Efficient Management of Extractable & Leachable Data in Process Development

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Purpose

Extractable and Leachable (E&L) studies are an important part of successful drug product development. Unfortunately, the large quantity of analytical and numerical data collected and compiled for E&L studies is often scattered among a variety of systems including email, Microsoft applications (e.g. Excel) and electronic notebooks, to name a few. While scientists have developed practices and processes to compile E&L data to help make decisions, this remains a tedious manual process where simple questions are often difficult to answer.

Objective

In this presentation, we introduce a CMC decision support application (Luminata®) built to help project teams address the challenge of effective data management across product development. Luminata offers the capability for scientists investigating product enclosure systems to easily construct E&L study maps from data processed in the software of their choice. The software provides an interface for all E&L data to be assembled and connected for easy visual comparison and decision-support.

Methods

Analytical data collected for Agomelatine (an atypical antidepressant), synthesized via a six-stage process route (**Figure 1**), was used in this work.

The analytical data was collected on an Agilent-1200-Series HPLC with an Agilent VWD-G1314B UV detector, acquiring spectra at 210 nm and an Agilent 6110 Quadropole API-ES MS, collecting low resolution spectra in a mass range of 45-1000 Da. Column separation was performed using an isocratic method with an ammonium formate/acetonitrile buffer combination (35:65) at pH 4.5. The flow rate was 1.2 ml/min with a run time of 50 min, and the column used was a Zorbax Eclipse XDB C18 5 µm – 4.6 x 150 mm.

Luminata (v2019.2), built in the ACD/Spectrus platform, was employed to manage the analytical and chemical data for Agomelatine synthesis.

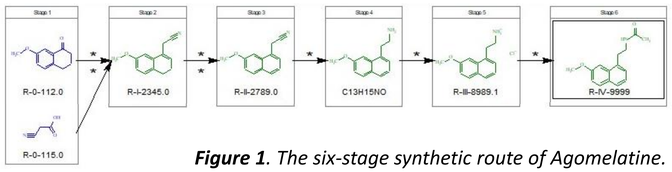


***Figure 1**. The six-stage synthetic route of Agomelatine.*

Results

1. Spectrus Processor Platform

ACD/Labs enables data processing, manual to automated, with scripting configuration to handle aspects of comparisons, semi-quantitation, collation of data, and results. Identification steps are aided by powerful algorithms for extracting features and conducting searches against databased information, whether spectra from commercial libraries or self-built ones. Data, structures, and results are stored in the knowledgebase and can be queried to find or recognize already known information. Reports can be generated and also stored in the knowledgebase (**Figure 2**).

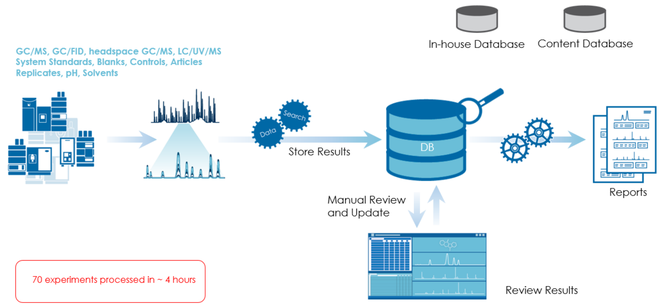
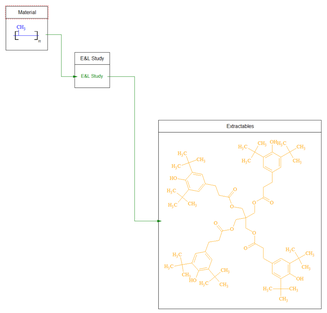


***Figure 2.** One of the approaches for automated data processing for the Extractable and Leachable workflow.*

2. Adaptability of Luminata

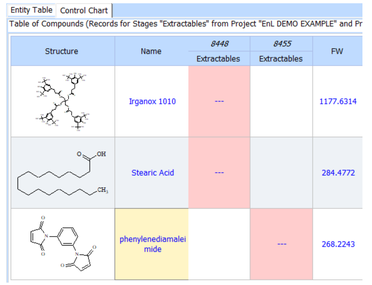
One of the strengths within the software is the ability to configure the process map to a synthetic route, degradant pathway, formulation map and in this case, focusing on extractable and leachable studies. This adaptability allows the software to store extractable and leachable chemical and analytical information for medical devices and drug delivery systems.



In **Figure 3**, we can take a material of interest, such as Polypropylene and generate an E&L map. In this case, the extractable would be Irganox 1010. It can also store the degradants that occur for Irganox 1010 as well.

***Figure 3.** Assembly of project record containing an Extractable for Polypropylene.*

3. Assessments on differing Extraction Procedures



By creating all of these E&L maps, you can leverage this knowledge by comparing other test procedures for the same material and observing which substances are in a specific study. In **Figure 4**, we are directly comparing two differing procedures for the material and viewing all substances. These values can be area percent's or Toxlogical levels for those extractables

***Figure 4.** Using the filtering capability in Luminata to view all substances for differing procedures for the same Material.*

Another important functionality that the software offers is the capability to take a sample and search if the spectrum and/or peak(s) have been seen before. **Figure 5** shows the capability to search an the mass spectrum and match it with extractables in Luminata.

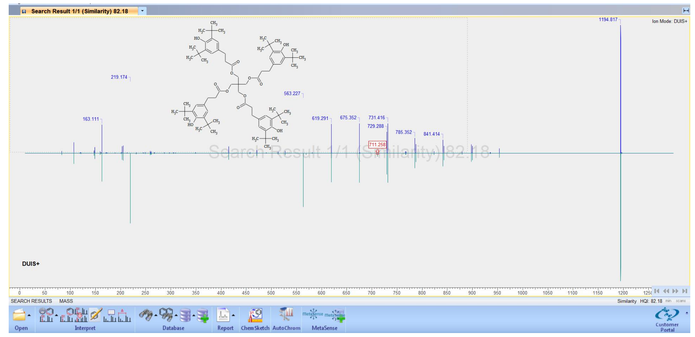


***Figure 5**. Searching unknown Mass Spectrum with Luminata.*

Conclusion

E&L contains large amount of analytical datasets and chemical information of all impurities associated to each study. Luminata's ability to be configurable, allows it to handle each step within the extractable and leachable process, to store all meta data for each compound found in the study with its corresponding data.

ACD/Labs would like to thank
Dr. Valter Russo, Director, Zirkon Ltd.