MMSL
Military Medical Science Letters
Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2018, 87(2), 92-94
ISSN 0372-7025
DOI: 10.31482/mmsl.2018.012

LETTER TO THE EDITOR

NOVICHOK AGENTS - MYSTERIOUS POISONOUS SUBSTANCES FROM THE COLD WAR PERIOD

On March 4, Sergei Skripal, a former Russian spy who was convicted and imprisoned in Russia for working as a double agent, and his daughter were found unresponsive and slumped on a shopping-center bench in Salisbury, England. On 12 March 2018, British Prime Minister Theresa May said in Parliament that the two had been poisoned with Novichok, a "military grade" nerve agent developed by Russia, and she moved swiftly to retaliate against the government of President Vladimir Putin (BBC News, 12 March 2018). It was the first use of a nerve agent on European soil since World War II. Russian authorities have rejected May's claims as nonsense. On 14 March 2018, the UK expelled 23 Russian diplomats after the Russian government refused to meet the UK's deadline of midnight on 13 March 2018 to give an explanation for the use of the substance (BBC News, 14 March 2018).

The whole world has learned about the existence of a highly toxic neuro-paralytic substance called Novichok, which should have been destroyed under the Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction (https://treaties.un.org/Pages/ViewDetails.aspx?src=TREATY&mtdsg_no=XXVI-3&chapter=26&lang=en). It will not hurt to tell what's behind Novichok, what substances are involved and how dangerous they are.

Novichok (Russian: Новичо́к) is a series of nerve agents the Soviet Union and Russia developed between 1971–1993 (Tucker, 2006; Ellison, 2007). They were designed as part of a Soviet program codenamed "FOLIANT" (Pitschmann, 2014), nevertheless Russia officially denies producing or researching Novichok agents (Borger, 2018). Novichok agents were developed during the Cold War period and have never been used on the battlefield.

In 2011, the Organisation for the Prohibition of Chemical Weapons (OPCW) Scientific Advisory Board reported that no peer reviewed paper on Novichok agents in scientific literature exist (OPCW Report, 2011) and in 2013 OPCW reported that it had insufficient information to comment on the existence or properties of Novichok agents (OPCW Report, 2013). Since then, new information has emerged that confirms the existence of Novichok agents and brings more information about them.

Novichok agents are binary weapons, in which precursors for the nerve agents are mixed in a munition to produce the agent just prior to its use (Darling and Noste, 2016). Because the precursors are generally significantly less hazardous than the agents themselves, this technique makes handling and transporting the munitions a great deal simpler. Additionally, precursors to the agents are usually much easier to stabilize than the agents themselves, so this technique also made it possible to increase the shelf life of the agents. Binary weapons are safer to store, transport and handle.

Different dihalonitrosomethanes or nitromethanes serves as precursors of Novichok agents. These react with phosphorus halides, phosphite, phosphate and alkylphosphonate esters to form formaldoximes of general formula shown in Figure 1, where X and Y = F, Cl, Br, or stable pseudohalogen e.g., -CN, and R may be halogen,

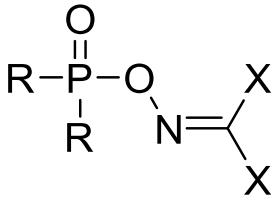

Figure 1. General structure of Novichok agents.

alkyl, alkoxyl, etc. Novichok family of analogs comprises more than a hundred structural variants. From a military standpoint, the most pronounced Novichok was A-232 (Novichok-5, Fig. 2). Other possible organophosphate molecules that can be ranked among Novichok agents are shown in Fig. 3.

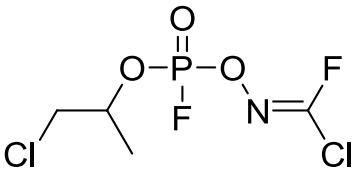

Figure 2. Chemical structure of Novichok A-232, also known as Novichok-5

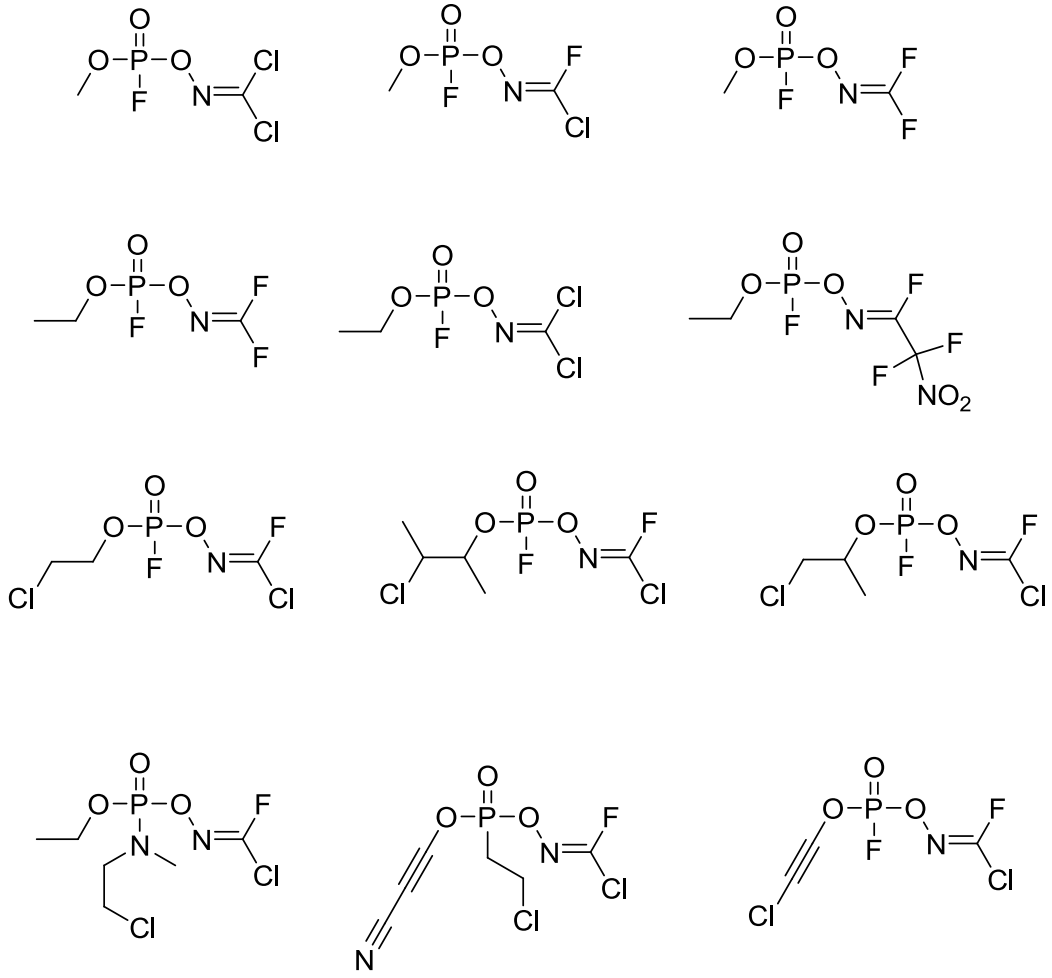

Figure 3. Possible molecules of organophosphates, ranked among Novichok agents.

Novichok agents belong to the class of organophosphate acetylcholinesterase inhibitors. These chemical compounds inhibit the enzyme acetylcholinesterase, preventing the normal breakdown of the acetylcholine, neurotransmitter in cholinergic nervous system. Acetylcholine concentrations then rapidly increase at neuromuscular junctions to cause involuntary contraction of all muscles (Antonijevic and Stojiljkovic, 2007). As a result, respiratory and cardiac arrest follow with death from heart failure or suffocation as copious fluid secretions fill the victim's lungs.

Novichok agents are exerts their action very rapidly, penetrate through the skin and respiratory system. Novichok A-232 exceeds effectiveness of soman by 10 times and of VX by 5 to 8 times (Vásárhelyi and Földi, 2007). As an antidote for Novichok poisoning, atropine and oxime reactivators are likely to be used, but the results of such therapy have not been published or even proved.

Declaration of conflict of interest

Author declares no conflict of interest.

References

1. Antonijevic B, Stojiljkovic MP. Unequal efficacy of pyridinium oximes in acute organophosphate poisoning. Clin Med Res. 2007;5(1):71-82.
2. BBC News. Russian spy: Highly likely Moscow behind attack, says Theresa May. BBC News, 12 March 2018.
3. BBC News. Russian spy: UK to expel 23 Russian diplomats. BBC News, 14 March 2018.
4. Borger J. UK spy poisoning: Russia tells UN it did not make nerve agent used in attack. The Guardian. 15 March, 2018.
5. Darling RG, Noste EE. Future Biological and Chemical Weapons. In Ciottone GR. Ciottone's Disaster Medicine (Second Ed.), Amsterdam: Elsevier, 2016. doi:10.1016/B978-0-323-28665-7.00080-7
6. Ellison DH. Handbook of chemical and biological warfare agents. Second Ed., CRC Press. 2007, 800 pp. ISBN 9780849314346
7. Pitschmann V. Overall View of Chemical and Biochemical Weapons. Toxins, 2014;6(6):1761–1784. doi:10.3390/toxins6061761
9. Report of the Scientific Advisory Board on developments in science and technology for the Third Review Conference (PDF). Organisation for the Prohibition of Chemical Weapons. 27 March 2013. p. 3. RC-3/WP.1.
10. Report of the Sixteenth Session of the Scientific Advisory Board (PDF) (Report). Organisation for the Prohibition of Chemical Weapons. 6 April 2011. p. 7. SAB-16/1.
11. Tucker JB. War of Nerves, New York: Anchor Books, 2006. ISBN 978-0-375-42229-4
12. Vásárhelyi G, Földi L. History of Russia's chemical weapons. Acad Appl Res Milit Sci. 2007;6(1):135-146.

✉
Jiri Patocka
University of South Bohemia in České Budějovice
Faculty of Health and Social Studies
Department of Radiology, Toxicologyand Civil Protection
J. Boreckého 1167/27
370 11 České Budějovice
Czech Republic
toxicology@toxicology.cz

Biomedical Research Centre
University Hospital
Hradec Kralove
Czech Republic

Received 13th March 2018.
Revised 20th March 2018.
Published 8th June 2018.