

Methamidophos

Insecticide, acaricide

Background Information

Methamidophos belongs to the group of organophosphorous pesticides, although widely used in the past, are much less so now because of toxicity concerns. Their registration is progressively expiring world-wide and are being replaced by less toxic compounds. The compound was patented by Bayer and Chevron in the late 1960s. Methamidophos is a broad spectrum insecticide for chewing, mining and sucking insects, e.g. aphids, leafhoppers, leaf-eating caterpillars and also has acaricidal side-effects.

Organophosphate insecticides, including methamidophos, act by the inhibition of the enzyme acetylcholinesterase, a key enzyme for nervous system function.

Worldwide crop protection uses of methamidophos include broccoli, cauliflower, corn, grapes, sugar beets, cotton, potatoes and tobaccos. Commercially available products may be found mainly as water soluble concentrate formulations. During the past years, methamidophos commercialization and usage has been severely restricted or banned. For example, in the EU, methamidophos has been excluded from Annex I listed under Dir. 91/414/EEC due to acute consumer exposure (based on food residues risk-assessment) and potential adverse effects to non-

target organisms. Methamidophos is on the Prior Informed Consent (PIC) list (Rotterdam Convention) and import is restricted in many countries. Where methamidophos is not registered anymore, its maximum residue limit (MRL) is generally set at the lower limit of analytical determination (LoD).

Methamidophos is also a main breakdown product in or on crops of another organophosphate insecticide – acephate. In the various national regulatory systems the definition of the residue for acephate is generally acephate per se, and methamidophos residues resulting from the use of acephate are accounted for by separate MRLs.

When comparing the toxicity of acephate and methamidophos towards insects and mammals, acephate has a higher activity toward insects, but seems to have low toxicity to other animals. The reason for this difference lies in the existence of a C=O bond in acephate that does not exist in methamidophos. The C=O bond can in mammals be cleaved in the major detoxification pathway leading to the formation of nontoxic fragments, whereas methamidophos cannot be detoxified in the same way.

The CORESTA Guide No.1 sets the Guidance Residue Level (GRL) for methamidophos¹.

Properties ²

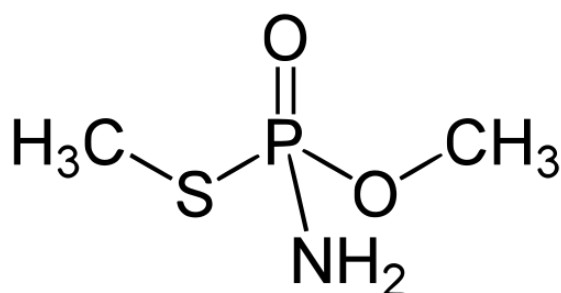


Figure 1. Structure of methamidophos.

IUPAC name: (RS)-O,S-dimethyl phosphoramidothioate

Formula: C₂H₆NO₂PS

Mass: 141.1

CAS RN 10265-92-6

Form: Colorless crystals

Solubility: Water and dichloromethane > 200 g/L; hexane 0.1-1 g/L; toluene 2-5 g/L [all at 20-25 °C]

Stability: Stable at ambient temperature, but decomposes on heating without boiling. Stable at pH 3–8; hydrolysed in acids and alkalis, DT₅₀ (22 °C) 1.8 y (pH 4), 110 h (pH 7), 72 h (pH 9); photodegradation is of minor importance.

pKa: - 15.57

Melting Point: 45 °C

Sample Extraction

Due to its good solubility properties and stability, methamidophos can be analyzed with a range of extraction and detection methods. Successful extraction of methamidophos from tobacco can be achieved using methanol or a combination of ethyl acetate and water^{2,3}. Applications relying on pressurized liquid extraction of tobacco samples are also amendable, but considerations of possible break-down of methamidophos due to higher extraction temperatures need to be controlled³.

When water is used for wetting the sample, a drying step with sodium sulfate or other drying agent is relevant for removing the water. The crude extracts are mostly subjected to concentration by rotary evaporation or solid phase concentration and clean-up³. Clean-up of extract by gel permeation chromatography is also frequently applied on samples prior to analysis. Modern LC-MS/MS instrumentation allows the direct injection of the extracts without any sample purification steps.

Analysis (chromatography and quantitation)

While gas chromatography utilizing a variety of different detectors (e.g. GC-FPD, GC-FID, GC-MS and GC-MS/MS) has been used for its analysis, as methamidophos is a highly polar compound it often exhibits excessive peak tailing and is subject to matrix effects at the injection port^{4,5}.

LC-MS/MS provides an effective means of analyzing methamidophos although extensive matrix effects arising from the tobacco must be eliminated, reduced or negated through the use of sample clean-up, internal standard, or matrix-matched standards, either alone or in combination^{6,7}. Methamidophos (mw 141.1) is easily protonated ($[M+H]^+$ at m/z 142) with LC-MS/MS using electrospray ionization in the positive mode and fragments readily (Figure 2).

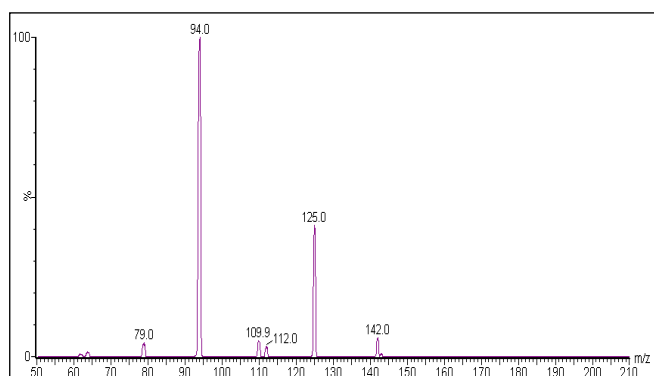


Figure 2. Product ion scan of methamidophos $[M+H]^+$; m/z 142 by LC-MS/MS using electrospray ionization (ESI) in the positive mode.

When analyzed by LC-MS/MS, the two major transitions produced are 142/94 and 142/125 with the former being the most intense in response (Figure 3).

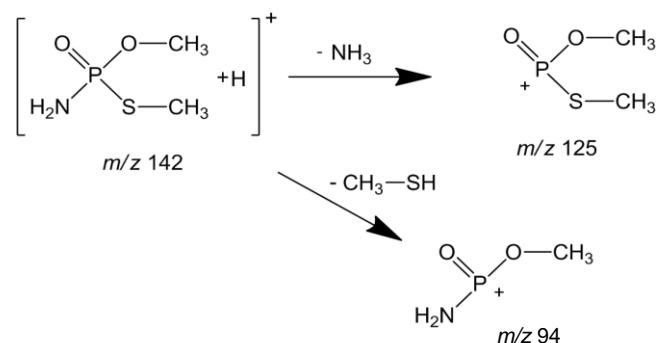


Figure 3. Fragmentation pathway for methamidophos.

Since tobacco is a very complex matrix, it is recommended that several transitions are evaluated when developing a method as a transition of lower response may be preferable for quantitation if it provides a 'cleaner' chromatogram compared to a more intense transition. Example chromatography by LC-MS/MS for methamidophos is provided (Figure 4).

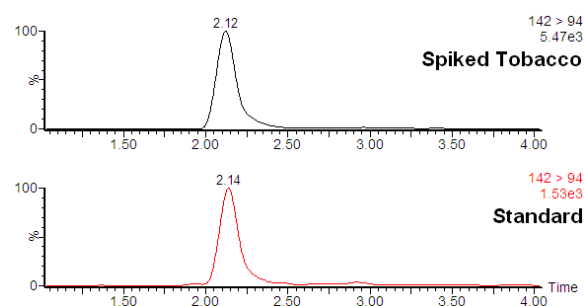


Figure 4. LC-MS/MS MRM chromatogram illustrating transition 142/94 for a tobacco extract fortified with methamidophos (upper trace) and a methamidophos calibration standard (lower trace).

References

- 1 Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA), *Guide No. 1: The Concept and Implementation of Agrochemical Guidance Residue Levels, July 2016 – fourth edition + additional CPA June 2018*, https://www.coresta.org/sites/default/files/technical_documents/main/Guide-No01-GRLs4th-Issue-July16added-fluopyram.pdf (verified September 2019).
- 2 *The Pesticide Manual 18th ed.*; C.D.S. Tomlin, (Ed.) British Crop Protection Council, 2018.
- 3 Blass W., Philipowski C.; *Gas-chromatographic method for the determination of methamidophos residues in material of plant origin, including processed products*; Bayer CropScience J. 48 (1995) 353-378.
- 4 Waliszewski S.M., Waliszewski K.N.; *Gas-chromatographic determination of acephate, methamidophos and terbufos in tobacco*; Fresenius Z. Anal. Chem. 325 (1986) 394.
- 5 Haib J., Hofer I., Renaud J. M.; *Analysis of multiple pesticide residues in tobacco using pressurized liquid extraction, automated solid-phase extraction clean-up and gas chromatography-tandem mass spectrometry*; J. Chromatogr. A 1020 (2003) 173-187.
- 6 Mayer-Helm B., Hofbauer L., Müller J.; *Method development for the determination of selected pesticides on tobacco by high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry*; Talanta 74 (2008) 1184-1190.
- 7 Mayer-Helm B.; *Method development for the determination of 52 pesticides in tobacco by liquid chromatography-tandem mass spectrometry*; J. Chromatogr. A 1216 (2009) 8953-8959.