DE-511, A NEW LOW-RATE TRIAZOLOPYRIMIDINE SULFONANILIDE HERBICIDE FOR CONTROL OF BROAD-LEAVED WEEDS IN CEREALS AND MAIZE

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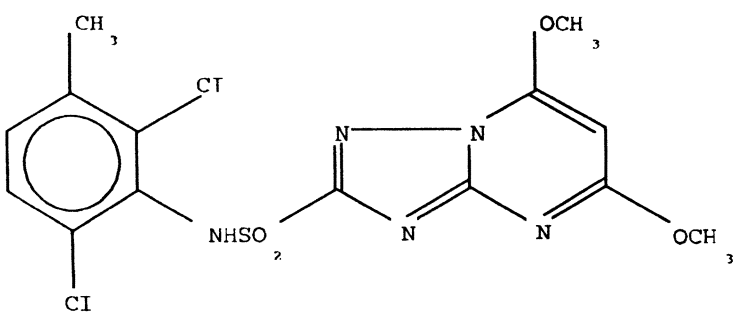
Summary. DE-511, N-(2,6-dichloro-*m*-tolyl)-5,7-dimethoxy[1,2,4]triazolo[1,5a]pyrimidine-2-sulfonamide (ISO proposed common name - metosulam) is a new selective herbicide for the control of broad-leaved weeds in cereals and maize. Typical application rates in cereals range from 5 to 15 g.a.i. ha^{-1} post-emergence and in maize from 20 to 30 g.a.i. ha^{-1} pre- or post-emergence. DE-511 is a representative of the chemical family triazolopyrimidine sulfonanilides and can be formulated in both aqueous and dry systems. Favourable results were obtained in toxicological and environmental studies. The latter studies suggest that no restrictions are required with regard to rotational crops.

INTRODUCTION

DE-511, N-(2,6-dichloro-*m*-tolyl)-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide (ISO proposed common name - metosulam) is a novel low-rate herbicide discovered by DowElanco. This representative of a new generation of herbicide chemistry, the triazolopyrimidine sulfonanilides is being developed by DowElanco Europe and affiliated companies for post-emergence control of broad-leaved weeds in all cereal species and for both pre- and early post-emergence control of key broad-leaved weeds in maize. The triazolopyrimidine sulfonanilide chemistry allows a high degree of formulation flexibility, and DE-511 can be formulated in both liquid and dry systems. This paper will summarise the chemistry, toxicology, environmental fate in soil and water, fate in plants and mode of action of DE-511. The herbicidal efficacy and selectivity in cereals and maize, as well as the aspect of safety to rotational crops under European conditions is reviewed by Snel *et al.* (3).

CHEMICAL AND PHYSICAL PROPERTIES

Structure.



Proposed common name (ISO): metosulam

Herbicide technology

Chemical name:
(IUPAC):
N-(,6-dichloro-*m*-tolyl)-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide.
(CA):
N-(2,6-dichloro-3-methylphenyl)-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide

Molecular weight: 418.26

Melting point: 210-211·5C

Solubility in water (at 20C):

distilled water	(pH 7.5)	200 mg L^{-1}
aqueous buffers	(pH 5.0)	100 mg L^{-1}
	(pH 7.0)	700 mg L^{-1}
	(pH 9.0)	5,600 mg L^{-1}

Dissociation constant: $pK_a = 4.8$

n-Octanol/Water partition Coefficient at 20C :
Aqueous phase (distilled water) log $P_o/W = 0.9778$

Vapour pressure: 4 x 10-13 Pa at 20°C

TOXICOLOGY

Acute mammalian toxicity.

- Acute Oral LD_{50}
  - Rat (Fischer 344) >5,000 mg kg^{-1} BW
  - Mouse (CD - 1) >5,000 mg kg^{-1} BW
- Acute Percutaneous LD_{50}
  - Rabbit (NZW) >2,000 mg kg^{-1} BW
- Inhalation LC_{50} at **maximum attainable** concentration.
  - Rat (Fischer 344) >1.9 mg L^{-1}

Primary irritation tests.

- Skin Irritation
  - Rabbit Non-irritant
- Eye Irritation
  - Rabbit Non-irritant

Skin sensitisation.
- Guinea pig Non-sensitiser

Mutagenicity tests. Five mutagenicity tests systems *(in vitro/in vivo)* were used to evaluate DE-511. This molecule did not induce genotoxic changes and is thus deemed to be non-mutagenic.

Sub-chronic and chronic toxicity. Renal toxicity was evident in both short and long-term feeding studies, with the rat identified as the most sensitive species (2-year NOEL 5 mg/kg BW/day). No adverse effects were observed in reproductive toxicity studies. The data generated indicate that the potential human exposure associated with the proposed agricultural uses should not present a hazard.

Ecotoxicology. Results of extensive ecotoxicological studies indicate that DE-511 and its formulations should not present a hazard to wildlife and desirable soil organisms when applied in accordance to good agricultural practices.

ENVIRONMENTAL FATE IN SOIL AND WATER

Soil. Aerobic degradation studies conducted under laboratory conditions showed a half-life in soil with an average DT_{50} value of 6 days (range : <1 to11 days). Further experiments showed that the degradation of DE-511 is microbially mediated with very little degradation taking place under anaerobic conditions. Metabolite formation was observed 3 days after the initiation of the aerobic study. Under actual field conditions over two seasons, an average DT_{50} value of 20 days, depending on soil type, weather conditions and geography was demonstrated in six geographically well separated experiments. These trials on the dissipation of DE-511 in soil under field conditions were conducted in England and Germany in 1992 and 1990/91, respectively. Standard laboratory leaching studies (BBA, 1986) showed that under the extremely adverse environmental conditions prescribed in the protocol of these experiments, DE-511 possessed only a very limited mobility in all soil types with the exception of sandy soils.

Water. DE-511 is stable to hydrolysis at 25°C across the normal environmental pH-range (pH 5 to 9).

FATE IN PLANTS AND MODE OF ACTION

Plant metabolism. A plant metabolism study in wheat has been conducted using a ^{14}C labelled DE-511 formulation. The radiolabelled formulation was applied at growth stage ZD30 (beginning of stem elongation) at an application rate equivalent to 100 g a.i. ha^{-1}, viz at 7-10 times the rate to be recommended. Only approximately 1% of the total applied radioactivity was absorbed by the plants. Metabolism was not very extensive because the major component (>80% of the radioactivity present) in green plant tissue at all sampling times was the parent molecule. The total levels of parent and any metabolites at harvest were very low especially when the elevated application rate is taken into account, viz. 0.01 and 0.125% applied radioactivity in grain and straw, respectively, which expressed as DE-511 equivalents represents levels of 0.005 ppm and 0.05 ppm, respectively.

Residues in plants. When applied at rates ranging from 15 to 40 g a.i. ha^{-1} in a wide range of cereal species/varieties at growth stage ZD30-39, DE-511 residues could not be detected in grain (lowest validated limit of determination: 0.01 mg kg^{-1}). Residues of DE-511 in straw were occasionally above the lowest validated limit of determination (0.1 mg kg^{-1}) but always <0.5 mg kg^{-1}. These extremely low residue levels in grain and straw combined with the favourable

mammalian toxicity allow the conclusion that there is negligible risk to consumers of treated crops.

Mode of action. Gerwick *et al.* (2) presented physiological and biochemical evidence that triazolopyrimidine sulfonanilides act by inhibition of the first common enzyme to branched-chain amino acid synthesis, acetolactate synthase (ALS). Most of these tests were conducted with N-(2,6-dichlorophenyl)-5,7-dimethyl[1,2,4]triazolo[1,5-a] pyrimidine-2-sulfonamide, an analogue of DE-511. Concentrations as low as 0.006-0.010 ppm of this analogue effectively caused total inhibition of growth in soybean suspension cultures. The herbicidal effect could be completely reversed in the presence of valine, leucine and isoleucine. *In vitro* studies with isolated ALS from susceptible and tolerant plant species showed that the concentrations at which the analogue of DE-511 gave 50% inhibition of the enzyme activity (I_{50}) fall within a narrow range (0.11 to 0.45 M), whilst the GR_{50} (50% growth inhibition) following foliar applications showed a spread of 9-500 mg L^{-1}. DE-511 produced an I_{50} value of 0.0012 M on barley ALS, which presents a significant advance in enzyme inhibition over the earlier analogue described above.

CONCLUSIONS AND SUMMARY

DE-511 (ISO proposed common name: metosulam) is a representative of a new generation of herbicide chemistry, the triazolopyrimidine sulfonanilides. DE-511 has been shown to be safe to all winter cereal species. The optimum time of application in winter cereals is post-emergence in the spring at a rate of 10-15 g a.i. ha^{-1}. These rates present no safety problems in key rotational broad-leaved crops such as oil seed rape and sugar beet. (Snel *et al.*, 3). In view of its flat dose response curves seen for the key cereal broad-leaved weeds, the optimal application rate is 10 g a.i. ha^{-1} under Northern European conditions.

LITERATURE CITED

1. BBA 1986. Richtlinien fur die amtliche Prüfung von Pflanzenschutzmitteln. Teil IV, 4-2. BBA. Braunschweig, Germany.
2. Gerwick, B.C., Subramanian, M.V and Loney-Gallant, V.I. 1990. Pestic-Sci. 29, 357-364.
3. Snel M., Watson P.A., Gray N.R., Kleschick W.A. and Carson C.M. 1993. Med. Fac. Landbouww., Univ. Gent (56, In Press)