FLUMIOXAZIN (No.578)

Small Scale Collaborative Trial

Small Scale Collaborative Trial on the Determination of Flumioxazin in Flumioxazin Technical and Formulation by High Performance Liquid Chromatography

by
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1. INTRODUCTION

1.1 Scope

The results of the small scale collaborative trial for flumioxazin technical product and flumioxazin wettable powder are reported.

1.2 Samples

1) Flumioxazin technical (TC-1)
2) Flumioxazin technical (TC-2)
3) Flumioxazin technical (TC-3)
4) Flumioxazin wettable powder (WP-1)
5) Flumioxazin wettable powder (WP-2)

1.3 Participants

Shingo Aoyagi	Sumika Chemical Analysis Service, Ltd. Osaka Laboratory (JAPAN)
Yasushi Asada	Sumitomo Chemical Co., Ltd. Organic Synthesis Research Laboratory (JAPAN)
Yoshikazu Asahi	Koei Techno Co., Ltd. (JAPAN)
Yumiko Kozuki	Sumitomo Chemical Co., Ltd. Agricultural Chemicals Research Laboratory (JAPAN)
Rika Matsumoto	Taoka Chemical Analysis Center Co., Ltd. (JAPAN)
Tomoko Uraga	Hayashi Agro Science, Ltd. (JAPAN)

2. ANALYTICAL METHOD

2.1 Outline of Method

Flumioxazin in the test samples is determined by reversed phase high performance liquid chromatography using an ODS column, UV detection at 288 nm and external standardization as stated in CIPAC/4713/m.

2.2 Program of Work

We requested the collaborators to:

1) conduct duplicate determinations on two different days for each sample;
2) inject each sample solution in duplicate and calculate the mean value;
3) check linearity before the determination;
4) describe operating conditions in detail; and
5) attach the calibration curve and all chromatograms for each sample.

3. REMARKS OF PARTICIPANTS

3.1 Analytical Conditions

Lab	Liquid chromatograph Integrator	Column	Mobile phase	Flow rate (ml/min)	Column temp. (°C)
Proposed Method		Phenomenex Gemini 5μ C18 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40
1	Shimadzu LC-20A Shimadzu LC-solution	Phenomenex Gemini 5μ C18 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40
2	Hitachi L-7000 Hitachi D-7000	L-column ODS (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40

3	Shimadzu LC-20A Shimadzu LC-solution	SUMIPAX ODS A-211 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40
4	Shimadzu LC-10ATvp Shimadzu C-R8A	Phenomenex Gemini 5μ C18 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40
5	Shimadzu Prominence Shimadzu LC-solution	CAPCELL PAK C18 SG120 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	0.8	40
6	Shimadzu LC-20A Shimadzu LC-solution	Phenomenex Gemini 5μ C18 (4.6 mm ID × 250 mm, 5 μm)	acetonitrile - water, 50 + 50 (v/v)	1.0	40

3.2 Remarks

- Lab.1
  - Ultrasonic wave was irradiated for about two minutes in order to reduce the preparation time.

- Lab.3
  - The technical material was not easily dissolved and ultrasonic wave was irradiated for 5 to 10 seconds.

- Lab.4
  - The HPLC system was shut down after the analysis on the first day, and linearity was checked again for confirmation on the second day.

- Lab.5
  - The technical material was not easily dissolved and ultrasonic wave was irradiated for about two minutes.

4. RESULTS AND DISCUSSION

Six data sets were obtained from six participants. Summary and detailed statistical evaluations are shown in Tables 1 and 2-1 to 2-5. The statistical evaluations were carried out according to ISO 5725.

The discussion on stragglers and outliers is as follows:

- WP-1
  The variance of Lab. 4 was identified as an outlier. The data were retained because there were no reasons to remove them.

5. CONCLUSION

For all samples, the values of RSD_R (reproducibility relative standard deviation) were smaller than those calculated by Horwitz's equation. The proposed method is considered appropriate for the determination of flumioxazin in technical product and wettable powder.
JAPAC recommends proceeding to a large scale collaborative trial.

Table 1 Summary of Statistical Evaluation of Flumioxazin Small Scale Collaborative Study

	TC-1	TC-2	TC-3	WP-1	WP-2
Average (g/kg)	994.41	994.99	995.80	516.33	516.80
Number of labs.	6	6	6	6	6
Repeatability standard deviation (S_r)	1.970	3.061	3.249	2.586	1.608
"Pure" between laboratory standard variation (S_L)	1.686	2.221	2.600	9.038	5.585
Reproducibility standard deviation (S_R)	2.593	3.782	4.161	9.400	5.812
Repeatability (r)	5.516	8.571	9.097	7.241	4.502
Reproducibility (R)	7.260	10.590	11.651	26.320	16.274
RSD_r	0.198	0.308	0.326	0.501	0.311
RSD_R	0.261	0.380	0.418	1.821	1.125
Horwitz's value	2.002	2.002	2.001	2.209	2.209

Table 2-1 Flumioxazin Technical -1

Lab		Analytical data (n=4)		Yi	$(Yi)^2$	Si	Si^2
1	Day1	994.5	995.4				
	Day2	994.6	996.7	995.30	990622.09	1.017	1.034
2	Day1	997.7	996.0				
	Day2	996.5	998.5	997.18	994367.95	1.135	1.288
3	Day1	996.6	997.3				
	Day2	990.8	997.1	995.45	990920.70	3.114	9.697
4	Day1	993.9	991.8				
	Day2	996.5	991.1	993.33	986704.49	2.428	5.895
5	Day1	991.7	990.4				
	Day2	994.1	990.4	991.65	983369.72	1.745	3.045
6	Day1	993.4	995.3				
	Day2	991.6	993.9	993.55	987141.60	1.529	2.338
S1 SUM		Yi =		5966.46			
S2 SUM		Yi^2 =			5933126.55		
S3 SUM		Si^2 =					23.297

p = 6

1) Cochran's test (p=6, n=4)

$C = Si^2max / S3$ = 0.416 < 0.532 (p=6, n=4, 5%)

2) Grubbs' test (p=6, n=4)

Yi(min) = 991.65 Yi(max) = 997.18 Y = S1/p 994.41

S = 1.953

Y - Yi(min) = 2.76

Yi(max) - Y = 2.77

lower = [Y-Yi(min)]/S = 1.413 < 1.887 (p=6, 5%)

upper = [Yi(max)-Y]/S = 1.418 < 1.887 (p=6, 5%)

3) Calculation of r and R

Mean; Y = S1 / p = 994.41

$Sr^2 = S3 / p$ = 3.883 Sr = 1.970

$SL^2 = [(pS2-S1^2)/p(p-1)]-(Sr^2/n)$ = 2.842 SL = 1.686

$SR^2 = Sr^2 + SL^2$ = 6.724 SR = 2.593

r = 2.8 x Sr =	5.516
R = 2.8 x SR =	7.260
RSDr = (Sr / mean) x 100 =	0.198
RSDR = (SR / mean) x 100 =	0.261

Horwitz's Value = 2 ^[1 - 0.5 x log(Y / 1000)] = 2.002

RSDr and RSDR < 2.002 (Horwitz's Value)

Table 2-2 Flumioxazin Technical -2

Lab		Analytical data (n=4)		Yi	$(Yi)^2$	Si	Si^2
1	Day1	1000.5	999.6				
	Day2	999.3	992.6	998.00	996004.00	3.636	13.220
2	Day1	992.2	994.8				
	Day2	1000.8	998.4	996.55	993111.90	3.807	14.493
3	Day1	1002.2	999.0				
	Day2	995.3	993.6	997.53	995066.10	3.847	14.799
4	Day1	993.8	991.2				
	Day2	996.1	993.0	993.53	987101.86	2.032	4.129
5	Day1	989.8	991.2				
	Day2	992.1	993.7	991.70	983468.89	1.635	2.673
6	Day1	994.5	995.3				
	Day2	990.1	990.7	992.65	985354.02	2.630	6.917
S1 SUM		Yi =		5969.96			
S2 SUM		Yi^2 =			5940106.77		
S3 SUM		Si^2 =					56.231

p = 6

1) Cochran's test (p=6, n=4)

$C = Si^2max / S3$ = 0.263 < 0.532 (p=6, n=4, 5%)

2) Grubbs' test (p=6, n=4)

Yi(min) = 991.70 Yi(max) = 998.00 Y = S1/p 994.99
S = 2.697

Y - Yi(min) = 3.29
Yi(max) - Y = 3.01
lower = [Y-Yi(min)]/S = 1.221 < 1.887 (p=6, 5%)
upper = [Yi(max)-Y]/S = 1.115 < 1.887 (p=6, 5%)

3) Calculation of r and R

Mean; Y = S1 / p = 994.99
$Sr^2 = S3 / p$ = 9.372 Sr = 3.061
$SL^2 = [(pS2-S1^2)/p(p-1)]-(Sr^2/n)$ = 4.931 SL = 2.221
$SR^2 = Sr^2 + SL^2$ = 14.303 SR = 3.782

r = 2.8 x Sr =	8.571
R = 2.8 x SR =	10.590
RSDr = (Sr / mean) x 100 =	0.308
RSDR = (SR / mean) x 100 =	0.380

Horwitz's Value = 2 ^[1 - 0.5 x log(Y / 1000)] = 2.002

RSDr and RSDR < 2.002 (Horwitz's Value)

Table 2-3 Flumioxazin Technical-3

Lab		Analytical data (n=4)		Yi	$(Yi)^2$	Si	Si^2
1	Day1	1002.4	1002.8				
	Day2	996.6	997.5	999.83	999660.03	3.229	10.426
2	Day1	998.9	993.4				
	Day2	998.4	995.6	996.58	993171.70	2.567	6.589
3	Day1	1000.7	1001.3				
	Day2	996.5	995.2	998.43	996862.46	3.030	9.181
4	Day1	1000.7	991.7				
	Day2	993.6	987.6	993.40	986843.56	5.473	29.954
5	Day1	990.0	990.8				
	Day2	992.4	993.7	991.73	983528.39	1.652	2.729
6	Day1	996.4	996.7				
	Day2	994.1	992.2	994.85	989726.52	2.114	4.469
S1 SUM		Yi =		5974.82			
S2 SUM		Yi^2 =			5949792.66		
S3 SUM		Si^2 =					63.348

p = 6

1) Cochran's test (p=6, n=4)

$C = Si^2max / S3$ = 0.473 < 0.532 (p=6, n=4, 5%)

2) Grubbs' test (p=6, n=4)

Yi(min) = 991.73 Yi(max) = 999.83 Y = S1/p 995.80
S = 3.066

Y - Yi(min) = 4.07
Yi(max) - Y = 4.03
lower = [Y-Yi(min)]/S = 1.329 < 1.887 (p=6, 5%)
upper = [Yi(max)-Y]/S = 1.313 < 1.887 (p=6, 5%)

3) Calculation of r and R

Mean; Y = S1 / p = 995.80

$Sr^2 = S3 / p$ = 10.558 Sr = 3.249

$SL^2 = [(pS2-S1^2)/p(p-1)]-(Sr^2/n)$ = 6.758 SL = 2.600

$SR^2 = Sr^2 + SL^2$ = 17.316 SR = 4.161

r = 2.8 x Sr =	9.097
R = 2.8 x SR =	11.651
RSDr = (Sr / mean) x 100 =	0.326
RSDR = (SR / mean) x 100 =	0.418

Horwitz's Value = 2 ^[1 - 0.5 x log(Y / 1000)] = 2.001

RSDr and RSDR < 2.001 (Horwitz's Value)

Table 2-4 Flumioxazin Wettable Powder-1

Lab		Analytical data (n=4)		Yi	$(Yi)^2$	Si	Si^2
1	Day1	509.7	507.5				
	Day2	512.4	510.6	510.05	260151.00	2.037	4.149
2	Day1	526.0	525.2				
	Day2	525.1	523.1	524.85	275467.52	1.234	1.523
3	Day1	525.6	524.2				
	Day2	521.6	522.1	523.38	273926.62	1.863	3.471
4	Day1	518.9	530.7				**
	Day2	527.6	523.3	525.13	275761.52	5.141	26.430
5	Day1	503.3	505.6				
	Day2	506.6	503.0	504.63	254651.44	1.756	3.084
6	Day1	511.0	508.5				
	Day2	510.9	509.4	509.95	260049.00	1.212	1.469
S1 SUM		Yi =		3097.99			
S2 SUM		Yi^2 =			1600007.10		
S3 SUM		Si^2 =					40.126

p = 6

1) Cochran's test (p=6, n=4)

$C = Si^2max / S3$ = 0.659 > 0.532 (p=6, n=4, 5%)
> 0.626 (p=6, n=4, 1%)

Outlier Lab 4 was included in the following evaluation.

2) Grubbs' test (p=6, n=4)

Yi(min) = 504.63 Yi(max) = 525.13 Y = S1/p 516.33
S = 9.130

Y - Yi(min) = 11.70
Yi(max) - Y = 8.80
lower = [Y-Yi(min)]/S = 1.282 < 1.887 (p=6, 5%)
upper = [Yi(max)-Y]/S = 0.964 < 1.887 (p=6, 5%)

3) Calculation of r and R

Mean; Y = S1 / p = 516.33
$Sr^2 = S3 / p$ = 6.688 Sr = 2.586
$SL^2 = [(pS2-S1^2)/p(p-1)]-(Sr^2/n)$ = 81.680 SL = 9.038
$SR^2 = Sr^2 + SL^2$ = 88.368 SR = 9.400

r = 2.8 x Sr =	7.241
R = 2.8 x SR =	26.320
RSDr = (Sr / mean) x 100 =	0.501
RSDR = (SR / mean) x 100 =	1.821

Horwitz's Value = 2 ^[1 - 0.5 x log(Y / 1000)] = 2.209

RSDr and RSDR < 2.209 (Horwitz's Value)

Table 2-5 Flumioxazin Wettable Powder-2

Lab		Analytical data (n=4)		Yi	$(Yi)^2$	Si	Si^2
1	Day1	518.7	517.8				
	Day2	519.5	519.5	518.88	269236.45	0.810	0.656
2	Day1	525.3	523.4				
	Day2	520.9	522.7	523.08	273612.69	1.819	3.309
3	Day1	523.7	522.1				
	Day2	517.0	521.3	521.03	271472.26	2.863	8.197
4	Day1	510.7	511.2				
	Day2	510.8	511.5	511.05	261172.10	0.370	0.137
5	Day1	509.4	508.4				
	Day2	508.5	509.1	508.85	258928.32	0.480	0.230
6	Day1	520.4	517.8				
	Day2	516.9	516.6	517.93	268251.48	1.727	2.983
S1 SUM		Yi =		3100.82			
S2 SUM		Yi^2 =			1602673.30		
S3 SUM		Si^2 =					15.512

p = 6

1) Cochran's test (p=6, n=4)

$C = Si^2max / S3$ = 0.528 < 0.532 (p=6, n=4, 5%)

2) Grubbs' test (p=6, n=4)

Yi(min) = 508.85 Yi(max) = 523.08 Y = S1/p 516.80

S = 5.643

Y - Yi(min) = 7.95

Yi(max) - Y = 6.28

lower = [Y-Yi(min)]/S = 1.409 < 1.887 (p=6, 5%)

upper = [Yi(max)-Y]/S = 1.112 < 1.887 (p=6, 5%)

3) Calculation of r and R

Mean; Y = S1 / p = 516.80

$Sr^2 = S3 / p$ = 2.585 Sr = 1.608

$SL^2 = [(pS2-S1^2)/p(p-1)]-(Sr^2/n)$ = 31.191 SL = 5.585

$SR^2 = Sr^2 + SL^2$ = 33.777 SR = 5.812

r = 2.8 x Sr =	4.502
R = 2.8 x SR =	16.274
RSDr = (Sr / mean) x 100 =	0.311
RSDR = (SR / mean) x 100 =	1.125

Horwitz's Value = 2 ^[1 - 0.5 x log(Y / 1000)] = 2.209

RSDr and RSDR < 2.209 (Horwitz's Value)

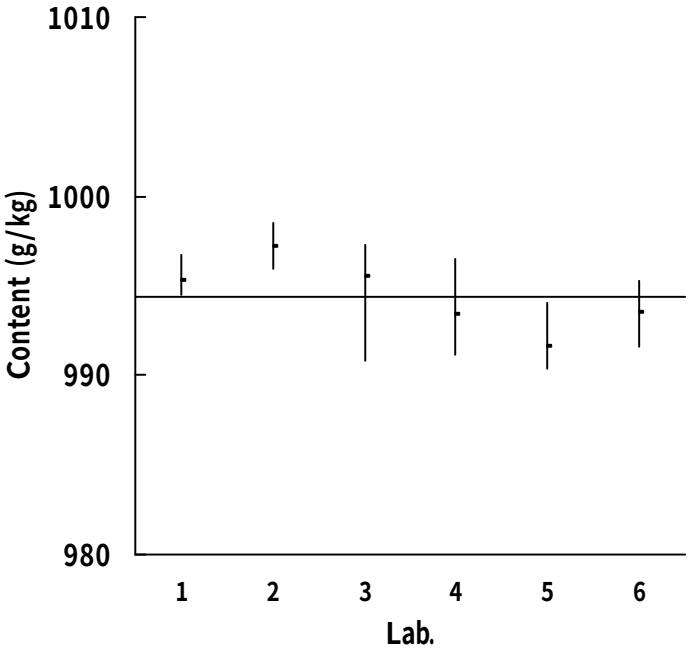

Fig. 1 Flumioxazin Technical-1

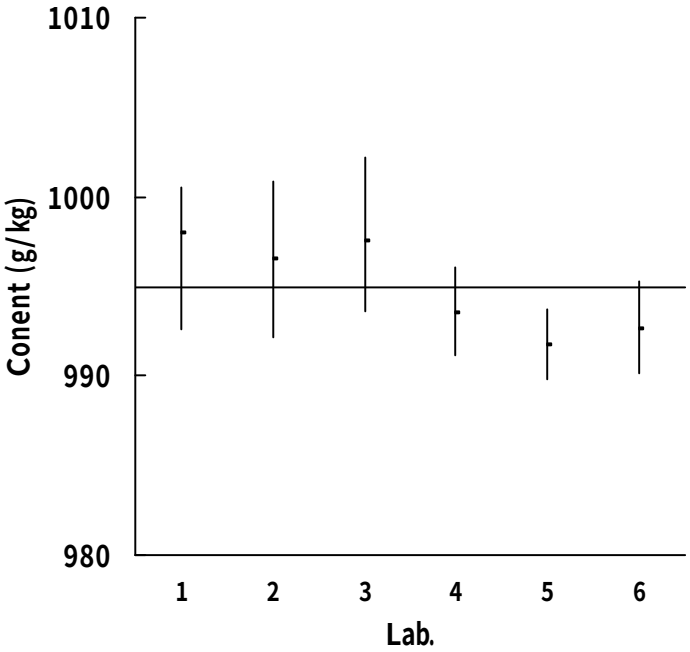

Fig. 2 Flumioxazin Technical-2

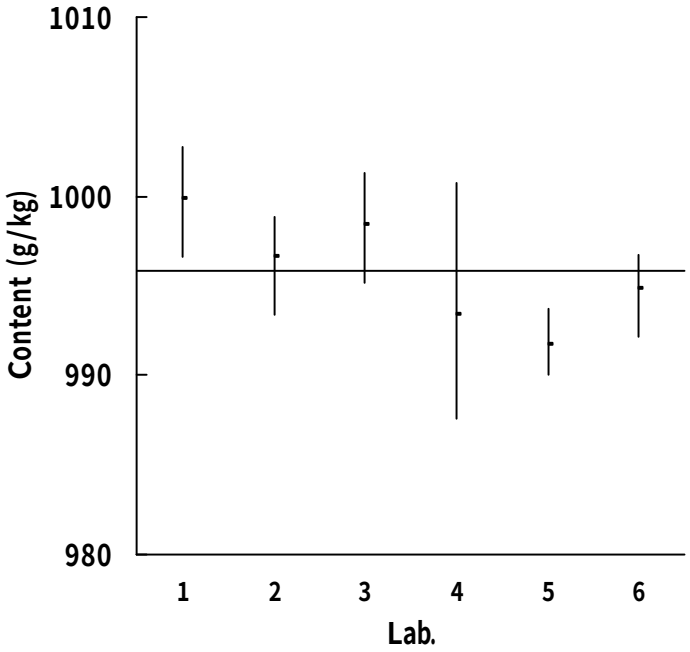

Fig. 3 Flumioxazin Technical-3

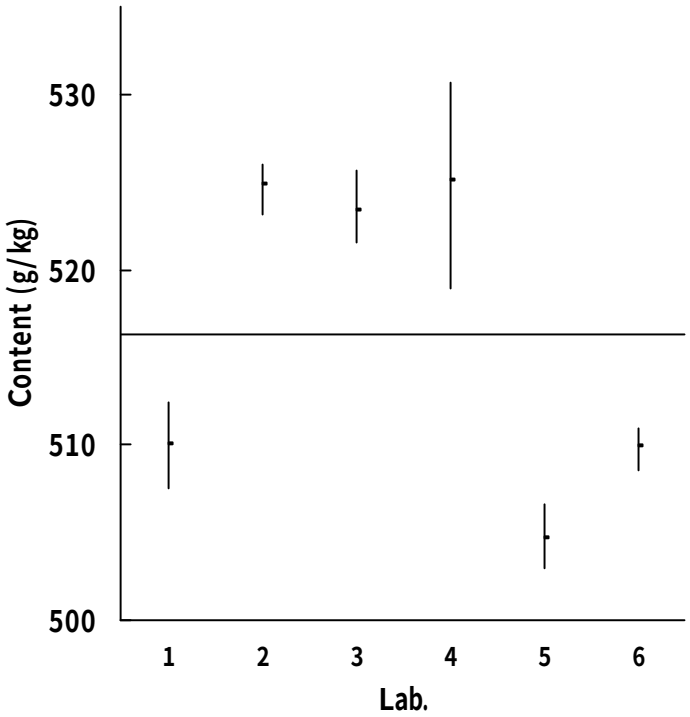

Fig. 4 Flumioxazin Wettable Powder-1

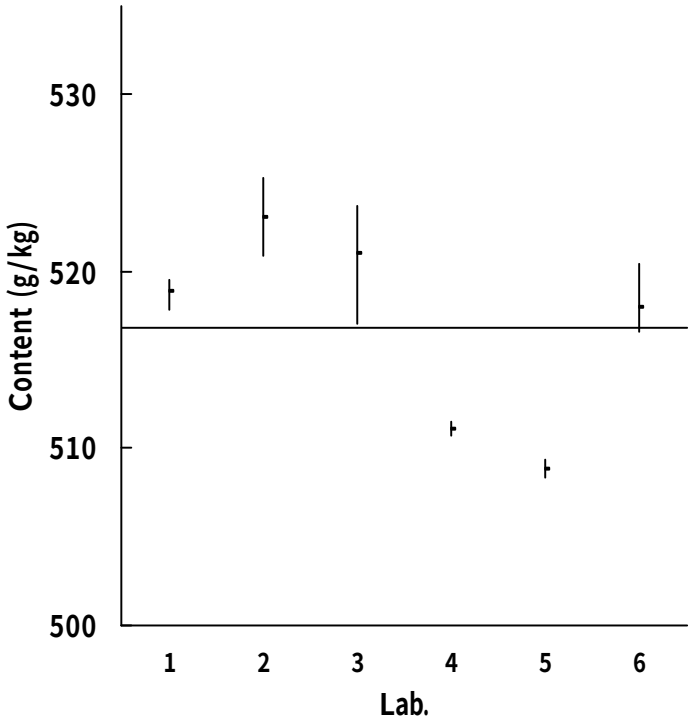

Fig. 5 Flumioxazin Wettable Powder-2