Average Polymer Length Determination for Polyoxyl 10 Oleyl Ether (Oleth-10) According to USP-NF Monograph Method Using ^{1}H Benchtop NMR

Background

Polyoxyl 10 oleyl ether, also known as oleth-10, is an oleyl alcohol-based polymer containing a terminal poly(oxyethylene) fragment. The structure of polyoxyl 10 oleyl ether is shown in **Figure 1**.

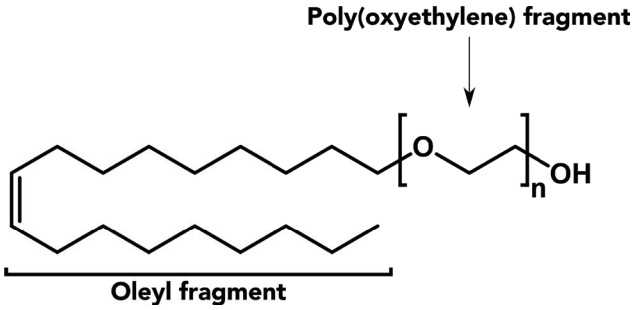

Figure 1. *Structure for polyoxyl 10 oleyl ether (n = 9.1–10.9). The oleyl and poly(oxyethylene) fragments are highlighted.*

At room temperature, polyoxyl 10 oleyl ether is a semi-solid that has found many uses as a surfactant and emulsifier in soaps, deodorants, creams, detergents, and many more.[1–4] Because of their incorporation in such a wide variety of commercial products, the quality control of these polymers is crucial on an industrial scale, and ^{1}H NMR can be used to determine the average polymer length of the poly(oxyethylene) fragment according to the USP-NF monograph method.[5]

Average polymer length test

To determine the number of repeating poly(oxyethylene) units, or the average polymer length, a sample is allowed to melt at 60°C with stirring to eliminate potential molecular weight gradients. A portion is transferred and dissolved in $CDCl_3$ containing 1% tetramethylsilane (TMS) as an internal chemical shift reference. Then, a ^{1}H NMR spectrum is collected and the integrations of the protons in the oleyl fragment ($\mathbf{A_1}$), minus those of the alkyl fragment and those directly adjacent to the ether oxygen, are compared to the combined integrations of the poly(oxyethylene) protons ($\mathbf{A_2}$).[6] A representative ^{1}H spectrum of **Brij® O10** is shown in **Figure 2**, along with the integration regions of interest.

In total, 3 different polyoxyl 10 oleyl ether products from different suppliers were analyzed, and the average polymer length values obtained using NMR were compared to the expected values for each product.

The polymers analyzed in this study were: **Brij® O10, ETHOXCARE® OA-10, and Procol™ OA-10**.[7] The analyses were performed on a 60 MHz benchtop NMR instrument, in addition to a traditional 400 MHz high-field NMR instrument.

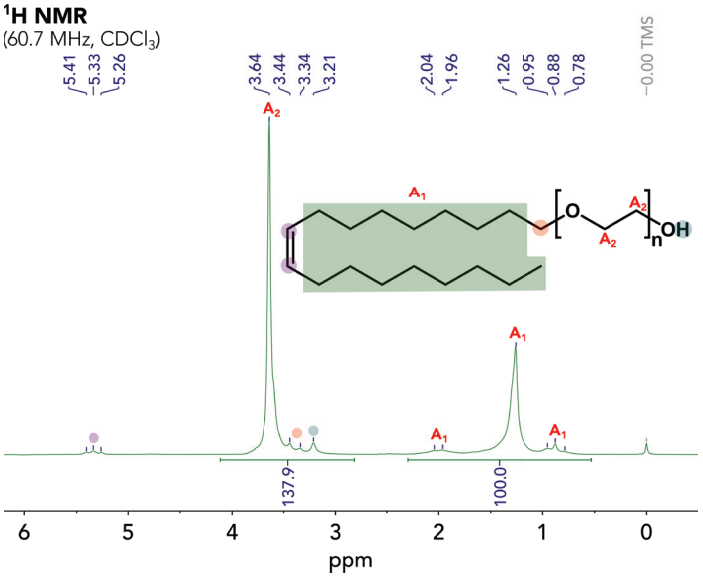

Figure 2. *^{1}H (60.7 MHz) NMR spectrum of Brij® O10 in $CDCl_3$ with the structure of polyoxyl 10 oleyl ether shown. The protons of the oleyl fragment (highlighted in green) are observed between 0.5-2.3 ppm ($\mathbf{A_1}$), while the poly(oxyethylene) protons are observed between 2.8-4.1 ppm ($\mathbf{A_2}$). The methylene protons of the oleyl fragment next to the poly(oxyethylene) oxygen (highlighted in red), in addition to the terminal hydroxyl proton (highlighted in blue), are subtracted from the $\mathbf{A_2}$ region during the calculations.*

Results

In total, 3 individual samples were prepared for each polymer, and each sample was analyzed in triplicate, for a total of 9 analyses per polymer. For all samples, very close agreement between the values obtained at 60 MHz and 400 MHz were obtained. These results are summarized in **Table 1**. Additionally, these values match the expected average polymer length for these products closely (n = 9.1–10.9), confirming that this monograph method can be performed at a benchtop level. For these analyses, the 60 MHz instrument can easily integrate the $\mathbf{A_1}$ and $\mathbf{A_2}$ regions separately, providing accurate and precise results. The analysis takes < 1 minute, and sample preparation is minimal.

Table 1. *Summary of the average polymer length at both 60 MHz and 400 MHz (expected value n = 9.1–10.9).*

Polymer	Sample	Average Polymer Length	
		60 MHz[a]	400 MHz[a]
Brij® O10	1	10.0 (0.7)	9.9 (0.0)
	2	9.9 (0.3)	9.8 (0.0)
	3	10.0 (0.5)	9.8 (0.0)
ETHOXCARE® OA-10	1	9.0 (0.5)	8.9 (0.0)
	2	9.0 (0.5)	8.9 (0.0)
	3	9.0 (0.1)	8.9 (0.0)
Procol™ OA-10	1	10.2 (0.3)	10.2 (0.1)
	2	10.2 (0.2)	10.1 (0.1)
	3	10.3 (0.3)	10.1 (0.0)

[a]*Average of triplicate analyses, the relative standard deviation (RSD) values for which are provided in parentheses.*

If you have any questions about the incorporation of benchtop NMR into your USP-NF workflows, or about the work presented herein, please don't hesitate to contact us!

References

(1) Rissi, N. C.; Aparecida Scatolin Guglielmi, D.; Corrêa, M. A.; Chiavacci, L. A. *Brazilian J. Pharm. Sci.* **2014**, *50*, 653–661.
(2) Sliwa, K.; Sliwa, P. *J. Funct. Biomater.* **2020**, *11*, 1–11.
(3) Fiume, M. M.; Heldreth, B.; Bergfeld, W. F.; Belsito, D. V; Hill, R. A.; Klaassen, C. D.; Liebler, D.; Marks, J. G.; Shank, R. C.; Slaga, T. J.; Snyder, P. W.; Andersen, F. A. *Int. J. Toxicol.* **2012**, *31*, 169S-244S.
(4) Park, E. S.; Chang, S. Y.; Hahn, M.; Chi, S. C. *Int. J. Pharm.* **2000**, *209*, 109–119.
(5) Polyoxyl 10 Oleyl Ether (2020). The United States Pharmacopoeia – The National Formulary. Rockville, MD, USA.
(6) The average polymer length can be calculated using the following equation: *Average polymer length = [(31 × A_2/A_1) - 3]/4*. Full details can be found in the official monograph method.
(7) Polymer samples were received from various suppliers and used without further purification. MilliporeSigma: Brij® O10 p/n: P6136, lot: MKCG0705. Ethox Chemicals: ETHOXCARE® OA-10 lot: 31H054. Protameen Chemicals: Procol™ OA-10 lot: 17-1280-21B03.