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A novel HNK-102 is multiple folds better compared to 2-PAM as an antidote against nerve agents intoxication in mice

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Background: The conventional therapy for the treatment, atropine (cholinolytic) and 2-PAM (Acetylcholinesterase enzyme reactivator) were not found to be effective against some of the nerve agents. This short coming demanded a search of a broad spectrum, more efficacious, stable and less toxic antidote for treatment of all nerve agents poisoning. In the present study, comparative evaluation of the newly synthesized HNK series oximes with 2-PAM was performed using Swiss albino male mice.

Material & Methods: (i) Protection Index in terms of survival against nerve agents i.e. sarin, tabun and soman, DFP and dichlorvos poisoning, *in vivo*; (ii) Acute and sub-acute toxicity in Swiss mice and Human cell lines; (iii) Evaluation of antidotal efficacy of shortlisted HNK-102 oxime against sarin vapor poisoning through inhalation route; were carried out. Atropine administration was common for all groups.

Results: In comparison to 2-PAM, HNK-102 oxime found to be (a) Multifold superior in terms of both survival of animals against multiple lethal doses of nerve agents poisoning and more reactivation of AChE enzyme (b) Fourfold more protection against acute toxicity of sarin vapor inhalation in the mice (c) Least toxic in all the used human cell lines (*in vitro*) and in Swiss mice (*in vivo*) via ip, im, iv routes of administration, (d) Safer by showing no irreversible adverse effects on general health on repeated 21 days oral administration at two dose levels ($0.20\times LD_{50}$ and $0.05\times LD_{50}$).

Conclusion: HNK-102 oxime was found to be (i) multifold better antidote compared to that of 2-PAM against nerve agents, dichlorvos and DFP poisoning in the mice, (ii) safe following *in vitro* and *in vivo* studies and (iii) can be considered for further studies in order to replace 2-PAM.

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