News from the Archives

Why do so many scientific research articles languish in obscurity? There is no single answer. No doubt many have earned their ignominy by their flawed scholarship, poor exposition, or arcane subject matter, but this is not always the case. A search of the old literature often uncovers many seemingly worthy contributions that have inexplicably fallen into oblivion. Probably the most common reason for the neglect of these papers is their publication in unsuitable journals or in journals of limited circulation. The exemplar par excellence of this phenomenon, of course, was Gregor Mendel’s inscrutable choice of the little-known Verhandlungen des naturforschenden Vereines im Brunn as a vehicle for his scientific communications. Mendel’s journal choice certainly accounted in part for the 35-year lag in the recognition of his fundamental contributions to the science of heredity. Mendel’s case also exemplifies a second reason why some papers may be overlooked: they are simply too ahead of their time to be fully appreciated. News from the Archives, which will be an occasional feature of Plant Physiology, doesn’t promise to expose any lost paradigms as big as Mendel’s. The goals of this column are much more modest: first, to bring to light some lost observations from the dusty recesses of the archives; and second, to redress historical oversights. Suggestions from the readers of Plant Physiology concerning specific articles that have been treated unfairly by history or which deserve renewed consideration in light of recent discoveries are most welcome. This month’s column explores the possible implications of some overlooked reports concerning the effects of two Na\(^+\) channel drugs, veratrine and tetrodotoxin (TTX), on plant cell mitosis.

Veratrine, a Na\(^+\) Channel Agonist, Inhibits Mitosis in Plants

Veratrine is a mixture of alkaloids produced by the sabadilla plant (Schoenocaulon officinale), a member of the Liliaceae or the Melanthiaceae (Fig. 1). The two major alkaloid components of veratrine are veratradine and cevaridine, both of which act as agonists of plasma membrane Na\(^+\) channels in animal cells. Na\(^+\) ions play a much more integral role in the basic transport processes of animal cells than they do in plant cells. In animal cells, the pumping activity of Na\(^+\)-ATPases are the primary source of the electrogenic component of the membrane potential, whereas the same function is served by H\(^+\)-ATPases in plant cells. This dichotomy in the use of Na\(^+\) and H\(^+\) is also seen in the cotransport systems of plant and animal cells, where Na\(^+\) is most often cotransported in animal cells and H\(^+\) is most often cotransported in plant cells. Perhaps most telling of the relative unimportance of Na\(^+\) to plant cell function is the fact that Na\(^+\) isn’t even an essential mineral nutrient of most plants. In retrospect, therefore, Witkus and Berger’s (1944) discovery that 0.1% solution of veratrine sulfate inhibits both spindle and cell plate formation in the meristematic cells of onion (Allium cepa) root tips is quite surprising. Of the veracity of Witkus and Berger’s (1944) observations, there can be little doubt since Sharma and Sarkar (1956) and Kubiak (1971a, 1971b) independently arrived at the same conclusion.

TTX, a Na\(^+\) Channel Antagonist, Also Inhibits Mitosis in Plants

TTX is a toxin extracted from the puffer fish Arothron nigropunctatus (Fig. 2). Khora et al. (1997) reported that TTX inhibited mitosis at concentrations greater than 30 \(\mu\)m as evident by the fall of mitotic index. TTX at far lower concentrations (0.1–5.0 \(\mu\)m) significantly enhanced the frequencies of sister chromatid exchange (SCE), indicating a possible interference of the toxin in DNA replication and repair. Other authors, however, have previously found no effect of TTX on an inward Na\(^+\) current in Zea mays (Roberts and Tester, 1997) or Triticum aestivum (Davenport and Tester, 2000) roots, or on the secretory network of Closterium acerosum (Domozycz, 1999), or on the resting or action potential of Nitella mucronuta (Kopperhöfer, 1972). It is conceivable that the putative veratrine- and TTX-sensitive channel in plants may only be important during certain stages of plant cell mitosis.

Figure 1. The sabadilla plant S. officinale is a source of the alkaloid mixture veratrine that is widely used as an agonist of Na\(^+\) channels in animal cells. (© Missouri Botanical Garden)

Figure 2. The puffer fish is a rich source of tetrodotoxin, a toxin most often used as a blocker of Na\(^+\) channels in animal cells. (© Jeffrey N. Jeffords)
Veratrine and TTX Also Affect Ca\textsuperscript{2+} Currents in Heart Cells

Ion channels are often named according to the dominant ion that they pass under physiological conditions, but this often leads to the impression that such channels are completely and absolutely specific for that ion. This is not always true, and the Na\textsuperscript{+} channel of animal cells is a case in point. Several studies have concluded that some Na\textsuperscript{+} channels in heart cells are also permeable to Ca\textsuperscript{2+} under certain conditions (Lemaire et al., 1997; Cole et al., 1997). Santana et al. (1998). Indeed, genomic evidence suggests that Ca\textsuperscript{2+} and Na\textsuperscript{+} channels have similar structures, reflecting a common ancestry (Spafford et al., 2001). Both are large monomeric proteins that include four homologous repeats and share extensive sequence homology in their transmembrane segments and S5-S6 linkers (Sato et al., 2001). Especially intriguing is the recent discovery that the activation of either the β-adrenergic receptor or protein kinase A transforms the Na\textsuperscript{+} channel in rat heart cells into one that is promiscuous with respect to ion selectivity, permitting Ca\textsuperscript{2+} ions to permeate as readily as Na\textsuperscript{+} (Santana et al., 1998).

Ca\textsuperscript{2+} Currents: The Site of Action for Veratrine and TTX in Plant Cells?

What is striking about the effect of veratrine on A. cepa cell mitosis is how similar it is to the effects of treatments such as caffeine (Samuels and Staehelin, 1996; Valser and Hepler, 1997) and intracellular Ca\textsuperscript{2+} chelators (Jurgens et al., 1994). These latter two agents are believed to act by disrupting intracellular Ca\textsuperscript{2+} gradients. In keeping with the new appreciation that some types of veratrine-sensitive Na\textsuperscript{+} channels may also serve as Ca\textsuperscript{2+} channels, it is tempting to speculate that veratrine may serve as a Ca\textsuperscript{2+} channel agonist in A. cepa meristematic root cells.

If the effect of TTX on Allium sister chromatid exchange during mitosis is related to its blocking effect on a Ca\textsuperscript{2+} current, then it follows that any factor that lowers [Ca\textsuperscript{2+}]\textsubscript{cyt} should also increase the frequency of SCE. Ortiz and Cortés (1990) reported that SCE frequency in the meristematic cells of A. cepa roots increased in a dose-dependent fashion when treated with EDTA. They proposed that deprivation of divalent cations (Ca\textsuperscript{2+} or Mg\textsuperscript{2+}) probably play an important role in DNA replication and repair processes. Thus, all pharmacological evidence is consistent with the hypothesis that mitotic plant cells may employ a veratrine- and TTX-sensitive Ca\textsuperscript{2+} channel.

LITERATURE CITED


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