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ionKey/MS System: Moving Toward Greener, More Sustainable Chemistry Methods by Reducing Mobile Phase Consumption

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This is an Application Brief and does not contain a detailed

Experimental section.

Abstract

In this work, we present the reduction in mobile phase consumption and the associated cost savings to perform bioanalytical work by utilizing the ionKey/MS System.

Benefits

ionKey/MS: Enhanced MS with the turn the Key. Reduce the consumption and storage of mobile phase chemicals when analyzing typical bioanalytical samples.

Introduction

Safety, ability to obtain critical information, and the cost associated with analysis, represent three important aspects in the bioanalytical laboratory. The combination of liquid chromatography and tandem quadrupole mass spectrometry (LC-MS/MS) has, over the past 20 years, become the analytical technique of choice for bioanalytical studies due to the specificity and sensitivity of the technique.[1-3] These analyses are most often accomplished by utilizing narrow-bore LC columns at flow rates of up to 800 µL/min with either acetonitrile, or methanol as the strong mobile phase.[4-5] Recently there has been momentum towards environmentally friendly or "green" chemistry approaches in the scientific community. One way in which scientists can address this issue is to limit the use of hazardous chemicals in their everyday processes. This very issue was recently highlighted in the June 2012 peer-reviewed journal ***Bioanalysis.*** Moreover, reduction in chemical usage further eliminates the need for specialized storage conditions for flammable chemicals such as acetonitrile and methanol.

One such approach to reduce the use of chemicals in the bioanalytical laboratory is to, therefore, reduce the amounts of strong mobile phase consumed during LC-MS analysis. This can be accomplished via reduction of the column diameter which results in lower required flow rates and therefore less overall consumption. In this work, we present the reduction in mobile phase consumption and the associated cost savings to perform bioanalytical work by utilizing the ionKey/MS System.

Results and Discussion

The ionKey/MS System, shown in Figure 1, consists of the ceramic-based separations device with an integrated emitter together in a single iKey Device that is placed directly into the source of the mass spectrometer. With ionKey/MS, all fluidic connections are made through the turn of a handle thereby creating a true “plug and play” capillary scale instrument. As previously stated most current LC-MS/MS assays employ 2.1 mm i.d. columns run at flow rates up to 0.8 mL/min. Optimal LC flow rates are dependent on a number of factors including: column diameter, particle size of the packing material contained in the LC column, the size of the analyte, as well as the ability for the mass spectrometer to desolvate the column effluent. One approach in reducing the amount of organic solvent required for a LC-MS/MS analysis is to use a chromatographic column of smaller diameter. Chromatographic theory suggests that as the column diameter is decreased; the flow rate at which the column is run is decreased by the square of the column diameter. For example, reduction from a 2.1 to a 0.15 mm i.d. column packed with the same chromatographic particle size will realize a $(2.1)^2/(0.15)^2 = 196$ fold decrease in the amount of solvent consumed. Therefore when analyzing a typical 96-well plate run by standard 2.1 x 50 mm column at 0.8 mL/min with a 5 minute cycle time, the total mobile phase consumption is 384 mL. The same analysis run on a 0.15 mm i.d. column at 0.004 mL/min would only require 2 mL total mobile phase consumption, a reduction of over 99%. This greatly reduces the amount of waste that is generated during analysis as well as the amount of space required to store the flammable, organic solvents used in the strong mobile phase preparation. This reduction in mobile phase delivers further benefits in the cost per analysis. The graph in Figure 2 shows a typical gradient profile during one inject to inject cycle used in bioanalytical LC-MS analysis.

Figure 1. ionKey/MS System: comprised of the Xevo TQ-S, the ACQUITY UPLC M-Class, the ionKey source and the iKey separation device.

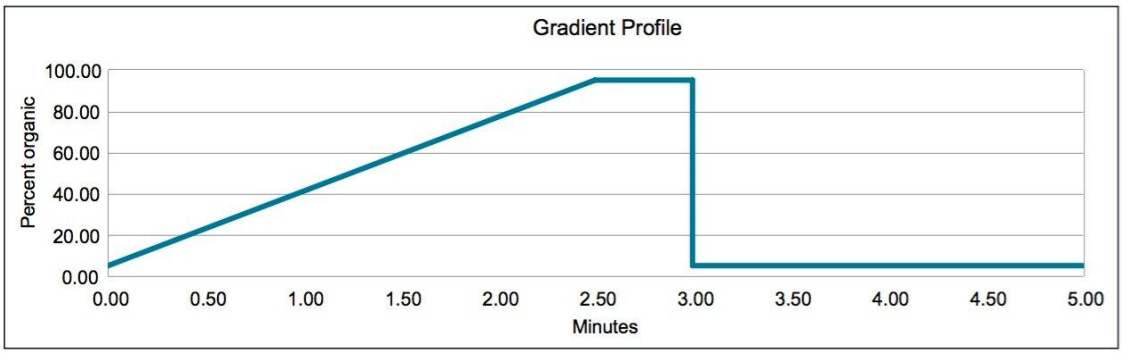

Figure 2. Typical, generic, LC gradient profile utilized for analysis of biological samples.

Often with the inherent high sensitivity of modern MS instruments, cleaner solvents must be used as a source for the strong, organic mobile phase. These solvents can be quite expensive, costing greater than $100.00 per liter. The use of the organic mobile phase changes throughout the LC-MS analysis as illustrated in Figure 2, therefore reduces the required consumption of these costly solvents, leading to lower cost-per-analysis. Table 1 illustrates the reduction in the cost-per-analysis of one 96-well plate utilizing a 2.1 mm i.d. column and a 0.15 mm i.d. column geometrically scaled and based of the cost of 1 L of acetronitrile of $123.00. In the example illustrated in Table 1, the cost saving can be substantial when reducing the column i.d. from 2.1 mm to 0.15 mm.

Column I.D./flow rate	Organic (mL consumed during cycle steps)			Total mL consumed	Cost/96-well plate (USD)
	2.5 min gradient	0.5 min wash	2 min condition		
2.1 mm 0.8 mL/min	1.0	0.4	0.08	1.48	$17.50
0.15 mm .004 mL/min	0.0051	0.00204	0.00408	0.00755	$0.09

Table 1. Cost associated with organic mobile phase consumption when compared versus column i.d.

Conclusion

Safety, the ability to obtain critical information, and cost associated with analysis, represent three aspects that must be balanced in the bioanalytical laboratory. Modifications to current techniques that can address these important business aspects will become even more critical moving forward in today's pharmaceutical environment. Approaches such as the strategy outlined in this work to reduce consumption and associated required storage of hazardous, flammable chemicals for LC-MS analysis, can address some of these concerns.

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