TARGET SIZE AND SITE-BASED HERBICIDE RESISTANCE

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Summary. The multiplicity of molecular receptor sites associated with the large binding domains of herbicide targets has been shown to account for the relatively small number of useful targets so far identified and for the development of site-based herbicide resistance.

INTRODUCTION

It is only relatively recently that some plants have been shown to acquire tolerance to particular herbicides under field conditions. Such herbicide resistance has been ascribed either to mutation of the target site leading to weaker binding of the herbicide or to modification of the metabolic activity of the host plant resulting in enhanced herbicide degradation.

This contribution is concerned with a relationship between the size of the target site, the discovery of new herbicides and the development of site-based herbicide resistance.

DISCUSSION

Relatively large and conformationally mobile endogenous molecules appear to be associated with many of the known herbicide target sites [1]. Thus plastoquinone interacts with the binding site for PS_{II} photosynthetic electron transport inhibitor herbicides such as atrazine, diuron, bromacil and metribuzin, protoporphyrinogen, with that for the bleaching herbicides (bifenox, oxyfluorfen, oxadiazon) [2] and phytoene with that for the carotenoid inhibiting herbicides (fluridone, norflurazon) [3]. Furthermore, it has been proposed that the site of action of inhibitors of acetohydroxy acid synthase (chlorsulfuron, sulfometuron methyl, etc.) is an evolutionary relic of an ubiquinone binding site [4].

The binding domains of such molecules as plastoquinone, phytoene, ubiquinone and protoporyphrinogen, i.e. the endogenous receptor (ER) sites, would be expected to be large and complex and possess many centres (amino acid residues) with which small molecules could interact. Different molecules would be likely to interact with different combinations of amino acid residues and this could lead to many potential herbicide receptor (HR) sites either within or overlapping the same ER site.

A multiplicity of inhibitor binding sites has been shown to occur within the PS_{II} reaction centre accounting for herbicides as structurally diverse as amide, urea, triazine, triazinone, pyrimidinone, phenol and cyanoacrylate derivatives inhibiting photosynthetic electron transport at the PS_{II} level [1]. Moreover, the unique character of each HR site accounts for the highly specific structure-activity relationships observed within closely related series of PS_{II} herbicides e.g. cyanoacrylates [5].

Evidence for multiple HR sites in non-photosynthetic herbicide targets is provided by the structural diversity of known inhibitors. Thus sulfonyl urea (chlorsulfuron) and imidazolinone herbicides (imazapyr) inhibit acetohydroxy acid synthase, an enzyme involved in branched amino acid biosynthesis [6] whilst phenoxyphenoxy propionic acids (haloxyfop) and cyclohexanediones (sethoxydim) inhibit acetylcoenzyme A carboxylase, an enzyme concerned with lipid biosynthesis [7]. Likewise, nitrodiphenyl ethers (oxyfluorfen) and oxadiazoles (oxadiazon) act as bleaching herbicides by inhibiting protoporphrinogen oxidase, an enzyme involved in chlorophyll formation [2] whilst phenylpyridazinones (norflurazon) and diphenyl pyridones (fluridone) act as carotenoid inhibitors by affecting phytoene desaturase [3].

The development of site-based herbicide resistance is yet another possible consequence of large endogenous receptor sites. The larger the binding domain the greater the opportunity for a change in a specific amino acid residue to significantly reduce the affinity of a particular herbicide for its receptor site without necessarily affecting the binding of the endogeneous molecule. This is reflected in the large number of mutants, isolated from algae, plants and photosynthetic bacteria, which show site-based resistance to PS_{II} inhibitor herbicides. Varying levels of cross resistance are shown by a given mutant to different PS_{II} herbicides presumably reflecting the degree of overlap between the HR sites involved and the point of mutation.

The relationship between the size of the ER site and the number of potential HR sites available has implications with respect to the discovery of herbicides and the development of site-based herbicide resistance. New herbicides will tend to be biased in favour of those affecting targets with large binding domains because of their greater number of potential HR sites. This is reflected by the current situation where, although many herbicides are known, relatively few herbicide targets have been identified and most of these targets are associated with large endogenous molecules.

Large targets with many interaction sites are more likely to develop resistance to herbicides than those with fewer sites so that future resistance problems will tend to increase. On the other hand the ability of large target sites to interact with a variety of compounds offers an opportunity to discover alternative herbicides showing no cross resistance.

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