

Quantification of Carbohydrates and Glycols in Pharmaceuticals

Val Hanko and Jeff Rohrer
Thermo Fisher Scientific, Sunnyvale, CA, USA

Introduction

The United States Food and Drug Administration (U.S. FDA)¹⁻³ and the regulatory agencies in other countries require that pharmaceutical products be tested for composition to verify their identity, strength, quality, and purity. Recently, attention has been given to inactive ingredients as well as active ingredients. Some of these ingredients are nonchromophoric and cannot be detected by absorbance. Some nonchromophoric ingredients, such as carbohydrates, glycols, sugar alcohols, amines, and sulfur-containing compounds, can be oxidized, and therefore can be detected using amperometric detection. This detection method is specific for those analytes that can be oxidized at the selected potential, leaving all other nonoxidizable compounds transparent.⁴⁻⁵ Amperometric detection is a powerful detection technique with a broad linear range and very low detection limits.

This application note describes the use of three different anion-exchange columns with amperometric detection to analyze common simple sugars, sugar alcohols, and glycols in pharmaceutical formulations. Two oral, over-the-counter medications were selected as representative pharmaceutical products. A cough suppressant and a multisymptom cold/flu medication were chosen because they contain a complex mixture of simple sugars, glycols, and sugar alcohols. These carbohydrates and glycols are also commonly found in other medications. Furthermore, these formulations contain inorganic and organic anionic ingredients that have been analyzed using the Thermo Scientific Dionex IonPac AS14 and AS11 anion-exchange columns with suppressed conductivity detection.⁶

In the methods outlined in this Note, the selectivities of the Dionex IonPac™ ICE-AS1 ion exclusion, Thermo Scientific Dionex CarboPac PA10, and CarboPac MA1 anion-exchange columns for the analysis of carbohydrate and glycol ingredients in pharmaceutical formulations are compared. The Dionex IonPac ICE-AS1 resin bead is a completely sulfonated polystyrene/divinylbenzene polymer with a capacity of about 27 meq/column and with moderate hydrophilic characteristics. The retention mechanisms possible in this column include ion exclusion, steric exclusion, and adsorption. Weakly-ionized acids are separated by pKa differences, size, and hydrophobicity. This column is ideal for the determination of aliphatic organic acids and alcohols in complex or high-ionic strength samples.

The Dionex CarboPac™ PA10 column packing consists of a non-porous, highly crosslinked polystyrene/divinylbenzene substrate agglomerated with 460-nm diameter latex. The Thermo Scientific Dionex MicroBead latex is functionalized with quaternary ammonium ions, which create a thin surface rich in anion-exchange sites. The packing is specifically designed to have a high selectivity for monosaccharides. The PA10 has an anion-exchange capacity of approximately 100 µeq/column.

The Dionex CarboPac MA1 resin is composed of a polystyrene/divinylbenzene polymeric core. The surface is grafted with quaternary ammonium anion-exchange functional groups. Its macroporous structure provides an extremely high anion-exchange capacity of 1450 µeq/column. The Dionex CarboPac MA1 column is designed specifically for sugar alcohol and glycol separations. The ICE-AS1 and PA10 columns, but not the MA1 column, are compatible with eluents containing organic solvents, which can be used to clean these columns.

Expected detection limits, linearity, selectivity, accuracy, and precision are reported for the CarboPac MA1 column. The performance of the CarboPac PA10 column for monosaccharide analysis is presented in Technical Note 40.⁷

Equipment

Thermo Scientific Dionex DX-500 system consisting of:

- GP40 Gradient Pump, with degas option
- ED40 Electrochemical Detector
- LC30 or LC25 Chromatography Oven
- AS3500 Autosampler

Thermo Scientific Dionex PeakNet Chromatography Workstation

Reagents and Standards

Reagents

Fisher Scientific sodium hydroxide, 50% (w/w)

Fisher Scientific perchloric acid, 70% (w/w)

Deionized water, 18 M Ω -cm resistance or higher

Standards

Propylene glycol, anhydrous (Sigma-Aldrich®, St. Louis, USA)

Glycerol (EM Science®, Billerica, USA)

Sorbitol (Eastman™ Chemical Company Kingsport, USA)

Mannitol, ACS grade (J.T.Baker®, Mansfield, USA)

Maltitol (Sigma-Aldrich)

Glucose, reference grade (Pfanstiehl® Laboratories)

Fisher Scientific sucrose, ACS certified

	Conditions								
	System 1			System 2			System 3		
Columns:	Dionex IonPac ICE-AS1 Analytical (P/N 43197) NG1 Neutral Guard (P/N 39567)			Dionex CarboPac PA10 Analytical (P/N 46110) Dionex CarboPac PA10 Guard (P/N 46115)			Dionex CarboPac MA1 Analytical (P/N 44066) Dionex CarboPac MA1 Guard (P/N 44067)		
Flow Rate:	2.0 mL/min			1.5 mL/min			0.4 mL/min		
Injection Volume:	10 μ L			10 μ L			10 μ L		
Oven Temperature:	30 °C			30 °C			30 °C		
Detection (ED40):	Integrated amperometry, platinum electrode			Integrated amperometry, gold electrode			Integrated amperometry, gold electrode		
Waveform for ED40:	Time (s)	Potential (V)	Integration (Begin/End)	Time (s)	Potential (V)	Integration (Begin/End)	Time (s)	Potential (V)	Integration (Begin/End)
	0.00	+0.30		0.00	+0.05		0.00	+0.05	
	0.05	+0.30	Begin	0.20	+0.05	Begin	0.20	+0.05	Begin
	0.25	+0.30	End	0.40	+0.05	End	0.40	+0.05	End
	0.26	+1.40		0.41	+0.75		0.41	+0.75	
	0.60	+1.40		0.60	+0.75		0.60	+0.75	
	0.61	+0.10		0.61	-0.15		0.61	-0.15	
	1.00	+0.10		1.00	-0.15		1.00	-0.15	
Eluent Components:	A: 100 mM Perchloric acid			A: Water B: 200 mM Sodium hydroxide			A: Water B: 1.0 M Sodium hydroxide		
Eluent Concentration:	100 mM Perchloric Acid			18 mM Sodium hydroxide			480 mM Sodium hydroxide		
Method:	Time (min)	A (%)		Time (min)	A (%)	B (%)	Time (min)	A (%)	B (%)
	0.0	100		0.0	91	9	0.0	52	48
	End	100		11.0	91	9	60.0	52	48
				11.1	0	100			
				17.6	0	100			
				17.7	91	9			
				40.0	91	9			

On-line degassing is necessary because the amperometric detector is sensitive to oxygen in the eluent. High flow rates of 2 mL/minute, such as those used in the Dionex ICE-AS1 system, require more frequent on-line degassing intervals (every 5 minutes) to eliminate cyclic baseline drift.

Preparation of Solutions and Reagents

Perchloric Acid Eluent

100 mM Perchloric acid

Degas 1983 mL of deionized water for 20 min and mix with 17.1 mL 70% (w/w) perchloric acid. Connect the eluent reservoir to the instrument and pressurize with helium.

Sodium Hydroxide Eluents

200 mM Sodium hydroxide

It is essential to use high-quality water of high resistivity (18 M Ω -cm) as free of dissolved carbon dioxide as possible. Biological contamination should be absent. Additionally, borate, a water contaminant that can break through water purification cartridges (prior to any other indication of cartridge depletion), can be removed by placing a Thermo Scientific Dionex BorateTrap column (P/N 47078) between the pump and the injection valve. It is extremely important to minimize contamination by carbonate, a divalent anion at high pH that binds strongly to the columns, causing a loss of chromatographic resolution and efficiency. Commercially available sodium hydroxide pellets are covered with a thin layer of sodium carbonate and should not be used. A 50% (w/w) sodium hydroxide solution is much lower in carbonate and is the preferred source for sodium hydroxide.

Dilute 20.8 mL of a 50% (w/w) sodium hydroxide solution into 1980 mL of thoroughly degassed water to yield a 200 mM sodium hydroxide solution. Keep the eluents blanketed under 5–8 psi (34–55 kPa) of helium at all times.

1.0 M Sodium hydroxide

Follow the same precautions described above for the 200 mM sodium hydroxide eluent. Dilute 104 mL of a 50% (w/w) sodium hydroxide solution into 1896 mL of thoroughly degassed water to yield 1.0 M sodium hydroxide. Keep the eluents blanketed under 5–8 psi (34–55 kPa) of helium at all times.

Stock Standards

Solid standards were dissolved in purified water to 10 g/L concentrations. These were combined and further diluted with purified water to yield the desired stock mixture concentrations.

For determinations of linear range, combine 10 g/L solutions of propylene glycol, glycerol, sorbitol, mannitol, glucose, maltitol, and sucrose to make a 1.0 g/L standard mix solution. Dilute with water to concentrations of 800, 600, 400, 200, 100, 80, 60, 40, 20, 10, 8, 6, 4, 2, 1, 0.8, 0.6, 0.4, 0.2, and 0.1 mg/L. Maintain the solutions in a frozen state at –20 °C until needed.

Sample Preparation

Dilute viscous products with water on a weight per weight (w/w) basis. Combine 1 gram of medication with 9 grams of water to obtain a 10-fold dilution. Further dilute the medication to yield 100- and 1000-fold dilutions on a weight per weight (w/w) basis. Determine product densities by measuring the weights of known volumes. Calculate the final concentrations based on the densities of these medications. The ingredients of each medication are presented in Tables 1 and 2. The ingredients noted in bold-face type can be analyzed by anion-exchange chromatography with amperometric detection. Many of the other ingredients listed below can be analyzed using the Dionex IonPac AS14 and AS11 columns with suppressed conductivity detection.⁶

Any purified water used for dilutions should be tested for trace carbohydrates prior to its use. Test the sample containers for residual carbohydrates prior to use by adding pure water, shaking or vortexing, and then testing the liquid. Prerinsing the vials with purified water can eliminate artifacts and erroneous results.

Table 1. Cough suppressant ingredients

	Type
Dextromethorphan Hydrobromide	Active
Citric Acid	Inactive
FD&C Red 40	Inactive
Flavors	Inactive
Glycerin (glycerol)	Inactive
Propylene Glycol	Inactive
Saccharin Sodium	Inactive
Sodium Benzoate	Inactive
Sorbitol	Inactive
Water	Inactive

Table 2. Multisymptom cold/flu ingredients

	Type
Pseudoephedrine Hydrochloride	Active
Acetaminophen	Active
Dextromethorphan Hydrobromide	Active
Citric Acid	Inactive
FD&C Yellow #6	Inactive
Flavor	Inactive
Glycerin (glycerol)	Inactive
Polyethylene Glycol	Inactive
Propylene Glycol	Inactive
Purified Water	Inactive
Saccharin Sodium	Inactive
Sodium Citrate	Inactive
Sucrose	Inactive

Discussion and Results

Selectivity

Figure 1 shows the separation of sorbitol, glycerol, and propylene glycol standards using a 100 mM perchloric acid eluent with the Dionex IonPac ICE-AS1 analytical column and the NG1 guard column. The separation was isocratic, which decreases injection-to-injection run times and increases sample throughput. Glycerol, propylene glycol, and sugar alcohols were determined within 10 minutes. Sucrose, maltitol, and mannitol were not well resolved by this method (results not shown). Oxygen is reduced using the same waveform used to detect sugar alcohols. Oxygen dissolved in the sample eluted at the total permeation volume, and appeared as a dip in the baseline at just before 8 minutes. Use of the NG1 neutral guard column increased the total permeation volume and moved the oxygen dip away from the analytes. Without the NG1, sucrose, sorbitol, maltitol, and mannitol were slightly better resolved, but the oxygen dip encroached on the propylene glycol peak. An alternative way to reduce or eliminate the oxygen dip is to degas the sample prior to injection.

The Dionex CarboPac PA10 column separated propylene glycol, glycerol, sorbitol, mannitol, maltitol, glucose, and sucrose using an isocratic sodium hydroxide eluent (Figure 2). Propylene glycol and glycerol eluted near the void and were not baseline-resolved.

Propylene glycol, glycerol, sorbitol, mannitol, maltitol, and sucrose were completely resolved when analyzed on the Dionex CarboPac MA1 (Figure 3). Shorter run times are possible for both the PA10 and MA1 methods by adjusting the eluent strength, but resolution may be lost.

Although not presented here, nearly a dozen over-the-counter medications have been analyzed using the Dionex ICE-AS1 and MA1 columns with amperometric detection. These medications include both solid and liquid formulations such as nasal and oral decongestants, astringents, antacids, enemas, sleep aids, analgesics, cleaning and disinfecting solutions, antihistamines, and allergy syrups. In most cases, the known carbohydrate ingredients in each formulation were separated from each other using the MA1 column without any apparent interference.

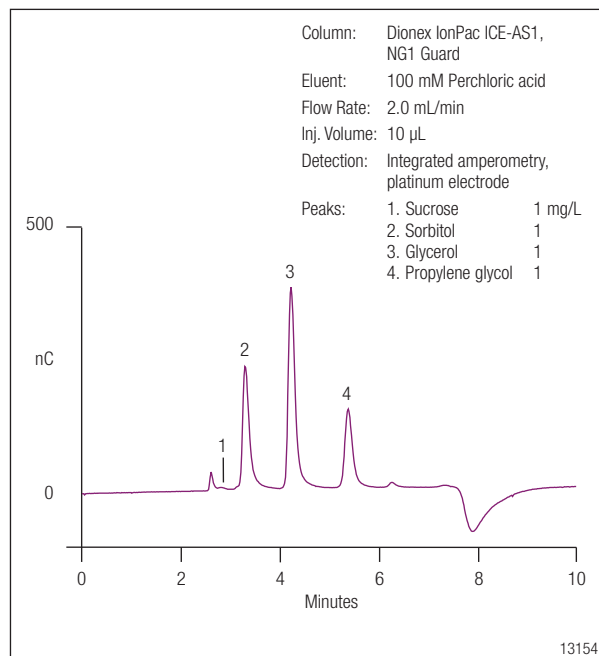


Figure 1. Separation of common glycols, sugar alcohols, and carbohydrates in pharmaceutical formulations on a Dionex IonPac ICE-AS1 column.

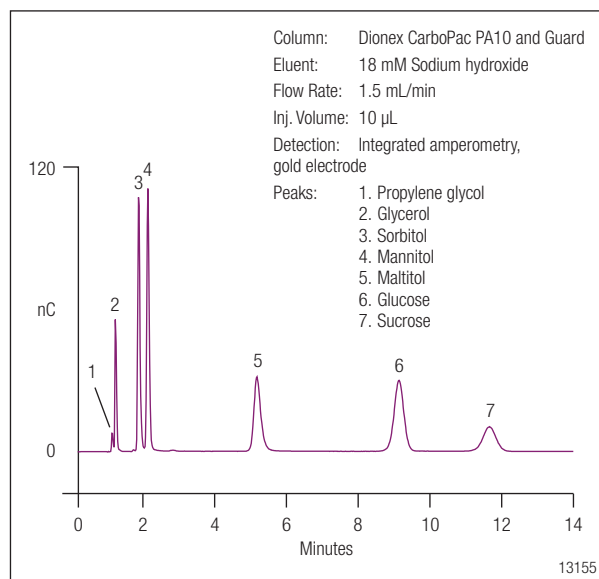


Figure 2. Separation of common glycols, sugar alcohols, and carbohydrates in pharmaceutical formulations on a Dionex CarboPac PA10 column.

Figures 4 and 5 compare the selectivity of the Dionex ICE-AS1 and MA1 columns for the analysis of a cough suppressant. Figure 5B is an expanded view of Figure 5A to better reveal the minor peaks. In general, peak elution order from the Dionex ICE-AS1 column is the reverse of that of the MA1 column. The early eluting peaks for sugar alcohols and carbohydrates were not resolved on the Dionex ICE-AS1 column. Propylene glycol and glycerol eluted later and were completely resolved on this column. Figure 6 shows the analysis of a multisymptom cold/flu medication using the MA1 column.

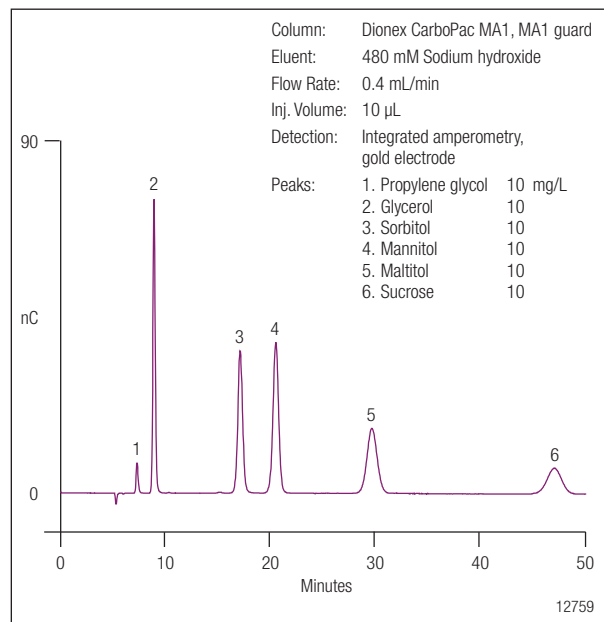


Figure 3. Separation of glycols, sugar alcohols, and carbohydrates using the Dionex CarboPac MA1 column.

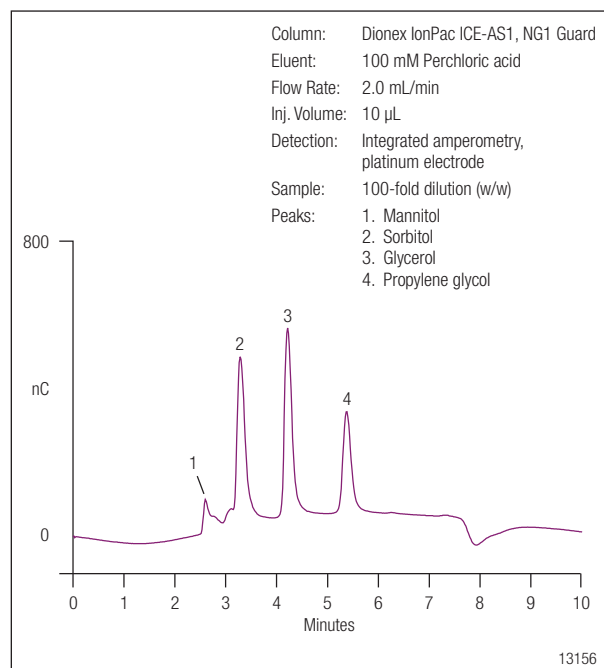


Figure 4. Separation of sugar alcohols and glycols in cough suppressant using the Dionex IonPac ICE-AS1 column.

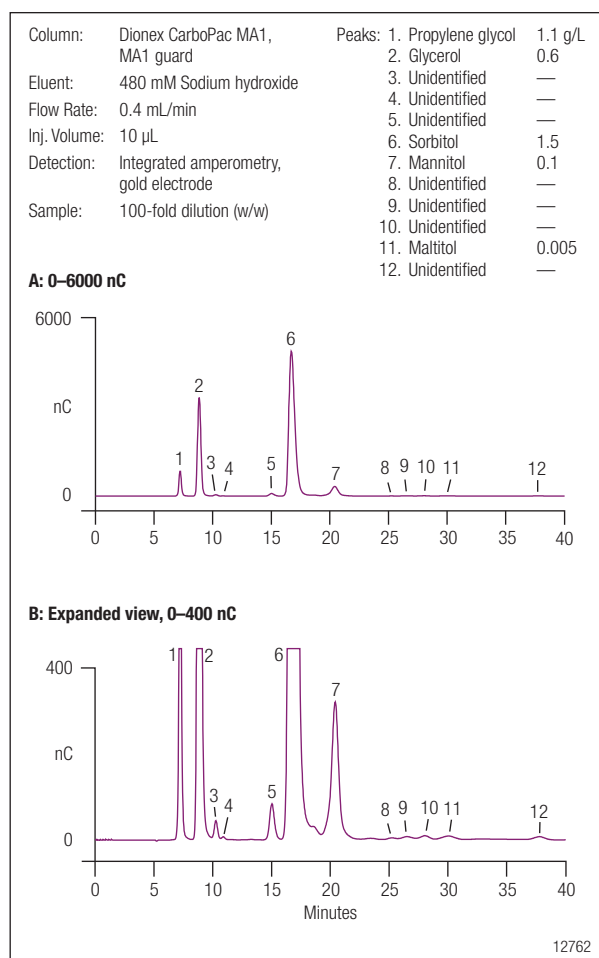


Figure 5. Separation of sugar alcohols and glycols in cough suppressant using the Dionex CarboPac MA1 column.

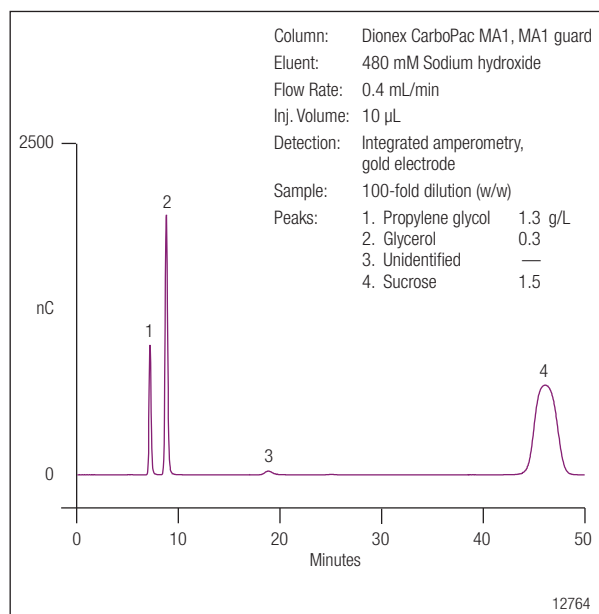


Figure 6. Sugar alcohols, glycols, and carbohydrates in multisymptom cold/flu medication.

The selection of the best method depends on the analytes tested. If a rapid analysis of sugar alcohols and simple sugars is needed, with little interest in propylene glycol or glycerol, the Dionex CarboPac PA10 column is the best choice. If a rapid analysis of glycerol and propylene glycol is desired, with little interest in carbohydrates, the Dionex IonPac ICE-AS1 is the best choice. If the analysis of all of these compounds is required, a Dionex CarboPac MA1 is the best choice.

Method Detection Limits

The method detection limits (MDL) for a 10- μ L injection of common pharmaceutical constituents using the MA1 column are shown in Table 3. The MDL is defined as the minimum concentration required to produce a signal-to-noise ratio of 3. The MDL can be further decreased by increasing the injection volume above the 10- μ L injection volume used in this application note, and by using smoothing algorithms available in PeakNet software.⁷

Linearity

Propylene glycol, glycerol, sorbitol, mannitol, glucose, maltitol, and sucrose standards ranging from 0.1–1000 mg/L (1–10,000 ng) were injected ($n = 2$ to 3 per concentration) onto a Dionex CarboPac MA1 column. The method was found to be linear for propylene glycol, sorbitol, mannitol, glucose, maltitol, and sucrose over this range ($r^2 \geq 0.999$). Glycerol was linear over the range of 0.1–200 mg/L (1–2,000 ng per injection; $r^2 = 0.999$). For the range of 0.1–1000 mg/L (1–10,000 ng), glycerol deviated from linearity ($r^2 = 0.995$). Using a second order polynomial regression, the r^2 for glycerol was 0.9998 over the range of 0.1–1000 mg/L (1–10,000 ng). For all analytes, linearity was demonstrated over at least three orders of magnitude. Broad linear ranges help eliminate the need to repeat sample analyses when components vary greatly in concentration.

Calibration curves for the MA1 column are presented in Figure 7.

Precision

The peak area and retention time RSDs for 10-mg/L injections of standards (10 μ L per injection, 12 injections) run on the MA1 are presented in Table 4. RSDs varied from 2–4% at this concentration. Precision is affected by concentration; RSD values increase as the concentrations approach the MDL. RSDs increase near the MDL because peak integration becomes less precise from the contribution of variation in baseline noise from run-to-run.

Recovery from Sample Matrix

To assess the accuracy of this method, evaluate both medications by the method of standard addition. Combine each 1000-fold (w/w) diluted formulation with an equal weight of a 100-mg/L mixture of propylene glycol,

Table 3. Estimated detection limits using the Dionex CarboPac MA1

	ng	μ g/L
Propylene glycol	4	400
Glycerol	0.7	70
Sorbitol	1	100
Mannitol	1	100
Glucose	1	100
Maltitol	2	200
Sucrose	7	700

Table 4. Peak area and retention time precision

	RSD (%)	
	Area	Retention Time (min)
Propylene glycol	2.4	0.0
Glycerol	3.0	0.2
Sorbitol	2.9	0.1
Mannitol	2.9	0.1
Glucose	2.7	0.1
Maltitol	2.6	0.1
Sucrose	3.7	0.1

Table 5. Recovery of carbohydrates in medications

Analyte	Percent Recovery	
	Cough Suppressant	Multisymptom Cold/Flu Medication
Propylene glycol	96	111
Glycerol	98	109
Sorbitol	87	105
Mannitol	99	105
Glucose	101	104
Maltitol	103	106
Sucrose	103	114

glycerol, sorbitol, mannitol, maltitol, sucrose, and glucose to yield a 50 mg/L spiked solution [2000-fold dilution (w/w)]. Subtract the amount of each analyte measured in the sample before it was spiked from the total amount of each analyte measured in the spiked sample to yield the amount of spiked analyte recovered. The amount of spiked analyte recovered relative to the known amount added then yields the percent recovery.

Figure 5 shows the separation of carbohydrate and glycol ingredients in cough suppressant using the MA1 column. Figure 6 shows the separation of carbohydrates and glycols in a multisymptom cold/flu formulation. The percent recovery after standard addition [50 mg/L spike, 2000-fold dilution, (w/w)] is presented in Table 5. Percent recovery ranged from 87–114% for the glycols, sugar alcohols, and carbohydrates tested.

Table 6. Concentration of carbohydrates in medications

Analyte	Concentration (g/L)	
	Cough Suppressant	Multisymptom Cold/Flu Medication
Propylene glycol	184*	215*
Glycerol	144*	56*
Sorbitol	288*	0.1
Mannitol	13	1.5
Glucose	0.2	0.2
Maltitol	0.2	Not Detected
Sucrose	Not Detected	459*

* Ingredients that are listed on the product containers.

Concentration of Known Ingredients in Pharmaceutical Products

Ingredients in pharmaceutical products that could be identified by retention times are listed in Table 6. Their respective concentrations were determined and also presented in Table 6. The ingredients listed on the product container are marked with an asterisk (*). It is not the normal practice of drug manufacturers to state the concentrations of inactive ingredients on their product labels; therefore, the accuracy of these formulations against the stated label concentrations could not be evaluated.

In addition to the labeled content of the pharmaceutical products, other carbohydrate or glycol ingredients may be present. Unlabeled ingredients are not marked with an asterisk. Trace levels of unlabeled carbohydrates were determined by injecting less dilute samples [1000 and 100-fold dilutions (w/w)]. Expanding the chromatogram for the cough suppressant (Figure 5B) reveals the presence of minor peaks. Besides sorbitol, which is a labeled ingredient of the cough suppressant, the unlabeled ingredients, mannitol and maltitol, were also identified based on their retention time. Mannitol and maltitol are probably trace impurities of sorbitol. Seven other peaks were detected in the cough suppressant (Figure 5B), but were not identified. The multisymptom cold/flu medication contained one unidentified minor peak (Figure 6).

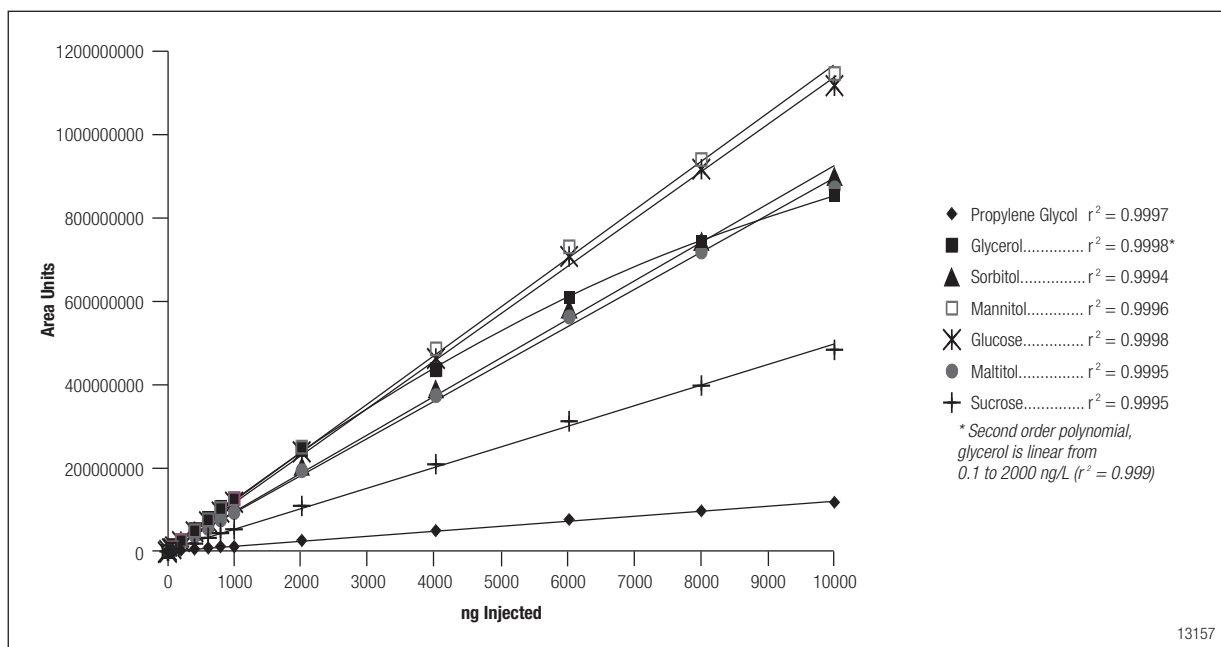


Figure 7. Method linearity for Dionex CarboPac MA1 with amperometric detection.

Conclusion

Pharmaceutical formulations can be analyzed for both glycols and carbohydrates using the Dionex CarboPac MA1 column with amperometric detection. The MA1 resolves glycols such as propylene glycol and glycerol. It also resolves sugar alcohols such as sorbitol, mannitol, maltitol, and carbohydrates such as sucrose and glucose in the same injection. The Dionex CarboPac PA10 also resolves sugar alcohols and carbohydrates, but is not suitable for glycols such as propylene glycol and glycerol. The Dionex IonPac ICE-AS1 with the NG1 can be used to rapidly separate propylene glycol and glycerol, but is less effective for many carbohydrates and some sugar alcohols. The Dionex ICE-AS1 reverses the elution order of glycols and carbohydrates when compared to the Dionex CarboPac columns.

All of these columns use isocratic eluents, which simplify analysis. The MA1 is a high-capacity column and generally has longer run times than the PA10 and the Dionex ICE-AS1. Amperometric detection eliminates potential interferences from the nonoxidizable ingredients in the formulation and provides a sensitive means to detect nonchromophoric analytes. Carbohydrates, glycols, and sugar alcohols can be detected at the 70–700 µg/L levels using the Dionex CarboPac MA1 column with amperometric detection. The three classes of compounds tested were linear over more than three orders of magnitude using this system. The recoveries from pharmaceutical formulations were greater than 87% based on the method of standard addition. This method can also be used to evaluate trace levels of carbohydrate, glycol, and sugar alcohol contaminants.

References

1. CFR Title 21, Food and Drugs, Chapter 1, FDA, B Part 211.22, “Responsibilities of quality control unit.”
2. CFR Title 21, Food and Drugs, Chapter 1, FDA, I Part 211.160, “General requirements.”
3. CFR Title 21, Food and Drugs, Chapter 1, FDA, I 211.165, “Testing and release for distribution.”
4. Rocklin, R. *A Practical Guide to HPLC Detection*; D. Parriott, Ed.; Chapter 6, Electrochemical Detection, Academic Press: San Diego, CA, 1993, pp 145–173.
5. Rocklin, R.D. J. *Chromatogr.* 1991, 546, 175–187.
6. Dionex Corporation (now part of Thermo Fisher Scientific), “Quantification of Anions in Pharmaceuticals”, Application Note 116.
7. Dionex Corporation (now part of Thermo Fisher Scientific), “Glycoprotein Monosaccharide Analysis Using High-Performance Anion-Exchange Chromatography with Pulsed Amperometric Detection (HPAE-PAD)”, Technical Note 40.

Suppliers

Fisher Scientific, 711 Forbes Ave., Pittsburgh, Pennsylvania, 15219-4785, U.S.A., 1-800-766-7000.

Aldrich Chemical Company, Inc., 1001 West Saint Paul Avenue, P.O. Box 355, Milwaukee, Wisconsin, 53233, U.S.A., 1-800-558-9160.

Sigma Chemical Company, P.O. Box 14508, St. Louis, Missouri, 63178, U.S.A., 1-800-325-3010.

EM Science, P.O. Box 70, 480 Democrat Road, Gibbstown, New Jersey, 08027, U.S.A., 1-800-222-0342.

Eastman Chemical Company, 1001 Lee Road, Rochester, New York, 14652-3512, U.S.A., 1-800-225-5352.

J. T. Baker Incorporated, 222 Red School Lane, Phillipsburg, New Jersey, 08865, U.S.A., 1-800-582-2537.

Pfanstiehl Laboratories, Inc., 1219 Glen Rock Avenue, Waukegan, Illinois, 60085-0439, U.S.A., 1-800-383-0126.

www.thermoscientific.com/dionex

©2012 Thermo Fisher Scientific Inc. All rights reserved. ISO is a trademark of the International Standards Organization. Sigma-Aldrich is a registered trademark of Sigma-Aldrich Co. LLC. EM Science is a registered trademark of EMD Millipore. Eastman is a trademark of Eastman Chemical Company. J.T.Baker is a trademark of Covidien. Pfanstiehl Laboratories is a registered trademark of Ferro Corporation. All other trademarks are the property of Thermo Fisher Scientific Inc. and its subsidiaries. This information is presented as an example of the capabilities of Thermo Fisher Scientific Inc. products. It is not intended to encourage use of these products in any manners that might infringe the intellectual property rights of others. Specifications, terms and pricing are subject to change. Not all products are available in all countries. Please consult your local sales representative for details.

Africa +43 1 333 50 34 0
Australia +61 3 9757 4300
Austria +43 810 282 206
Belgium +32 53 73 42 41
Brazil +55 11 3731 5140
Canada +1 800 530 8447
China 800 810 5118 (free call domestic)
 400 650 5118

Denmark +45 70 23 62 60
Europe Other +43 1 333 50 34 0
Finland +358 9 3291 0200
France +33 1 60 92 48 00
Germany +49 6103 408 1014
India +91 22 6742 9494
Italy +39 02 950 591

Japan +81 6 6885 1213
Korea +82 2 3420 8600
Latin America +1 561 688 8700
Middle East +43 1 333 50 34 0
Netherlands +31 76 579 55 55
New Zealand +64 9 980 6700
Norway +46 8 556 468 00

Russia/CIS +43 1 333 50 34 0
Singapore +65 6289 1190
Sweden +46 8 556 468 00
Switzerland +41 61 716 77 00
Taiwan +886 2 8751 6655
UK/Ireland +44 1442 233555
USA +1 800 532 4752



Thermo Fisher Scientific, Sunnyvale, CA
 USA is ISO 9001:2008 Certified.

Thermo
 SCIENTIFIC

A Thermo Fisher Scientific Brand