

UV reflectance imaging-based component mapping of spironolactone tablets using a UV-sensitive camera compared with NIR and Raman chemical imaging

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ABSTRACT

UV reflectance imaging-based machine vision can provide a fast alternative to established spectroscopic imaging methods for mapping the surface distribution of tablet components. In this study, the applicability of this approach was assessed by comparison with reference techniques using visually white model tablets containing spironolactone as a low-dose active pharmaceutical ingredient (2 w/w%), together with microcrystalline cellulose and lactose monohydrate as the main excipients. Five tablet batches containing different spironolactone particle size fractions were prepared. Selected samples representing the smallest, intermediate, and largest API particle size fractions were analyzed by UV reflectance imaging, NIR chemical imaging, and Raman chemical imaging for direct method comparison. UV reflectance imaging provided sufficient grayscale contrast to distinguish spironolactone, lactose monohydrate, and microcrystalline cellulose on the tablet surface, and the resulting maps showed qualitative agreement with the NIR and Raman distributions. In addition, UV-based full-surface component maps were successfully obtained for all five particle size fractions. UV reflectance imaging required only a single short exposure for full-surface acquisition, whereas NIR and especially Raman mapping required substantially longer measurement times. These findings indicate the potential of UV reflectance imaging-based mapping as a rapid screening approach, yielding surface-distribution patterns that show reasonable agreement with established reference imaging techniques.

1. Introduction

Vibrational spectroscopic chemical imaging is an essential analytical technique in the pharmaceutical industry, used to characterize materials and pharmaceutical dosage forms (Bunaciu et al., 2020; Gowen et al., 2008; Ewing and Kazarian, 2018; Smith et al., 2015). Raman and near-infrared (NIR) chemical imaging are the most widely applied methods, with the choice depending on the chemical composition of the formulation, the available analysis time, and the spatial resolution required to obtain the necessary information (Šašić Slobodan and Ozaki, 2010;

Clark and Šašić, 2006). Both Raman and NIR chemical images can provide a broad range of surface information from solid dosage forms, such as tablets (Carruthers et al., 2021; An and Analysis, 2007; Carruthers et al., 2022; Galata et al., 2023). Using Raman chemical imaging, several critical quality attributes of tablets can be determined, including active pharmaceutical ingredient (API) content, component particle size distribution, and homogeneity (Gordon and McGoverin, 2011; Szabó-Szócs et al., 2025).

Although Raman spectroscopy provides high-resolution chemical images with detailed information on domain morphology, it requires

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long data acquisition times. In contrast, NIR imaging allows much faster measurements, offering a lower-resolution yet rapid means of characterizing the spatial distribution of components within tablets (Galata et al., 2023). According to the study of Carruthers et al., even with advanced fast Raman techniques, measuring a $3000 \times 3000 \mu\text{m}$ area typically requires a few hours when using a 0.1 s acquisition time and a $10 \mu\text{m}$ step size. The same region can be analyzed by NIR chemical mapping in a few minutes with a $25 \mu\text{m}$ step size and a 0.05-second acquisition time. Laser direct infrared (LDIR) imaging is a newer mid-infrared chemical imaging technique that uses a tunable quantum cascade laser and automated scanning optics to acquire spectrally resolved images at high speed. Using LDIR, the spectral data needed to construct a chemical map of the same area can be collected in a few seconds with a $10 \mu\text{m}$ step size (Carruthers et al., 2022; Ficzer et al., 2025).

In chemical mapping experiments (Ewing and Kazarian, 2018; Smith et al., 2015), spectral information is typically collected at multiple spatial points by acquiring a full spectrum at each location. To reduce data acquisition time, research has focused on methods that probe specific vibrational transitions to generate distribution maps of individual components, provided that each component possesses unique spectral bands. These approaches, however, require prior knowledge of all components present in the tablet (Galata et al., 2023). To extract the desired information from chemical images, the collected hyperspectral data cubes must first be transformed into concentration maps for easier interpretation, which can be a challenging process (Su et al., 2022). These maps can then be further analyzed using traditional image analysis methods or, with recent advances, convolutional neural networks (Cheng et al., 2025).

In this field of pharmaceutical research, another applicable technique for examining tablet surfaces is scanning electron microscopy combined with energy-dispersive X-ray spectroscopy (SEM-EDX). When the sample surface is irradiated with a focused electron beam, the atoms in the material emit X-rays with element-specific energies, allowing the elemental composition to be determined from the detected radiation. SEM-EDX has been widely used to visualize the surface topography of pharmaceutical tablets and to generate elemental distribution maps that assist in understanding the spatial arrangement of drug and excipient particles (Scoutaris et al., 2014; Gupta et al., 2022).

While Raman, NIR, LDIR, and SEM-EDX imaging can provide chemically or elementally specific information, these methods generally require spatially resolved spectroscopic or elemental measurements, specialized instrumentation, and subsequent data processing. Consequently, there remains a need for simpler and faster imaging approaches that can provide spatially resolved information on tablet surface composition without extensive analysis. In this context, UV-based techniques have emerged as promising tools for the rapid surface characterization of pharmaceutical dosage forms.

Multispectral ultraviolet (UV) imaging has gained increasing attention as a rapid and non-destructive chemical mapping technique for pharmaceutical applications (Al Ktash et al., 2021). Early studies demonstrated that UV imaging can provide both chemical and physical information about solid dosage forms with high spatial resolution and significantly shorter acquisition times compared to conventional vibrational spectroscopic methods. Wu et al. first applied multispectral UV imaging for surface characterization of compacted pharmaceutical solids, showing that the technique could distinguish between crystalline and amorphous domains of the active ingredient and visualize the distribution of excipients (Wu et al., 2014). Klukkert et al. further expanded the applicability of this method by demonstrating its potential for quantitative assessment of tablet properties, such as API content, density near the surface, and mechanical strength, through multivariate analysis of UV images (Klukkert et al., 2016). These studies collectively established multispectral UV imaging as a promising analytical approach for rapid, surface-sensitive characterization of pharmaceutical tablets.

UV imaging using narrow-band light-emitting diode (LED)

illumination represents a powerful approach for the rapid characterization of pharmaceutical tablets (Péterfi et al., 2024; Ficzer et al., 2024; Mészáros et al., 2020; Péterfi et al., 2026). When tablets are illuminated with UV light centered at a specific wavelength, the components can exhibit distinct optical responses due to differences in fluorescence and absorption. This inherent optical contrast enables effective differentiation between components, allowing visualization of the spatial distribution of APIs and excipients on the tablet surface. By capturing images of the illuminated surface using an RGB camera, several critical quality attributes can be evaluated within a few milliseconds. Mészáros et al. (2024) demonstrated that UV/VIS imaging can be effectively applied to tablets containing a white API, caffeine, enabling the prediction of API content, crushing strength, friability, disintegration time, and dissolution profile from the acquired images (Mészáros et al., 2024). In the study by Ficzer et al., UV imaging-based mapping method was introduced as a novel approach for the analysis of pharmaceutical tablets, and its results were directly compared with Raman chemical maps to assess spatial correspondence and the component distribution (Ficzer et al., 2025).

More recently, not only camera platforms but also sensor technologies have advanced substantially, and UV-sensitive sensors are now available that enable UV reflectance imaging with improved sensitivity and image quality. In our previous study by Ficzer et al., the analytical contrast was obtained using a camera equipped with a sensor operating in the visible range, and component discrimination was based on the visible fluorescence response of the tablet components under UV excitation (Ficzer et al., 2025). In contrast, the measurement principle differs in the present work, which uses direct UV reflectance imaging with a UV-sensitive camera. Here, the recorded grayscale intensity is primarily determined by the amount of incident UV radiation reflected from the tablet surface, thus reflecting differences in absorption and scattering at the selected wavelength rather than fluorescence emission. Thus, while the earlier approach relied on fluorescence-based contrast detected in the visible range, the current method is based on direct UV reflectance contrast, yielding grayscale intensity patterns and extending the concept toward a purely UV-based surface mapping strategy.

The aim of this study was to evaluate the applicability of UV reflectance imaging, based on direct UV imaging with narrow-band UV illumination, as a rapid and surface-sensitive mapping method for visually white pharmaceutical tablets containing a low-dose API and multiple commonly used excipients. The motivation for this work was to determine whether a single UV reflectance image can provide sufficiently informative maps of surface component distribution to reveal the key spatial distribution patterns obtained by established Raman and NIR chemical imaging techniques. Such information is relevant because the spatial arrangement of API and excipient domains reflects formulation structure and may reveal differences associated with component segregation and particle size-dependent distribution patterns.

The method was evaluated using five tablet batches containing spironolactone as a low-dose API (2 w/w%) with different particle size fractions. Selected tablets representing the smallest, intermediate, and largest API particle size fractions were investigated. UV reflectance imaging was subsequently extended to all particle size fractions to assess whether the observed trends remained detectable across the full range of API particle sizes.

The statistical comparison was intended to assess whether direct UV reflectance imaging can provide surface-distribution information broadly consistent with that obtained by established Raman and NIR chemical imaging techniques, while substantially reducing measurement time and enabling full-surface evaluation.

The model composition was intentionally designed to represent a typical formulation environment in which component distribution is challenging to resolve. To position the UV reflectance imaging approach within the existing analytical toolbox, its performance was also compared with Raman and NIR chemical mapping in terms of component distribution, spatial representation, and the time required for

Table 1

Spironolactone particle size fractions obtained after sieving.

Particle size fraction [μm]
<50
50–100
100–150
150–200
200–300

Table 2

Composition of the spironolactone-containing tablet formulation.

Components	Concentration [w/w%]
Spironolactone	2
MCC	62
LAC	35
Aerosil	0.5
MgSt	0.5

image acquisition and data processing. The objective of the comparison was not to identify a universally best technique, but to determine whether UV reflectance imaging can provide sufficiently informative surface maps as a rapid screening tool for this formulation type.

2. Materials and methods

2.1. Materials

The model tablet composition was designed to represent a commercially available pharmaceutical formulation with a low concentration of the API and multiple commonly used excipients, allowing the benchmarking of each spectroscopic imaging technique in resolving the spatial distribution of components. The investigated tablets contained spironolactone, supplied by Gedeon Richter Plc. (Budapest, Hungary), as a model API. Microcrystalline cellulose (MCC, Vivapur® 200) by JRS Pharma (Rosenberg, Germany) was used as the binder. Lactose monohydrate (LAC, Flowlac® 100), a spray-dried lactose grade produced by MEGGLE Pharma (Wasserburg, Germany), served as the filler. Colloidal silicon dioxide (Aerosil® 200, Evonik Industries AG, Essen, Germany) was incorporated as a glidant, while magnesium stearate (MgSt), obtained from Hungaropharma Ltd. (Budapest, Hungary), was used as the lubricant.

2.2. Methods

2.2.1. Crystallization of spironolactone

The initial spironolactone was a micronized anhydrous crystalline material. To enable evaluation of the method across multiple API particle size fractions, the API was recrystallized and subsequently separated into different size fractions. This step was used to reproducibly generate larger particle size fractions under controlled laboratory conditions while maintaining the same anhydrous crystalline form of spironolactone.

To reproduce the anhydrous form with different particle sizes under laboratory conditions, a slow, water-free crystallization method was applied. In this procedure, 60 mL of n-butanol was heated to 75 °C under continuous stirring at 200 rpm, and 12.9 g of spironolactone was dissolved to obtain a clear solution. The solution was then cooled to 5 °C with 0.1 °C/min linear cooling rate. At 68 °C, 60 mg of micronized spironolactone, corresponding to 0.5% of the dissolved material, was added as seed crystals to promote slow nucleation and uniform crystal growth.

Following crystallization, the product was separated by filtration (G2 glass filter) and dried in air at ambient temperature. The crystalline form of the prepared samples was confirmed by Raman spectroscopy, which

verified that the anhydrous form of spironolactone had been successfully produced. The dried material was subsequently sieved to obtain fractions based on sieve mesh size ranges, which are shown in Table 1.

2.2.2. Preparation of tablets

For each API particle size fraction, a separate batch of powder blend was prepared with an identical qualitative composition. Approximately 5 g of powder was obtained by manually pre-mixing all components except MgSt for 5 min, in an amount sufficient to produce multiple tablets. MgSt was then added to the blend, and mixing was continued for an additional 1 min to ensure uniform lubrication. All components in this formulation are white; therefore, the final homogenized powder blend and the resulting tablets exhibited a uniform white appearance. The detailed compositions of the formulations are presented in Table 2.

Tablet compaction was performed using a Styl'One Evo compaction simulator (Medelpharm, France), an instrumented single-punch press designed for precise replication and analysis of industrial tableting conditions. Flat-faced punches were used to produce cylindrical tablets with a diameter of 11.28 mm and a target weight of 300 mg. The compression force was set to 10 kN, applying a V-shaped punch displacement profile with a tableting speed of 25 mm/s.

For each formulation, multiple tablets were manufactured from the corresponding powder blend, and one tablet was randomly selected from each batch for direct UV mapping. To enable comparison between the imaging techniques, tablets representing the smallest (<50 μm), intermediate (100–150 μm), and largest (200–300 μm) API particle size fractions were additionally analyzed by NIR and Raman chemical mapping. Furthermore, a second tablet containing the intermediate fraction was analyzed as a replicate. These fractions were selected to cover the lower, middle, and upper limits of the investigated particle size range. In addition, full-surface UV reflectance mapping was performed for all five API particle size fractions to evaluate the applicability of the UV workflow across the entire particle size range studied.

To identify and visually distinguish the components on the tablet surface and to determine their grayscale intensities, a dedicated reference compact for UV reflectance imaging was produced using the same formulation components. The reference compact was prepared in the same manner as the sample tablets. First, MCC was placed into the die of the tablet press, then spironolactone and LAC were carefully layered on top with a spatula in a predefined order to enhance spatial separation. After positioning the powders in the desired sequence, the material was compressed into a tablet, resulting in a compact with well-separated surface regions representing each component, as illustrated in Fig. 1. This design enabled direct side-by-side comparison of the grayscale responses of the components within the same image and provided a grayscale reference palette. Although a single multi-component reference compact was used in the present study, separate reference compacts prepared from the individual components could also be used, provided that the images are acquired under reproducible imaging conditions. The use of a multi-component reference compact may also be advantageous when material availability is limited or when individual components do not readily form mechanically stable compacts.

For NIR and Raman mapping, separate reference compacts were prepared from the pure components, which were then used to acquire reference spectra for the chemometric models and to aid in the interpretation of the chemical images. To ensure that the same orientation of the sample tablet was compared across all techniques, the investigated tablet was marked on its side before the measurements, and this mark was used to reproduce the same positioning during UV reflectance, NIR and Raman imaging.

2.2.3. UV reflectance imaging: Hardware setup and image acquisition procedure

Under UV reflectance imaging at ~ 270 nm, the recorded grayscale intensity reflects how much of the incident UV radiation is diffusely reflected back to the detector from each surface location. Domains that

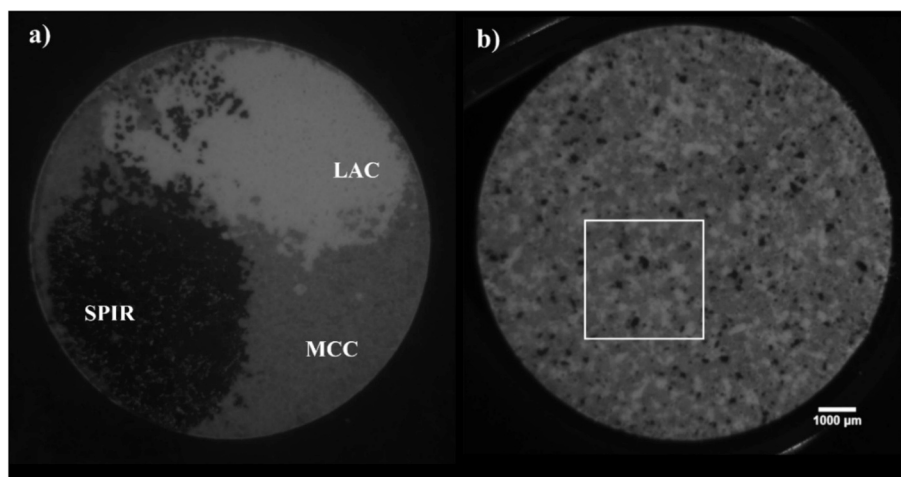


Fig. 1. Reflectance images acquired under UV ~ 270 nm illumination using the UV camera from the reference compact (a) and from the surface of the evaluated sample containing the 100–150 μm API particle size fraction (b), used for comparison of the different mapping methods. The region selected for Raman chemical mapping is indicated by a white rectangle.

absorb more strongly at the illumination wavelength appear darker, while domains with low absorption and strong scattering appear brighter in the grayscale image (Jentoft, 2004).

Reflectance images of the examined tablets were recorded using an Alvium 1800 U-812 monochrome UV camera (Allied Vision, Germany) equipped with an IMX487 sensor (Sony, Japan) (Allied Vision Alvium 1800 U-120m). This sensor is a 2/3-type, 8.13-megapixel industrial CMOS device designed for high-sensitivity direct UV imaging in the 200–400 nm range (Alvium 812 UV camera | Sony IMX487, 2026). It uses a back-illuminated pixel structure together with Pregius S^{TM} global shutter technology, which provides high quantum efficiency in the UV region, enables distortion-free image capture, and supports high-speed operation even in applications requiring precise inspection of fast-moving objects. The optical setup included a 25 mm standard UV fixed-focal-length lens (Edmund Optics, USA), which was attached to the camera via three, 5 mm extension rings. Increasing the distance between the sensor and the lens allowed the system to achieve higher magnification, thereby improving the visibility of fine surface features and enhancing the detail in the recorded UV reflectance images. This configuration ensured stable focusing and allowed the absorption responses of the tablets to be captured with sufficient clarity for further analysis.

Illumination was provided by custom-designed ring lights equipped with ultraviolet LEDs, arranged to deliver uniform lighting over the tablet surface. For visual inspection and assessment of the component appearance, images were acquired under UV ~ 270 nm illumination, using the same geometry and intensity settings for all samples to ensure reproducible imaging conditions.

Under the applied instrumentation, optical configuration, and measurement conditions described above, the UV reflectance images were acquired with a spatial resolution corresponding to a pixel size of 4.1 μm . The acquisition time for a single image was 0.09 s.

2.2.4. UV reflectance imaging-based mapping of component distribution

The image processing workflow aimed to identify and spatially map the major tablet components (the API and the main excipients) based on their distinct optical responses captured with a UV camera under UV ~ 270 nm illumination. Although only a monochromatic intensity map is available in this case, it provides sufficient contrast to support component evaluation. This was accomplished through intensity-based clustering using a predefined reference palette, enabling discrimination of components based on their absorption behavior. To separate the individual constituents in the UV images and generate corresponding UV reflectance-based component maps, the acquired images were processed

using a custom algorithm developed in MATLAB R2023a (MathWorks, Natick, MA, USA).

Gaining preliminary knowledge of the sample and the reference compact was essential to assess the grayscale intensity and visual appearance of the individual components to determine whether these could be differentiated under UV ~ 270 nm illumination. The first step of the analysis involved removing the background to isolate the tablet area. For the reference compact, after locating suitable regions, three 200×200 pixel rectangular areas were manually selected on each image to represent the components included in the formulation. The average grayscale intensity values extracted from these regions were then used to compare the intensity characteristics of the components. Based on these values, a shade order was established from the darkest to the lightest appearance, corresponding to the lowest and highest grayscale intensities, and this served as the foundation for the following mapping procedure.

After gaining preliminary knowledge of the surface appearance of the components, the mapping procedure was executed on the prepared sample set. Automatic segmentation of the components was performed using k-means clustering (k-means clustering in MATLAB), based on the grayscale intensities of the sample and the reference compact. The number of clusters (k) was set equal to the number of known main components in the tablet formulation ($k = 3$). To minimize the risk of convergence to local minima, the algorithm was repeated 100 times and the solution with the lowest total within-cluster variance was retained. The resulting clusters were assigned to the corresponding formulation components by matching their mean grayscale values to those of the shade order obtained from the reference compacts. The outcome of this step was a cluster map representing the spatial distribution of each component.

After clustering-based segmentation, continuous membership maps were generated that describe the degree to which each pixel belongs to each cluster. This approach is particularly important for accurately representing boundary regions. For each cluster, the median intensity and its interquartile range were calculated. Then, for every pixel, the difference between its intensity value and the cluster median was determined and divided by the interquartile range. On these scaled differences, a Gaussian membership function was applied. This yielded a value between 0 and 1 for each pixel, where values close to 1 mean that the pixel is very similar to the cluster center, and values close to 0 mean that it is very different. In this way, “soft” component maps were obtained that keep the fine spatial details but also show how strongly each pixel belongs to a given component.

The UV reflectance imaging-based maps were aligned with the other

Table 3

Summary of data acquisition parameters used for UV reflectance imaging, NIR and Raman chemical imaging experiments.

Parameter	UV reflectance imaging	NIR imaging	Raman imaging
Instrument	Alvium UV camera	Spotlight 400 FT-NIR	LabRAM Raman microscope
Light source	~270 nm UV LED ring	Internal NIR source	785 nm laser
Spectral range	~270 nm	4000–7800 cm ⁻¹	327–1586 cm ⁻¹
Detector / sensor configuration	Sony IMX487 monochrome CMOS sensor, 12.75 mm diagonal (Type 2/3)	Liquid-nitrogen-cooled 16-element linear MCT detector array	Air-cooled Synapse 1024 × 256 OECCD detector (–75 °C)
Step size	4.1 μm (pixel size)	25 μm	25 μm
Acquisition time	0.09 s (per image)	0.05 s (per spectrum)	20 s (per spectrum)
Number of scans	–	2	2
Measured area	Full tablet surface	Full tablet surface	3000 × 3000 μm ²
Total mapping time	~0.1 s	~77 min	~83 h

chemical imaging datasets to allow a meaningful comparison. For the Raman measurements, a predefined 3000 × 3000 μm surface area of the tablet was mapped. The same region was then identified and manually selected on the full-surface UV reflectance images, ensuring that exactly the same tablet area was evaluated by all three techniques.

2.2.5. Applied setup for NIR mapping

For NIR mapping, reference spectra of the three main components were recorded using a PerkinElmer Spectrum 400 FT-IR/FT-NIR spectrometer equipped with a NIRA reflectance accessory and an InGaAs detector. Spectra were acquired in the 10,000–4000 cm⁻¹ wavenumber range with a spectral resolution of 2 cm⁻¹. 32 scans were accumulated to achieve an appropriate signal-to-noise ratio.

Full-surface NIR imaging of the tablets was performed using a Spotlight 400 FT-IR/FT-NIR Imaging System (PerkinElmer, Inc., Waltham, MA, USA), equipped with a liquid-nitrogen-cooled 16-element linear mercury cadmium telluride (MCT) detector (PerkinElmer, 2026). A 12 × 12 mm² area was defined so that the entire tablet fitted into the field of view, and this region was scanned in diffuse reflectance mode with a spatial resolution of 25 μm, yielding 230,400 spectra. For each pixel, a NIR spectrum was recorded in the 7800–4000 cm⁻¹ range with a spectral resolution of 8 cm⁻¹, using 2 scans per spectrum. The total acquisition time for the NIR map was approximately 1.3 h.

Since the spectral range and resolution of the reference and mapping spectra differed, the reference spectra were resampled using SpectrumIMAGE R 1.6.5 software. The reference spectra were interpolated to match the resolution of the imaging data, and a reduced spectral window between 6000 and 4000 cm⁻¹ was then selected, retaining 251

variables for subsequent analysis.

2.2.6. Applied setup for Raman mapping

Raman measurements were first performed on the pure components to obtain reference spectra for the subsequent chemical mapping. Hyperspectral surface images were then recorded using a Horiba Jobin–Yvon LabRAM system (Longjumeau, France) (LabRAM confocal Raman microscope) equipped with an 80 mW, 785 nm laser, focused onto the sample through an Olympus BX-40 optical microscope (Shinjuku, Tokyo, Japan) using a 20 × objective. Chemical imaging was performed by moving the sample using an automated, preprogrammed stage prior to each spectral acquisition. A 3000 × 3000 μm² surface area was mapped with a step size of 25 μm, resulting in a 121 × 121 grid of spectra. At each point, spectra were acquired using 2 accumulations of 10 s (20 s total), and the accumulated spectra were averaged, giving a total mapping time of approximately 83 h. The spectral range of 327–1586 cm⁻¹ was evaluated.

2.2.7. Generation of Raman and NIR chemical images

The acquired hyperspectral datasets were converted into concentration maps using the classical least squares (CLS) method in PLS Toolbox 9.2 (Eigenvector, Manson, WA, USA). For this purpose, reference spectra of the pure tablet components were collected in advance for both Raman and NIR measurements, serving as input for the CLS models. The non-negative CLS algorithm (Bro, 1997) estimates the relative contribution of each component in each recorded spectrum, yielding mass fraction values scaled to 0–1, thereby visualizing the spatial distribution of components on the tablet surface.

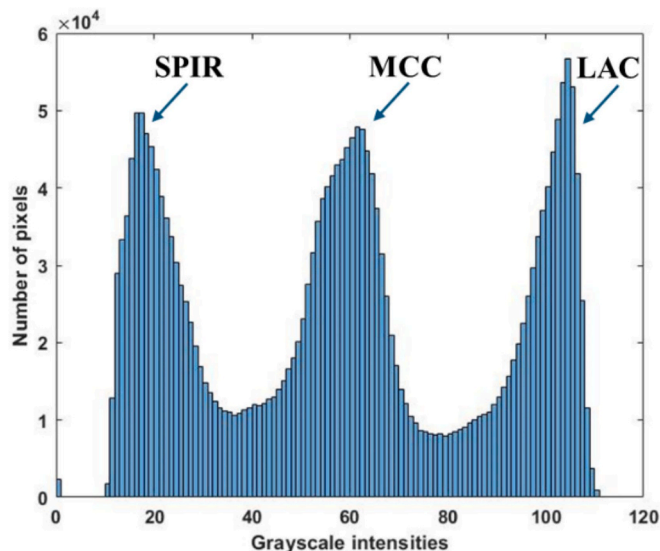


Fig. 3. Grayscale intensity histogram of the tablet components in the reference compact under UV ~270 nm illumination.

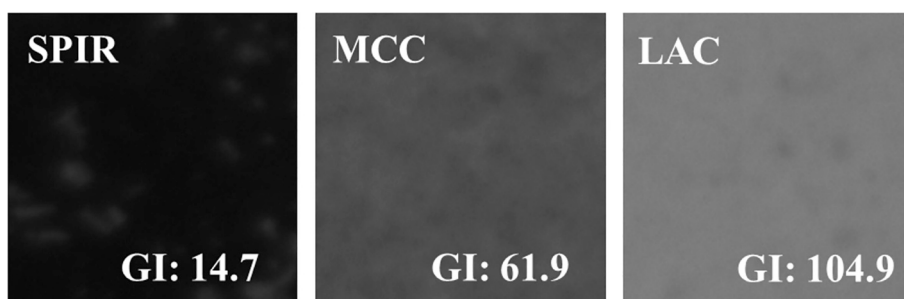


Fig. 2. Shade series from the reference compact under UV ~270 nm illumination with mean grayscale intensity values (GI) for each component.

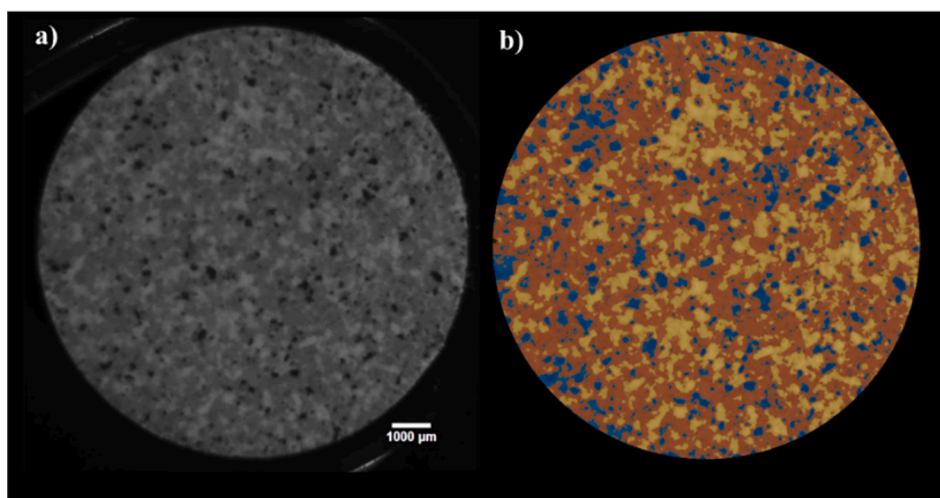


Fig. 4. The original image (a) and the cluster map (b) of the evaluated tablet containing spironolactone in the 100–150 µm particle size fraction, obtained from direct UV imaging (blue: SPIR, orange: MCC, yellow: LAC).

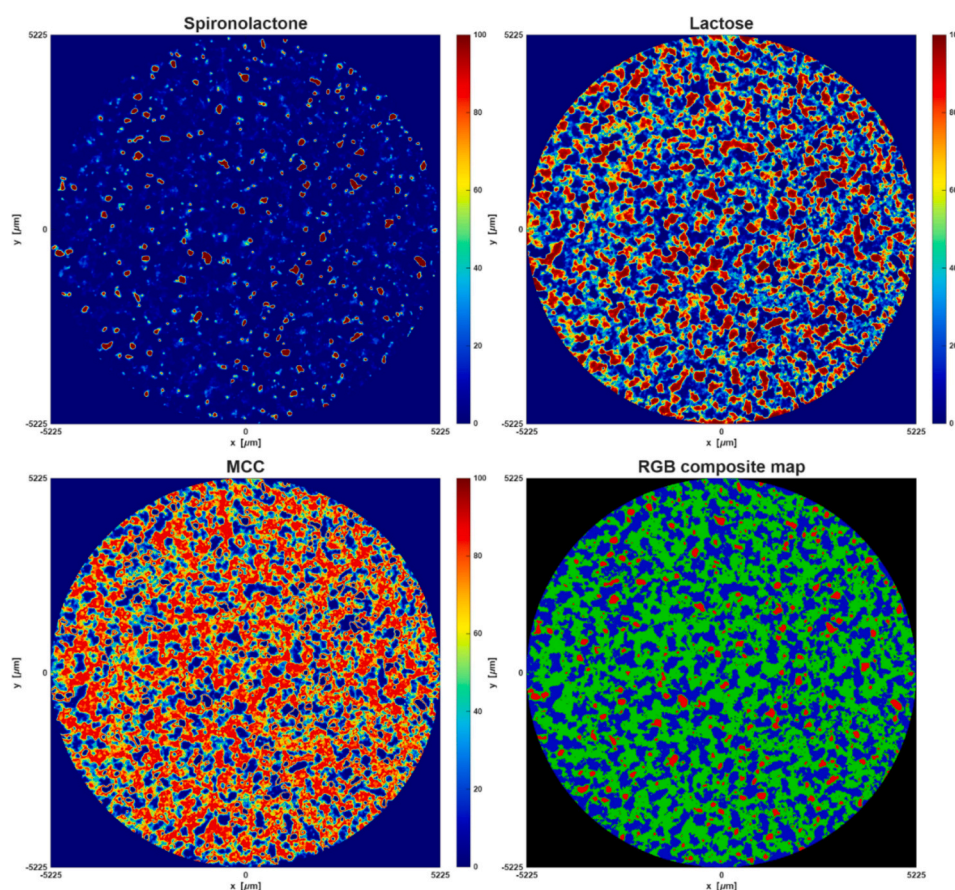


Fig. 5. Full-surface UV reflectance-based component maps and the corresponding RGB composite map of the tablet containing 100–150 µm spironolactone particles. In the composite map, red areas represent spironolactone, blue areas represent lactose, and green areas represent MCC.

Prior to CLS evaluation, spectral preprocessing was performed to improve signal quality and to compensate for baseline distortion and scattering effects. Raman spectra were preprocessed using baseline correction with an automatic Whittaker filter ($\lambda = 10,000$; $p = 0.005$), followed by area-based normalization (1-norm). The same preprocessing was applied to the Raman reference spectra shown in Fig. 8; therefore, the figure presents preprocessed spectra rather than raw Raman spectra. For the NIR spectra, the previously selected absorption spectral

region underwent Whittaker filter correction ($\lambda = 10,000$; $p = 0.001$) and area-based normalization.

2.2.8. Statistical comparison of the distribution maps obtained by the different methods

To quantitatively compare the distribution maps obtained by UV reflectance imaging, NIR chemical imaging, and Raman mapping, the generated component maps were first spatially aligned and rescaled to

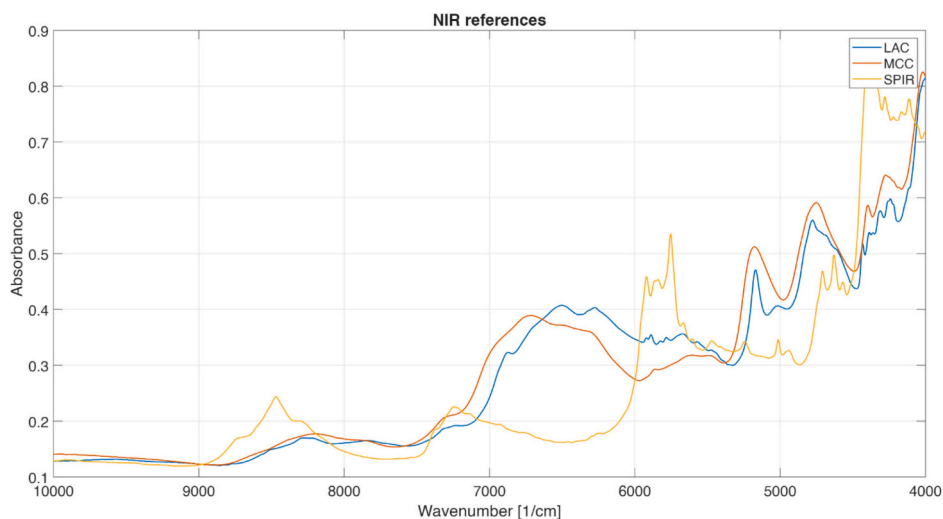


Fig. 6. NIR reference spectra of spironolactone (yellow), lactose monohydrate (blue) and microcrystalline cellulose (green).

the size of the NIR-based maps. Prior to evaluation, all maps were normalized to the range of 0–1.

Similarity between the aligned maps was evaluated using threshold-independent statistical metrics that directly compare the continuous spatial intensity distributions of the component maps.

For overall method comparison, global similarity metrics were calculated by concatenating the normalized pixel intensities from the spironolactone, lactose monohydrate, and microcrystalline cellulose maps obtained with each imaging method. Consequently, the reported values describe the overall agreement between imaging methods across the complete set of investigated component distributions rather than individual component maps.

Pearson correlation coefficients were calculated to assess linear spatial correspondence between the compared datasets, whereas Spearman rank correlation coefficients were used to evaluate monotonic relationships and the preservation of relative intensity rankings. Higher correlation values indicate stronger agreement between the spatial distributions obtained using the different imaging methods ([Linear or rank correlation - MATLAB, 2026](#)).

To compare the overall intensity distributions independently of spatial location, Jensen–Shannon divergence and the first-order Wasserstein distance were calculated from normalized intensity histograms. Jensen–Shannon divergence quantifies the similarity between intensity distributions, with lower values indicating greater similarity ([Lin, 1991](#)). The Wasserstein distance measures the average amount of intensity redistribution required to transform one distribution into another; the smaller the value, the greater the similarity between distributions ([Rubner et al., 2000](#)).

Differences in intensity concentration patterns were assessed using the Gini coefficient, which quantifies the degree of inequality in the distribution of normalized pixel intensities ([Ceriani and Verme, 1912](#)). The absolute difference between the Gini coefficients of the compared datasets was calculated, with smaller values indicating greater similarity in the degree of intensity concentration and spatial heterogeneity.

Continuous coverage was defined as the mean normalized pixel intensity of the compared component maps. For global comparison, continuous coverage values were calculated from the concatenated spironolactone, lactose monohydrate, and microcrystalline cellulose maps obtained with each imaging method. The absolute difference between the resulting continuous coverage values was used as an additional descriptor of overall agreement, with smaller values indicating greater similarity.

All calculations were performed using custom scripts developed in MATLAB R2023a (MathWorks, Natick, MA, USA).

3. Results and discussion

Tablets containing spironolactone as a model API were investigated in this study. In addition to the API, the two main excipients in the formulations were lactose monohydrate (LAC) and microcrystalline cellulose (MCC). Aerosil and magnesium stearate were present as minor components, but only spironolactone, lactose monohydrate, and MCC were included as mapped components in the present workflow, as discussed below.

Five different tablet batches were examined using UV reflectance imaging, each containing spironolactone with a different particle size fraction. From these, the small (<50 µm), intermediate (100–150 µm), and large (200–300 µm) particle size fractions were selected for further analysis and were subsequently measured using NIR and Raman chemical mapping as well. In addition, a replicate measurement was performed on a second sample containing the intermediate particle size fraction (100–150 µm). A summary of acquisition parameters for UV reflectance, NIR, and Raman imaging is given in [Table 3](#).

3.1. UV reflectance imaging-based mapping

3.1.1. Gaining preliminary knowledge of the components for direct UV imaging-based mapping

The UV reflectance images of the reference compact and the evaluated sample surface containing the 100–150 µm API fraction, which were used to compare the direct UV imaging-based approach with NIR and Raman chemical mapping, are summarized in [Fig. 1](#).

The components appeared with clearly different intensities on the surface of the reference compact ([Fig. 1a](#)). Consequently, discrete regions corresponding to each component can also be observed on the sample surface in [Fig. 1b](#), showing the same intensity differences. This behavior can be attributed to the similar particle size of the components, which promotes the formation of well-separated surface domains.

The minor components, Aerosil and magnesium stearate, were not reliably resolved as separate phases under the applied imaging conditions. In addition to their low concentration (0.5 w/w% each), both materials are typically present as very fine particles that are relatively uniformly distributed throughout the formulation rather than forming larger, spatially distinct surface domains. Consequently, they were less likely to generate identifiable contrast features under the applied UV reflectance imaging conditions. This observation should not be interpreted as a strict particle size limitation of the method, since smaller particles may also be detectable when sufficient UV contrast and surface representation are present. Rather, the limited detectability of Aerosil

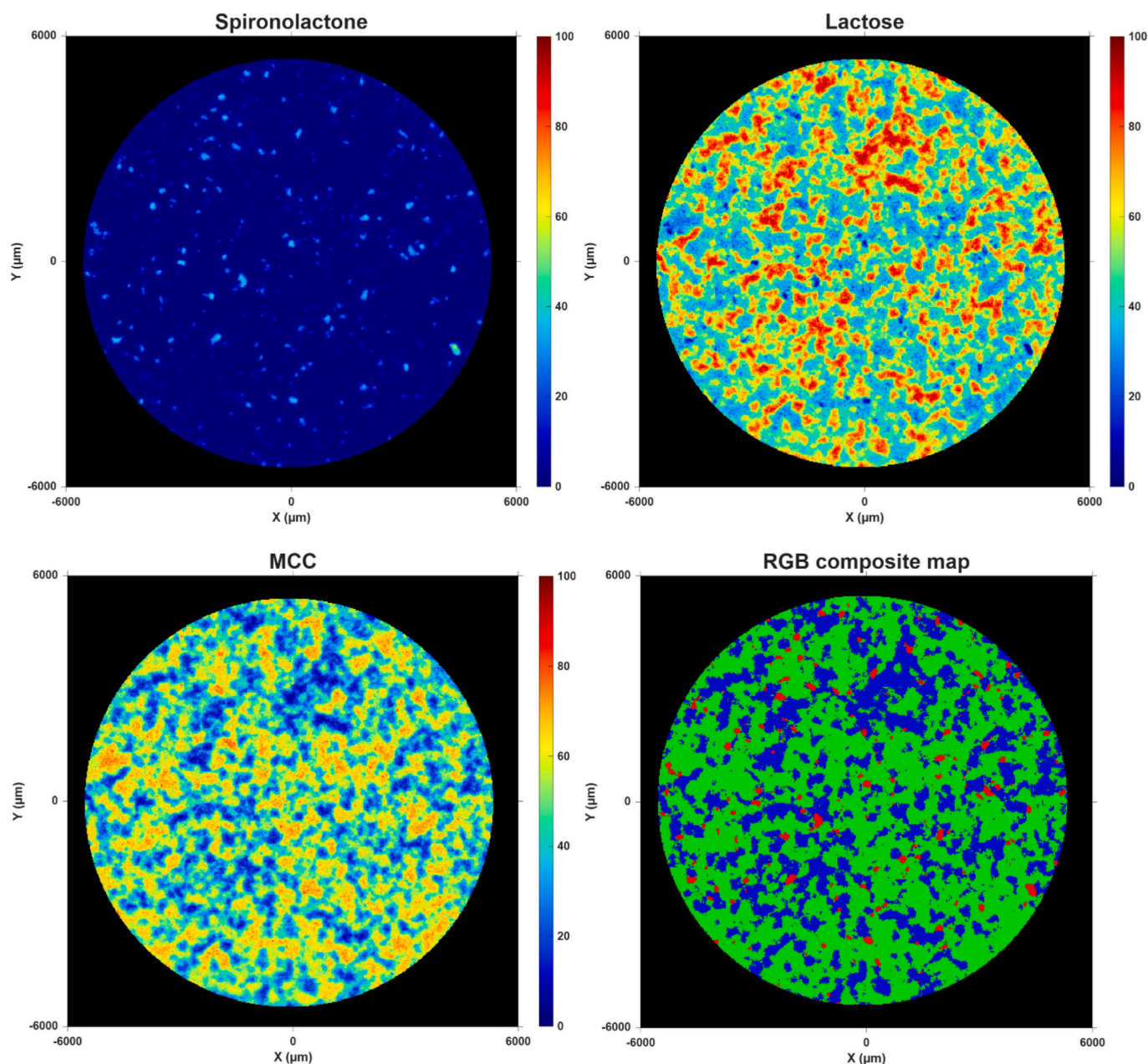


Fig. 7. NIR-based full-surface component maps and RGB composite map of the tablet containing 100–150 μm spironolactone particles. In the composite map, red areas represent spironolactone, blue areas represent lactose, and green areas represent MCC.

and magnesium stearate in the present formulation is attributed to the combined effects of their low concentration, fine particle size, and relatively uniform surface distribution.

A shade series was generated from the reflectance image of the reference compact shown in Fig. 1a by cropping 200×200 pixel rectangular regions corresponding to each component. The average grayscale intensity was then calculated for each material from these regions. The resulting shade series is presented in Fig. 2.

Based on the shade series obtained from the UV reflectance images, the individual components could be clearly distinguished from one another. Under UV reflectance imaging at ~ 270 nm, the recorded grayscale intensity reflects the amount of incident UV radiation returned from the surface, which is governed by the balance between absorption and scattering. Lactose monohydrate is expected to exhibit only weak absorption at ~ 270 nm; therefore, under illumination at this wavelength, it returns a high reflectance signal and appears bright in the UV

reflectance images (Janssen et al., 2022; Vlčková et al., 2023). Microcrystalline cellulose showed comparatively higher effective attenuation in this region than lactose. Although its strongest intrinsic absorption is typically observed at shorter UV wavelengths, MCC exhibited an intermediate grayscale intensity under the applied imaging conditions (Yong et al., 2024; Peng and The, 2021). Spironolactone, in contrast, is a UV-active compound with pronounced absorption in the near-UV region, commonly quantified by UV absorbance around ~ 238 nm; consequently, it attenuates the returned ~ 270 nm signal more strongly than the carbohydrate excipients and appears as the darkest phase in the UV reflectance images (Salama et al., 2019; Lotfy et al., 2022). This visual impression was consistent with the calculated grayscale intensity values for the three components, which were then used in the subsequent mapping procedure.

From the image of the reference compact, a histogram was constructed to display the components as a function of their grayscale

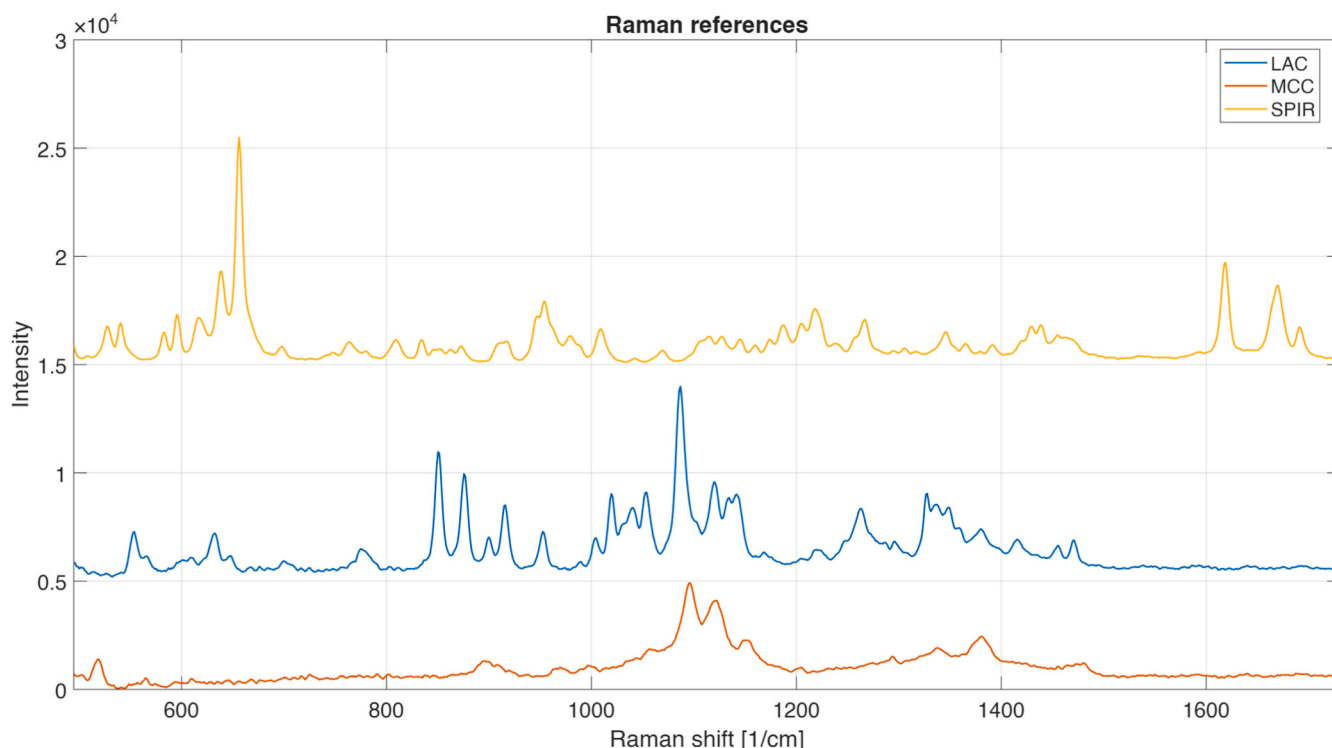


Fig. 8. Preprocessed Raman reference spectra of spironolactone (yellow), lactose monohydrate (blue) and microcrystalline cellulose (orange).

intensities, as shown in Fig. 3. The results indicate that the three examined components form three distinct intensity clusters with adequate separation. Although some overlap is present at the edges of the peaks, this does not hinder the differentiation of the components or their mapping in the following steps.

These differences and results indicate that direct UV imaging-based mapping can be successfully carried out using the UV camera. In this setup, the spatial resolution was 4.1 μm , and an exposure time of 0.09 s was used for image acquisition. The grayscale intensity obtained by UV reflectance imaging may be influenced by physical properties of the compact, such as density, porosity, surface roughness, and scattering behavior. Although identical compaction conditions help reduce experimental variability, they cannot completely eliminate formulation-dependent differences in these properties.

In the present study, the reference grayscale values were determined from representative 200×200 pixel regions of interest rather than individual pixels. This approach reduces the influence of local surface irregularities and minor physical variations on the reference grayscale values. Furthermore, the reference compact exhibited distinguishable grayscale intensities for the major components, indicating that, under the applied experimental conditions, the contrast between the major components was sufficient to enable the mapping procedure. It is important to note that reproducible imaging conditions remain essential for reliable measurements. Future studies should further investigate the influence of formulation-dependent physical properties and develop image-processing and correction procedures where required.

3.1.2. Generation of the UV reflectance imaging-based maps

The generation of the UV reflectance imaging-based maps is demonstrated using the sample containing the 100–150 μm spironolactone particle size fraction. The same procedure was subsequently applied to all investigated samples. In this phase, k-means clustering was applied to identify the dominant intensity-based regions in the images. The number of clusters was set to three, corresponding to the known number of main formulation components, and the same clustering strategy was used for all five samples.

The result of the clustering step in the UV reflectance-based machine vision mapping for the selected region is shown in Fig. 4. Intensity-based clustering allowed three main domains to be distinguished, corresponding to spironolactone, LAC and MCC. The segmentation is in good agreement with the visual appearance of the components on the direct UV images.

For better comparability with the full-surface NIR maps, a thin outer band at the tablet edge was excluded from the direct UV maps. This peripheral region contained increased noise and surface irregularities, which made alignment with the NIR images less reliable and would have reduced the clarity of the comparison.

Full-surface UV reflectance-based maps were then generated for each of the three components. In terms of grayscale intensity, spironolactone showed the strongest contrast relative to the excipients, which enabled clear separation from the remaining components. These maps are shown in Fig. 5.

These maps showed that LAC and MCC dominate the tablet surface, while spironolactone appears in discrete, well-localized regions with much lower frequency. This is consistent with the formulation, where the API is present at low concentration. A key advantage of the UV reflectance-based approach is the very short image acquisition time, since the entire surface can be mapped from a single exposure in less than a second. To aid interpretation, RGB composite maps were also created, in which each pixel was assigned to the component that showed the highest relative intensity at that position.

3.2. NIR chemical mapping

NIR chemical mapping was carried out on tablets containing spironolactone in the < 50 μm , 100–150 μm , and 200–300 μm particle size fractions to provide a vibrational spectroscopic reference for direct UV-based mapping. The reference NIR spectra of spironolactone, LAC and MCC are shown in Fig. 6. The spectra of LAC and MCC overlap to a large extent, which is consistent with the known similarity of excipient signals observed in pharmaceutical NIR imaging studies, whereas spironolactone exhibits more distinct spectral features, including two

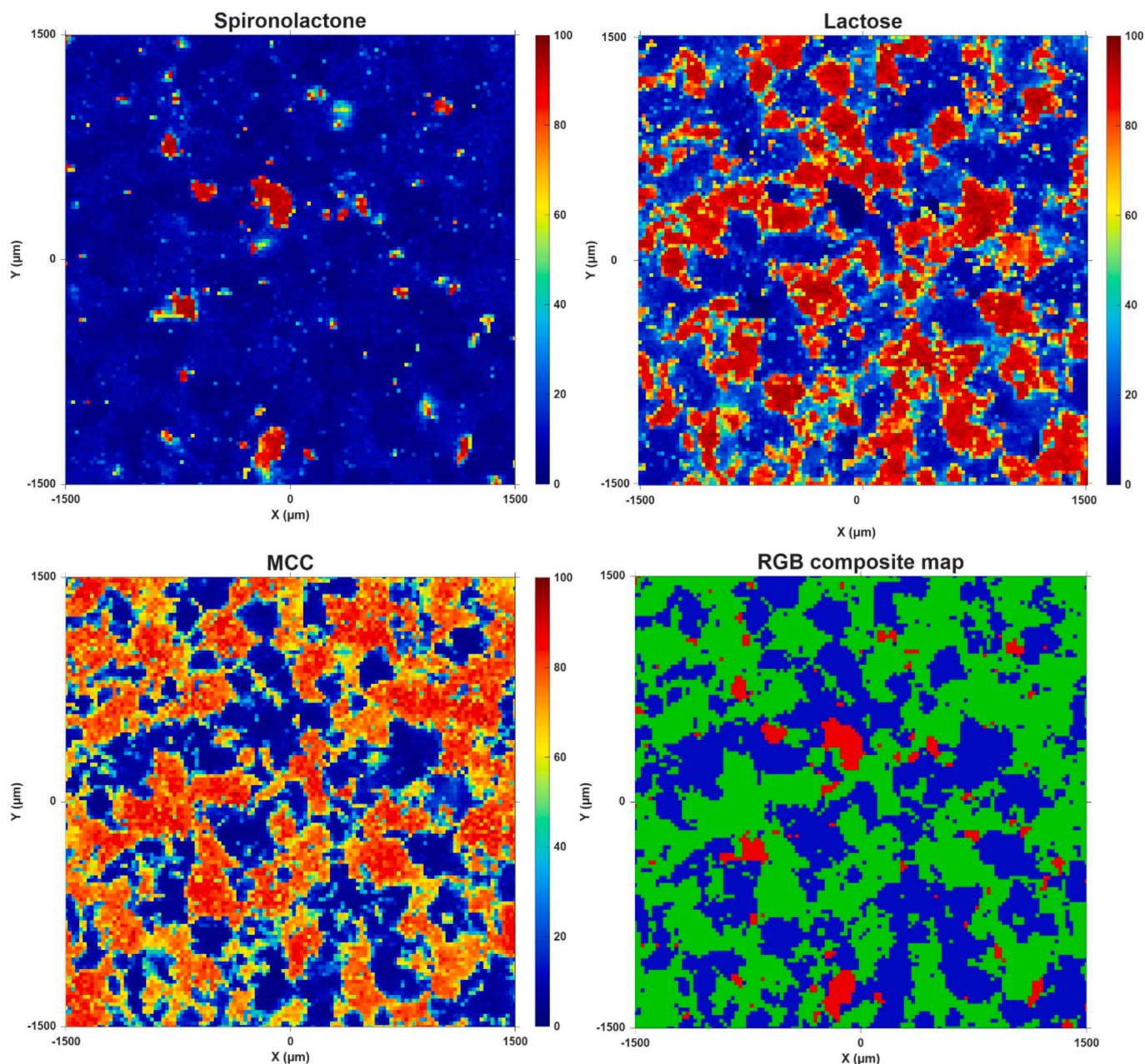


Fig. 9. Raman-based component maps and RGB composite map for the $3000 \times 3000 \mu\text{m}^2$ region of the tablet surface. In the composite map, red areas represent spironolactone, blue areas represent LAC, and green areas represent MCC.

characteristic bands around 4360 and 5752 cm^{-1} (Carruthers et al., 2021; Sasić, 2007). These bands improve the detectability of spironolactone even at low content. For the evaluation, the spectral range was restricted to $4000\text{--}6000 \text{ cm}^{-1}$.

The NIR-based component maps of the full tablet surface of the same $100\text{--}150 \mu\text{m}$ sample are presented in Fig. 7. The hyperspectral acquisition required 77 min, with a spatial resolution of $25 \mu\text{m}$. All three components could be identified: spironolactone appears as a minor phase in small, discrete regions, while LAC and MCC dominate the surface. In the NIR distribution and composite maps, mixed regions are observed between MCC and LAC, indicating partial overlap of the excipient domains. For practical interpretation of the LAC maps, intensity values above 60% were therefore taken as characteristic of lactose-rich areas.

Although spectral overlap between LAC and MCC contributes to the difficulty of component separation in the NIR data, this factor alone does

not fully explain the softer appearance of the NIR-based maps. Pre-processing and CLS can improve spectral discrimination, but diffuse reflectance NIR imaging is also influenced by the effective sampling volume of each pixel, which extends beneath and laterally beyond the nominal pixel area because of photon migration within the sample. As a result, adjacent-pixel cross-talk can occur, leading to blurred phase boundaries and less sharply resolved domains. In this sense, the softer appearance of the NIR maps in the present study is more appropriately attributed to the combined effects of spectral similarity, deeper sampling, and lateral photon spread. Previous comparative work has likewise shown that Raman mapping generally provides sharper and more clearly discriminated surface domains than NIR mapping when the objective is to represent tablet surface distribution patterns (Carruthers et al., 2021; Shi and Anderson, 2010).

To allow direct comparison, RGB composite images from the UV reflectance-based and NIR-based maps were aligned to the same

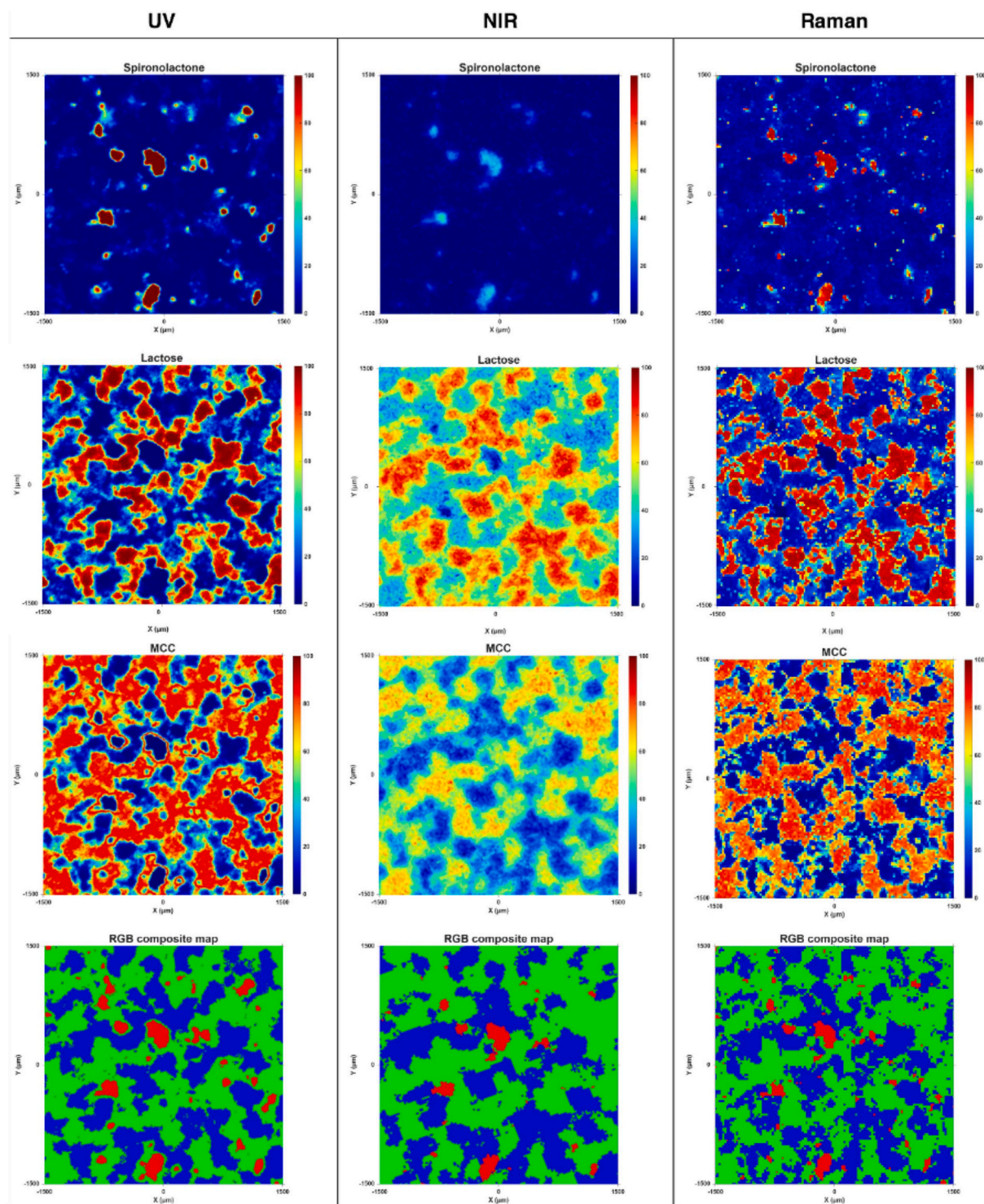


Fig. 10. Comparison of UV reflectance-, NIR- and Raman-based maps for the same $3000 \times 3000 \mu\text{m}^2$ region of the tablet surface. In the composite maps, red areas represent spironolactone, blue areas represent lactose, and green areas represent MCC.

orientation. The spatial distributions of spironolactone and LAC showed good agreement between the two techniques, and MCC appeared as the most abundant component in both cases. These findings indicate that UV reflectance-based and NIR-based full-surface maps provided a broadly consistent description of the sample, while also reflecting the different contrast mechanisms and effective sampling volumes of the two methods.

3.3. Raman chemical mapping of the selected region

Raman chemical mapping was performed on the predefined $3000 \times 3000 \mu\text{m}^2$ region to obtain a chemically specific vibrational reference. The spatial resolution for Raman mapping was set to $25 \mu\text{m}$, and acquisition required approximately 83 h. The preprocessed Raman reference spectra of spironolactone, LAC and MCC are shown in Fig. 8. In comparison with the NIR spectra, the Raman spectra are more clearly separated. LAC shows a spectrum rich in sharp peaks, while

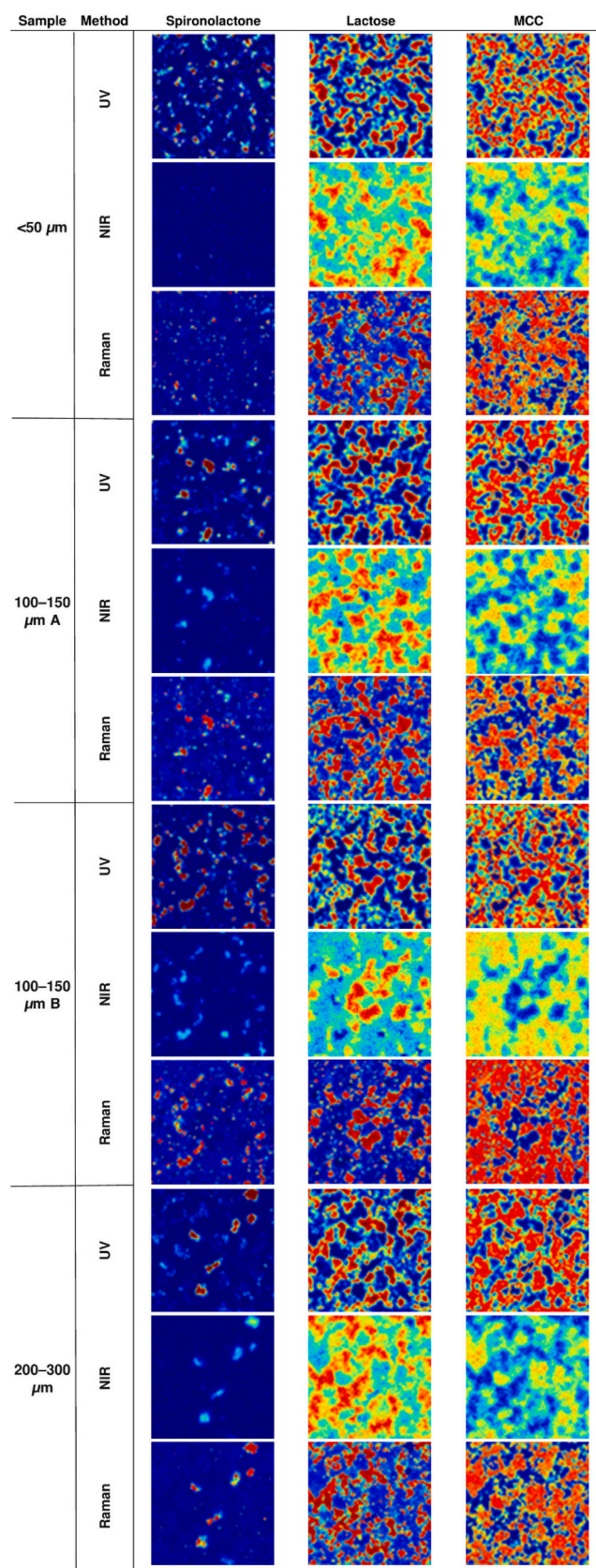


Fig. 11. Comparison of UV reflectance-, NIR-, and Raman-based component maps obtained for the investigated particle size fractions and the replicate sample used for statistical evaluation.

spironolactone exhibits several strong and selective Raman bands, allowing reliable identification at low concentration. Although the results for the 100–150 μm particle size fraction are presented here as a representative example for better visual comparison, Raman mapping was also performed for the additional particle size fractions and replicate sample included in the comparative statistical evaluation.

The Raman-based component maps and the corresponding composite map for the investigated region are summarized in Fig. 9. The spatial patterns are in good agreement with the direct UV-based and NIR-based mappings. Spironolactone again appears in small, well-localized domains with low overall surface coverage, while LAC and MCC form more extended regions. Compared with NIR, fewer mixed regions with intermediate intensities are observed between these two excipients in the Raman map, and in the examined region they appear in more similar proportions.

3.4. Comparative evaluation of UV reflectance, NIR and Raman mapping

The results of the three imaging techniques, namely UV reflectance-based machine vision, NIR chemical imaging, and Raman mapping, were compared for the same $3000 \times 3000 \mu\text{m}^2$ area. In all three methods, LAC appeared as high-intensity regions, while MCC generally exhibited lower intensities. The strongest overlap and mixing between LAC and MCC were observed in the NIR maps. Although spectral similarity between these excipients contributes to this effect, the softer appearance of the NIR-based maps is more appropriately attributed to the larger effective sampling volume of diffuse reflectance NIR imaging rather than to spectral overlap alone. Spironolactone appeared as discrete, high-intensity domains in both the Raman and direct UV-based maps, and a similar spatial pattern was also visible in the NIR maps, although with lower contrast. Overall, the composite images showed that the three techniques converged to a broadly similar spatial distribution of the components.

To assess whether the observed agreement was limited to the representative region shown in Fig. 10, additional UV, NIR, and Raman measurements were performed for the investigated particle size fractions and the replicate sample (Fig. 11). Similar distribution patterns were observed across the different samples. In particular, spironolactone appeared as discrete domains in all three imaging methods, while LAC and MCC formed complementary continuous regions. The replicate sample showed comparable distribution characteristics, suggesting that the mapping approaches were reproducible under the applied experimental conditions.

To complement the visual comparison, quantitative global similarity metrics were calculated from the aligned component maps. The results are summarized in Table 4 for each evaluated sample. For the 100–150 μm API particle size fraction, two tablets were evaluated and are denoted as sample A (which corresponds to the tablet discussed in detail above and shown in Fig. 10) and sample B.

The calculated similarity metrics confirmed the qualitative observations obtained from visual inspection of the maps. Pearson correlation coefficients ranged from 0.61 to 0.82 for the UV–Raman comparison, from 0.64 to 0.78 for the UV–NIR comparison, and from 0.69 to 0.82 for the NIR–Raman comparison. Similar trends were observed for the corresponding Spearman correlation coefficients. These values indicate that the different imaging methods captured largely comparable spatial distribution patterns across the investigated samples, with regions of high and low component abundance occurring at similar locations. The differences in similarity metrics obtained within the 100–150 μm API particle size fraction may reflect tablet-to-tablet variability.

The intensity distribution-based metrics further supported these observations. Jensen–Shannon divergence values remained low throughout the investigated particle size fractions, indicating minor differences between the intensity distributions obtained by the different methods. The relatively higher Jensen–Shannon divergence values observed for certain NIR–Raman comparisons likely arise from the

Table 4

Global similarity metrics calculated from the aligned component maps obtained by UV reflectance imaging, NIR chemical imaging, and Raman mapping.

Sample	Comparison	Global pearson coefficient	Global spearman coefficient	Global jensen-shannon divergence	Global Wasserstein distance	Global gini difference	Global continuous coverage difference (%)
<50 μm	UV–NIR	0.72	0.74	0.24	0.06	0.08	4.50
<50 μm	UV–Raman	0.72	0.73	0.10	0.03	0.01	0.89
<50 μm	NIR–Raman	0.75	0.78	0.42	0.10	0.09	3.77
100–150 μm A	UV–NIR	0.78	0.81	0.19	0.07	0.10	7.79
100–150 μm A	UV–Raman	0.82	0.81	0.13	0.03	0.04	4.43
100–150 μm A	NIR–Raman	0.82	0.84	0.33	0.09	0.06	7.33
100–150 μm B	UV–NIR	0.64	0.66	0.22	0.09	0.13	7.37
100–150 μm B	UV–Raman	0.61	0.60	0.18	0.06	0.00	4.76
100–150 μm B	NIR–Raman	0.75	0.74	0.45	0.13	0.13	9.45
200–300 μm	UV–NIR	0.66	0.70	0.19	0.08	0.10	9.34
200–300 μm	UV–Raman	0.75	0.77	0.13	0.02	0.01	3.53
200–300 μm	NIR–Raman	0.69	0.75	0.33	0.09	0.09	6.12

smoother intensity distributions generated by NIR mapping compared with Raman mapping. Likewise, the generally small Wasserstein distances suggest that only limited redistribution of intensity values would be required to transform one distribution into another. The low Gini coefficient differences further indicate that the compared maps exhibited similar degrees of intensity concentration and spatial heterogeneity.

The continuous coverage differences were also generally low, particularly for the UV–Raman comparisons, indicating similar estimates of the apparent relative abundance of the mapped components. Together, these metrics demonstrate that the three imaging techniques provided highly similar information regarding the overall component distributions and their spatial organization.

Overall, the quantitative evaluation demonstrated that UV reflectance imaging, NIR chemical imaging, and Raman mapping yielded closely comparable descriptions of the spatial distribution of spironolactone, lactose monohydrate, and microcrystalline cellulose across the investigated samples. These findings support the use of UV reflectance imaging as a rapid alternative for assessing tablet surface distribution patterns while providing information that is consistent with that obtained by the spectroscopic imaging methods.

Although the quantitative metrics demonstrated a high degree of similarity between the resulting maps, some differences between the methods were observed and are related to their effective sampling depth and sampling volume. In the present study, UV reflectance imaging was interpreted as a predominantly surface-sensitive technique, since the grayscale signal was obtained from the UV radiation returned from the tablet surface under ~ 270 nm illumination; however, the penetration depth of UV/Vis radiation in tablets is material-, wavelength-, and particle size-dependent, and exact penetration depths were not determined in the present work (Brands et al., 2025). In contrast, diffuse reflectance NIR imaging probes a larger effective sampling volume, and photon migration within the sample can extend both beneath and laterally beyond the nominal pixel area, leading to adjacent-pixel cross-talk and the contribution of multiple particle layers to a single NIR pixel (Shi and Anderson, 2010). This effect may partly explain the softer LAC/MCC boundaries observed in the NIR maps and is particularly relevant when components show partially overlapping NIR spectra, as observed for lactose monohydrate and MCC in the present formulation. Raman mapping provided sharper local discrimination in this system because of its higher chemical specificity, and previous comparative studies on pharmaceutical tablets have similarly shown that Raman maps can provide more clearly resolved surface-domain information than NIR

maps (Carruthers et al., 2021). Nevertheless, the actual Raman sampling depth also depends on the optical configuration, focusing conditions, and sample properties. Therefore, the observed differences between UV, NIR, and Raman maps should be interpreted not only in terms of spectral selectivity, but also in terms of effective sampling volume and surface sensitivity.

Taken together, the results show that direct UV-based machine vision, NIR chemical imaging, and Raman mapping can all identify the main components of the investigated formulations and resolve their spatial distributions. At the same time, their relative performance should be interpreted in the context of the studied model system, which contained spironolactone as the API and MCC and LAC as the main excipients. These excipients were selected due to their widespread use in pharmaceutical formulations. The relative strengths and limitations of the three methods are influenced by the optical and spectroscopic properties, concentration, particle size, and spatial distribution of the components. Therefore, the present results highlight the complementary strengths of the three imaging approaches and demonstrate their applicability for characterizing component distribution in typical pharmaceutical formulations.

In the present work, spironolactone served as a suitable model API. Despite its low concentration, it showed distinct spectroscopic features in the vibrational measurements and pronounced UV absorption under the applied imaging conditions. These results suggest that the UV-based approach may also be applicable to other formulations containing APIs with similarly strong UV contrast behavior. Nevertheless, this assumption requires further validation in additional systems. From a practical perspective, UV reflectance imaging is most advantageous for rapid surface screening and high-throughput comparison of related samples. NIR chemical imaging is useful when chemically specific full-surface information is required. In the present system, Raman mapping provided clearer chemical discrimination because the pure-component Raman spectra contained more distinct and component-specific bands. Since no independent ground-truth surface map was available, the Raman map should be interpreted as a chemically more specific reference within this comparative framework, rather than as an absolute representation of the true component distribution. This improved chemical discrimination was achieved at the cost of substantially longer acquisition time and a smaller mapped area. Despite these differences, the three techniques provided a coherent and mutually supportive picture in the present system.

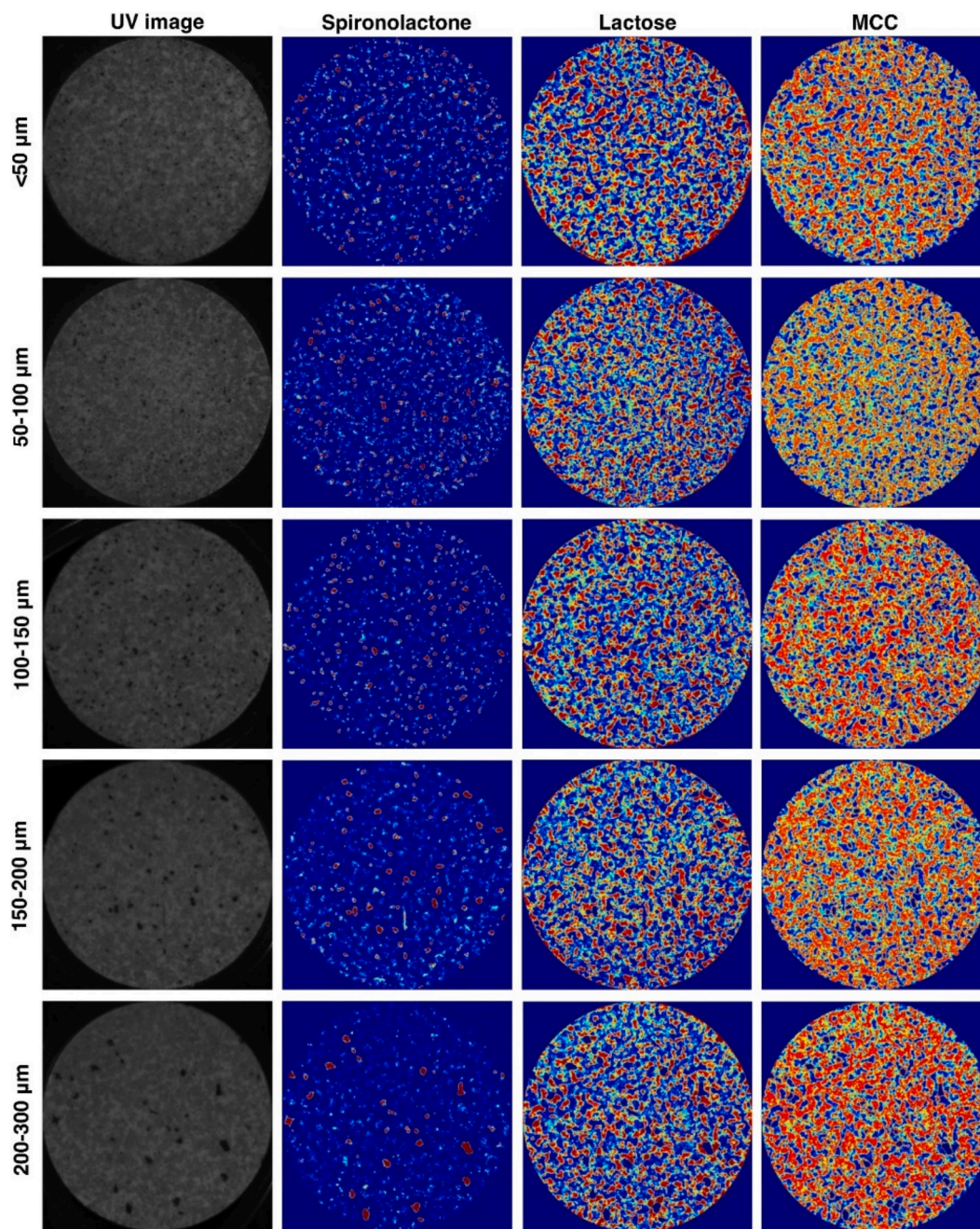


Fig. 12. Full-surface UV reflectance-based component maps for all five tablet batches with different spironolactone particle size fractions.

3.5. Full-surface UV reflectance mapping of tablets containing different API particle size fractions

After the evaluation of similarity between UV reflectance imaging, NIR chemical imaging, and Raman mapping had been established on the selected regions, the UV workflow was applied to complete tablet surfaces in order to demonstrate its practical applicability beyond the localized comparative measurements. A major advantage of the UV-based approach is its ability to rapidly generate full-surface component maps, enabling the investigation of formulation-scale heterogeneity and the analysis of larger sample sets.

To illustrate this capability, full-surface UV reflectance maps were generated for five tablet batches containing spironolactone with different particle size fractions. The same direct UV-based mapping procedure was applied to all samples, and the resulting component maps

are presented in Fig. 12. The purpose of this section is not to provide an additional comparison with the reference techniques, but rather to demonstrate how the validated UV workflow can be used to characterize complete tablet surfaces and to assess spatial variations in API distribution across related samples within the same formulation system. Because the distribution of API-containing domains is not spatially uniform across the tablet surface, the selection of a limited region of interest may not always provide a fully representative picture of the overall distribution. Full-surface imaging reduces the risk of drawing conclusions from locally unrepresentative areas and provides a more comprehensive assessment of tablet-scale component distribution. In component-distribution studies, this is particularly important because the spatial organization of API-rich domains directly influences the interpretation of component segregation and the representativeness of the analyzed region.

The resulting maps demonstrate that the UV workflow remained applicable across the investigated particle size fractions and revealed differences in the size, frequency, and spatial distribution of API-containing domains between the investigated samples. These observations indicate that the method is capable of capturing particle size-related variations in API distribution while maintaining full-surface coverage of the tablet.

However, as with any method, this approach also has limitations. Additional experiments are required to determine the smallest API particle size that can be reliably detected under the applied UV imaging conditions.

4. Conclusion

In addition to demonstrating the feasibility of UV reflectance imaging-based machine vision as a potential novel analytical tool for tablet surface mapping, this study placed the method in context through comparison with NIR chemical imaging and Raman mapping. The results showed that, across the investigated API particle size fractions, UV reflectance imaging was able to provide surface-distribution information broadly consistent with that obtained by NIR chemical imaging and Raman mapping, while offering a clear advantage in measurement speed and full-surface coverage from a single short exposure. Furthermore, the UV-based workflow remained applicable across the investigated API particle size fractions, demonstrating its ability to reveal particle-size-dependent differences in surface distribution patterns and supporting its use for comparative assessment of formulation variants.

Importantly, the method can be suitable for the investigation of visually white tablets, in which component-related differences are not discernible by visual inspection under visible illumination. In addition, the present approach was able to resolve the API and the major excipients, whereas minor formulation components present at low concentrations and with limited spatial contrast were not reliably distinguished under the applied conditions.

From a practical perspective, the method may serve as a rapid screening tool for identifying surface regions that may indicate component segregation or localized API-enriched domains, supporting region-of-interest selection, and enabling high-throughput comparison of multiple samples, for example, across different API particle size fractions. At this stage, UV reflectance imaging can be used to complement the presented chemical imaging methods by providing fast, surface-sensitive information that can guide more time-consuming, chemically specific measurements.

The present results should be interpreted within the scope of the investigated formulation and measurement design. Future studies should extend the approach to more complex industrial formulations, larger datasets, and broader validation across formulation variables, including different API concentrations, excipient systems, compression conditions, and tablet geometries. Additional information may also be gained by combining UV reflectance imaging with fluorescence imaging or by exploring wavelength optimization and multispectral UV approaches. Such developments may further expand the range of formulations and components that can be reliably differentiated when direct grayscale contrast is insufficient under single-wavelength UV imaging conditions.

Overall, UV reflectance imaging-based machine vision appears to be a rapid and information-rich surface-screening method for solid dosage forms, most appropriately used alongside slower reference techniques when detailed chemical confirmation is required. The rapid acquisition speed and full-surface coverage of the technique may also justify future investigation of its applicability in process-oriented analytical workflows.

CRedit authorship contribution statement

Bence Szabó-Szócs: Writing – original draft, Visualization,

Validation, Investigation, Data curation, Conceptualization. **Lilla Alexandra Mészáros:** Writing – review & editing, Validation, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Attila Farkas:** Supervision, Investigation, Data curation. **Hajnalka Pataki:** Methodology, Investigation. **Barbara Honti:** Investigation. **Gábor Drávavölgyi:** Resources, Conceptualization. **Szilveszter Gergely:** Investigation, Data curation. **Lajos Madarász:** Writing – review & editing, Supervision, Software, Conceptualization. **Dorián László Galata:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Zsombor Kristóf Nagy:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

References

- Bunaciu A.A., Aboul-Enein H.Y., Hoang V.D., V.D., Vibrational spectroscopy applications in biomedical, pharmaceutical and food sciences. Published online 2020:266.
- Gowen, A.A., O'Donnell, C.P., Cullen, P.J., Bell, S.E.J., 2008. Recent applications of chemical imaging to pharmaceutical process monitoring and quality control. *Eur. J. Pharm. Biopharm.* 69 (1), 10–22. <https://doi.org/10.1016/j.ejpb.2007.10.013>.
- Ewing, A.V., Kazarian, S.G., 2018. Recent advances in the applications of vibrational spectroscopic imaging and mapping to pharmaceutical formulations. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* 197, 10–29. <https://doi.org/10.1016/j.SAA.2017.12.055>.
- Smith, G.P.S., McGovern, C.M., Fraser, S.J., Gordon, K.C., 2015. Raman imaging of drug delivery systems. *Adv. Drug Deliv. Rev.* 89, 21–41. <https://doi.org/10.1016/j.ADDR.2015.01.005>.
- Šašić Slobodan, Ozaki Y. Raman, infrared, and near-infrared chemical imaging. Published online 2010:317.
- Clark, D., Šašić, S., 2006. Chemical images: technical approaches and issues. *Cytometry A* 69 (8), 815–824. <https://doi.org/10.1002/CYTO.A.20275>.
- Carruthers, H., Clark, D., Clarke, F.C., Faulds, K., Graham, D., 2021. Comparison of Raman and near-infrared chemical mapping for the analysis of pharmaceutical tablets. *Appl. Spectrosc.* 75 (2), 178–188. <https://doi.org/10.1177/0003702820952440>.
- Šašić S. An In-Depth Analysis of Raman and Near-Infrared Chemical Images of Common Pharmaceutical Tablets. *Applied Spectroscopy*. 61(3) 2007 239-250. Accessed October 27, 2025. <https://opg.optica.org/abstract.cfm?uri=as-61-3-239>.
- Carruthers, H., Clark, D., Clarke, F.C., Faulds, K., Graham, D., 2022. Evaluation of laser direct infrared imaging for rapid analysis of pharmaceutical tablets. *Royal Society of Chem. Published Online*. <https://doi.org/10.1039/D2AY00471B>.
- Galata, D.L., Gergely, S., Nagy, R., et al., 2023. Comparing the performance of raman and near-infrared imaging in the prediction of the in vitro dissolution profile of extended-release tablets based on artificial neural networks. *Pharmaceutics* 16 (9), 1243. <https://doi.org/10.3390/PH16091243/S1>.
- Gordon, K.C., McGovern, C.M., 2011. Raman mapping of pharmaceuticals. *Int. J. Pharm.* 417 (1–2), 151–162. <https://doi.org/10.1016/j.IJPHARM.2010.12.030>.
- Szabó-Szócs, B., Ficzer, M., Péterfi, O., Galata, D.L., 2025. Simultaneous prediction of the API concentration and mass gain of film coated tablets using Near-Infrared and

- Raman spectroscopy and data fusion. *Int. J. Pharm.* 668 (15), 124957. <https://doi.org/10.1016/j.ijpharm.2024.124957>.
- Ficzere, M., Madarász, L., Kádár, S., Farkas, A., Mészáros, L.A., Nagy, Z.K., 2025. UV imaging as a novel, ultrafast chemical mapping tool for pharmaceutical tablet analysis. *Microchem. J.* 217. <https://doi.org/10.1016/j.microc.2025.115032>.
- Su, X., Wang, Y., Mao, J., et al., 2022. A review of pharmaceutical robot based on hyperspectral technology. *J. Intell. Rob. Syst.* 105 (4), 75. <https://doi.org/10.1007/S10846-022-01602-7>.
- Cheng, M.F., Mukundan, A., Karmakar, R., Valappil, M.A.E., Jouhar, J., Wang, H.C., 2025. Modern trends and recent applications of hyperspectral imaging: a review. *Technologies* 13 (5), 170. <https://doi.org/10.3390/TECHNOLOGIES13050170>.
- Scoutaris, N., Vithani, K., Slipper, I., Chowdhry, B., Douroumis, D., 2014. SEM/EDX and confocal Raman microscopy as complementary tools for the characterization of pharmaceutical tablets. *Int. J. Pharm.* 470 (1–2), 88–98. <https://doi.org/10.1016/J.IJPHARM.2014.05.007>.
- Gupta, S., Omar, T., Muzzio, F.J., 2022. SEM/EDX and Raman chemical imaging of pharmaceutical tablets: a comparison of tablet surface preparation and analysis methods. *Int. J. Pharm.* 611, 121331. <https://doi.org/10.1016/J.IJPHARM.2021.121331>.
- Al Ktash, M., Stefanakis, M., Boldrini, B., Ostertag, E., Brecht, M., 2021. Characterization of pharmaceutical tablets using UV hyperspectral imaging as a rapid in-line analysis tool. *Sensors* 21 (13), 4436. <https://doi.org/10.3390/S21134436>.
- Wu, J.X., Rehder, S., Van Den, B.F., et al., 2014. Chemical imaging and solid state analysis at compact surfaces using UV imaging. *Int. J. Pharm.* 477 (1–2), 527–535. <https://doi.org/10.1016/J.IJPHARM.2014.10.064>.
- Klukkert, M., Wu, J.X., Rantanen, J., Carstensen, J.M., Rades, T., Leopold, C.S., 2016. Multispectral UV imaging for fast and non-destructive quality control of chemical and physical tablet attributes. *Eur. J. Pharm. Sci.* 90, 85–95. <https://doi.org/10.1016/J.EJPS.2015.12.004>.
- Péterfi, O., Mészáros, L.A., Szabó-Szőcs, B., et al., 2024. UV–VIS imaging-based investigation of API concentration fluctuation caused by the sticking behaviour of pharmaceutical powder blends. *Int. J. Pharm.* 655, 124010. <https://doi.org/10.1016/J.IJPHARM.2024.124010>.
- Ficzere, M., Alexandra Mészáros, L., Diószegi, A., et al., 2024. UV imaging for the rapid at-line content determination of different colourless APIs in their tablets with artificial neural networks. *Int. J. Pharm.* 657, 124174. <https://doi.org/10.1016/J.IJPHARM.2024.124174>.
- Mészáros, L.A., Galata, D.L., Madarász, L., et al., 2020. Digital UV/VIS imaging: a rapid PAT tool for crushing strength, drug content and particle size distribution determination in tablets. *Int. J. Pharm.* 578, 119174. <https://doi.org/10.1016/J.IJPHARM.2020.119174>.
- Péterfi, O., Mészáros, L.A., Szabó-Szőcs, B., et al., 2026. ANN-assisted UV imaging for non-destructive dissolution prediction of HPMC matrix tablets. *Int. J. Pharm.* 692, 126649. <https://doi.org/10.1016/j.ijpharm.2026.126649>.
- Mészáros, L.A., Madarász, L., Ficzere, M., Bicsár, R., Farkas, A., Nagy, Z.K., 2024. UV/VIS-imaging of white caffeine tablets for prediction of CQAs: API content, crushing strength, friability, disintegration time and dissolution profile. *Int. J. Pharm.* 663, 124565. <https://doi.org/10.1016/J.IJPHARM.2024.124565>.
- Jentoft F. Diffuse reflectance IR and UV-vis spectroscopy modern methods in heterogeneous catalysis. Published online 2004.
- Allied Vision Alvium 1800 U-120m, 1/3" 1.2MP S-Mount, USB 3.0 Monochrome Camera. Accessed March 4, 2026. https://www.edmundoptics.eu/p/allied-vision-alvium-1800-u-120m-13-12mp-s-mount-usb-31-monochrome-camera/42977/?gad_source=1&gad_campaignid=20956749007&gbraid=0AAAAACOW0GMEYNef-uQAAWc-SHUYN_i_n&gclid=CjwKCAiAzZ_NBhAEEiwAMtqKy3NNAgUH_MooUEk35SQ4clDIrXx-UyrQLW-16EVJE5nPi0yJ2jCbxcCkLQAvD_BwE.
- Alvium 812 UV camera | Sony IMX487. Accessed March 4, 2026. <https://www.axiomoptics.com/products/alvium-uv-camera/>.
- MATLAB Help Center. Kmeans - k-means clustering - MATLAB. Accessed November 20, 2025. <https://www.mathworks.com/help/stats/kmeans.html>.
- PerkinElmer. Spotlight™ 400 FT-IR and 400N FT-NIR Imaging Systems FT-IR IMAGING THAT'S CLEARLY MEASURABLY AMAZING. Accessed June 16, 2026. www.perkinelmer.com/spotlight.
- Spectroscopy R, Raman A/, Labram X. A Full Range of Solutions LabRAM Series: High Performance Raman with Automation XploRA Series: Simply Better Raman System: The XploRA series, compact and rugged confocal Raman microscope.
- A fast non-negativity-constrained least squares algorithm - Bro - 1997 - Journal of Chemometrics - Wiley Online Library. Accessed July 9, 2026. [https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/\(SICI\)1099-128X\(199709/10\)11:5%3C393::AID-CEM483%3E3.0.CO;2-L](https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/(SICI)1099-128X(199709/10)11:5%3C393::AID-CEM483%3E3.0.CO;2-L).
- corr - Linear or rank correlation - MATLAB. Accessed June 17, 2026. <https://www.mathworks.com/help/stats/corr.html>.
- Lin, J., 1991. Divergence measures based on the Shannon entropy. *IEEE Trans. Inf. Theory*, 37.
- Rubner, Y., Tomasi, C., Guibas, L.J., 2000. The earth mover's distance as a metric for image retrieval. *Int. J. Comput. Vis.* 40 (2), 99–121.
- Ceriani L, Verme P. The origins of the Gini index: extracts from Variabilità e Mutabilità (1912) by Corrado Gini. *The Journal of Economic Inequality*. 10(3) 2011 421-443. doi:10.1007/S10888-011-9188-X.
- Janssen, P.H.M., Kulkarni, S.S., Torrecillas, C.M., et al., 2022. Effect of batch-to-batch variation of spray dried lactose on the performance of feeders. *Powder Technol.* 409, 117776. <https://doi.org/10.1016/j.powtec.2022.117776>.
- Vlčková, N., Šimonová, A., Duriš, M., Čokrtová, K., Almquist, S., Krížek, T., 2023. Detection techniques for carbohydrates in capillary electrophoresis – a comparative study. *Monatshfte für Chemie - Chemical Monthly* 154 (9), 967–975. <https://doi.org/10.1007/s00706-023-03109-9>.
- Yong, W.S., Yeu, Y.L., Chung, P.P., Soon, K.H., 2024. Extraction and characterization of microcrystalline cellulose (MCC) from durian rind for biocomposite application. *J. Poly. Environ.* 32 (12), 6544–6575. <https://doi.org/10.1007/s10924-024-03401-7>.
- Peng, Y., Via, B., 2021. The effect of cellulose nanocrystal suspension treatment on suspension viscosity and casted film property. *Polymers* 13 (1). <https://doi.org/10.3390/polym13132168>.
- Salama, A., Badran, M., Elmowafy, M., Soliman, G.M., 2019. Spironolactone-loaded lecithin as potential topical delivery systems for female acne: in vitro appraisal and ex vivo skin permeability studies. *Pharmaceutics* 12 (1), 25. <https://doi.org/10.3390/pharmaceutics12010025>.
- Lotfy, H.M., El-Hanboushy, S., Fayz, Y.M., Abdelkawy, M., 2022. Smart spectrophotometric methods for concurrent determination of furosemide and spironolactone mixture in their pharmaceutical dosage forms. *Brazilian J. Pharmaceutical Sci.* 58. <https://doi.org/10.1590/s2175-97902022e19487>.
- Shi, Z., Anderson, C.A., 2010. Application of Monte Carlo simulation-based photon migration for enhanced understanding of near-infrared (NIR) diffuse reflectance. Part II: photon radial diffusion in NIR chemical images. *J. Pharm. Sci.* 99 (10), 4174–4182. <https://doi.org/10.1002/JPS.22125>.
- Brands, R., Fuchs, L., Seyffer, J.M., et al., 2025. Penetration depth and effective sample size characterization of UV/Vis radiation into pharmaceutical tablets. *J. Pharm. Sci.* 114 (12), 103889. <https://doi.org/10.1016/J.XPHS.2025.103889>.