CIPAC STATUS REPORT

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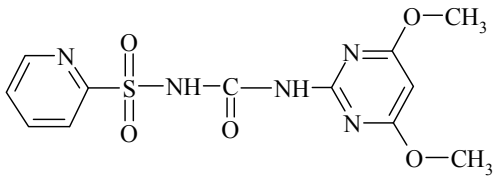

0595 Flazasulfuron

Allocated to ESPAC
CIPAC methods published in:

CIPAC

CIPAC 54th meeting, June 2010 in Ljubljana

Mr Jim Garvey presented the results of a small scale trial on the determination of flazasulfuron in TC and WG formulations using HPLC-UV at 230 nm using internal standard, organised by ESPAC in conjunction with ISK Belgium. 4 labs participated.
Comments from labs:
Ultrasonication not long enough for dissolution; for WG would be better to add some water as solvent; baseline interference for internal std for all WGs; the proposed sample preparation of adding internal std. up to volume is not ideal; would prefer to have a more concentrated internal standard and make up to volume.
2 Cochran outliers in the data. None of the outliers were removed. The TCs were within Horwitz value, but WGs weren't. Removing the outliers didn't really help.
Visual inspection of the results from Lab 3 showed much higher results than the other. Removing laboratory 3 gave results within Horwitz (but these were not identified as outliers). No internal std. was provided by the company which might have introduced variables in the results as all labs sourced their own.
Comments:
CIPAC guidance says HPLC method should not used internal std. unless it's really justified.
Were calculations made without the internal std., too? Propose that it's recalculated without the internal std. and discuss within ESPAC.
It was proposed to go to full scale trial but to use 3 point calibration without internal standard and as many laboratories as possible.
ISK will check back to see if the internal std. can be removed.
Decision: If all the information raised is taken into consideration and the method adapted then they could perhaps go to full scale trial? Meeting agreed that ESPAC should discuss with the company and see if they can develop something further (i.e. recalculated the result without the internal standard) and if needed conduct a small scale trial. Then, if all OK, go to full-scale trial to present at the next year. Timelines are tight.
Why use acetic acid to buffer a compound that has a pKA lower than acetic acid?
With the submitted data set it was not possible to make a reliable recommendation.
It was proposed to have further consideration within ESPAC.

CIPAC 55th meeting, June 2011 in Beijing

Mr Jim Garvey presented the results of a **small scale** collaborative trial on the determination of flazasulfuron in technical product (TC) and water dispersible granule (WG) formulations using HPLC-UV with detection at 230 nm and external standard calibration. The trial was organised by ESPAC in conjunction with ISK Belgium. A small scale trial was presented to CIPAC in 2010 for the same method but using an internal standard, which gave unacceptable results. ESPAC re-evaluated the data without the internal standard and the data were acceptable, however in after discussions with company, it was proposed by the company to conduct another small scale trial.

5 laboratories participated in the study. 2 samples of TC and 3 samples of WG were provided.
3 participating laboratories commented that there were difficulties in separating the a.i. and formulants in the WG samples, with Laboratory 5 commenting that using detection at 260 nm instead of 230 nm limited the influence of interferences. Laboratory 4 commented that the Day 1 results for both TCs were slightly lower than on Day 2.
The statistical evaluation was carried out according to the CIPAC guidelines.
For TC 2 Lab 3 was a Cochran's straggler. For WG 1, WG 2 and WG 3 Lab 3 was a Cochran's outlier. For WG1 Lab 5 was a Grubb's straggler and for WG 3 and Lab 5 was a Grubb's outlier. No data were excluded from the initial evaluation.
TC 1 and TC 2 meet the Horwitz criteria when all the data are included. All 3 WG samples fail the Horwitz criteria when all the data are included. When the results from Lab 3 (Cochran's outlier) were omitted and the statistical evaluation was repeated the Horwitz criteria were met in all cases.
ESPAC considers that the proposed method was considered appropriate for the determination of flazasulfuron in TC and WG and that a full scale trial can be conducted.
The following comments were received from the meeting:

- ➢ It would be preferred to have a fixed operating temperature for the HPLC analysis as ambient temperature can vary from country to country.
- ➢ What was the preferred wavelength to use 230 nm or 260 nm? Mr Garvey replied that only one laboratory had an issue with interference at 230 nm. This was resolved by using 260 nm, but no other labs had this problem therefore 230 nm was the preferred wavelength.
- ➢ The issues with the results for the WG could be due to the extraction procedure as fluzasulfuron is not particularly stable to hydrolysis in acidic conditions. It might be better to use a different extraction solution at a higher pH to achieve a better recovery of flazasulfuron from the WG.

CIPAC 56th meeting, June 2012 in Dublin

Mr Joris presented the results of a **full scale** collaborative study on the determination of flazasulfuron in technical product (TC) and water dispersible granule (WG) formulations using HPLC-UV, detection at 260nm and external single point standard calibration. Two samples of TC and three samples of WG were provided. 16 laboratories participated however only results for 15 labs were presented for the TC due to problems with sample shipment to 1 lab.
Several changes were made to the method based on the result of the small scale trial:

- ➢ A grinding step was included for preparation of the WG samples
- ➢ All samples need to be analysed within 8 hours of preparation. This is because flazasulfuron is not particularly stable in acetonitrile solutions.
- ➢ The internal standard was removed.
- ➢ The temperature of the HPLC analysis was changed to 40°C
- ➢ Injection volume
- ➢ The detection wavelength was changed from 230 nm to 260 nm to get better resolution from interferences.

One lab commented that it was not necessary to grind WG samples – instead they added water. Another lab commented that the sonication time for WG was not sufficient.
No data were excluded from the initial evaluation. With all the data included all samples meet the Horwitz criteria. One laboratory was identified as an outlier for most samples however the Horwitz criteria were met with all data included.
Mr Joris concluded that the proposed method is appropriate for the determination of flazasulfuron in TC and WG and proposed that the method be adopted by CIPAC as a provisional method.
The meeting raised concerns about the need to analyse samples within a certain time after extraction as this may indicate instability of active substance. It was noted that the samples that were sonicated for extraction gave consistently lower results but were within the acceptable range.
The meeting agrees that there were some reservations with the method but the statistical results indicate that the method is working acceptably.

Decision:

The reversed phase HPLC method (CIPAC/4831) for the determination of flazasulfuron in TC and WG formulations was accepted as a **provisional** CIPAC method.

CIPAC 57th meeting, June 2013 in Kyiv

At the 56th meeting, 2012 in Ireland the method was adopted as provisional. No further comments were received.
The method can be promoted to a **full CIPAC method**.

Decision: The reversed phase HPLC method (CIPAC/4831) for the determination of flazasulfuron in TC and WG formulations was accepted as a **full** CIPAC method.