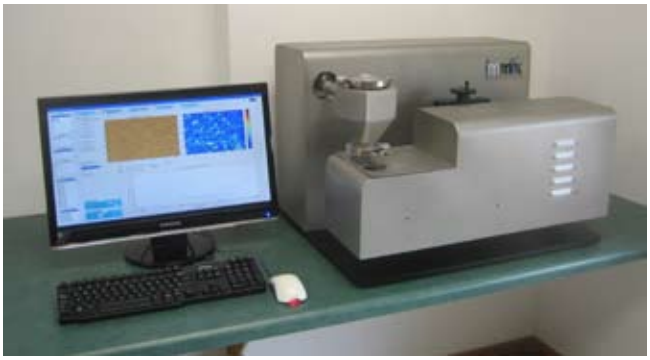
middleton research

imMix™ MICROMIXING IMAGER

PRODUCT SHEET
MRC-920-060

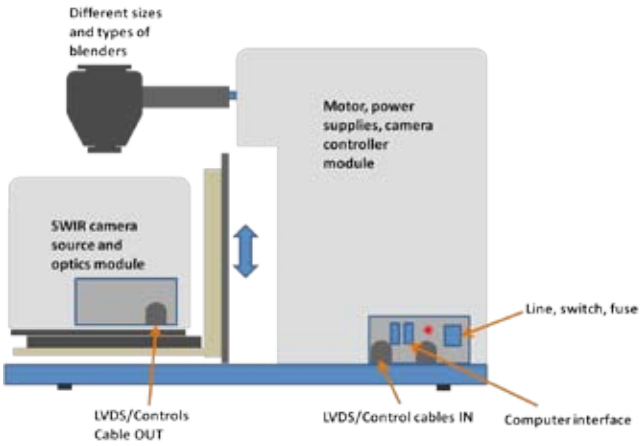
imMix™ Micromixing Hyperspectral Imager*



Background

Micromixing is a process in which ingredient particles rearrange to form a blend. Development of pharmaceutical formulations requires understanding how the ingredients blend with each other and how the blending progresses through different stages. It is also important to establish in a scientific manner when the blending is considered complete, establishing the margins of blending performance, so that in production the blending is complete before the blending process stops.

In order to achieve optimal blending, the micromixing process must be studied to determine mixing parameters such as blending time, blending speed, type and size of blender. When blending is performed too long, overblending may occur, with particles re-aggregating, resulting in segregation of the previously ideal blend.



Features and Benefits

- Understand micromixing of particles during blending
- Study the effect of rotation speed
- Study the effect of different sizes and types of blenders
- Study the effect of blending time
- Study the effects of different excipients and ratios of excipients
- Shorten formulation development time
- Hyperspectral measurements at all or selected rotations
- Automated data collection
- No calibration set required
- Automated prediction of all ingredients
- Integrated image analysis routines
- Micromixing parameters calculated for all blender rotations

Formulation scientists and technologists need tools to select ingredients for new formulations. Tablets contain multiple ingredients beyond the active pharmaceutical ingredients (API) such as fillers, tableting agents, disintegrants, and absorption enhancers or agents that slow down and control absorption. Choice of materials is important to assure the flow characteristics, potency and absorption of specific formulations. In addition, proper particle size grades of the ingredients must be selected to produce an optimum blend for capsule filling.

In order to study the rate and uniformity of blending, destructive analytical methods, such as dissolution followed by chromatographic separation and detection are often used. These methods require samples to be pulled from the blend, followed by time consuming laboratory analysis. In production, such analysis delays may lengthen time required for production formulation development.

Near-infrared hyperspectral imaging can show the distribution of ingredients in pharmaceutical tablets. In addition to laboratory analysis, imaging of near line pull-samples has been used to indicate whether the mixing endpoint has been achieved. However, such measurements were performed once blending was completed, and therefore, did not yield information about the progression of micromixing during the blending process.

imMix™ Concept

The imMix system is a hyperspectral imaging tool that can be used to optimize the blending process. Hyperspectral data is collected through an optical window on the blender, and composition maps (spatial dispersion) are created of all of the blend ingredients throughout the blending process. The very large amount of imaging data is condensed to a limited number of useful micromixing parameters.

* Patent pending

imMix System Components

The imMix system consists of a push-broom SWIR hyperspectral camera, which is positioned to view the blend inside the rotating blender. The blender is rotated by a computer-controlled motor, and the camera is programmed to scan the blender window on all or certain specified rotations. The camera is protected in a stainless steel housing; the motor, power supply, and camera controller and other electronics are housed in another stainless steel module. The imMix is compatible with different sizes and different types of blenders. The camera position is adjustable to adapt to different blenders. To empty the blender, the camera module can be easily moved away from the blender. Additional accessories include: a white reference for background measurements and devices to establish proper focus and measure pure components or smaller quantities of materials without filling the blender.

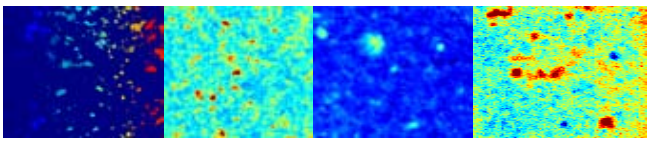
The imMix comes complete with software to control data collection and analyze the images afterward. The data collection software allows the user to:

- view live camera data
- store white and dark references
- adjust camera settings such as exposure time and frame rate
- adjust blend speed
- select measurement resolution
- specify which blend rotations (or all) should be measured

Development of Composition Maps

The very large amount of hyperspectral data is automatically collected, sequentially arranged by blender rotation, and analyzed very efficiently. The composition maps provide the first level of data compression, resulting in the images of the predicted compositions of all ingredients. The analysis software allows the user to look at prediction images for selected rotations and components, or view them all in a slide show.

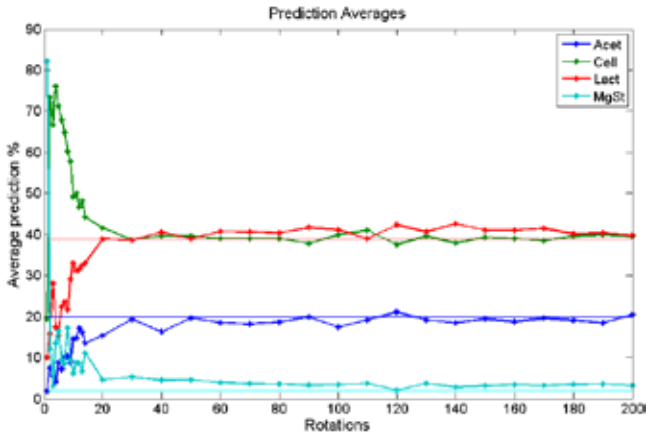
The analysis portion of the imMix system allows the user to predict the composition of the hyperspectral images with the Science-Based Calibration (SBC) method. This method requires the input of the pure analytes' spectra which can be collected with the imMix system or imported as a single spectrum obtained from other instruments. The imMix software can use prediction equations developed by other techniques, such as PLS or PCA, or equations generated on other near infrared instruments.



Analysis of Composition Maps

In the subsequent analysis, the images are further compressed into parameters that are meaningful for the blending process and displayed as a function of the rotation of the blender. Various image analyses can be performed with the prediction images, including standard statistical measures such as image average, standard deviation, and the fraction of pixels above/below/within a certain threshold, and spatial uniformity measures such as the distribution of aggregate sizes and the homogeneity of the blend.

The user can zoom in on a certain portion of the blending to understand the underlying micromixing process. Pharmaceutical formulation scientists can select the most relevant parameters to monitor micromixing and blending as well as display side-by-side comparisons of relevant parameters.



Specifications

Rotation speed	up to 60 revolutions per minute
Physical size	28" long x 23.5" deep x 19.375" high
Physical weight	~ 50kg
Body material	Stainless Steel Housing and blender, Anodized aluminum base plates
Blender sizes	Standard: 1Liter (~1 Qt.) IBC drum blender Other options: 2L and 4L IBC drum blenders; 1/2 Qt and 2 Qt V-blenders 8 oz. glass blender for small samples
Accessories	White reference and holder, small sample holder with sapphire window, focus target
Input voltage	Standard North American input wall voltage (120 VAC)
Storage temp.	-20 to 50 C
Operating temp.	5 to 40 C, non-condensing

Middleton Research is committed to continually update the software with additional user-friendly controls and displays, chemometric and image analysis techniques.