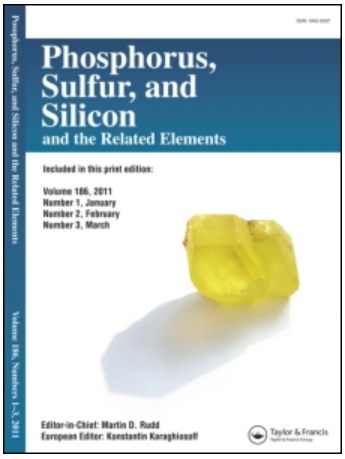

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Recent Advances in the Research on Herbicidally Active Aminomethylenebisphosphonic Acids

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Influence of the mode of application of herbicidally active N-pyridylaminomethylenebisphosphonic acids on their uptake by plants was studied in some detail. The experimental evidence is given that accounts for a multiple mode of action of these herbicides.

Keywords: aminophosphonate; herbicide; glutamine; aromatic amino acids

INTRODUCTION

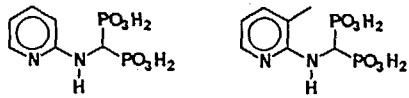
N-substituted aminomethylenebisphosphonic acids, developed in Japan,[1] constitute a new class of promising herbicides. These acids posses two strongly acidic residues and one positively charged amino group, and thus closely resemble popular herbicide glyphosate. Most of them exert the remarkable phytotoxic effects at both the plant and cell culture level.[2,3] Although some attempts have been made for the determination of their mechanism of action, it still remains unclear and the literature data suggest that they are multiple target herbicides.[4–6]

In this paper we report some new results on the herbicidal activity of N-substituted aminomethylenebisphosphonic acids.

RESULTS AND DISCUSSION

Influence of the mode of application on herbicidal activity

In order to find out if the transportation in plants accounts for the potency of this new class of herbicides we have tested how the mode of the application influenced the physiological activity of four N-pyridylaminomethylenebisphosphonates (compounds 1-4).



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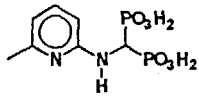

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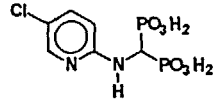

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They were applied as post-emergence herbicides in 1% water solutions in a doses accounting for 3 kg/ha using three test plants: two brands of horse bean (*Vicia faba* var. *faba* and *Vicia faba* var. *minor*) and tomato (*Lycopersicon lycopersicum*). Four modes of application included: standard spraying of the plant leaves, direct application to the soil, cultivation of the plants under hydroponic conditions with herbicide present in the growth medium, and application of the herbicides directly to the stem of plants by means of capillary tubes. The tested compounds exhibited nearly identical pattern of activity as reported earlier [3] with compounds 2 and 4 being the most active and compound 3 exhibiting weak herbicidal action. The herbicidal activity was practically non-dependent on the mode of application, thus showing that the transportation of the herbicides in plant tissues is quite effective. The only exception was herbicidal activity of compound 3 towards tomato plant which appeared only if compound was given directly to the plant stem.

Thus, we have shown that N-pyridylaminomethylenebisphosphonates are effective herbicides and their activity does not depend on their mode of application.

Mode of action of N-2-(5-chloropyridyl)aminomethylenebisphosphonic acid

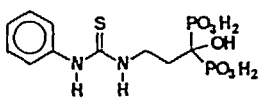
Compound **5** was previously found to inhibit *in vitro* the activity of the first enzyme in the pre-chorismate pathway 3-deoxy-D-*arabino*-heptulosonate-7-phosphate synthase (DAHPS, EC 4.1.2.15).[4] At milimolar level it inhibited the activity of Co^{2+}-dependent, cytosol-localized DAHPS isoform but such effect was shown to rely entirely on its chelating properties. On the contrary, it reduced the activity of plastidial and Mn^{2+}-stimulated isozyme competitively to the substrate erythrose-4-phosphate and the inhibition did not simply base upon metal chelation. To ascertain whether DAHPS activity could really represent the main target of compound **4** *in vivo* we undertook study of the effect of sublethal concentrations of the inhibitor on cultured *Nicotiana plumbaginifolia* cells. Amino acid pools measurement showed an actual reduction of phenylalanine, tyrosine and tryptophan level following the addition of the compound to the growth medium. However, even stronger effect was noticed for other amino acids, mainly for glutamine. When the activity of the enzymes involved in the glutamate cycle was measured in the presence of the compound 4, glutamate synthase appeared unaffected, while glutamine synthetase (EC 6.3.1.12) was significantly inhibited.

To allow adequate kinetic analysis, the enzyme was purified near to homogeneity from actively proliferating cells. During the purification procedure no evidence for multiple enzyme forms was found. Catalytic properties of the enzyme were consistent with those previously described for the enzyme from other plant species: a strikingly high apparent affinity for ammonia (27 μM) and K_m values in the milimolar range for ATP and glutamate (1.2 and 5.5 mM respectively).[7] Compound 4 appeared to be uncompetitive inhibitor with respect to ammonia, glutamate and ATP, with K_i values of 113, 97 and 39 μM, respectively. Contrary to phosphinothricin, the inhibitor bonds to the enzyme reversibly.

Exogenous supply of glutamine, however, failed to reverse the toxicity of compound 4. The same procedure significantly relieved the physiological activity of a comparable level of phosphinothricin. Similarly as shown before,[5] not even a mixture of aromatic amino acids was able to counteract the effect of compound 4, whereas the same mixture alleviated that of a similar concentration of glyphosate. On the contrary, when cells were fed with both supplements, full reversal was obtained. Thus, we assume that these data support the indication that the inhibition of the synthesis of both glutamine and aromatic amino acids might be the real basis of the herbicidal activity of N-2-(5-chloropyridyl)aminomethylenebisphosphonic acid (**4**).

New bisphosphonates of herbicidal activity

Previous studies on herbicidal activity of the derivatives of aminomethylenebisphosphonic acids revealed that for compound to be active the presence of two strongly acidic residues and one positively charged substituted amino group is required.[3] An attempt of this part of work was to find out how the structural modifications of amino moiety influence herbicidal action of these compounds. Thus, using common cress (*Lepidium sativum*) we have studied physiological activity of compounds in which amino group was replaced by hydroxyl-, ureido- or thioureido-function and those which contain imino group (an oxidized form of amino group). Compounds **5**, **6** and **7** appeared to be the most active. Our results indicate that substituted, protonated amino group is not an indispensable structural feature of bisphosphonates in order to exhibit phytotoxicity.



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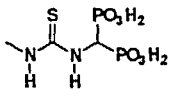

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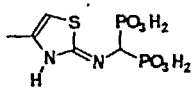

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