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Streamlining Identification of Compounds in Pharmaceutical Drug Products

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Identifying compounds in pharmaceutical tablets is important for a variety of reasons in a regulated industry. Factors such as drug quality, drug purity, identification of degradants and distribution of materials assure the highest quality of finished drug products. The nature of the active pharmaceutical ingredients (APIs) and excipients in tablet form makes x-ray microanalysis challenging due to electron beam conditions and sample sensitivity to the electron beam, potential for sample damage, and beam spread within the matrix of the material. While techniques such as x-ray phase mapping have been successfully used for compound identification [1], there are limitations due to electron beam interaction with surrounding material. Low kV microanalysis has further been used to optimize collection, limiting the area of analysis to smaller spatial resolution which more distinctly identifies compounds [2]. Yet there are still challenges associated with using this method because it is more difficult to accurately quantify the elements present in the material.

This work shows how the spectrum library matching software method facilitates compound identification and matching in pharmaceutical drug products. A library is built from x-ray spectra of known or previously identified compounds; this reference library is then used as a basis for comparison for unknown compound spectra. The method for compound matching is full spectrum energy peak intensity fitting, which removes the dependence on an accurate quantitative analysis which can be challenging for the above identified reasons.

In the example used here, data is collected from a multivitamin in tablet form. First, several spectra from unique areas in the electron image are collected, the major elements are identified and the spectrum is labelled. Each spectrum is then entered into the spectrum library, as seen in Figure 1 showing Calcium Phosphate, Magnesium Oxide and Potassium Chloride. Phase mapping of a different area of the sample is then performed to highlight the presence of various phases, or multi-element compounds, with a unique color display. The phase spectra, which are considered unknown materials, are then compared to the match library which provides a conclusive match, with a fit percentage, as compared to the previously identified compounds, Figure 2.

The benefits of the spectrum matching method are well suited for regulated industry for several reasons. First, the process follows the documented collection of identified materials to build a reference library and then uses this as the basis for comparison of future materials. Next, the software routine displays a match fit percentage, which removes the need for the analyst to make subjective conclusions, and does not depend upon interpretation of the data by an analyst. Finally, it is a simple software procedure that is well suited for novice analysts who can perform the method and provide documented, substantiated results.

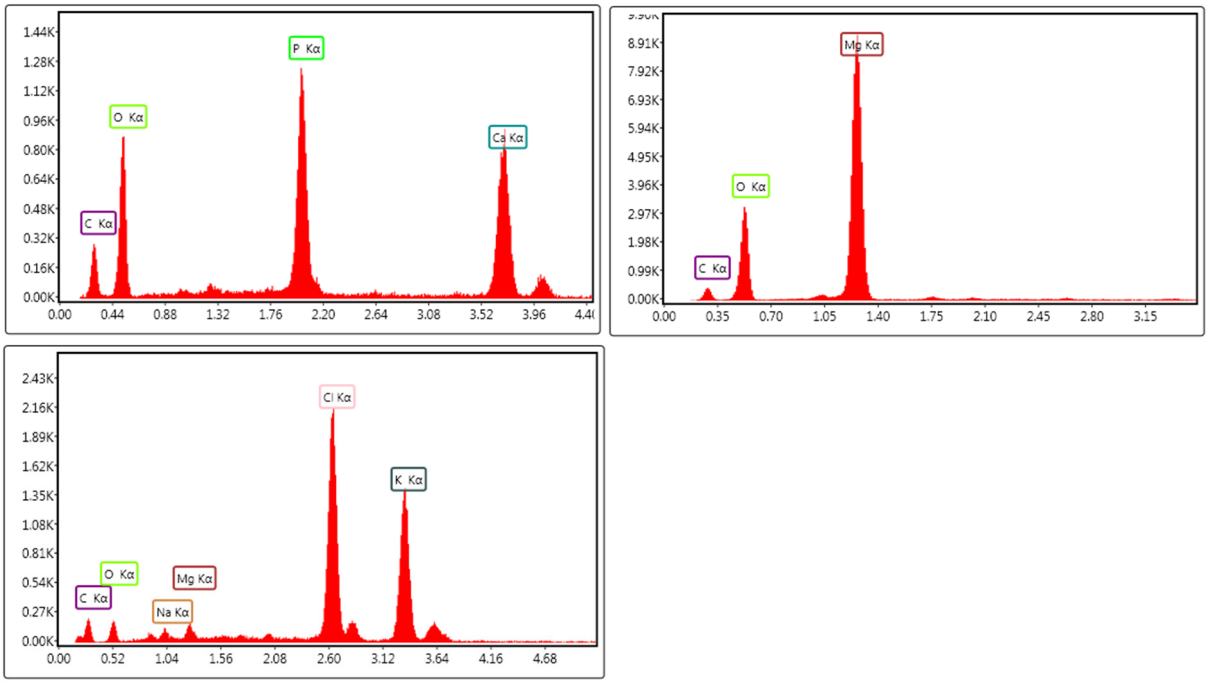

Figure 1 shows Calcium Phosphate, Magnesium Oxide and Potassium Chloride compounds from the tablet which were used to create the multivitamin spectrum library.

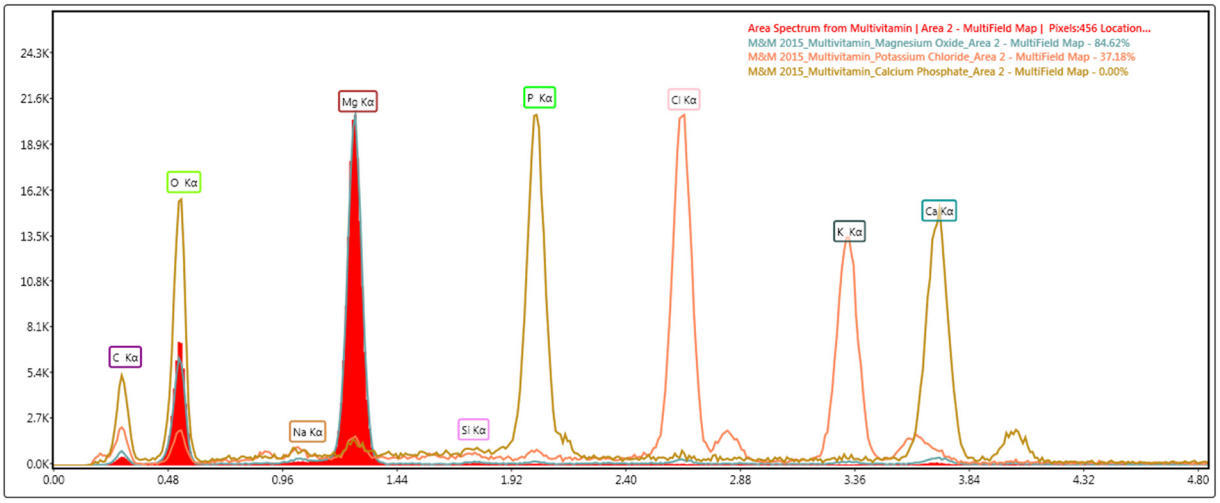

Figure 2 shows a spectrum extracted from the phase map (red) as matched to the library. An 85% fit match confirms it matches Magnesium Oxide.

[1] Anderhalt *et al*, Microscopy & Microanalysis Proceedings (2010).
[2] Nylese *et al*, Microscopy & Microanalysis Proceedings (2013).

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