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***IN VITRO* AND *IN VIVO* CHARACTERIZATION OF RECOMBINANT HUMAN
BUTYRYLCHOLINESTERASE (PROTEXIA™) AS A POTENTIAL
NERVE AGENT BIOSCAVENGER**

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Previous studies in rodents and nonhuman primates have demonstrated that pretreatment with a variety of enzymes that can scavenge nerve agents can provide significant protection against behavioral and lethal effects of nerve agent intoxication. Human butyrylcholinesterase (HuBuChE) purified from plasma is currently being evaluated for efficacy against nerve agents in guinea pigs and non-human primates. A recombinant form of HuBuChE has been expressed in the milk of transgenic goats as a product called Protexia™. Protexia™ was supplied by Nexia Biotechnologies (Quebec, Canada) as a purified solution with a specific activity of 600U/mg. Initial *in vitro* studies using radiolabeled ³H-soman or ³H-DFP (diisopropyl fluorophosphate) demonstrated that Protexia™ bound specifically to these inhibitors. When Protexia™ was mixed with soman, sarin, tabun or VX under conditions of varying molar ratios of enzyme to nerve agent (8:1, 4:1, 1:1 and 1:4, respectively), the data indicated that 50% inhibition of enzyme activity occurs around the 1:1 molar ratio for each of the nerve agents. Protexia™ was further characterized for its interaction with pyridostigmine bromide and four unique carbamate inhibitors of cholinesterase activity. IC₅₀ and K_i values for Protexia™ were determined to be very similar to those of HuBuChE purified from human plasma. These preliminary data suggest that Protexia™ has properties very similar to HuBuChE when compared *in vitro*. The pharmacokinetics of Protexia™ in guinea pigs after intramuscular injection were determined, and the *in vivo* efficacy of Protexia™ against the nerve agent soman was examined. Administration of Protexia™ in the absence of other pretreatments or therapy protected guinea pigs (n=10) against 3 x LD₅₀s of soman for 14 days, after which their tissues were harvested for histological examination. Together these data suggest that the goat milk-produced recombinant HuBuChE Protexia™ has the potential to be a highly useful bioscavenger of organophosphorus nerve agents.