A novel sample delivery method for powder X-ray diffraction at Turkish Light Source

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Abstract

Powder X-ray diffraction is highly sensitive to sample-delivery conditions, particularly when measurements are performed on platforms originally designed for single-crystal diffraction. In this study, we developed a modified Terasaki-plate-based sample-delivery method for PXRD using a laboratory single-crystal diffractometer implemented with the XtalCheck-S plate-reader module at Turkish Light Source. The method was evaluated against standard loop/pin-based loading and a grease-based Terasaki setup using [4-(2-methoxyphenyl)piperazin-1-yl]methyl}-1,3,4-oxadiazol-2-thiol as a model analyte. While the loop-based method allowed initial PXRD measurements, it provided limited sample volume and insufficient particle statistics. The grease-based plate setup enabled multi-well data collection at a time, but yielded weaker, more diffuse patterns due to increased background noise. Inversely, modification of the Terasaki wells with Kapton tape enabled secure low-volume powder loading, improved diffraction clarity, and supported batch-mode data collection. Comparative search–match and profile-fitting analyses showed that all three loading strategies sampled the same crystalline material, whereas the Kapton-based setup presented the most reliable diffraction profile, with the lowest profile residual (Rp = 9.6%). These findings indicate that this novel sample-delivery method, rather than instrument hardware, can largely improve PXRD performance on an existing in-situ crystallography platform. The Kapton-Terasaki method provides a simple, cost-effective, and practical pipeline for high-throughput PXRD analysis of small powder samples under laboratory conditions.

Keywords: Powder X-ray diffraction, sample delivery, Kapton-tape, profile fitting

1. Introduction

Powder X-ray diffraction (PXRD) is one of the most widely used methods for characterizing crystalline materials, providing rapid, informative access to phase identity, crystallinity, and overall structural features without the need for single-crystal diffraction [1], [2]. For molecular and pharmaceutical powders in particular, PXRD plays an important role in screening, phase comparison, and verifying sample content [1]. At the same time, the analytical value of PXRD depends strongly on the quality of the collected diffraction signal, which is affected not only by instrumental setup but also by sample preparation, particle statistics, sample geometry, and background contributions [3]. These factors become especially important when powder measurements are performed on instruments and pipelines originally optimized for single-crystal diffraction rather than for routine powder analysis [4]. Recent advances in laboratory X-ray instrumentation have expanded the practical flexibility of home-source diffractometers and created new opportunities to adapt available crystallographic platforms to non-conventional measurement strategies [5]. In Türkiye, the installation of a modern home X-ray source in 2022 provided a new local framework for laboratory-based crystallographic data collection and method development [4], [5]. Accordingly, the Rigaku XtaLAB Synergy system allows data collection not only through the standard loop-/pin-based single-crystal pipeline, but also via the XtalCheck-S plate-reader module, primarily intended for in-situ screening of multiple crystal samples [5] (Rigaku Oxford Diffraction, 2021). Although this capability offers a practical starting point for high-throughput analysis, its direct application to powder X-ray diffraction is not straightforward, because powder specimens require a different sample-delivery logic than isolated single crystals and are more sensitive to issues such as low sample volume, poor particle statistics, and background scattering [6]. To address related practical limitations in crystallographic screening, we previously developed

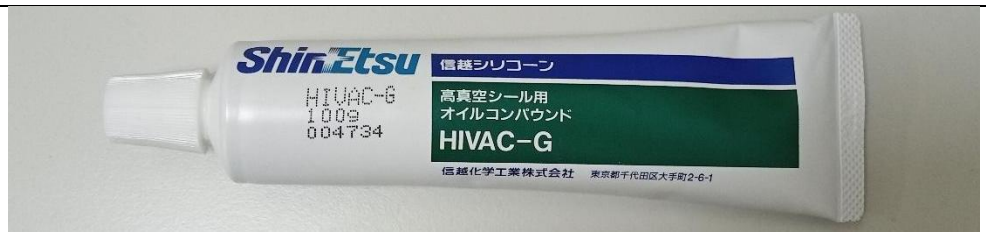
a 3D-printed adapter that enabled Terasaki plates to be used in the XtalCheck-S module for crystal-handling applications [5]. Building on this idea, the present work explores whether the same general platform can be extended to powder X-ray diffraction by redesigning the sample-delivery format. In this context, Terasaki plates are cost-effective and very useful, as they allow multi-well loading, enabling data collection from multiple samples at a time [7], [8]. However, successful practice needs a support strategy that can keep very small amounts of powder, remain compatible with the plate-reader geometry, and minimize undesirable background noise. Here, we developed a modified Terasaki-plate-based sample-delivery method for PXRD on a laboratory single-crystal diffractometer implemented with the XtalCheck-S module. The method was evaluated by comparing a standard loop/pin-based method with a grease-based Terasaki loading strategy. Particular attention was focused on diffraction signal quality, practical handling, multi-well data collection, and the reproducibility of the resulting powder diffraction after batch-mode data processing. Using {[4-(2-methoxyphenyl)piperazin-1-yl]methyl}-1,3,4-oxadiazol-2-thiol as a model analyte [9], we noticed that modification of the Terasaki plate with Kapton-sealed wells provides a simple and low-cost method to obtain clearer and more representative PXRD data than can be collected with either loop-based or grease-based loading under the present experimental conditions. Beyond the specific analyte examined here, the study aims to demonstrate that improving sample delivery can largely extend the PXRD use of an available in-situ crystallography platform.

2. Results

The powder sample examined in this present study corresponds to {[4-(2-methoxyphenyl)piperazin-1-yl]methyl}-1,3,4-oxadiazol-2-thiol, previously reported as compound 3 in the synthesis study of highly substituted piperazine–azole hybrids by Mermer et al [9]. This molecule contains a 1,3,4-oxadiazole core linked to a 2-methoxyphenyl-substituted piperazine moiety through a methylene bridge, thus combining two pharmaceutically relevant heterocyclic fragments within a single scaffold. In the original report, the compound was prepared from the corresponding hydrazide precursor, characterized by elemental and spectroscopic analyses (NMR, MS, etc.), and further identified as a biologically active intermediate for subsequent derivatization. Importantly, compound 3 also showed measurable antimicrobial activity against both Gram-negative and Gram-positive bacteria, as well as Mycobacterium smegmatis, supporting its relevance as a structurally defined and chemically meaningful model analyte for the present PXRD method-development study.

2.1. Conventional single-measurement-loop/pin method and its limitations. PXRD data were collected using standard single-crystal instrumentation and sample-mounting procedures. For sample preparation, the powder was first spread on a glass slide (**Fig. 1a**) and examined under a microscope (**Fig. 1b-c**); the most suitable particles were then picked up using a standard loop (**Fig. 1d**) or a pin coated with ShinEtsu HIVAC-G grease (**Table 1**).

Table 1. Sample delivery tools for powder X-ray diffraction.

Grease			
Tungsten needle probe			
Magnetic wand			
Sample pin		Sample puck (for cryogenic sample delivery)	
Standard laboratory tools, including a spatula, tweezers, glass slides, and a mortar and pestle, were used for sample preparation.			

The mounted pin was placed on the Intelligent Goniometer Head (IGH) of the Rigaku XtaLAB Synergy diffractometer for data collection (**Fig. 1e**) [4]. The data collection parameters were set similarly to those used in single-crystal experiments, with a HyPix-Arc 150° detector-to-source distance of 60 mm, a resolution limit of 2θ = 50°, and an exposure time of 10 s. Following data collection, the diffraction images were processed to assess the quality of the powder signal. Representative 2D diffraction frames and the corresponding integrated powder pattern obtained from these images are shown in **Figure 2**. Although this approach enabled initial PXRD

measurements, it demonstrated clear limitations when applied to powder samples. In practice, the loop-based setup yielded only one or two frames, relative intensity is low, and the amount of powder that could be mounted remained limited. Because reliable powder diffraction data require a necessary large number of randomly oriented crystallites within the X-ray beam, these conditions were not enough to provide robust particle statistics [3], [6]. As a result, while the standard loop-based method was useful for preliminary assessment, it was not optimal for routine PXRD analysis. These limitations motivated the development of an alternative sample-loading strategy that could accommodate a larger number of measurements, improve signal quality, and enable more efficient batch data collection [5], [10], [11].

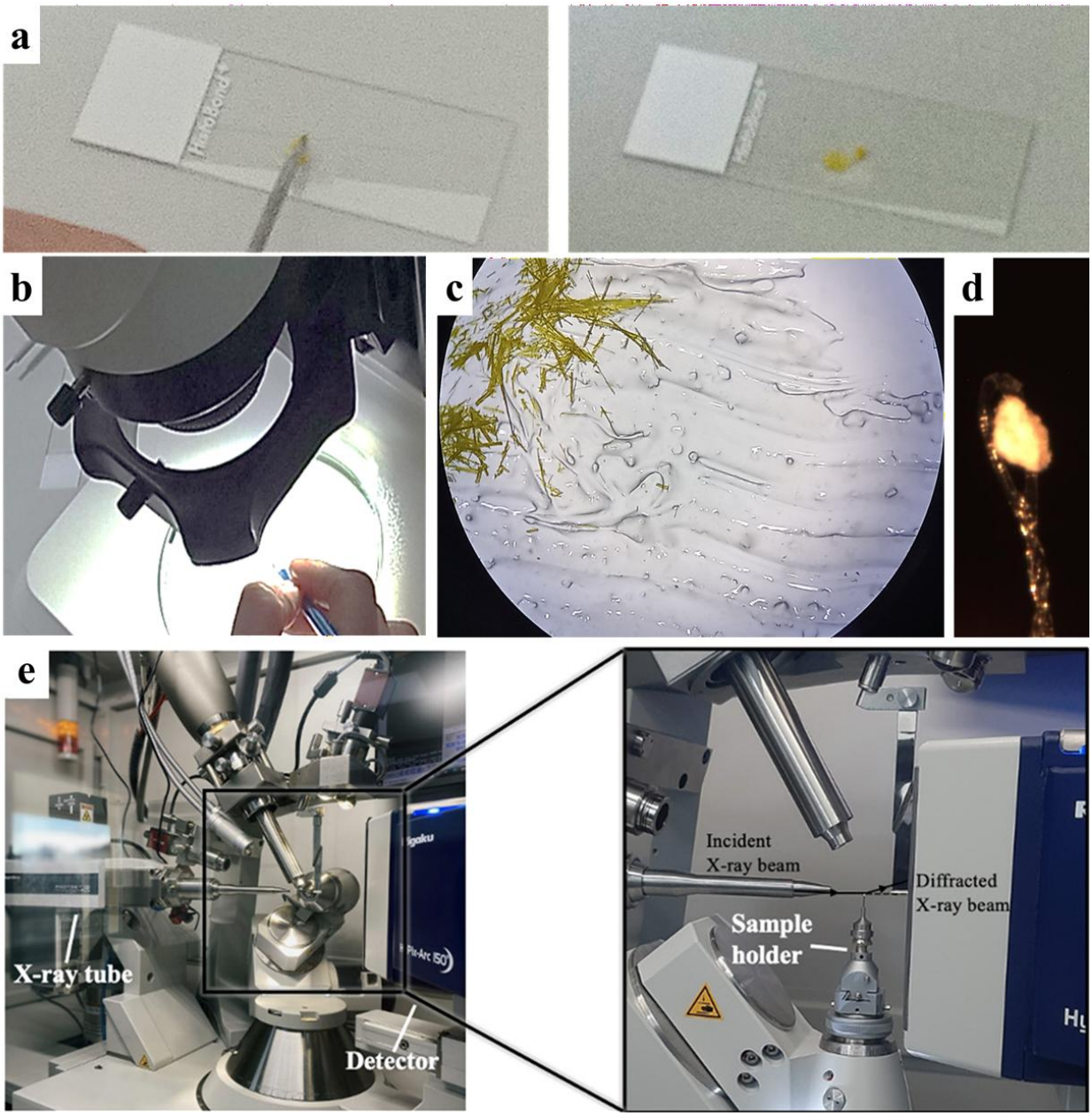


Figure 1. Standard loop-based powder sample preparation and mounting procedure for PXRD data collection. (a) A powder sample was spread on a glass slide, and selected particles were collected using a grease-coated loop. (b) Microscopic inspection during sample picking. (c) Representative microscopic view of the powder dispersed on the glass slide. (d) Powder is mounted on the loop prior to measurement. (e) Experimental setup on the Rigaku XtaLAB Synergy diffractometer, showing the X-ray tube, detector, and mounted sample. The magnified inset highlights the sample position relative to the incident and diffracted X-ray beams (Panel e, adopted from Atalay et al. [4]).

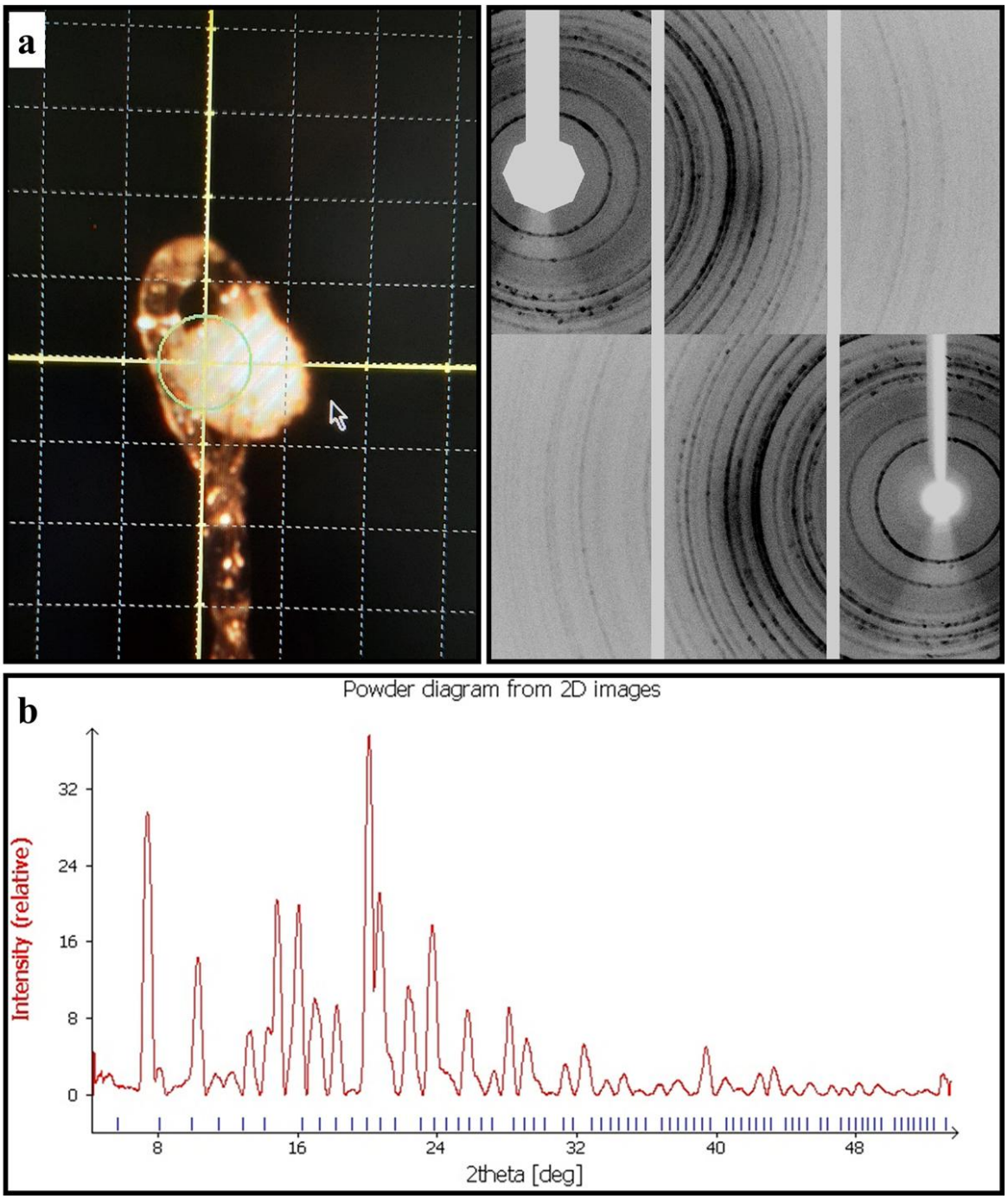


Figure 2. Representative diffraction obtained from the standard loop-based PXRD measurement after data collection and initial processing. (a) Optical view of the powder sample mounted on the loop and centered in the X-ray beam. The near panels show representative 2D diffraction images collected from the mounted sample, displaying powder diffraction rings. (b) One-dimensional powder diffraction pattern generated by integration of the 2D diffraction images, shown as intensity versus 2θ.

2.2. High-throughput Terasaki plate modification: grease- and Kapton-based approaches. To overcome the limitations of the standard loop-based method in terms of both data quality and throughput, the XtalCheck-S plate reader module, originally designed for in situ multiple-crystal screening [5], was adapted for powder X-ray diffraction measurements. In this approach, 72-well Terasaki plates were used to enable batch data collection from multiple (up to 72) samples at a time [5]. In the initial optimization experiments, powder samples were loaded directly into Terasaki wells containing grease, without any physical modification of the plate (**Fig. 3a**). Although this approach enabled data collection, it imposed several practical limitations. In particular, the sample volume could not be reduced enough, and the loading procedure was not ergonomically convenient. In addition, as also noted in the literature, amorphous binders such as grease or petroleum jelly may reduce data quality by absorbing X-rays and/or increasing background noise [10]. Consistently, the diffraction data collected using the grease-based method showed a well-defined, but relatively weaker, diffuse signal (**Fig. 3b-c**). To address these limitations, an alternative and more effective modification of the Terasaki plate was developed. The bottom of each well was perforated and sealed with Kapton tape (polyimide), a material known for its high X-ray transparency (**Fig. 4a**) [12], [13]. This modification enabled loading powder samples into the wells in very small amounts while preventing sample loss. Polymer films such as Kapton and Mylar are widely recognized as suitable supports in transmission and diffraction experiments because of their low mass absorption coefficients and minimal interference with diffraction signals [12]. In line with these properties, the Kapton-based setup provided a stronger, clearer diffraction signal (**Fig. 4b-c**) than the grease-based method (**Fig. 3b-c**), while also offering a more practical pipeline for rapid, high-throughput PXRD data collection (**Fig. 5-6**).

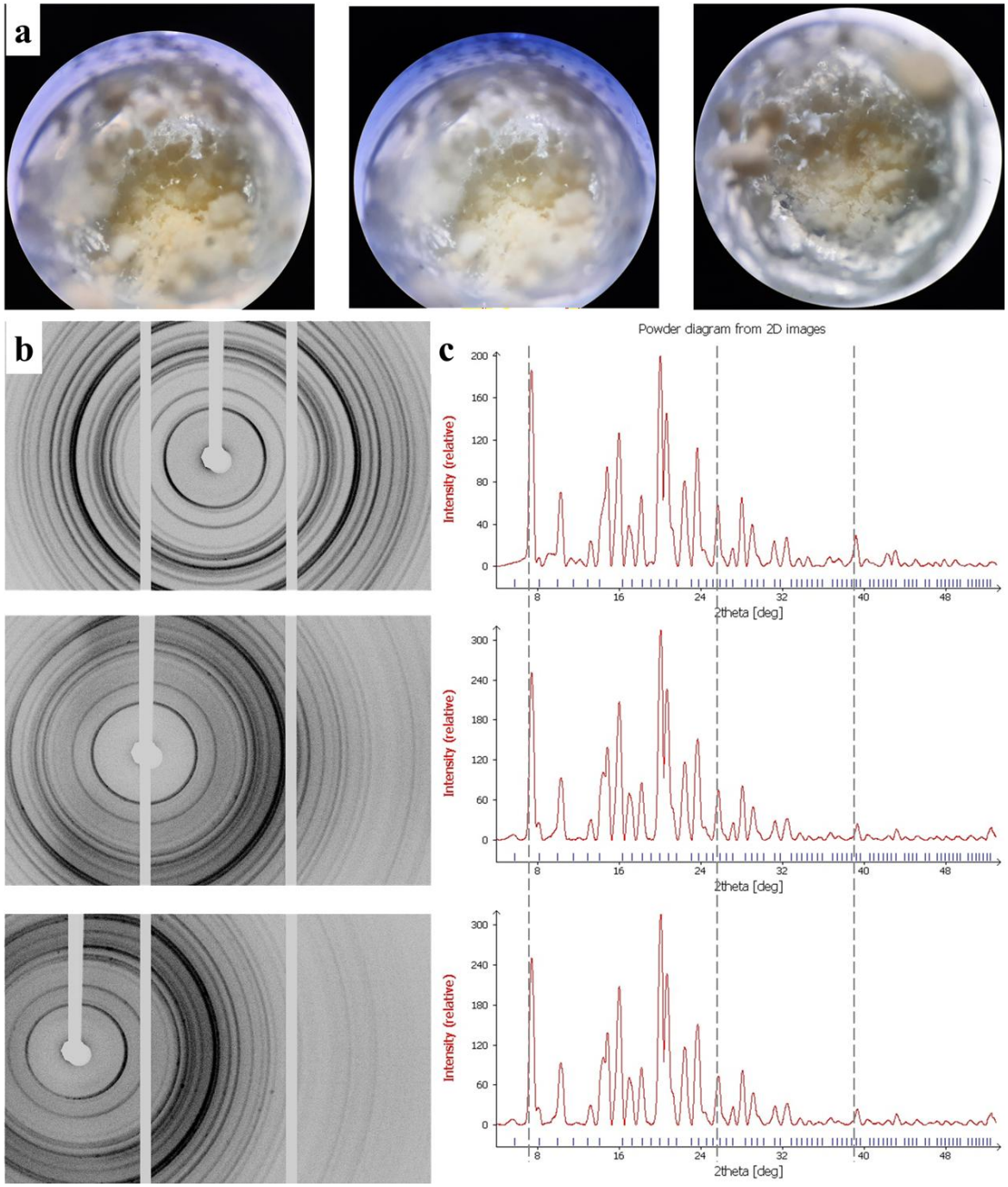


Figure 3. Powder X-ray diffraction data collected from grease-loaded Terasaki wells. (a) Representative optical images of powder samples placed in grease within Terasaki plate wells. (b) 2D diffraction frames obtained from the grease-based sample-loading configuration. (c) Corresponding integrated powder diffraction profiles derived from the 2D images. For batch-mode processing, over 126 frames × 3 replicates were processed.

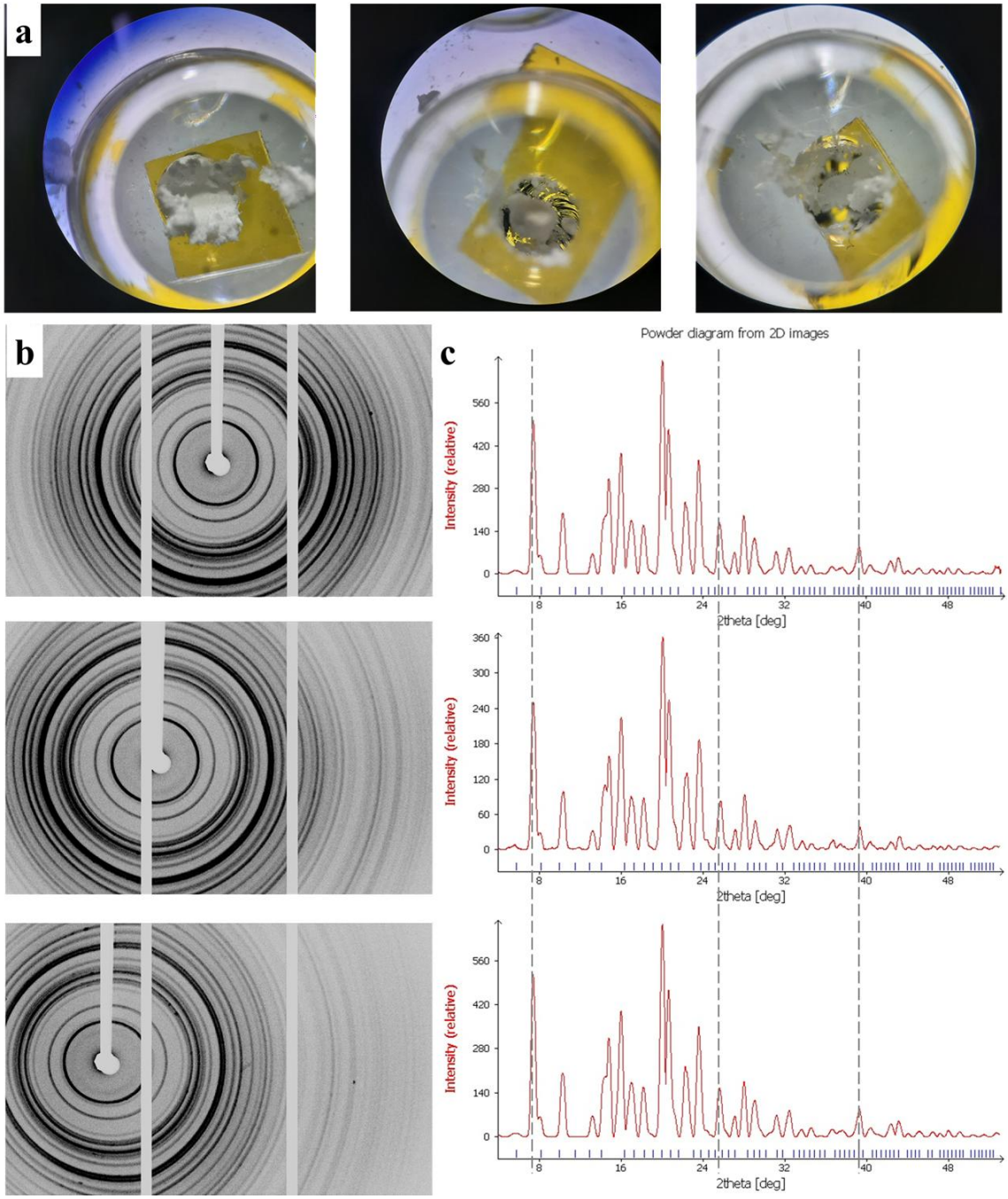


Figure 4. Kapton-Terasaki plate model for powder X-ray data collection. (a) Representative optical images of powder samples loaded into modified Terasaki wells sealed with Kapton tape. (b) Corresponding 2D diffraction images collected from the Kapton-supported powder samples, showing well-defined powder diffraction rings. (c) Integrated 1D powder diffraction patterns generated from the 2D images. For batch-mode processing, over 126 frames × 3 replicates were processed.

Accordingly, once the modified Kapton-Terasaki plate that is loaded with an appropriate amount of powder sample is installed into the 3D-printed plate-holder adapter (**Fig. 5a-d**), the assembly is introduced into the XtalCheck-S module for PXRD data collection (**Fig. 5e**). The parameters were optimized to improve both angular coverage and data-collection efficacy. The detector distance was increased to 100 mm, and the 2θ range was extended from 0 to 126° with a step size of 1.00°. In addition, the omega scans were oscillated with 0.2° increments over the accessible scan range, and the exposure time was reduced to 0.2 s per frame. Representative diffraction images collected at approximately ω = −17°, −1°, and +30° are shown to illustrate the beginning, middle, and end of the oscillation range (**Fig. 5f-h**).

After multi-well data collection, the diffraction frames were reprocessed in CrysAlis^{Pro} (**Fig. 6a**) using the HighScore *.asc output format together with smoothing and baseline-correction options (**Fig. 6b**). This pipeline enabled the collection of 116 frames for each of three independent replicates, followed by merging in batch-mode within CrysAlis^{Pro}. The combination of many frames with replicate-based merging improved particle statistics by increasing the representation of randomly oriented crystallites in the X-ray beam. As a result, the modified Kapton-Terasaki plate provided more robust results (**Fig. 6c$_{i}$**) and an efficient PXRD pipeline (**Fig. 5**) than the grease-based (**Fig. 3** and **Fig. 6c$_{ii}$**) and standard loop-based methods (**Fig. 1** and **Fig. 6c$_{iii}$**), while also being well suited for rapid multi-sample analysis.

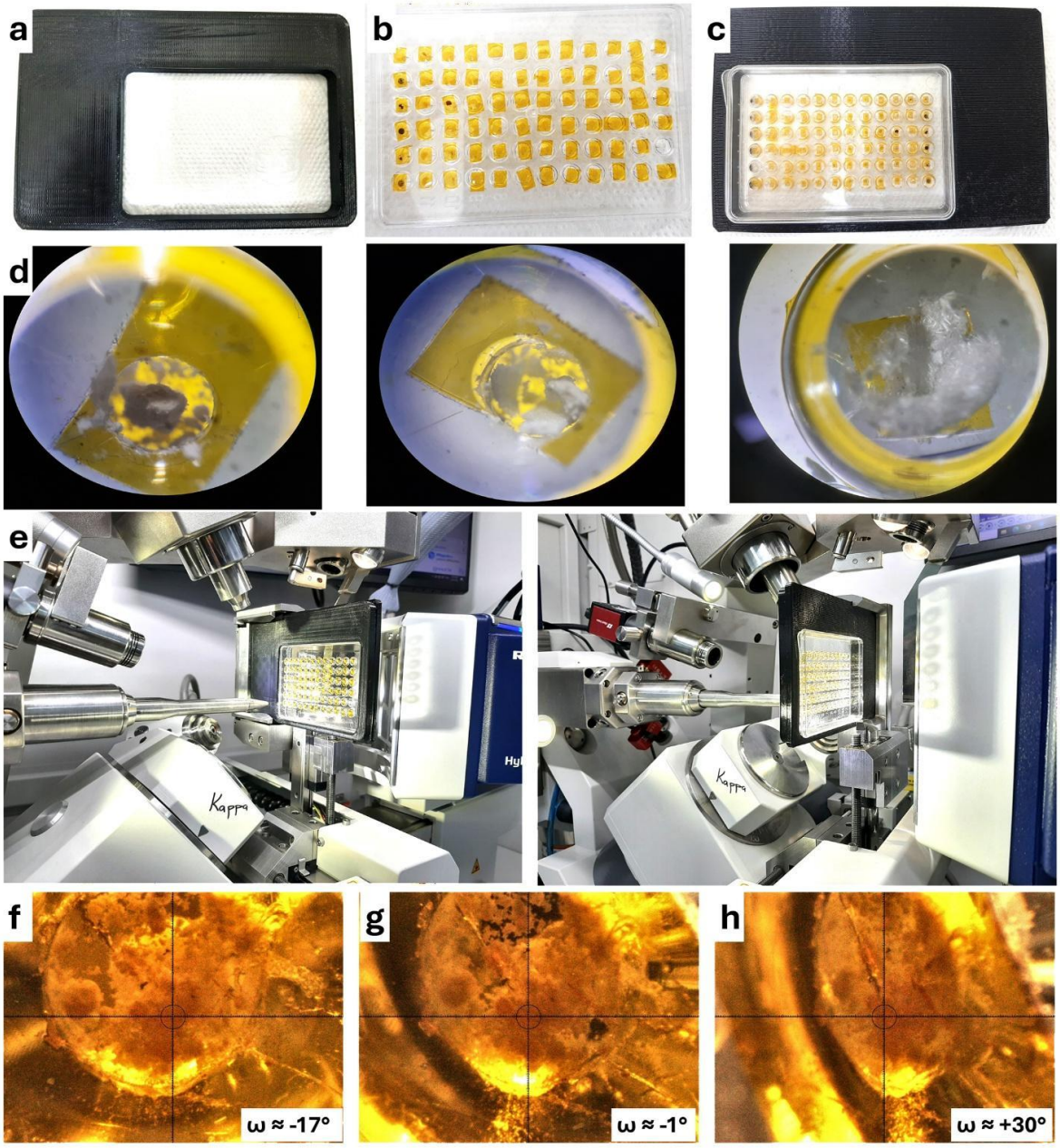


Figure 5. Kapton- Terasaki plate setup for high-throughput PXRD data collection using the XtalCheck-S module. (a) Previously developed 3D-printed plate-holder adapter [5]. (b,c) Modified Terasaki plate prepared for insertion into the adapter and compatible with the plate-holder adapter. (d) Representative powder samples loaded in small amounts onto Kapton-sealed wells. (e) Experimental setup showing the mounted plate–adapter assembly positioned in the XtalCheck-S module for PXRD data collection. (f–h) Representative optical views of the sample at approximately ω = −17°, −1°, and +30°, corresponding to different stages of the ω oscillation during data collection.

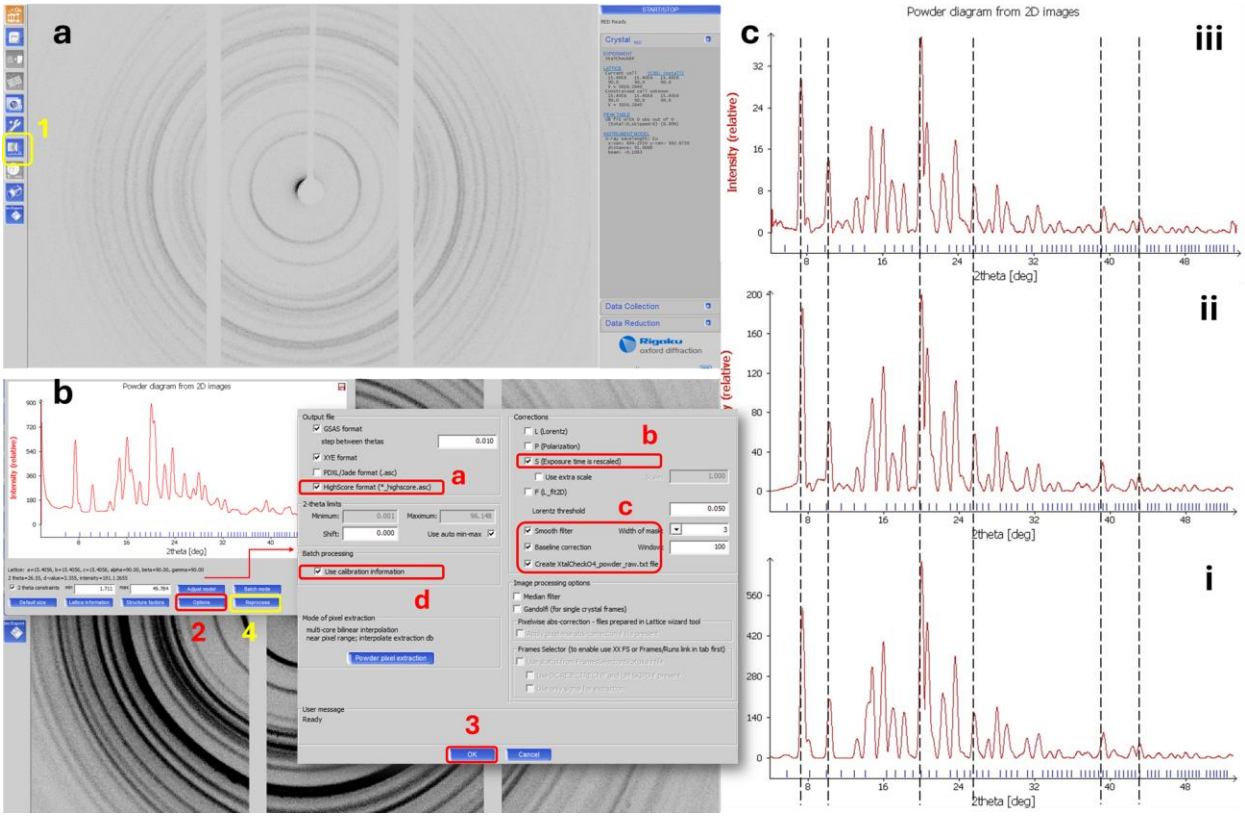


Figure 6. Data processing pipeline in CrysAlis^{Pro} and comparison of powder diffraction profiles obtained using the three sample-loading approaches. (a) Representative 2D diffraction file opened in CrysAlis^{Pro}; the yellow box (#1) indicates the processing/reprocessing command used to initiate data treatment after collection. (b) Export and reprocessing window used to generate the final powder diagram from the 2D images. In this panel, #a indicates selection of the output format as HighScore (*.asc), #b indicates the selection of the exposure-time rescaling correction, #c indicates application of smoothing and baseline-correction settings, and #d indicates the selection of the calibration-information option in the processing settings. The numbered labels highlight the processing sequence: #2, selection of the relevant export/process function; #3, confirmation of the selected settings (for insets a-d; OK); and #4, execution of the reprocessing/export step to produce the final diffraction profile. (c) Comparison of the integrated 1D powder diffraction patterns obtained from the three sample-loading strategies: i, conventional loop-based collection; ii, grease-based Terasaki well collection; and iii, Kapton-based modified Terasaki well collection. The vertical dashed lines mark corresponding peak positions across the three datasets, showing that all methods produced similar diffraction peaks, while the Kapton-based approach yielded the strongest overall intensities (~700 a.u.).

To better separate differences in diffraction quality from possible differences in phase identity, the processed powder profiles were further examined by database-assisted search–match and profile-fitting analyses. Search–match analysis was performed in *Match!4* software using the COD database with organic-phase restrictions. As expected for a newly synthesized organic compound [9], no satisfactory reference phase was identified for the analyte examined in this study (**Fig. 7**). This result is consistent with the fact that the powder sample corresponds to the methoxyphenylpiperazine–oxadiazole derivative reported as compound 3 in the original synthesis study [9] and is therefore not represented by an appropriate reference powder entry in the database used here. Importantly, the absence of a database match did not indicate any inconsistency among the three PXRD datasets (**Fig. 8**). On the contrary, the profiles obtained from the loop-, grease-, and Kapton-based loading approaches showed the same characteristic reflection positions, indicating that all three methods probed the same crystalline material. To compare the quality of the measured profiles more directly, profile-fitting analysis was performed on all three experimental datasets. In each case, the overall diffraction pattern was reproduced well, further supporting phase consistency across the loading strategies. The quality of the fit was evaluated using the profile residual (Rp) [1], defined as $Rp = \frac{\sum|yobs - ycalc|}{\sum yobs} \times 100$ which quantifies the absolute difference between observed and calculated intensities across the diffraction profile [14]. Regarding our analysis, the fitting residuals differed among the methods: the Kapton-based configuration yielded the lowest Rp value (9.6%), followed by the loop-based measurement (12.5%), whereas the grease-based approach gave the highest residual (21.2%). Together with the stronger diffraction signal and lower background contribution observed for the Kapton-Terasaki measurements, these findings indicate that the Kapton-Terasaki setup provides the most reliable representation of the powder sample under the present experimental conditions.

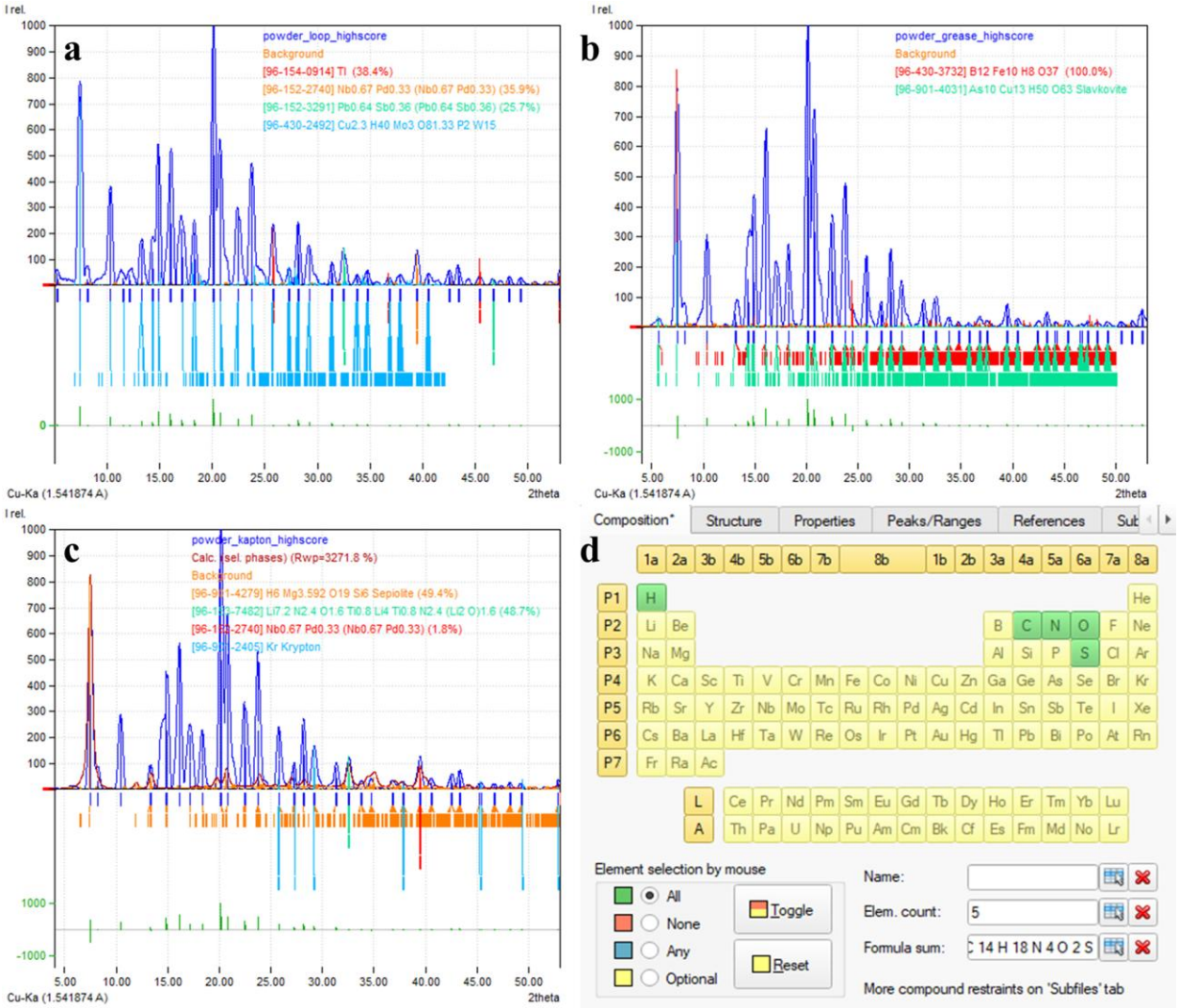


Figure 7. Database-assisted search–match analysis of PXRD data obtained from different sample-loading strategies. (a) Search–match results for the loop-based measurement. (b) Search–match results for the grease-based measurement. (c) Search–match results for the Kapton-Terasaki measurement, showing no satisfactory phase assignment and high mismatch between experimental and calculated patterns. (d) Elemental and compositional parameters applied during the search–match analysis, including selection of organic compounds and specification of the empirical formula (C14H18N4O2S; m/z=307.36, M+1) [9].

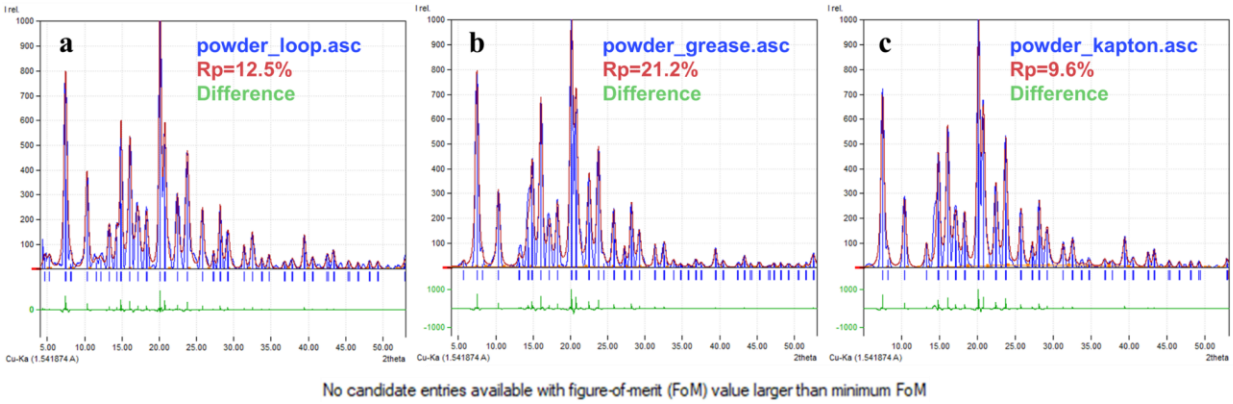


Figure 8. Comparison of powder diffraction profiles obtained using three different sample-loading methods. (a) Loop-based measurement, (b) grease-based loading, and (c) Kapton-Terasaki plate setup. While three methods show no candidate entries available with FoM in *Match! 4*, all yield consistent peak positions, confirming that the same crystalline phase is probed, while differences in profile quality are reflected in the Rp values, with the Kapton-based method providing the lowest residual and best overall fit.

3. Discussion

The present study shows that a single-crystal diffractometer equipped with a plate-reader module [5] can be adapted into a practical platform for powder X-ray diffraction by redesigning the sample-delivery setup rather than modifying the core instrument hardware [4], [5]. The results indicate that data quality was determined not only by detector and scan parameters, but also by the method of introducing the powder into the X-ray beam (**Fig. 1** and **Fig. 5**). This observation is consistent with the orthodox principles of powder diffraction, in which reliable intensity data depend on sufficient particle statistics, enough sampling of randomly oriented crystallites, and the minimization of artifacts arising from specimen geometry, background scattering, and preferred orientation [15]. Accordingly, the traditional loop-based setup provided a useful starting point, but it was intrinsically limited for practical PXRD measurements, since only a very small amount of powder could be mounted, giving disposable measurements alone [10], and only a limited number

of diffraction frames could be collected, whereas many frames should be collected for data merging instead. Therefore, too few crystallites contribute to the diffraction event to achieve a representative powder pattern [15].

The novel method, which moved from the loop-based format to Terasaki-plate-based loading, addressed two practical issues simultaneously: throughput and diffraction accuracy. ***(i)***, the multi-well format enabled serial or batch (up to 72 samples) data collection at a time (using a single Terasaki plate), offering a clear, standardized, and ergonomic setup over repeated manual pin-mounting of individual loop samples (**Fig. 5**). ***(ii)***, the Terasaki enabled evaluation of the powder in different support setups (**Fig. 3** and **Fig. 4**). The grease-containing wells showed that higher powder samples could be measured in plate-reader mode (**Fig. 3**); however, they also revealed an important limitation. Although well diffraction patterns were obtained, they were weaker, less distinct, and noisier due to the plate and grease background. This is a reasonable necessity for a bonding agent setup, as non-crystalline mounting media (such as plate and grease) may increase background and reduce the diffraction clarity [16]. By contrast, the Kapton-supported setup [12], [13] provided a cleaner interface between the powder and the X-ray beam, while also allowing small amounts of powder to be retained more securely in a vertical measurement geometry. In practice, this design improved both handling and data quality (**Fig. 4**).

A particularly important aspect of the Kapton-Terasaki setup is that it improved the statistical representativeness of the powder measurement (**Fig. 6**). Namely, large numbers of frames were collected and merged across necessary and sufficient frame replicates (up to 116 frames x 3 replicates), thereby increasing the effective sampling of crystallites contributing to the final diffraction profile. This is central to powder diffraction methodology [14], [15] because the

observed intensity distribution is strongly influenced by both the number of crystallites determined and their orientation within the beam [10], [14], [15].

Here, the Kapton-Terasaki setup produced a stronger and clearer diffraction pattern, and better overall profile quality and intensity than either the grease-containing or loop-based methods. These findings suggest that the modified Terasaki setups provided a more representative powder specimen under the present experimental conditions. The lower-profile-fitting residual (Fig. 8c; Rp = 9.6%) obtained for the Kapton-adopted data further supports this idea. Thus, the main advantage of the novelty was not simply the generation of a stronger signal, but the collection of more reliable powder diffraction data.

The further search–match and profile-fitting analyses were also important for interpreting the significance of the differences observed among the three loading strategies. No satisfactory database match was obtained for the analyte, which is not unexpected for a newly synthesized organic compound lacking an appropriate reference entry [1], [2], [9], [17] (**Fig.7** and **Fig. 8**). However, the absence of a database match should not be taken to indicate a collapse of the PXRD pipeline. Importantly, the loop-, grease-, and Kapton-Terasaki datasets showed the same characteristic reflection, indicating that all three methods were in the same crystalline phase (**Fig. 6** and **Fig. 8**). Accordingly, search–match analysis primarily defined whether a known reference phase could be assigned, whereas profile fitting provided a more informative basis for comparing how faithfully each sample-delivery method reproduced the experimental diffraction pattern. This gap is momentous because, in method-development studies, alignment in peak positions across loading differs may be more informative than definitive phase identification, particularly when the material under question is novel [1], [15], [17].

Taken together, these results suggest that the modified Kapton-Terasaki setup is more than an alternative sample holder. Rather, it represents an improved PXRD sampling strategy for a laboratory single-crystal diffractometer implemented with a plate-reader module. Its principal advantages include low sample consumption, in line with rapid multi-sample collection, stronger diffraction intensity, and more reliable whole-pattern representation. These features make the method particularly significant for preliminary screening, comparative multi-powder studies at a time, and applications in which innumerable powder samples must be examined within too limited instrument time. Additionally, the method could be considered the best practical screening and data-collection approach rather than a universal substitute for dedicated high-resolution powder diffractometry in Türkiye. As widely recognized in the powder diffraction literature [15], [17], quantitative phase analysis and full structure determination remain sensitive to specimen effects, instrumental geometry, peak overlap, and the availability of suitable reference data. However, here, the Kapton-Terasaki method provides a simple, cost-efficient, and experimentally pragmatic way to extend the PXRD capabilities of an existing in situ crystallography platform.

4. Conclusion

This study demonstrates that the novel sample delivery method can significantly improve powder X-ray diffraction on a laboratory single-crystal diffractometer without requiring modifications to the instrument hardware. Among the tested setups, the Kapton-Terasaki plate provided the most reliable PXRD results, combining low sample consumption, practical handling, compatibility with the XtalCheck-S module, and superior diffraction quality. Compared with both the standard loop/pin-based method and the grease-based Terasaki format, the Kapton-supported method produced higher diffraction intensity, lower background, and a more reliable whole-pattern profile

after batch-mode data processing. These findings indicate that the major challenge in adapting single-crystal-oriented platforms for powder analysis lies in sample delivery as much as in data collection itself. By improving sample delivery, enabling high-throughput multi-well measurements, and enhancing particle statistics through batch-mode, the Kapton-Terasaki method provided the most robust pipeline for the powder sample under the present experimental conditions. Taken together, the results establish this method as a simple, cost-effective, and efficient strategy for extending the PXRD capability of available in-situ crystallography module and support its broader use in rapid laboratory-based powder screening.

Author Contributions

The analyte was synthesized by A.M. The Kapton–Terasaki setup was installed by E.A. and A.K., and data collection, processing, and further analysis were performed by E.A.

Competing interests

The authors declare no competing interests.

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