Rapid Evaporation Solutions for Natural Product Extraction Processes

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Introduction

Working with natural products as candidates for pharmaceutical leads has a reputation of being very difficult. Sample collection, preparation, extraction, and drying is extremely labor intensive and not easily reproducible from a process standpoint. The traditional bottleneck in the natural product pipeline has been the drying of solvent extracted sample. Recently, the use of new technology has facilitated and sped up this process, helping to eliminate the bottleneck.

The National Center for Natural Products Research (NCNPR), a research entity within the School of Pharmacy at the University of Mississippi, has a long history of discovering novel compounds from natural products. NCNPR has a dedicated team of research scientists whose expertise is very diverse. Teams of botanists, biologists, and chemists have developed models to identify and isolate new active components from natural products. The repository at the NCNPR is responsible for producing plant extract for such research efforts.

Repository Natural Product Process

Teams of botanists who harvest plant material and create the taxonomic vouchers for our expanding plant collection harvest plants or marine organisms. These samples are lyophilized and ground, and stored in our repository. Each sample is weighed out and extracted with ethanol using the Dionex ASE®300 (Accelerated Solvent Extraction) unit. The unit has been programmed to repeat the extraction process to ensure we remove as much of the organic material as possible. This extracted material is collected in 250 mL glass bottles. This extracted solvent is dried using various pieces of equipment until the sample is condensed to a typically dark, crude "sludge." This process is an art rather than an exact science. The Associate R&D Chemist who conducts this work has to make a judgment call to determine how much plant material is needed to generate enough crude extract "sludge" for our bioassay work. Often times, the same sample is extracted again or another sample is extracted to achieve this required amount. This "sludge" is used for primary bioassay discovery. Results from these efforts dictate which natural products are fractionated for further work. These fractions are also screened in our bioassays. Again, the active fractions are isolated to identify the pure compound(s) for verification of activity again in the bioassays. Once a novel pure compound has identified, synthetic chemists work to scale up synthesis for further work.

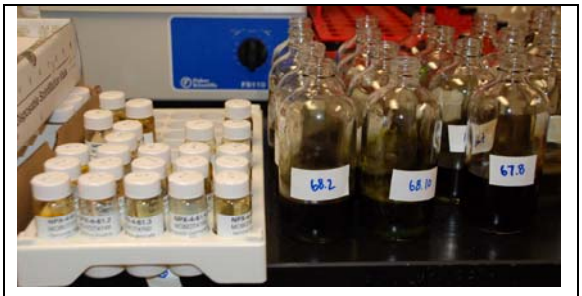

Figure 1: Solvent Extract from Dionex ASE®300 and Final Dried Extract Samples

The Bottleneck…

The Dionex ASE®300 produces 11 samples per a production run which generates ~150-200 mL of extract in solvent per sample. The time consuming task is to dry the solvent

down to produce the "sludge" extract. Historically we utilized RotoVap®, SpeedVac®, and Genevac® HT-12 evaporation methods in combination to remove the solvent from the extract. This typically could take anywhere from a couple of hours per sample to days to completely dry. Various natural product samples contain many essential oils which often take time in a desiccator or even some lyophilization to get the sample to its "sludge" state. Often times, a single sample would have to be dried in a SpeedVac® to reduce the total volume from ~200 mL to ~50 mL. Most times when the SpeedVac® was used, the sample bottle would have to be solvent washed to remove all organic material. This obviously creates more sample to dry. This was a necessary step to ensure that all material would be transferred to an 8 dram vial before its final drying step. These 8 dram vials were used as the permanent storage container for our crude "sludge" extract.

The Rocket™ & SampleGenie™ as a solution:

The NCNPR was first exposed to SampleGenie™ technology at ALA (Association of Lab Automation) Expo 2008. At this meeting, the Genevac® sales reps showed how the SampleGenie™ could take a bulk sample and dry it into a very small container, one where you want the sample to finally reside. The key benefit to the NCNPR Repository of the SampleGenie™ was that we could potentially eliminate the transfer step. Early 2009 the Genevac® sales representative sent me literature of the Rocket™. We received a trial unit in the fall of 2009 and for the first time used it to dry down natural product extracts. This unit performed the same task in such a manner that would allow us to dry down a week's worth of samples in a single day. The Rocket's® unique design and operational parameters allowed us to quickly dry down the sample, under low vacuum and low temperatures, and not affect the integrity of the sample. The Rocket™ can typically dry six samples in approximately 1 to 2 hours. We do have to deal with the phenomenon of "crashing" using the Rocket™ with natural products (crashing is where some of the sample clings to the wall of the SampleGenie™ during the drying process). Crashing requires a rinse, however this is not an issue as the Rocket will dry the remaining solvent down in less than an hour. The final sample is dried down into 20 mL Scintillation vials. This is another benefit as we now can store more of our samples in our long-term storage freezer. The use of the Rocket and the SampleGenie™ allows us to run samples in a more efficient manner which removes the biggest bottleneck in the natural product extraction process.

Figure 2: SampleGenie™ using Natural Product Extract

Figure 3: Rocket™ in Operation

Conclusions

The use of natural products for pharmaceutical research presents a unique challenge. Besides the chemistry issues of isolation, the fundamental process of extracting and preparing the natural product can be very time consuming. The use of the Rocket™ and the SampleGenie™ has allowed the NCNPR Repository to save time. Time is saved in eliminating a transfer step by the quick patented drying process of the Rocket™ and the SampleGenie®.

The author

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Acknowledgements

- Dionex ASE®300 is a registered trade mark of Dionex Inc., 3000 Lakeside Drive; Suite 116N; Bannockburn, IL; 60015 United States.
- Genevac® is a registered trademarks and SampleGenie™ and Rocket™ are trademarks of Genevac Ltd, Ipswich, UK.

Illustrations

Figure 1: Dionex ASE®300 Solvent Bottles with Natural Product Extract and 20 mL Scintillation vials with dried Natural Product extract "sludge" from SampleGenie™ and Rocket™.

Figure 2: Comparison of Natural Product Sample before and after drying using SampleGenie™ in the Genevac Rocket™

Figure 3: Illustration of Genevac Rocket™ in use with Natural Products.