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Detection of APIs in Pharmaceutical formulations using ARL X'TRA Companion X-ray Diffractometer

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Introduction

X-ray diffraction (XRD) is a powerful analytical technique widely used in the pharmaceutical industry for the identification and characterization of active pharmaceutical ingredients (APIs) and excipients such as hydroxypropyl methylcellulose (HPMC) and other diluents. XRD provides detailed information about the crystalline structure, phase composition, and purity of materials, which are critical for ensuring the quality and efficacy of pharmaceutical products. By analyzing the diffraction patterns produced when X-rays interact with the crystalline lattice of a substance, XRD enables the precise identification of chemical compounds and polymorphic forms. This is crucial for APIs, whose therapeutic effectiveness can be influenced by their crystalline form. Additionally, XRD helps in evaluating the compatibility and stability of excipients like HPMC, which are used to control drug release and enhance product performance. The ability to detect low levels of APIs within excipients ensures that the final product meets stringent quality standards. Overall, XRD is an essential tool in the pharmaceutical industry for quality control, formulation development, and regulatory compliance.

Instrument & software

The Thermo Scientific™ ARL™ X'TRA Companion X-ray Diffractometer (c.f. Figure 1) is a simple, easy-to-use benchtop XRD instrument for routine phase analysis as well as more advanced applications. The ARL X'TRA Companion XRD uses a θ/θ goniometer (160 mm radius) in Bragg-Brentano geometry coupled with a 600 W X-ray source (Cu or Co). The radial and axial collimation of the beam is controlled by divergence and Soller slits, while air scattering is reduced by a variable beam knife. An integrated water chiller is available on demand. Thanks to the innovative solid state pixel detector (55 x 55 µm pitch), the ARL X'TRA Companion XRD provides very fast data collection and comes with one-click Rietveld quantification capabilities and automated result transmission to a LIMS (laboratory information management system).

Figure 1: ARL X'TRA Companion X-ray diffraction system.

Experimental

A HPMC pure sample and mixtures of the latter with 5 wt.% and 1 wt.% resveratrol (3,5,4'-trihydroxy-trans-stilbene) were measured using a zero-background sample holder (30 minutes) in reflection mode using Cu Kα (1.541874 Å) radiation with sample spinning (c.f. Figures 2). Profex [1] software and COD (crystallography open database) were used to compare the data with theoretical peak positions. [2] The HPMC/resveratrol system acts as a good test case also for other potential formulations to determine a general estimate of the LoD (limit of detection).

Results & Discussion

By comparing the data to the theoretical XRD peak positions of resveratrol (Figure 2) it is possible to identify this compound in mixtures down to 1 wt.% fraction. This allows to identify low levels of API as well as contaminations with polymorphs or unwanted materials. From a linear regression the LoD was calculated (3*standard error of estimate) to 0.2 wt.% for this specific experiment.

Your Benefits

The ARL X'TRA Companion XRD yields data perfectly suited to identify APIs in mixtures with excipients like HPMC down to at least a LoD of 0.2 wt.%, which is required to control the quality of pharmaceutical formulations. This ensures compliance with stringent quality standards and supports the development of effective pharmaceutical products.

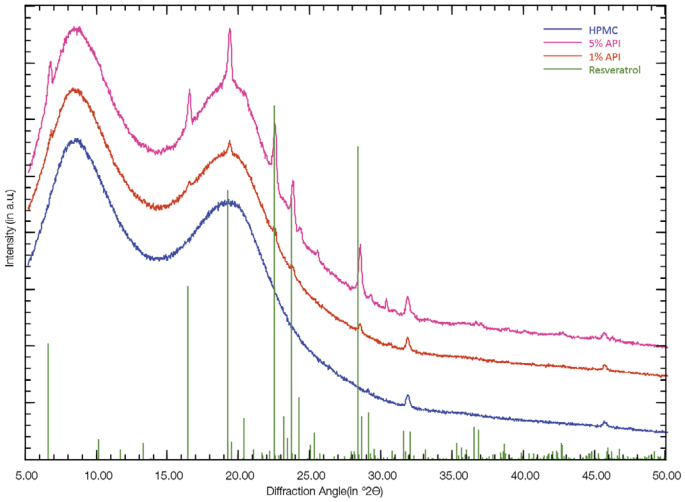

Figure 2: XRD pattern (30 min) of 100 % HPMC (blue) and mixtures of HPMC with 5 % (pink) and 1 % (orange) resveratrol compared to theoretical peak positions of resveratrol (green lines).

[1] N. Döbelin, R. Kleeberg, J. Appl. Crystallogr. **2015**, 48, 1573-1580.

[2] F. Caruso, J. Tanski, A. Villegas-Estrada, M. Rossi, J. Agric. Food Chem. **2004**, 52, 7279-7285.

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