Diisopropyl fluorophosphate (DFP) and hexaethyl tetraphosphate (HETP) have been shown to be remarkably potent inhibitors of cholinesterase both in vitro and in vivo. Higher concentrations of DFP were needed for the inhibition of true cholinesterase (brain and erythrocyte) than for the pseudocholinesterase (serum). The DFP inhibition was irreversible as opposed to eserine inhibition. With the serum enzyme the presence of DFP did not produce a progressive inactivation, but rather the hydrolysis proceeded as if less enzyme were present from the start and no preliminary incubation of the enzyme with DFP was necessary. Koelle has shown that eserine will protect cholinesterase against DFP inactivation.

The effect of DFP on enzymes of plant origin was studied with the view of determining whether any were more or less specifically inhibited. Of the enzymes jack bean urease, papain, crystalline $\beta$-amylase, citrus pectinesterase, and citrus acetyl esterase, only the acetyl esterase was found to be inhibited by incubation with DFP previous to assay. The characterization of citrus acetyl esterase, an enzyme which best hydrolyzes esters of acetic acid and which possesses no true lipase activity, has only recently been reported. The inhibition of this enzyme by DFP is shown in the table.

DFP at $10^{-3}$ M failed to inhibit the other enzymes under similar conditions. From these results it is apparent that the DFP did not react with

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5 Jansen, E. F., Jang, R., and MacDonnell, L. R., in press.
essential —SH groups, since it failed to inhibit urease and papain, and that
the inhibition is specific, since pectinesterase (obtained from the same
source as the acetylesterase) was not inhibited. The inhibition of wheat
“lipase” by DFP is consistent with the previous suggestion that this
enzyme is acetylesterase.

The reaction of DFP with acetylesterase was not dependent upon pH
over the range studied (4.9 to 7.5). Dialysis of acetylesterase inactivated
with DFP failed to restore the activity; hence the reaction is probably
irreversible. The kinetics of the reaction show it to be a bimolecular re-
action. Longer incubation times required less DFP to produce the same
inhibitions reported above.

In the presence of the substrate (0.23 M triacetin) the inhibition reaction
proceeded much more slowly for a given concentration of DFP. This
decrease in activity with time in the presence of the substrate is opposed to
that observed for cholinesterase. Eserine (which has been shown not to
inhibit the hydrolysis of acetylcholine by citrus acetylesterase) was found
not to inhibit the inactivation of acetylesterase by DFP.

Similar to its effect on cholinesterase, HETP inhibited acetylesterase in
lower concentrations than did DFP. With acetylesterase only one-fiftieth
as much HETP as DFP was needed to cause the same inhibition in a given
time. In situ inhibition of acetylesterase and the resulting effect on me-
tabolism are being investigated.

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APPARENT SPECIFIC INHIBITION OF PLANT ACETYLESTERASE BY DIISOPROPYL FLUOROPHOSPHATE

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