

IonicX Portable XRF Analyzer Device and Algorithm

A detailed look into the algorithm used to authenticate ionic salts

The Thermo Scientific™ IonicX™ Portable XRF Analyzer utilizes XRF (X-ray Fluorescence) spectroscopy. The IonicX Portable XRF Analyzer is based on Energy-Dispersive XRF, so called ED-XRF. The basic elements of XRF spectrometer systems are a radiation source, a sample, and an X-ray detector. The analysis relies on the interaction of radiation source output (an X-ray tube) with a sample, in this case, the cup of ionic salt material, such as Sodium Chloride, Potassium Chloride, etc. The XRF system can characterize materials, due to the fundamental principle that each element has a unique atomic structure, which in turn has a unique set of peaks (or bands) in its emission spectrum. The energy dispersive X-ray detector separates (disperses) the detected radiation emitted from the sample by energy, thus providing a spectrum from which the different elements present in the sample can be identified and/or quantified.

Principles of XRF

To stimulate the emission of X-rays from a sample, a beam of high energy photons (X-rays), is focused on the sample. At rest, an atom within the sample contains ground state (or unexcited) electrons in discrete energy levels, or electron shells, bound to the nucleus. The incident beam may excite an electron in an inner shell (primarily K & L shells), ejecting it from the shell while creating an electron-hole where the electron was located. An electron from an outer shell, the higher-energy shell, then quickly fills the hole. The difference in energy between the higher-energy shell and the lower energy shell may be released in the form of an X-ray (photon) of that energy. The number and energy of the X-rays emitted from a specimen can be measured by an energy-dispersive XRF spectrometer.

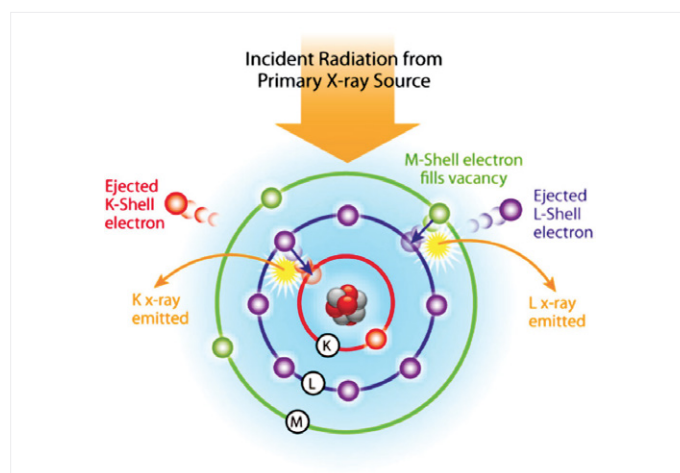


Figure 1. Stimulation of characteristic XRF emission lines.

X-ray tube emission spectrum

Arising from an X-ray tube source, electrons with high kinetic energy (typically 10-50 KV) strike atoms in the X-ray tube source target (typically Rh or Ag) and transfer energy.

The interaction of X-ray source photons with the X-ray tube target generates several features of the X-ray tube's emission spectrum, including:

Bremsstrahlung — meaning braking radiation, is produced by the deceleration of charged particles (including electrons), when deflected by other charged particles. The moving particle loses kinetic energy, which is converted to radiation (photons). Bremsstrahlung has a continuous (broad) spectrum, which has a peak intensity that shifts towards higher energies as the energies of the charged particle increase.

Characteristic radiation — is produced by the interaction of energetic electrons with the inner shell electrons of the atoms that make up the X-ray tube target. Once an inner shell electron is ejected from an atom, an electron from a higher shell fills the inner shell vacancy, and the difference in the shell binding energies propels the emission of a photon (X-ray) of that energy. Characteristic radiation is emitted in discrete energies that are specific to the elements present in the X-ray tube target. If the tube target is Ag and the tube voltage is sufficiently high, then the characteristic radiation emitted from the tube will include the Ag-Ka1 (22.16 KeV), Ag-Ka2 (21.99 KeV), Ag-Kb1 (24.94 KeV), Ag-La1 (2.98 KeV), and Ag-Lb1 (3.15 KeV) X-rays, among others.

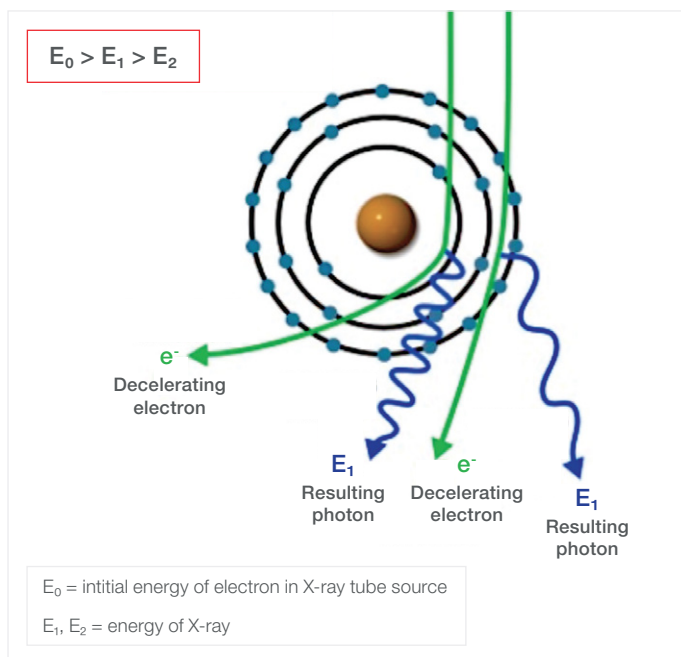


Figure 2. Mechanisms for the production of scattered radiation.

Understanding the XRF spectrum

The XRF spectrum comprises several components of radiation that return to the detector from the sample. These components include X-rays emitted from the X-ray tube (continuous spectrum and characteristic lines) which have been scattered by the sample, and fluorescence X-rays (discrete energies) emitted from the sample atoms upon exposure of the sample to the X-ray tube emissions.

Fluorescence X-rays provide unambiguous evidence that a chemical element is present, since every element has a unique pattern of X-ray fluorescence emission. But not all chemical elements produce fluorescence X-rays that can be detected by a handheld XRF instrument. In general, handheld XRF devices cannot detect X-rays with energies below 1 KeV, which excludes fluorescence from the lightest elements, those having atomic numbers 1 through 10 (hydrogen through neon). Even so, the presence of very light elements can often be observed indirectly through the scatter spectrum.

The scatter X-rays are incident X-rays that have come from the tube and have been scattered by the sample by two main mechanisms: coherent (or Rayleigh) scatter, and incoherent (or Compton) scatter.

Coherent scatter, scatter from a whole atom or a group of atoms, results a change in the direction of the X-ray's travel, but no change in the X-ray's energy. The coherent portion of the scatter spectrum essentially mirrors the incident spectrum; it contains the same discrete (characteristic) lines and the same broad continuum. Coherent scatter from heavy elements tends to be more intense than coherent scatter from light elements.

Incoherent scatter, scatter from a free or loosely bound (outer shell) electron, causes the transfer of a relatively small portion of the X-ray's energy to the electron, so the incident X-ray's energy is shifted (slightly) toward lower energy. The incoherent portion of the scatter spectrum similarly mirrors the incident spectrum, except it is shifted somewhat toward the left (lower energies). The incoherently scattered tube characteristic lines therefore appear at slightly lower energies. For example, an Ag-target X-ray tube's Ag-La1 characteristic line (22.16 KeV) shows up in the incoherent portion of the scattered spectrum at around 20.6 KeV. The incoherently scattered characteristic lines are often noticeably broadened. Incoherent scatter from light elements tends to be more intense than incoherent scatter from heavy elements.

The ratio of coherent scatter to incoherent scatter (from the scattered characteristic lines) can be used as a rough indicator of the average atomic number of a material, which can aid in the identification of materials that may contain elements too light to produce detectable fluorescence peaks.

A special case of coherent scatter is called X-ray diffraction (XRD). In XRD, X-rays are reflected from the atomic planes of a crystalline lattice provided that the Bragg condition (which is related to lattice spacing, angle of reflection, and X-ray wavelength) is satisfied. Due to XRD, specific discrete wavelengths (energies) can be selectively reflected to the detector from a continuum of incident X-ray energies. XRD is particularly strong at lower X-ray energies, below 10 KeV, say. To emphasize diffraction, relatively low tube voltage (15-20 KV, say) is paired with minimal tube filtering. Discrete diffraction peaks can be used to identify ionic salts even if no fluorescence peaks can be detected.

An example XRF spectrum

Plotted below in figure 3 is a main filter spectrum of Potassium Chloride (KCl). The tube voltage is 45 KV and the tube target is Ag. The spectrum has several X-ray fluorescence bands associated with Potassium (K) and Chlorine (Cl) lines at low energy. At around 20-25 KeV various lines from the tube internal elements can be seen. These lines are the tube's characteristic radiation (Ag-K lines) scattered by the sample. In the 18-45 KeV range, a broad spectral response is observed. This response results from the sample's scatter of the tube's bremsstrahlung emission. The relatively small peaks near 4.5 KeV, 11.9 KeV, and 13.3 KeV may be due to trace concentrations of Ti and Br in the sample.

Algorithm

Handheld XRF devices may not be able to identify certain compounds in a sample due to some, or all, of the elemental constituents lacking detectable characteristic X-ray fluorescence spectral features in response to the X-ray source in a portable device. A need therefore existed for a portable device that can identify certain compounds in a sample where primary X-ray fluorescence spectral features of constituent elements are not distinguishable or discernible.

Handheld X-ray fluorescence devices excite one or more elements of a test compound, such as magnesium or higher atomic mass, that can be detected based on characteristic fluorescence peaks generated in response to X-rays to identify or quantify a test compound being analyzed.

The test compound can include one or more elements that do not exhibit a detectable or distinguishable fluorescence peak at the first voltage level/filter configuration, such as elements having an atomic mass lower than magnesium, and so a positive identification of the test compound cannot be determined based on the primary elemental spectral fluorescence peaks alone.

However, the fluorescence peaks obtained at the first voltage level can be used to identify possible identities of the test compound from within a library of compounds by selecting a subset of library compounds with the same elements identified by the fluorescence peaks. A second spectrum of the test compound is obtained using X-rays at a higher voltage level/filter configuration. The second spectrum is matched to a reference spectrum of a compound within the subset of library compounds to identify the test compound. Reference spectra at the higher voltage level are obtained for a series of compounds to form a library of reference spectra to be compared with test spectra at the higher voltage level.

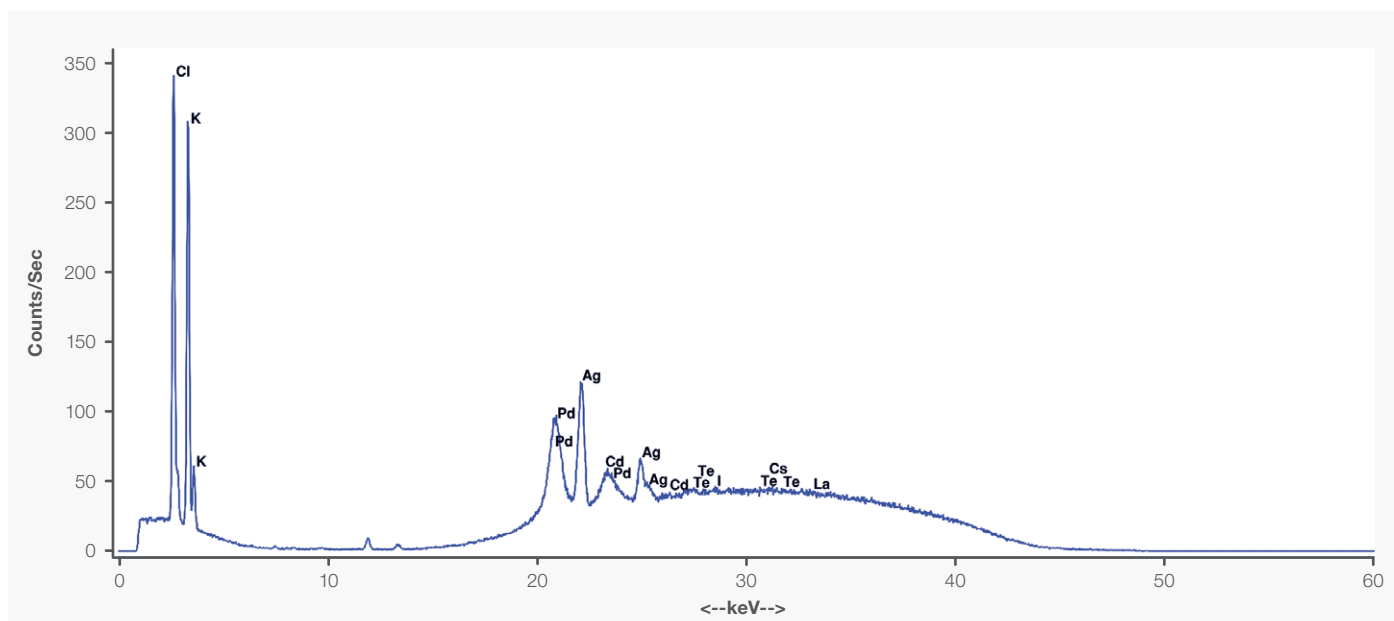


Figure 3. XRF spectrum of KCl sample.

A least squares slope and intercept may be calculated comparing one or more spectrum/spectra in the library with the scan (spectrum obtained from the sample) being analyzed. A perfectly matched sample spectrum to a library spectrum will have a slope of 1.0 and an intercept of 0. For example, a correlation score (C-Val) is calculated for each potential match using the square roots sum of squares for slope and intercept according to $C\text{-Val} = 1.0 - \sqrt{(\text{slope}^2 + \text{offset}^2)}$.

Each spectrum from the evaluation set is iteratively compared using a linear fitting model to each spectrum from the training set. The first set of preconfigured irradiation parameters is particularly advantageous for the detection of fluorescence lines of elements that include K, Cl, Mg, Ca or S. Such elements are low Z (or light elements) elements where characteristic L lines can be seen with the IonicX device.

The current IonicX Portable XRF Analyzer algorithm supports the verification of five different chemicals, NaCl, KCl, MgCl₂, CaCl₂ and NaOH. During the development and testing of the IonicX device and software, it has shown excellent selectivity when challenging the device with those chemicals and associated methods. Figure 4 indicates the c-values for the five methods vs. five chemicals (challenges). When those methods are selected and challenged, a user can expect one of two clear unambiguous results, as shown in figure 5, a pass (i.e. c-value ≥0.7) or a fail (i.e. c-value <0.7).

Summary

The IonicX Portable XRF Analyzer is a powerful addition for the verification of ionic salt type chemicals, utilizing XRF technology in a versatile, easy to use, small form factor. IonicX provides clear, easy to understand, unambiguous results and tools to assist with compliance and data integrity. IonicX is a robust verification tool which allows pharmaceutical companies to more efficiently verify incoming chemicals that typically have been tested using wet-chemistry techniques.

Methods					
XL501122	C-Values				
Challenges	NaCl	KCl	MgCl ₂	CaCl ₂	NaOH
NaCl	0.94	0	0	0	0
KCl	0	0.96	0	0	0
MgCl ₂	0	0	0.91	0	0
CaCl ₂	0	0	0	0.83	0
NaOH	0	0	0	0	0.88

Figure 4. C-values.

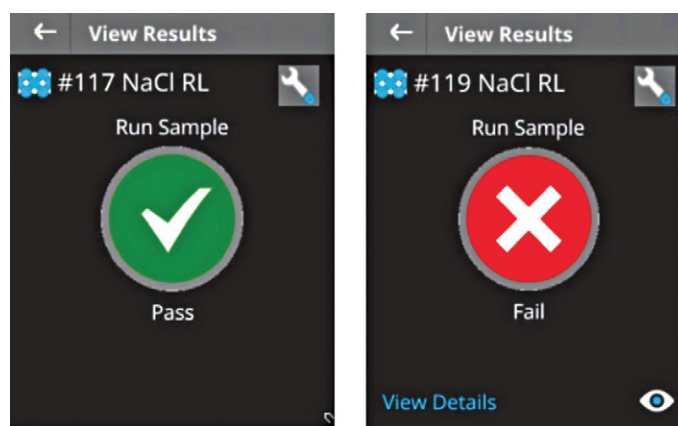


Figure 5. Results.

Learn more at thermofisher.com/qaqcsolutions or email us at mcspharma@thermofisher.com