Application Note

September 2024

Eliminating the Need for Cobalt Anode X-Ray Sources

Stephan X.M. Boerrigter, Triclinic Labs.

The ability to use XRF suppression for iron-containing samples renders the historical reliance on cobalt X-ray sources obsolete. Using XRF reduction detector technology offers a more efficient, cost-effective, and precise method of material characterization. XRF reduction can easily be implemented in a Good Manufacturing Practices (GMP) laboratory, and we have demonstrated the robustness of this approach across multiple detectors on different instruments. Therefore, the approach facilitates the development of methods and the release testing of iron-containing pharmaceutical ingredients and drug products.

Keywords: *Powder X-ray Diffraction, Cobalt Anode, Copper Anode, X-ray Fluorescence suppression, Iron-containing pharmaceuticals*

Triclinic Labs

Chemical Development and Analysis Expertise

2660 Schuyler Ave, Suite A, Lafayette, IN 47905 USA
+1.765.588.6200 *www.tricliniclabs.com*

Introduction

In traditional X-ray diffraction (XRD) analysis, cobalt (Co) anode X-ray sources have been used for analyzing iron-containing samples, as copper (Cu) sources induce fluorescence. This fluorescence significantly increases the background signal and reduces the limit of detection (LOD), making accurate analysis difficult. However, more modern technology such as the latest generation Rigaku SmartLab HyPix Detectors (SLHPD)[1], have demonstrated that cobalt sources are no longer required for iron-containing samples.

Background: The Challenge with Copper Sources

Copper-anode X-ray sources are most commonly used in XRD analysis because Cu offers a good tradeoff between the wavelength of the X-ray radiation it produces, the stability of the anode material, its heat conductivity, and cost. However, when it comes to iron-containing samples, using Cu sources introduces background fluorescence due to the iron's interaction with the Cu Kα X-rays. This fluorescence contaminates the diffraction pattern with non-elastic scattering, making it harder to resolve important features such as the Bragg peaks produced the crystalline analytes. The traditional solution has been to switch to a cobalt source, which does not induce this fluorescence, but this comes with significant downsides: cobalt X-ray tubes are expensive and swapping out X-ray tubes requires the entire instrument to be re-calibrated and therefore causes extensive labor and instrument downtime. The tubes are also labile and have a limited shelf life when being stored, so occasional use of a Co source is not viable.

New Solution: XRF Reduction Detector Technology

Modern X-ray detectors, such as the SLHPD, have a tunable energy range over which X-ray photons are collected. Photons produced due to X-ray fluorescence (XRF) are a form of so-called non-elastic scattering. This means that the energy of the photons is slightly lower than the energy of the photons produced by the X-ray source. By tuning the detection window to the energy close to the incident radiation, the detector effectively ignores the XRF signal. This mode therefore effectively mitigates the fluorescence problem without the need for cobalt sources (Figure 1). In addition to the XRF signal, the SLHPD detector other sources of non-elastic scattering are also eliminated. This significantly reduces the background noise in the XRD pattern and enhances the signal-to-noise ratio.

As demonstrated in testing, iron-containing samples such as ferric oxide (Fe_2O_3) produce nearly zero-background diffraction patterns when analyzed using the SLHPD detector's XRF reduction mode. In a comparative study, data was collected using both standard detector settings and with the XRF suppression feature enabled.

The results showed a remarkable reduction in background noise when the suppression feature was activated. While the total counts for the Bragg peaks were lower due to the narrow energy range, the reduction in random noise resulted in a net improvement in signal clarity, as shown in Figure 2, where the same data are plotted after scaling to a common maximum intensity. The overlay in Figure 2 demonstrates clearly that, for the same intensity of the Bragg peaks, the level of noise is significantly lower using the XRF mode.

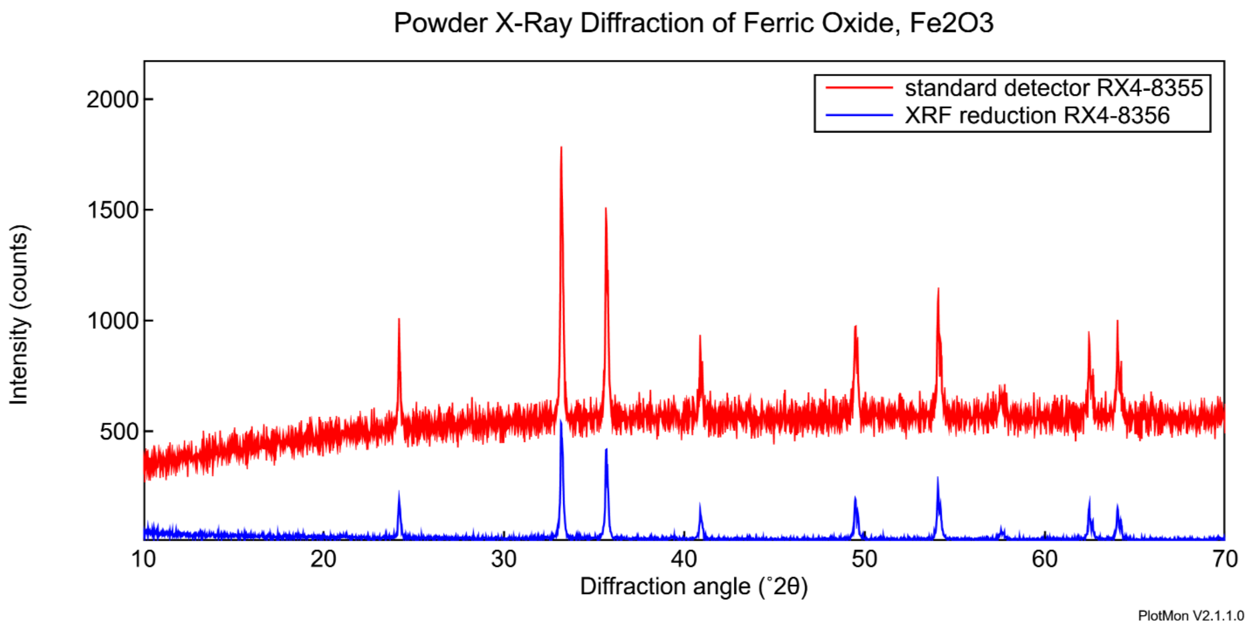

Figure 1. PXRD of Ferric Oxide, Fe_2O_3, when analyzed using the standard detector settings (red). The blue pattern shows the pattern when collected with the XRF suppression feature turned on.

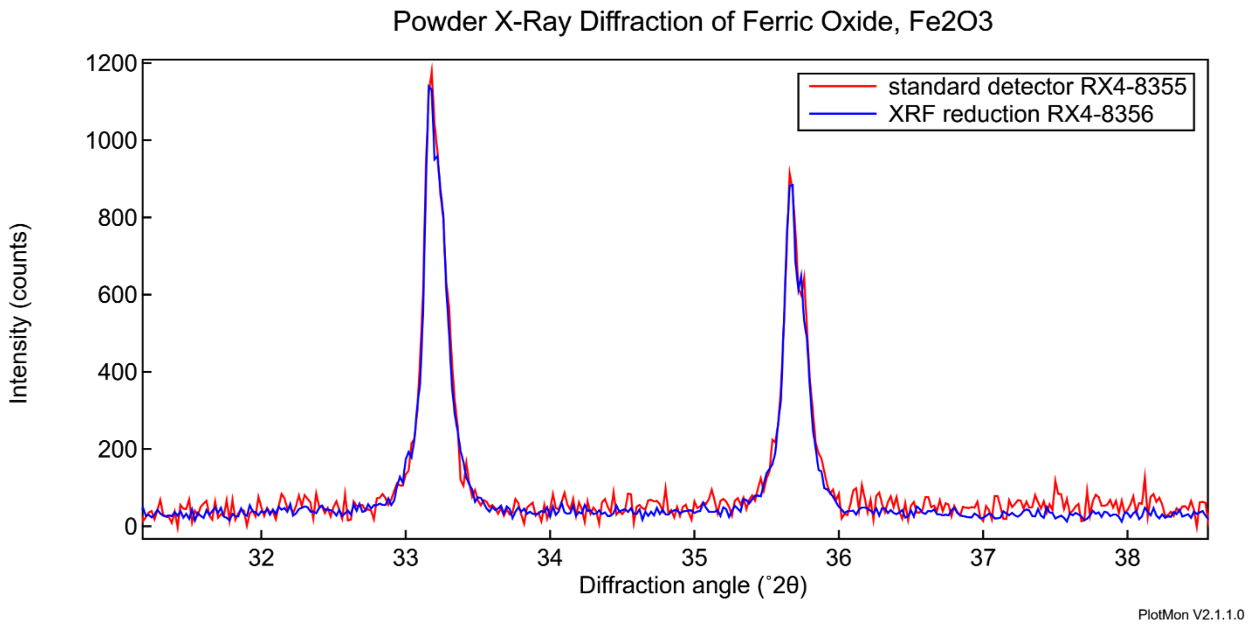

Figure 2. The standard detector mode data (red) has been scaled down to match the intensity of the XRF data. In overlay, it is clear that the noise level is lower using XRF filtering. Thus, the XRF reduction mode improves the signal-to-noise ratio.

Implications for Cobalt Source Usage:

This advancement suggests that the need for cobalt X-ray sources can be eliminated in many cases, particularly when working with iron-containing materials. The benefits include:

- **Cost Reduction**: Eliminating the need for expensive cobalt tubes.
- **Operational Efficiency**: Reducing downtime and labor associated with swapping X-ray tubes for iron-containing samples.
- **Improved Detection Limits**: Enhanced signal-to-noise ratios even when using Cu sources, allowing for better detection of weak features in diffraction patterns.

Practical Considerations

XRF reduction can be particularly beneficial in environments where cost and efficiency are crucial, such as pharmaceutical and materials science labs. XRF reduction can easily be implemented in a Good Manufacturing Practices (GMP) environment laboratory and we have demonstrated the robustness of this approach across multiple diffractometers. Therefore, it facilitates the release testing of iron-containing pharmaceutical ingredients and drug products. The ease of testing and implementing this feature on GMP instruments makes it a scalable solution for industry-wide adoption.

Conclusion

The ability to use XRF suppression for iron-containing samples renders the historical reliance on cobalt X-ray sources obsolete. Using XRF reduction detector technology offers a more efficient, cost-effective, and precise method of material characterization.

Contact Information :

Triclinic Labs, Inc,
2660 Schuyler Ave., Suite A
Lafayette IN 47905
USA
TriclinicLabs.com
rfi@triclinicabs.com

