Purity Test of Sucralose, Pharmaceutical Excipients Standard 2018

Sucralose is an artificial sweetener used as an excipient in pharmaceuticals. The purity test for sucralose listed in the Pharmaceutical Excipients Standard 2013 original required analysis using packed column GC. However the updated Pharmaceutical Excipients Standard 2018, announced in March 2018, was amended and required a method for the analysis of methanol in sucralose using a capillary column with headspace GC. In this application note, we report an analysis conducted in accordance with the revision, and that the results were excellent.

Measurement procedure

Standard

Methanol 0.25 g
↓
Dilute to 100 mL with water.
↓
Prepare 10 mL
← Standard stock solution2 mL
↓
Dilute to 250 mL with water.
↓
10 mL dispense into 20 mL headspace vials
↓
Headspace Autosampler
↓
GC/FID

[Final concentration]
Methanol: 100 µg/mL
Internal standard: 20 µg/mL

Test sample

Sucralose 1.0 g
← Internal standard 10 mL
[Final concentration] Internal standard: 20 µg/mL
↓
Add to a 20 mL headspace vial
↓
Headspace Autosampler
↓
GC/FID

Preparation of the internal standard stock solution and the internal standard

Standard stock solution	Internal standard
The *tert*-butyl alcohol 0.25 g is diluted to 100 mL with water.	2 mL of the internal standard stock solution is diluted to 250 mL with water.

Determine the ratios, Qs and Qt, for the peak area of methanol with t-butyl alcohol with the standard and test sample. Calculate the amount of methanol using the following formula: it should be no greater than 0.1 %.

Amount (%) of methanol = Ms/Mt × Qt/Qs × 2/5

Ms : Amount (g) of methanol
Mt : Amount (g) of sucralose

Assay conditions

Conditions

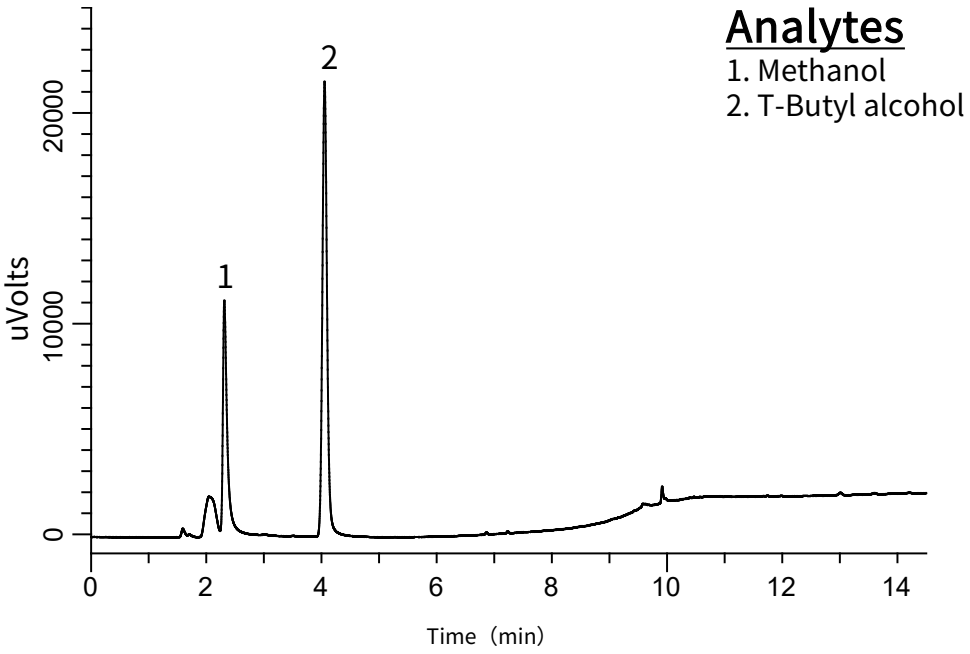
System	: GC - FID
Column	: InertCap 624MS 0.53 mm I.D. x 60 m df = 3.00 µm
Col. Cat. No.	: 1010-64968
Col. Temp.	: 40 ˚C (1 min) - 5 ˚C/min - 60 ˚C - 40 ˚C/min - 240 ˚C (5 min)
Carrier Gas	: He 15 mL/min
Injection	: Splitless 2 min 180 ˚C
Detection	: FID Auto Range 250 ˚C
Injection Vol.	: 0.4 mL
Syringe Size	: 2.5 mL

HS Conditions

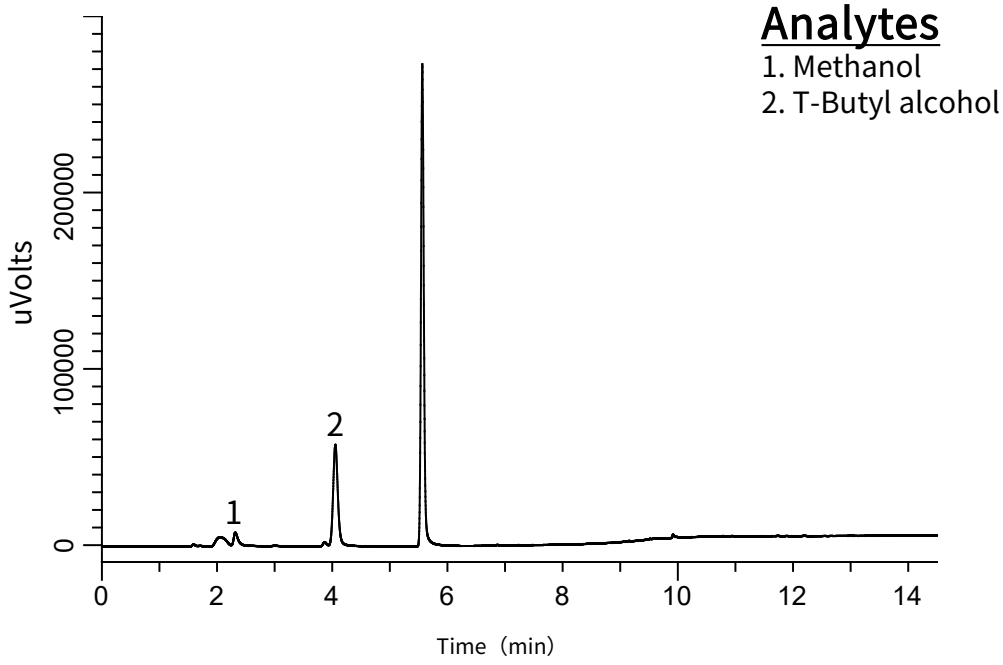
System	: Alpha MOS HT2000H
Sample Equil. Temp.	: 60 ˚C
Sample Equil. Time	: 20 min

Measurement

Chromatogram of the standard



Chromatogram of the test sample



Relative standard deviation

The relative standard deviation was determined to confirm the reproducibility of this test.

Table 1. Repeatability of area values

	Standard			Test Sample		
	Methanol	Internal Standard (*1)	Qs (*2)	Methanol	Internal Standard (* 1)	Qt (* 2)
1 st	194839	385690	0.50517	49715	332906	0.14934
2 nd	189309	363322	0.52105	50804	337456	0.15055
3 rd	194007	371652	0.52201	51812	337046	0.15372
4 th	199621	386311	0.51674			
5 th	181684	369258	0.49202			
6 th	189696	371890	0.51009			
Ave.	191526	374687	0.51118	50777	335803	0.15120
SD	6128	9294	0.01140	1049	2517	0.00227
RSD (%)	3.20	2.48	2.23	2.07	0.75	1.50

*1 The internal standard used is t-Butyl alcohol.
*2 Qs and Qt refer to the ratios of the peak area of methanol to that of t-butyl alcohol in the standard and test sample.

Purity of sucralose

Table 2. Methanol Content

	Methanol
Content (%)	0.0296

Calculating the methanol content using the formula described in Technical Note, P.1, it was found to be 0.0296 %.

Reference: Pharmaceutical Excipients 2018-Ministry of Health, Labour and Welfare
http://wwwhourei.mhlw.go.jp/hourei/doc/tsuchi/T180330I0030.pdf

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