# *IN VITRO* REACTIVATION OF CHLORPYRIFOS-INHIBITED RAT BRAIN ACETYLCHOLINESTERASE FROM PYRAZOLE-OXIME DERIVATIVES

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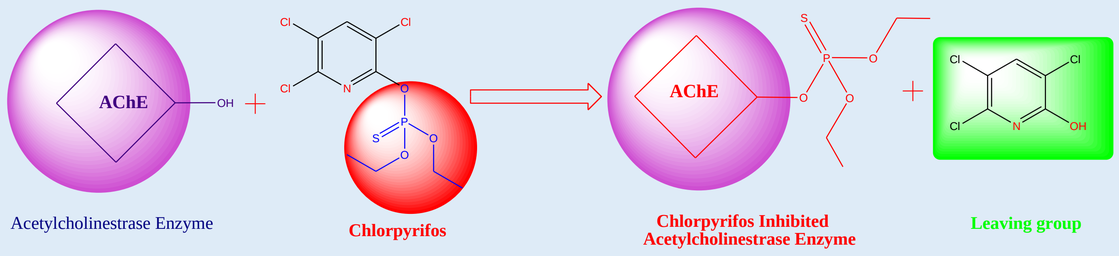
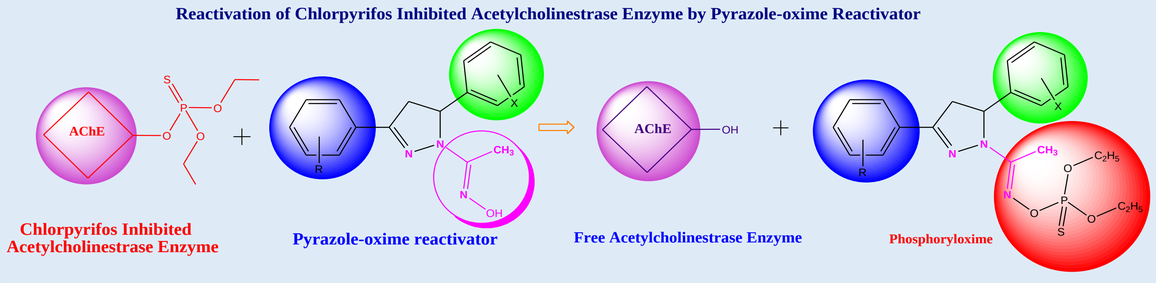
## Introduction:

Poisoning with organophosphorus compounds (OPC) is frequent because OPC are widely used as insecticides or pesticides. According to World Health Organization (WHO) report, more than two million suicidal poisoning cases with the insecticides or pesticides occur worldwide every year, and approximately 200,000 die, mostly in developing countries.[1-2]




Acetylcholinesterase reactivator is defined as compounds which have able to cleave phosphorylated bond between enzyme & OPC[3].

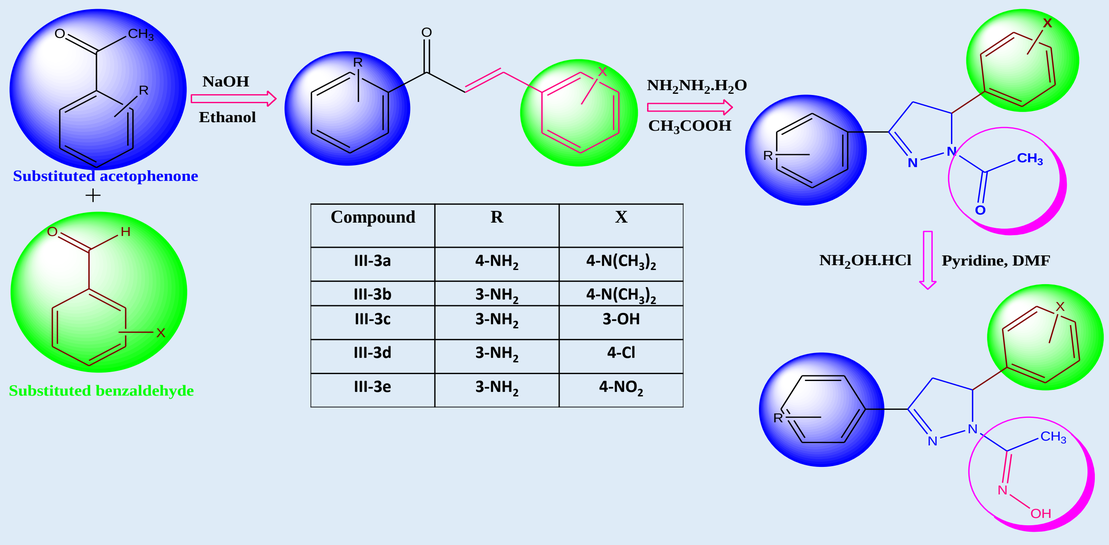



## Objective:

To synthesize a series of pyrazole-oxime derivatives and evaluating for their reactivating potency against chlorpyrifos inhibited AChE by Ellmann's method.

## Method:

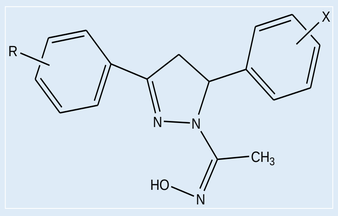
A series of chalcone were prepared by treating substituted acetophenone with various substituted aromatic aldehydes to form respective chalcone. The chalcone treated with hydrazine hydrate, which undergoes cyclisation to yield N-Acetyl pyrazole derivatives. Further, carbonyl group of N-Acetyl pyrazole subjected for oximation by treating hydroxylamine hydrochloride in presence of pyridine to yield.




| Compound | R | X |
|---|---|---|
| III-3a | 4-$NH_2$ | 4-$N(CH_3)_2$ |
| III-3b | 3-$NH_2$ | 4-$N(CH_3)_2$ |
| III-3c | 3-$NH_2$ | 3-OH |
| III-3d | 3-$NH_2$ | 4-Cl |
| III-3e | 3-$NH_2$ | 4-$NO_2$ |

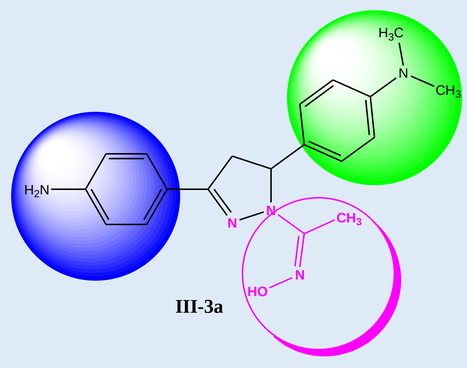
## Results:

Physicochemical data of pyrazole-oxime III-(3a-3f).

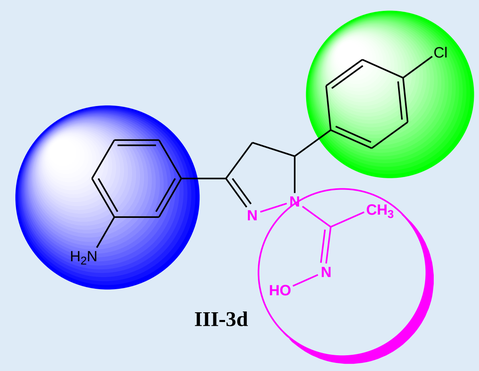



| Comp. | R | X | Mol. Formula | Mol. Wt | MP | % Yield | *Rf Value |
|---|---|---|---|---|---|---|---|
| III-3a | 4-$NH_2$ | 4-$N(CH_3)_2$ | $C_{19}H_{22}ON_4$ | 337.42 | 260-264 | 42.1 | 0.90 |
| III-3b | 3-$NH_2$ | 4-$N(CH_3)_2$ | $C_{19}H_{22}ON_4$ | 337.42 | 278-280 | 36.4 | 0.78 |
| III-3c | 4-$NH_2$ | 3-OH | $C_{17}H_{17}N_3O_2$ | 310.35 | 244-248 | 53.8 | 0.76 |
| III-3d | 3-$NH_2$ | 4-Cl | $C_{17}H_{16}ClN_3O$ | 328.8 | 282-284 | 47.4 | 0.84 |
| III-3e | 3-$NH_2$ | 4-$NO_2$ | $C_{17}H_{16}N_4O_3$ | 339.35 | 296-298 | 39.0 | 0.96 |

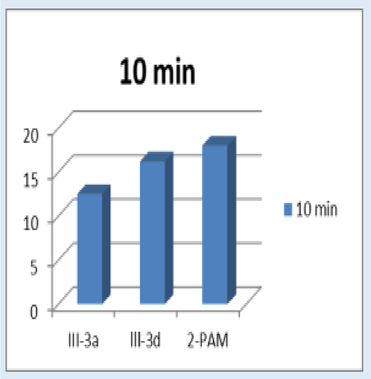
The data reveal that all the newly developed reactivators were not able to reactivate Chlorpyrifos-inhibited AChE. Only two compounds of pyrazole oxime, III-3a (35.2%, 60 min) and III-3d (37.2%, 60 min) were found to be potent reactivators of chlorpyrifos inhibited AChE as compared to standard (40%, 60 min).

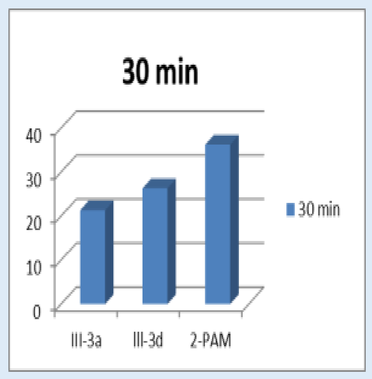


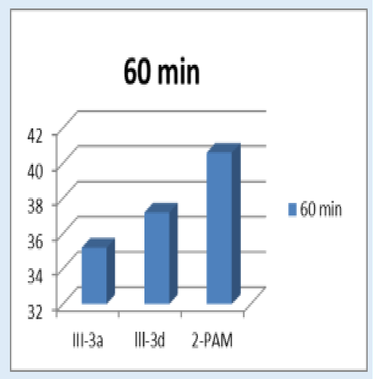

III-3a




III-3d




## Conclusion:

Despite continued efforts to discover improved reactivators, there has been little success towards discover of AChE reactivators. But compounds having diethylamine & chloro substitution at 4th positions showed satisfactory reactivation potency. Moreover, these pyrazole-oximes seem to be promising because of their sufficient reactivation potency at lower concentration ($10^{-3}$M).

## Acknowledgements:

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## References:

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