# The Effects of Temperature on the Blocking Action of Methyisopropoxyflurophosphine Oxide (Soman) of the Propagated Action Potential of the Bullfrog Sciatic Nerve[1]

by ERNEST R. WHITCOMB
*8405 S.W. 144th Street*
*Miami, Florida*

The present study is a continuation and expansion of earlier studies using a wide spectrum of acetylcholinesterase (AChE) inhibitors (1,2,3,4,5).

Attenuation of the action potential was used as an index of effectiveness of the inhibitor as in previous investigations (1,6,7,8,9,10).

Soman was investigated for its effectivenss in blocking the propagated action potential at different temperatures, to better define the role of temperature in the blocking action of organophosphate inhibitors on peripherial nerve.

## Materials and Methods

The nerve preparation, electrical recording, and solution preparation were similar to those used previously (4). The excised nerves were incubated in Ringer's solution overnight in the refrigerator (approx. 10°C). The nerve was desheathed just before mounting in the recording chamber. The control period (1-2 hours) was of sufficient duration to obtain a constant potential amplitude. During this period the drug chamber was filled with Ringer's solution. For the exposed period the Ringer's solution was replaced with a solution of the inhibitor. At the end of the exposure time the drug chamber was flushed several times with Ringer's solution and then refilled with Ringer's solution for

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[1] This work was done at the Medical Research Laboratories, Edgewood Arsenal, Maryland. The opinions or assertions contained herein are the private ones of the author and are not to be construed as official or reflecting the views of the Army Department or the Army Services at large.



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the recovery period. The action potential was recorded at the distal electrodes (4) using a Type RM Dual Tetronix Oscilloscope with a Type 2A61 Differential Amplifier. The steady state height of the action potential during the control period was designed as 100%. The amplitude at the end of the exposed and recovery periods were reported as percent of the control level. Ringer's phosphate solution (pH 7.6) was used.

## Results and Discussion

Of the three organophosphate inhibitors (Soman, Sarin, and Tabun) used in preliminary trials, Soman was the most effective as indicated by the rate of blocking the propagated action potential.

The blocking action of Soman was measured at two concentrations (5.5 and 15 mM) and at three temperatures (27°, 17°, and 7°C). The results are summarized in Table 1.

TABLE 1
Action of Soman on the Propagated Action Potential

| Trials | Conc. mM/L | Temp. C° | Contact Time (mins.) | Amplitude of Action Potential % Control End of Contact | End of Recovery |
|---|---|---|---|---|---|
| 2 | 5.5 | 27 | 30 | 76±6 | 100 |
| 8 | 5.5 | 27 | 60 | 49±19 | 59±11 |
| 5 | 5.5 | 27 | 90 | 27±20 | 29±12 |
| 4 | 5.5 | 27 | 120 | 24±15 | 24±9 |
| 4* | 5.5 | 27 | 60 | 55±19 | 54±8 |
| 4* | 5.5 | 7 | 60 | 82±4 | 96±7 |
| 4 | 15 | 27 | 8 | 0 | 57±12 |
| 11 | 15 | 27 | 15 | 0 | 29±8 |
| 4 | 15 | 17 | 15 | 0 | 84±20 |
| 4 | 15 | 7 | 30 | 0 | 98±5 |
| 8 | 15 | 7 | 60 | 0 | 76±14 |
| 2 | 15 | 7 | 90 | 0 | 58±2 |

* Paired nerves

It is apparent from these results that temperature altered the rate of blocking and the degree of irreversibility of the blocking action.

At 27°C the recovery upon washing with Ringer's solution was characterized by a biphasic response. A typical trial (Exp.#3-26) is shown in Figure 1. Upon washing there was an initial recovery followed by a secondary blocking action. Increasing the number of washings did not prevent this secondary blocking action. This biphasic response was not observed at either 17°C or 7°C. A typical trial for 7°C (Exp. #11-2) is shown in Figure 1. However, if the temperature during recovery was increased from 7°C to 27°C the secondary blocking action occurred.

The empirical findings reported here have indicated the important role of temperature in the blocking action of Soman in peripherial nerve. Some investigators attribute this blocking action by inhibitors at the concentrations used as due to a non-specific concentration effect. However, this does not account for the inability of acetylcholine, neostigmine and sucrose to block at a concentration of 20 mM.

No definitive explanation can be offered at this time for the observed effect of temperature. One possibility is that the blocking action is composed of two components; namely, a reversible and irreversible blocking effect. While both are responsive to temperature the irreversible effect is highly temperature dependent.

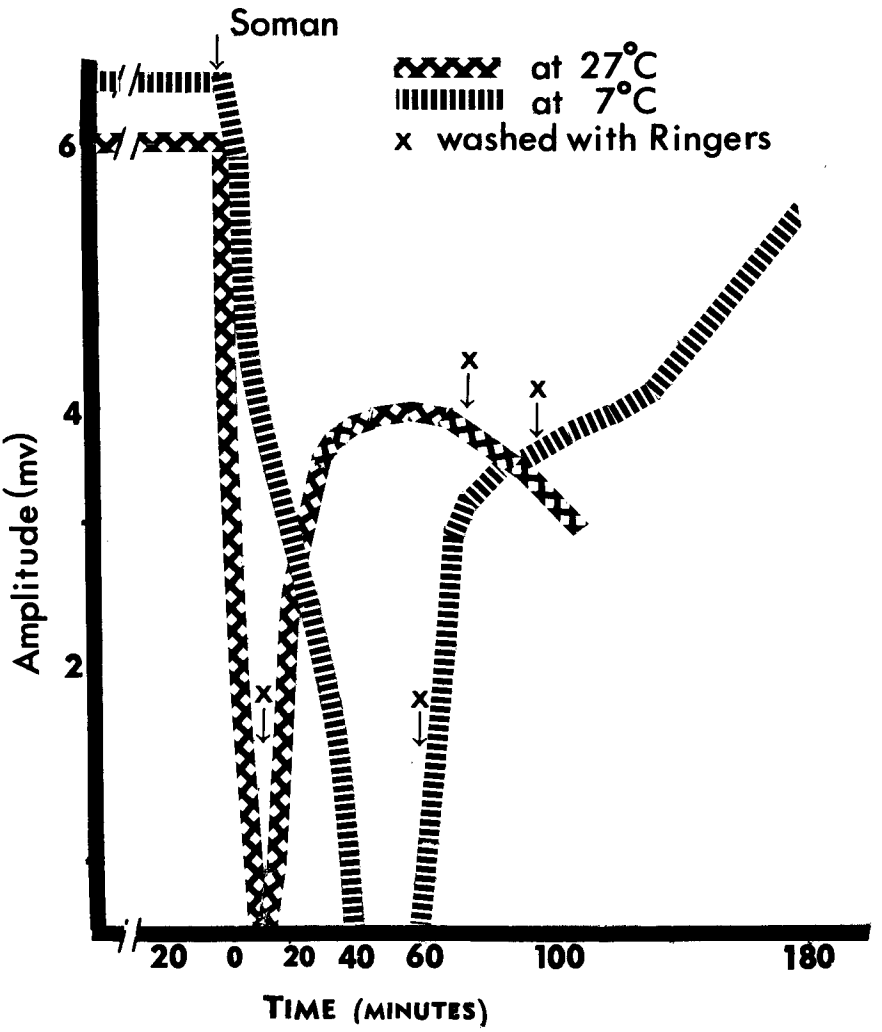


Figure 1. Effect of Temperature on the Reversibility of the Blocking Action of Soman (15 mM).

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