&D Division, Business Creation Division, USHIO INC., 6409 Motoishikawa, Aoba, Yokohama, Kanagawa 225-0004, Japan
[c] National Institute of Health Sciences, MHLW, 3-25-26 Tonomachi, Kawasaki, Kawasaki, Kanagawa 210-9501, Japan

ARTICLE INFO

Keywords:
Near-infrared spectroscopy
Transmission spectroscopy
Time-stretch spectroscopy
High-speed measurement
Pharmaceutical tablets
API content

ABSTRACT

We explored the feasibility of high-speed and high-accuracy quantification of active pharmaceutical ingredient (API) content in tablet products by near-infrared (NIR) spectroscopy to improve the reliability of pharmaceuticals. For this purpose, we employed a high-power NIR time-stretch transmission spectrometer recently developed by us. By using this transmission spectrometer with a multivariate calibration model, we demonstrated the ability to quantify API content with a short measurement time of 3.9 ms per tablet for model pharmaceuticals. For the model tablet, the quantification ability of our spectrometer was comparable to that achieved by a commonly used Fourier-transform NIR (FT-NIR) spectrometer with a measurement time of several seconds. We also confirmed that the effect of irradiating tablets with the NIR pulses used in our spectrometer was negligible.

1. Introduction

Near-infrared (NIR) spectroscopy is a non-destructive analytical method that does not require sample preparation, and thus it has been widely adopted for process control in a variety of fields, including agriculture and food industries. In recent years, it has also been employed in the pharmaceutical industry for quality checks of final pharmaceutical products and as a process analytical tool (PAT) [1–4].

The aim of the present study is to realize rapid, highly accurate measurement of active pharmaceutical ingredient (API) content in solid preparations for improving the quality of pharmaceuticals. Currently, quality checks of final tablet products are generally performed by sampling inspection with chromatography. Even with modern high- or ultra-performance liquid chromatography (HPLC/UPLC), the number of samplings is limited because of the need for sample destruction and the long measurement time caused by sample treatment, such as dissolving. We believe that if we could increase the number of samplings for the content measurement by means of NIR spectroscopy, we could further reduce the risk of distributing products that deviate from content standards. To realize this, it is essential to further improve the measurement throughput of NIR spectroscopy. To date, commercially-available Fourier-transform NIR spectrometers (FT-NIRs) have been mainly adopted for the spectroscopic measurement of tablets; however, it takes a few seconds to tens of seconds to observe the NIR spectrum of a tablet with a signal-to-noise ratio (SNR) sufficient for quantitative analysis [5,6]. Therefore, the number of samplings is still not enough even with conventional NIR spectroscopy. Recently, novel high-speed NIR spectroscopic instruments have been developed with the goal of achieving 100 % in-line quality control [7,8]. Although they have successfully achieved high measurement speeds of a few milliseconds to tens of milliseconds per tablet, their measurements were based on a (diffuse) reflection method. For highly accurate quantification of API content in tablets, transmission spectroscopy is preferred over the diffuse reflection method, as demonstrated in previous studies [9–11]. Since the transmission light interacts with a greater mass of the tablet, transmission spectroscopy can provide more accurate and robust results, for example, results that are insensible to inhomogeneity of the materials in the tablets and the surface properties of the tablets, such as coatings.

In this study, we investigated the feasibility of rapid, highly accurate quantification of API content in tablets by using a custom-built time-

* Corresponding author.
E-mail address: k-nakayama@towayakuhin.co.jp (K. Nakayama).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jpba.2024.116372
Received 24 April 2024; Received in revised form 17 July 2024; Accepted 18 July 2024
Available online 20 July 2024

stretch NIR transmission spectrometer [12]. Time-stretch spectroscopy, also known as dispersive FT spectroscopy, is an emerging method using ultra-short pulse lasers and is capable of acquiring the absorption spectrum of the sample at a high acquisition rate on the order of MHz or higher [13,14]. Our time-stretch spectrometer achieved 10-times higher output power compared with previous time-stretch spectrometers by using optical waveguides [12]. The high acquisition rate and high output power of our spectrometer will allow us to observe the transmission spectrum of a tablet with a sufficient SNR even within milliseconds measurement time. The present study demonstrated the quantification of API content in model tablets using our spectrometer and a multivariate calibration model. The quantification ability was compared with that obtained by a conventional FT-NIR. The influence of irradiating the tablets with NIR optical pulses was also evaluated.

2. Materials and methods

2.1. Model pharmaceutical

2.1.1. Formulation

In experiments to quantify the API content in tablets, we prepared model tablets containing allopurinol as an API. The standard contents of the ingredients in the tablet were: allopurinol 16.7 % w/w, lactose hydrate 55.6 % w/w, microcrystalline cellulose (MCC) 26.9 % w/w, and magnesium stearate (Mg-St) 0.8 % w/w. The total mass of the tablet was 180 mg. The tablet form was round uncoated convex tablets with a score line on one surface. The diameter and thickness were 8.0 and 3.2 mm, respectively. The photograph of the model tablet is shown in Supplemental Fig. S1.

Fig. 1 show the NIR absorption spectra of each ingredient contained in the model tablet measured with a commercially available FT-NIR (spectral resolution of 16 cm^{-1}). In Fig. 1(b), Savitzky-Golay (SG) first derivative and standard normal variate (SNV) were applied. The API shows characteristic NIR absorption in the 8700–9200 cm^{-1} range, different from the additive substances.

2.1.2. Preparation of model tablets

In the present study, we prepared two sets of model tablets, namely, calibration and test tablets, for developing a multivariate calibration model and demonstrating quantification of the API content in tablets, respectively. The target API contents in the calibration tablets were 70 %, 85 %, 100 %, 115 %, and 130 % (100 % corresponds to 16.7 % w/w with respect to the total mass of the tablet) [15]. For each API content, 10 tablets were prepared. For the test tablets, another 40 model tablets whose API content was about 100 % were prepared.

2.2. NIR spectrometers

2.2.1. High-power NIR time-stretch spectrometer

For quantification of the API content in the tablets, we used a custom-built NIR time-stretch spectrometer described in ref. 12. Spectroscopic measurement was conducted in the same manner as conventional absorption spectroscopy using a wavelength-tunable laser, except that our spectrometer emitted optical pulses rather than a continuous wave. The center wavelength of the optical pulse was scanned pulse by pulse every 56 cm^{-1} over the range of 7692–11111 cm^{-1} (900–1300 nm wavelength), resulting in 61 spectral channels in the spectrum. The wavelength scan rate was 1.2 MHz; therefore, the spectral acquisition rate was also 1.2 MHz when no spectral integration was applied. The average output power of our spectrometer was ~60 mW. The pulse duration was ~800 ps, and thus the peak power of the optical pulse was estimated to be ~1 W. The spectral range we measured was selected taking into account previous works of NIR transmission spectroscopy of tablets. The spectral response of a standard indium gallium arsenide (InGaAs) photodetector is in between 5880 and 11111 cm^{-1} (900–1700 nm wavelength). However, the strong absorption by excipients of mainly lactose hydrate and microcrystalline cellulose hinders the light transmission in 4000–7000 cm^{-1} [16,17], leading the quite low signal-to-noise ratio (SNR) of the detected signal in the spectral range [9,18]. Due to the low SNR of the detected signal, it seems to be challenging to improve the prediction ability of the calibration model even when the signals in the spectral range are incorporated into the model. As a result, the useful range is limited to about 7000–11111 cm^{-1} in the NIR transmission spectroscopy of tablets.

The spectral measurement of tablets was performed with a custom-built rotating holder (Supplemental Fig. S2). The sample beam constituted by the NIR optical pulses was focused onto a tablet. The $1/e^2$ diameter of the focused beam on the tablet mounted in the rotating holder was 0.7 mm. The diffuse transmission light exiting from a 2 mm-diameter area on the tablet back surface was collected by lenses (numerical aperture of 0.6) and detected by using an InGaAs photodetector (G12180–010A, Hamamatsu Photonics, 60 MHz cutoff frequency, φ1 mm). The photodetector was selected because of the cutoff frequency high enough to detect the intensity of optical pulses at different wavelengths as a waveform and the relatively large photosensitive area for collecting more transmission photons. The detection optics were tilted by 30 degrees to the optical axis of the sample beam in order to protect the photodetector from damage due to direct irradiation of intense optical pulses. Because the detected signal was weak due to the low-transmittance and highly-scattering properties of the tablet, the signal was amplified by an electrical amplifier (PE15A1007, Pasternack). The amplified signal was recorded with a digitizer (ADQ7DC, Teledyne SP Devices) at 5 GHz sampling rate. The transmission spectrum of the tablet

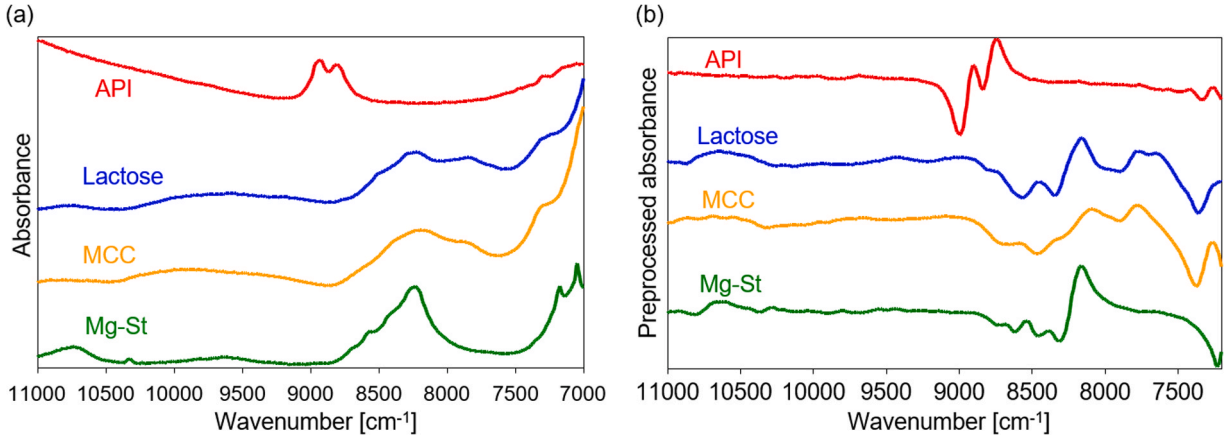

Fig. 1. NIR absorption spectrum of each ingredient contained in the model tablet. (a) raw spectrum. (b) preprocessed spectrum.

was calculated by integrating the signal intensity for each of the 61 pulses at different wavelengths in the waveform. The power fluctuation of the supercontinuum source in our spectrometer was compensated numerically by using a reference signal [12]. For each tablet, we integrated 4700 transmission spectra successively measured while the irradiation position on the tablet was scanned over 3.9 mm by rotating the holder. Accordingly, the measurement time was 3.9 ms for each tablet.

2.2.2. FT-NIR spectrometer

In this study, to compare the quantification ability of our spectrometer, we also quantified the API content in tablets with a conventional FT-NIR spectrometer (Multi-Purpose Analyzer (MPA), Bruker), which has been widely used for the spectral analysis of tablets [5,19]. A transmission unit for the MPA was used to detect the transmission light through the tablet. The transmission spectrum of each tablet was formed from an average of 32 scans over the range 7000–12500 cm^{-1}. The spectral acquisition time was 13 s for each tablet. The spectral resolution was set to 16 cm^{-1}.

2.3. Development of calibration model for quantitative NIR analysis

For the quantification of the API content in the tablets, a multivariate calibration model was developed. First, we obtained a training dataset for developing the calibration model by recording transmission spectra of the calibration tablets with our spectrometer. For each calibration tablet, eight transmission spectra were measured while changing the orientation of the tablet (i.e., laser light was radiated onto the surface with or without a score line) and the angle of the score line. The total number of spectra was 400 in the training dataset for our spectrometer. Then, PLSR calibration models [20] were developed with the training dataset. We compared the preprocessing methods of SNV, multiplicative scatter correction (MSC), SG first derivative, and their combinations. Mean centering was applied for every model. The spectral range and number of latent variables used in the models were selected based on the figure of merits obtained by leave-one-out cross-validation (LOOCV) and our empirical knowledge to avoid models those are overfitted and low-robustness. The comparison results of preprocessing methods are discussed in the Results section. Spectral preprocessing and PLS-LOOCV were performed by using the OPUS QUANT software (version 7.0, Bruker).

We developed another calibration model for the FT-NIR spectrometer because its spectral response was slightly different from our spectrometer. The corresponding model was developed by using transmission spectra of the same calibration tablets measured by the FT-NIR. The total number of spectra was 100 in the training dataset for the FT-NIR (two spectra for each calibration tablet). The comparison of preprocessing was performed in the same manner as the ones for our spectrometer.

2.4. Quantification of API content in test tablets by NIR transmission spectroscopy

We examined the quantification of the API content in the test tablets by using our spectrometer and the FT-NIR spectrometer with the corresponding calibration model. For each test tablet, we measured 10 transmission spectra while changing the tablet orientation and angle of the score line. The same spectral preprocessing used to develop the calibration model was also applied to the observed transmission spectra of the test tablets.

The prediction ability (accuracy and precision) of the calibration models was evaluated by the root mean square of prediction (RMSEP) for each tablet, as expressed by:

$$RMSEP = \sqrt{\frac{\sum_{i=1}^{N}\left(y - \hat{y}_{(i)}\right)^2}{N}} \quad (1)$$

where N is the number of spectra (N=10 for each tablet), y is the reference result of the corresponding tablet (Section 2.5), and $\hat{y}_{(i)}$ are the predicted results of each model for the spectrum i.

2.5. Reference analysis for API content

The actual API content in the tablets was evaluated with a UV-Vis spectrometer (UV-1800, Shimadzu) as a reference result. After the NIR measurement, the tablets were dissolved using a mixture of a sodium hydroxide solution (0.05 mol/L) and a hydrochloric acid solution (0.1 mol/L). The absorbance of the tablet solutions at a wavelength of 250 nm was measured with a quartz cuvette, and the API content in the tablets was calculated from the resultant absorbance.

2.6. Evaluation of the influence of NIR optical pulse irradiation on pharmaceuticals

Because the peak power of NIR pulses emitted from our spectrometer was relatively high, we investigated the influence of the irradiation of the sample with the NIR pulses. We examined this for three pharmaceuticals having different properties as below: (A) unstable to irradiation of visible light, but stable to heat, (B) stable to irradiation of visible light, but unstable to heat, and (C) unstable to both irradiation of visible light and heat. In the present study, because the stability of general formulations to NIR light has not been explored yet, we chose pharmaceuticals that are unstable to visible light. The API contents in the three pharmaceuticals were: (A) 2.9 % w/w, (B) 4.0 % w/w, and (C) 8.8 % w/w, respectively. Each sample was irradiated with 40-times more NIR pulses than the measurement conditions used for the API content (Section 2.2.1). We also analyzed the samples not being irradiated by the NIR pulses as a control. The control samples were treated and kept in the same manner as the irradiated samples, except for NIR pulse irradiation. The amount of photolysis products, thermolysis products, and total related substances, including unexpected modifications, were evaluated by an HPLC (LC-2050 C, Shimadzu).

3. Results and discussion

3.1. NIR calibration models

Comparison results of the models developed by using several preprocessing are summarized in Supplemental Table S1. For our time-stretch spectrometer, the model with SNV and SG first derivative was the most favorable, with RMSECV better than the other models. For FT-NIR spectrometer, the model with only SNV was just a little better than the model with SNV and SG first derivative. In the present study, we decided to use the latter model because the model without the derivative seems to be low robustness in the prediction of new samples based on our empirical knowledge. This will be further investigated in our future work. The optimal number of latent variables was determined by visually looking for the inflection point on the RMSECV profile to avoid overfitting. As a result, five and three latent variables were used for the models based on our spectrometer and FT-NIR spectrometer, respectively. Using different numbers of latent variables for different NIR spectrometers is reasonable since their spectral response were slightly different. A similar conclusion was seen in ref. 21.

Fig. 2 show the preprocessed transmission spectra of the calibration tablets at different API contents observed with (a) our spectrometer and (b) the FT-NIR spectrometer. As expected from the absorption spectrum of the pure API shown in Fig. 1, the intensity of the transmission spectra of the tablets varied in the range 8700–9200 cm^{-1} corresponding to the

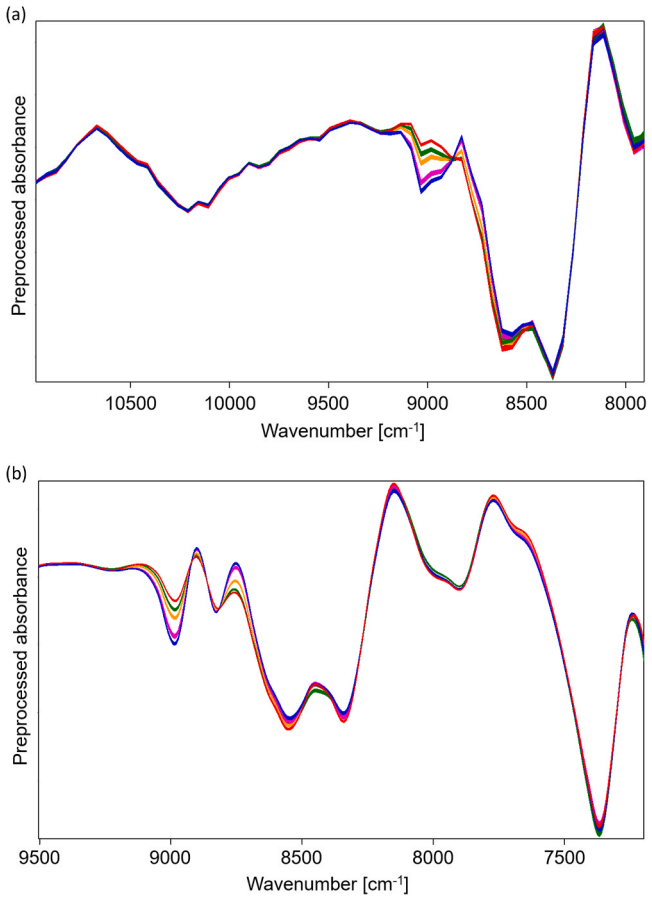

Fig. 2. Preprocessed transmission spectra of the calibration tablets measured with (a) our spectrometer and (b) the FT-NIR spectrometer. The API contents in the tablet were (red) 70 %, (green) 85 %, (orange) 100 %, (pink) 115 %, and (blue) 130 %, respectively. All spectra used for developing calibration models are plotted in the figure (for each API content, 80 and 20 spectra for (a) and (b), respectively).

API content in the tablets. Even with the sparce spectral sampling in our spectrometer (~56 cm^{-1} interval), the spectral change related to the API content was sufficiently observed.

The loading plots obtained by PLSR are shown in Fig. 3. For both NIR instruments, the first loading spectrum resembled the API absorption spectrum (Fig. 1) and had a significant contribution of >99 %. Those results indicate that the developed PLS calibration models were specific to the API content in the model tablet. The developed NIR calibration methods were validated in accordance with the recommendations of International Conference of Harmonization (ICH) guidelines (Q2(R2)). The figure of merits of the models calculated by using LOOCV results are shown in Table 1. The recovery values indicate the good trueness of our methods over the 70–130 % concentration levels. The precision was calculated as the repeatability at the five content levels. The precision for the two NIR spectrometers was comparably high enough for content uniformity assay considering that the standard width of API content in tablets is 100±5 % in general in the pharmaceutical industry. The concentration correlation plots are shown in Supplementary Fig. S3. The regression equations for the API concentration predicted by NIR (API_{pred}) are $API_{pred} = 0.996 \times API_{HPLC} + 0.421$ and $API_{pred} = 0.996 \times API_{HPLC} + 0.410$ for the models based on our spectrometer and FT-NIR spectrometer, respectively (API_{HPLC} is the reference value measured by HPLC). For both models, the slope included 1 within the 95 % confidence interval and the R^2 was almost 1, indicating the good linearity of our models for the API concentration quantification assay.

3.2. Quantification result of API content by NIR transmission spectroscopy

Fig. 4 plots the RMSEP for the test tablets obtained with our spectrometer and the FT-NIR spectrometer. Prediction results for all measured spectra are listed in Supplemental Table S2. The RMSEP values obtained by our spectrometer were almost entirely in the range between 0.5 % and 3.0 %. The high prediction error for the tablet #7 is probably due to the large segregation of the API in the tablet of interest because we made the test tablets by hand. Because the standard width of API content in tablets is 100±5 % in general in the pharmaceutical industry, the prediction ability of our spectrometer was good enough for quality checks of tablet products. A paired t-test showed no significant differences between the results obtained by our spectrometer and the FT-NIR spectrometer (t(39)=0.36 and p=0.72 for predicted API content, and t(39)=0.33 and p=0.74 for RMSEP). As shown here, our spectrometer demonstrated API content quantification results comparable to those obtained with conventional FT-NIR for the model tablet, even with a short measurement time of 3.9 ms per tablet. Finally, we confirmed that the calibration models we used were not over-fitted by evaluating the RMSEP as changing the number of latent variables in the model (Supplemental Table S3).

Although we examined the one model tablet only in the present study, we believe that our proposed method would be applicable to the

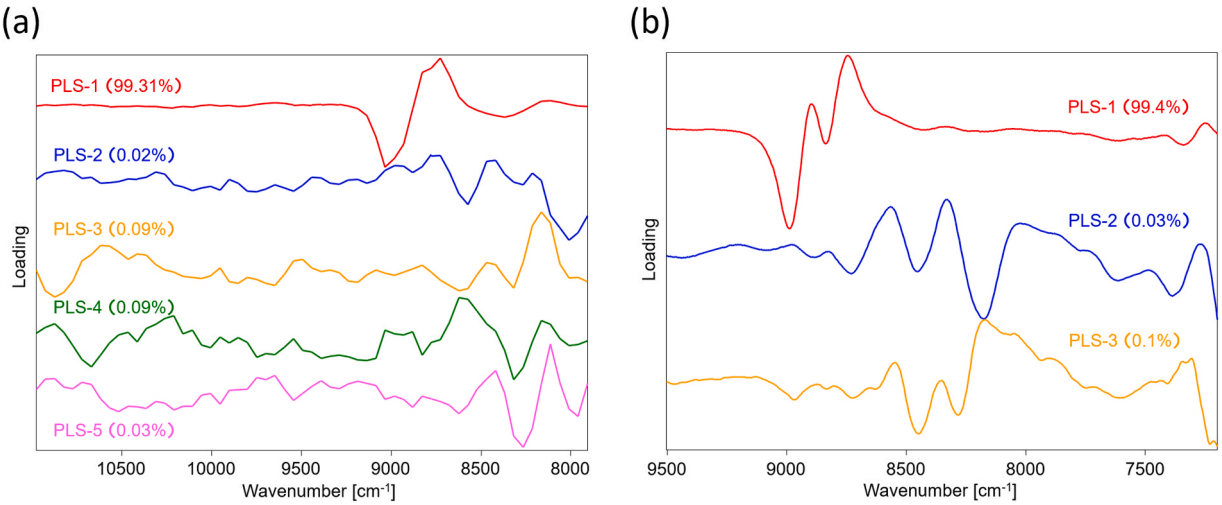

Fig. 3. Loading plots used for PLS calibration models for (a) our and (b) FT-NIR spectrometers. The contribution of each loading component is also indicated.

Table 1
Validation results of NIR methods.

NIR spectrometer	Concentration by HPLC [%]	NIR average [%]	Trueness		Precision
			Relative bias [%]	Recovery [%]	Repeatability [RSD%]
Our spectrometer	69.2	69.5	0.43	100.43	0.82
	81.7	81.4	−0.27	99.73	0.81
	93.8	93.7	−0.02	99.98	0.75
	118.7	118.5	−0.18	99.82	0.60
	127.8	128.0	0.14	100.14	0.62
FT-NIR	69.2	69.4	0.28	100.28	0.34
	81.7	81.5	−0.19	99.81	0.29
	93.8	93.7	−0.02	99.98	0.37
	118.7	118.8	0.07	100.07	0.31
	127.8	127.8	−0.05	99.95	0.24

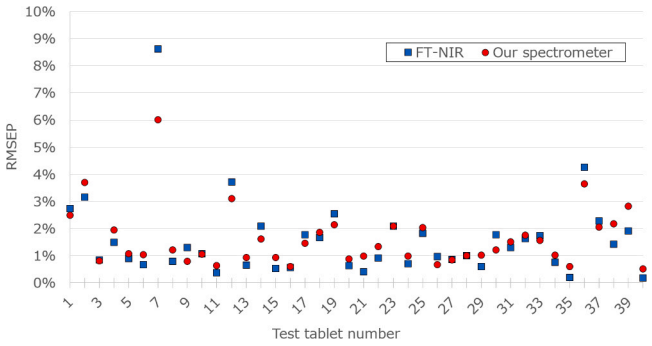

Fig. 4. RMSEP results for the test tablets.

rapid quantification of the API concentration for tablets with various APIs due to the following reason. Most APIs contain aromatic rings (aryl group, Ar) whereas most excipients are aliphatic and/or saccharide [22]. Because the vibration frequency of Ar-H is different from that of C-H appeared in aliphatic and saccharide, one can identify the API specifically in spectral domain. In the spectral region used in transmission NIR spectroscopy of tablets, APIs have spectral peaks around 9000 cm^{-1} whereas excipients have peaks around 8500 cm^{-1}. Therefore, a good NIR calibration model for API concentration can be generated by appropriately selecting the spectral region used in the analysis even when the spectral peaks of API and excipients are somewhat overlapped. This is supported by many successful demonstrations of transmission NIR spectroscopy of tablets previously reported, such as refs. 9,15,18,23. We have now investigated the applicability of the proposed method for wide variety of tablets such as different APIs, API concentration, tablet's coating and thickness, and model robustness as well. The results of the investigation will be reported in future work.

Table 2
The amounts of related substances of pharmaceuticals with and without NIR pulse irradiation.

	Condition	Photolysis products	Thermolysis products	Total related substances
Pharmaceutical A	Pulse irradiated	0.00 %	N/A	0.13 %
	Control	0.00 %	N/A	0.17 %
Pharmaceutical B	Pulse irradiated	N/A	0.10 %	0.21 %
	Control	N/A	0.10 %	0.21 %
Pharmaceutical C	Pulse irradiated	0.03 %	0.03 %	0.25 %
	Control	0.02 %	0.02 %	0.23 %

3.3. Evaluation of the influence of irradiation with NIR pulses

Table 2 shows the measurement results of the amounts of related substances in three pharmaceuticals tested with and without NIR pulse irradiation. Even when we irradiated the pharmaceuticals with 40-times more NIR pulses than the standard number used for the quantification of API content, there were no significant increases in the amounts of related substances compared with controls. This result indicates that the measurement for quantification of API content by our spectrometer does not affect the tablets being measured.

4. Conclusions

In this study, we demonstrated rapid, highly accurate quantification of the API content in a pharmaceutical tablet by transmission NIR spectroscopy with our high-power time-stretch spectrometer. For the model tablet, with a short measurement time of 3.9 ms per tablet, the quantification ability of our spectrometer was comparable to that of an FT-NIR spectrometer widely used for tablet analysis. This measurement speed matches the current manufacturing speed of pharmaceutical tablets (several hundred thousand tablets per hour). We also confirmed that the measurement by our spectrometer does not affect the tablets. These results demonstrate the feasibility of inspection of all individual tablets on the production line by NIR transmission spectroscopy. In future work, we will incorporate the spectrometer presented in this study into a transport system of tablets to practically realize the rapid, highly accurate quantification of the API content in tablet products. Our high-speed spectroscopic method can be beneficial not only for the quantification of API content in tablets, as demonstrated here, but also other physiochemical analyses of pharmaceuticals used as a PAT tool during manufacturing processes.

CRediT authorship contribution statement

Koji Nakayama: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Conceptualization. **Junki Sahara:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Masaya Fujimoto:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis. **Yasufumi Yagisawa:** Writing – review & editing, Writing – original draft, Visualization, Investigation. **Keiko Kobata:** Methodology, Investigation. **Hiroyuki Kawagoe:** Writing – review & editing, Writing – original draft, Visualization. **Aya Ikarashi:** Writing – review & editing, Methodology, Conceptualization. **Takuma Yokoyama:** Writing – review & editing, Project administration, Methodology. **Tomoaki Sakamoto:** Supervision.

Declaration of Competing Interest

The authors declare the following financial interests/personal

relationships which may be considered as potential competing interests: Koji Nakayama reports writing assistance was provided by Japan Agency for Medical Research and Development. Koji Nakayama has patent #JPA2020159971, JPA2023036975 issued to Ushio Inc., TOWA PHARMACEUTICAL CO., LTD. Koji Nakayama has patent #EPA3951366, USA2022/0178848, CNA113614518, INA202117044615 pending to Ushio Inc., TOWA PHARMACEUTICAL CO., LTD. Aya Ikarashi (Ota) has patent #JPA2020159971, JPA2023036975 issued to Ushio Inc., TOWA PHARMACEUTICAL CO., LTD. Aya Ota has patent #EPA3951366, USA2022/0178848, CNA113614518, INA202117044615 pending to Ushio Inc., TOWA PHARMACEUTICAL CO., LTD. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgements

The authors thank Professor Emeritus Masahiro Kawasaki at Kyoto University, Japan, and Professor Emeritus Yukihiro Ozaki at Kwansei Gakuin University, Japan, for their helpful advice on the application of NIR spectroscopy for pharmaceuticals. This research was supported by Japan Agency for Medical Research and Development (AMED) under Grant Number JP23mk0101202.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpba.2024.116372.

References

[1] M. Jamrógiewicz, Application of the near-infrared spectroscopy in the pharmaceutical technology, J. Pharm. Biomed. Anal. 66 (2012) 1–10.
[2] M. Boiret, F. Chauchard, Use of near-infrared spectroscopy and multipoint measurements for quality control of pharmaceutical drug products, Anal. Bioanal. Chem. 409 (2017) 683–691.
[3] K. Järvinen, W. Hoehe, M. Järvinen, S. Poutiainen, M. Juuti, S. Borchert, In-line monitoring of the drug content of powder mixtures and tablets by near-infrared spectroscopy during the continuous direct compression tableting process, Eur. J. Pharm. Sci. 48 (2013) 680–688.
[4] J.G. Rosas, P. Brush, B. Thompson, C. Miller, P. Overton, N. Tugby, D. Stoliarskaia, S. Hurley, M. Ramasamy, S.L. Conway, Implementation of a fully integrated CM direct compression and coating process at a commercial pharmaceutical facility – Part 2: PAT and RTD results for normal operational conditions batches, Int. J. Pharm. 636 (2023) 122814.
[5] Y.M. Colón, J. Vargas, E. Sánchez, G. Navarro, R.J. Romañach, Assessment of robustness for a near-infrared concentration model for real-time release testing in a continuous manufacturing process, J. Pharm. Innov. 12 (2017) 14–25.
[6] E. Peeters, A.F. Tavares da Silva, M. Toiviainen, J. Van Renterghem, J. Vercruysse, M. Juuti, J.A. Lopes, T. De Beer, C. Vervaet, J.P. Remon, Assessment and prediction of tablet properties using transmission and backscattering Raman spectroscopy and transmission NIR spectroscopy, Asian J. Pharm. Sci. 11 (2016) 547–558.
[7] D. Brouckaert, F. Vandenbroucke, F. Chauchard, M. Dollinger, Y. Roggo, L. Pellegatti, M. Krumme, Towards real-time release of pharmaceutical tablets: 100% in-line control via near-infrared spatially resolved spectroscopy and 3D microwave resonance technology, J. Pharm. Biomed. Anal. 209 (2022) 114491.
[8] T. Nishii, K. Matsuzaki, S. Morita, Real-time determination and visualization of two independent quantities during a manufacturing process of pharmaceutical tablets by near-infrared hyperspectral imaging combined with multivariate analysis, Int. J. Pharm. 590 (2020) 119871.
[9] J. Gottfries, H. Depui, M. Fransson, M. Jongeneelen, M. Josefson, F.W. Langkilde, D.T. Witte, Vibrational spectrometry for the assessment of active substance in metoprolol tablets: a comparison between transmission and diffuse reflectance near-infrared spectrometry, J. Pharm. Biomed. Anal. 14 (1996) 1495–1503.
[10] S.S. Thosar, R.A. Forbess, N.K. Ebube, Y. Chen, R.L. Rubinovitz, M.S. Kemper, G. E. Reier, T.A. Wheatley, A.J. Shukla, A comparison of reflectance and transmittance near-infrared spectroscopic techniques in determining drug content in intact tablets, Pharm. Dev. Technol. 6 (2001) 19–29.
[11] P.F. Chavez, P.Y. Sacré, C. De Bleye, L. Netchacovitch, J. Mantanus, H. Motte, M. Schubert, P. Hubert, E. Ziemons, Active content determination of pharmaceutical tablets using near infrared spectroscopy as Process Analytical Technology tool, Talanta 144 (2015) 1352–1359.
[12] H. Kawagoe, H. Sera, J. Sahara, S. Akai, K. Watanabe, K. Shinoyama, T. Nagashima, T. Yokoyama, A. Ikarashi, G. Yamada, Near-infrared spectroscopy of low-transmittance samples by a high-power time-stretch spectrometer using an arrayed waveguide grating (AWG), Sci. Rep. 13 (2023) 17261.
[13] K. Goda, B. Jalali, Dispersive Fourier transformation for fast continuous single-shot measurements, Nat. Photonics 7 (2013) 102–112.
[14] T. Godin, L. Sader, A.K. Kashi, P.H. Hanzard, A. Hideur, D.J. Moss, R. Morandotti, G. Genty, J.M. Dudley, A. Pasquazi, M. Kues, B. Wetzel, Recent advances on time-stretch dispersive Fourier transform and its applications, Adv. Phys. X 7 (2022) 2067487.
[15] D. Sasakura, K. Nakayama, T. Sakamoto, T. Chikuma, Strategic development of a multivariate calibration model for the uniformity testing of tablets by transmission NIR analysis, Pharmazie 70 (2015) 289–295.
[16] J. Smetisko, S. Miljanic, Dissolution assessment of allopurinol immediate release tablets bynear infrared spectroscopy, J. Pharm. Biomed. Anal. 145 (2017) 322–330.
[17] H.R.H. Ali, H.G.M. Edwards, I.J. Scowen, Noninvasive in situ identification and band assignments of some pharmaceutical excipients inside USP vials with FT-near-infrared spectroscopy, Spectrochim. Acta A 72 (2009) 890–896.
[18] D. Ishikawa, T. Genkawa, K. Murayama, M. Komiyama, Y. Ozaki, Feasibility study of diffuse reflectance and transmittance near infrared spectroscopy for rapid analysis of ascorbic acid concentration in bilayer tablets using a high-speed polychromator-type spectrometer, J. Infrared Spectrosc. 22 (2014) 189–197.
[19] A. Sánchez-Paternina, A.D. Román-Ospino, M. Martínez, J. Mercado, C. Alonso, R. J. Romañach, Near infrared spectroscopic transmittance measurements for pharmaceutical powder mixtures, J. Pharm. Biomed. Anal. 123 (2016) 120–127.
[20] H. Bjørsvik, H. Martens, Data analysis: Calibration of NIR instruments by PLS regression, in: D.A. Burns, E.W. Ciurczak (Eds.), Handbook of Near-Infrared Analysis, 3rd Edition, Taylor & Francis Group, Boca Raton, 2008, pp. 189–207.
[21] Y. Ge, C.L.S. Morgan, S. Grunwald, D.J. Brown, D.V. Sarkhot, Comparison of soil reflectance spectra and calibration models obtained using multiple spectrometers, Geoderma 161 (2011) 202–211.
[22] L. Alvarenga, D. Ferreira, D. Altekruse, J.C. Menezes, D. Lochmann, Tablet identification using near-infrared spectroscopy (NIRS) for pharmaceutical quality control, J. Pharm. Biomed. Anal. 48 (2008) 62–69.
[23] N.W. Broad, R.D. Jee, A.C. Moffat, M.R. Smith, Application of transmission near-infrared spectroscopy to uniformity of content testing of intact steroid tablets, Analyst 126 (2001) 2207–2211.