

Book review

Plant Protease Inhibitors: Significance in Nutrition, Plant Protection, Cancer Prevention and Genetic Engineering

Yehudith Birk, Springer-Verlag, Berlin, 2003, 170 pages, ISBN 3-540-00118-2, £54.00 hardback

Many current day medicines act by inhibiting proteases. There remains considerable interest within the pharmaceutical industry in discovering new compounds and mechanisms for protease inhibition, and these investments have lead, for example, to novel anti-HIV therapeutics, blood coagulation treatments and anti-cancer drugs. But it is easy to forget that nature got there first. Plants, in particular, produce a stunning and diverse range of proteinaceous enzyme inhibitors, and form the subject of this monograph from Yehudith Birk. As discoverer of perhaps the best-known class of plant-derived protease inhibitors, Birk brings a whole career's worth of experience to this comprehensive and timely overview of the field.

Plant protease inhibitors have been studied for over 70 years, although Birk wisely restricts most of his discussion to research from the past 20 years or so. This is still a long time in protein chemistry. Marrying traditional biochemical approaches with the more sophisticated techniques now routinely deployed is not easy. Genetic and crystallographic studies in particular have evolved tremendously over this period, but have not been applied equally to the diverse range of inhibitors covered in this overview. This presents a challenge to the reviewer, but Birk responds well, stitching together the story of each family of inhibitors by selecting the most relevant studies on a range of examples for each group. The approach is structured and a little methodical—outline of the key features of a family first, followed by paragraphs describing each significant publication in the field—but it works.

The bulk of the volume comprises this systematic summary of eight recognised families of plant protease inhibitors, with more emphasis on the serine protease inhibitors that have attracted the lion's share of interest in the laboratory. This compilation is of considerable value to both workers already in the field, and those seeking an introduction to this area.

Having comprehensively defined the molecular materials of this field, Birk then provides four chapters surveying attempts to use these inhibitors in a variety of applications. The first of these chapters covers nutritional uses, where a wide range of studies have failed to

provide a clear picture of the potential for plant protease inhibitors to serve as 'nutraceuticals'. In his summary, Birk aptly notes that toxicity reports of these inhibitors are based on massive doses being fed to small animals—unlike the low levels that have probably always formed part of the human diet. These dietary implications tie up with a later chapter discussing the potential use of protease inhibitors as cancer chemopreventive agents. This is an exciting development with many encouraging preliminary studies, précised in this book, exhibiting the ability of these inhibitors to suppress the carcinogenic process. No consistent mechanism for this trait seems to emerge, but there is no doubt that further exciting advances will soon emerge in this area.

Perhaps the most interesting chapter, though, relates to the commonly perceived explanation for the existence of these inhibitors in plants—the ability of protease inhibitors to protect plants from predatory insects and other organisms. Again a plethora of often conflicting studies are summarised by Birk. The production of protease inhibitors as part of the defense response of plants is not just of idle academic curiosity—there is immense potential to exploit such 'natural' defenses in transgenic, 'GM' commercial crops. This does not go unremarked by the author, who wisely highlights the environmental and sociological implications of such modifications. This topical discussion of the current understanding of the role of protease inhibitors in the survival of plants is, in my view, the heart of this book. Although there is no overt statement that plant defense is the *raison d'être* for this considerable maze of inhibitory proteins, the simple logic of many of the studies described by Birk leaves little doubt of this central role.

Overall, Birk has provided a comprehensive, orderly and digestible overview of the plant protease inhibitor literature. Although a few journal reviews have attempted to cover this broad field before, none of these share the depth or personal flavour that can only be derived from someone who has devoted a whole career to this area. Although the figures appear dated and are a little disappointing, *Plant Protease Inhibitors* fills an obvious gap in the scientific literature and forms an excellent introduction to this curious field.

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