# New peroxocompounds for medicine, their crystal structure and neuroprotective capacity

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## Introdution

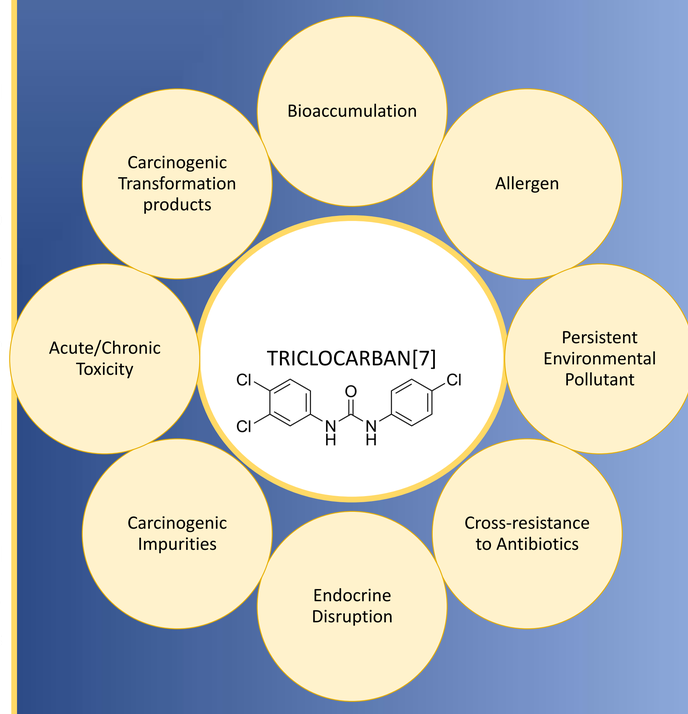
Peroxocompounds are featured by possibility of generation of dioxygen in its first excited singlet state ($^1O_2$). These compounds belong to a specific group of polyoxocompounds (POMs). One of the methods of their synthesis is based on reacting of an aqua solution of hydrogen peroxide with transition metal precursor like Mo, W, V. Peroxometalates are reactive, usually unstable and sometimes even explosive.

In our laboratory, we have obtained peroxocompounds with organic blocks directly connected with Mo atoms that results in unusual properties and/or interesting molecular architectures [5].

The investigated peroxomolybdates possess nicotinic or picolinic acid N-oxides fragments; the cations in these salts are: $K^+$ and $Na^+$. Although peroxocompounds have been found to possess antiviral, antibacterial and antitumor properties[1,2,3], their neuroprotective capacity needs to be clarified. The only available report on neuroprotective potential of POMs has been published recently [4]. In addition to the dioxygen in its first excited singlet state, the organic components like nicotinic/picolic acid N-oxides differ in the relative position of the N-oxide and carboxylic $COO^-$ groups, which could influence the catalytic properties and substantiate unique neuroprotective activity of the peroxocompounds.

## Methods

- Three peroxocompounds were tested in mouse primary neuronal cell cultures (K-nicO, K-picO, Na-picO).
- Damaging agent was triclocarban (TCB) IUPAC: 1-(4-chlorophenyl)-3-(3,4-dichlorophenyl) urea which is a phenyl ether that is often added to personal and health care products, including cloths, plastics, and even products dedicated for newborns, as well as pharmaceuticals.
- Cell toxicity was assessed in terms of lactate dehydrogenase (LDH) release at 6 and 24 h posttreatment (Fig. 4A-D).
- Apoptosis-related parameter was caspase-3 activity that was measured at 6 and 24 h of experiment (Fig. 5A-D).
- Statistical analysis – one way ANOVA: Levene test and post hoc Newman-Keuls; $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ versus control cultures and $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, and $^{\#\#\#}p < 0.001$ versus the cultures exposed to TCB.
- Fluorescence labeling of apoptotically fragmented nuclei and living cells utilized Hoechst 33342 and calcein AM, respectively (Fig. 6A-B).




## Crystal structure

| Name | K-nicO | K-picO | Na-picO |
|---|---|---|---|
| Chemical formula | $K_2[MoO(O_2)_2.ONC_5H_4COO]_2\ H_2O$ | $K[MoO(O_2)_2\ ONC_5H_4COO]$ | $Na[MoO(O_2)_2.ONC_5H_4COO].2H_2O$ |
| a[Å] | 9.1381(2) | 7.496(1) | 25.0697(4) |
| b[Å] | 10.132(2) | 17.692(3) | 6.31533(9) |
| c[Å] | 6.908(1) | 7.5605(1) | 14.5883(2) |
| α[°] | 95.66(2) | 90.0 | 90.0 |
| β[°] | 110.41(2) | 101.452(4) | 92.7553(14) |
| γ[°] | 74.34(2) | 90.0 | 90.0 |
| Space group | P-1 (2) | Cc(9) | C2/c (15) |
| V[Å$^3$] | 577.18 | 982.68 | 2307 |

K-nicO

Fig. 1A Asymmetric unit of K-nicO

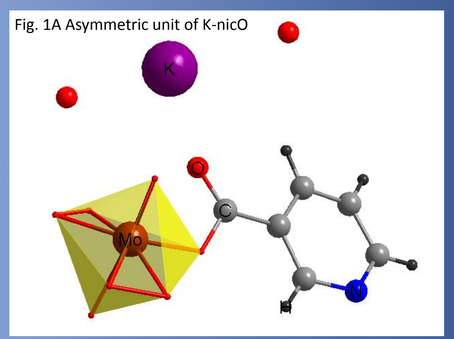
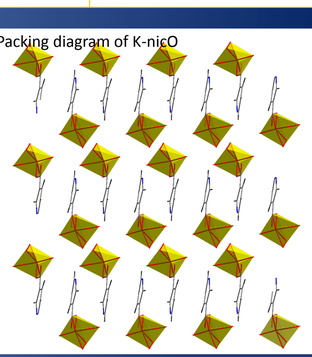



Fig. 1B Packing diagram of K-nicO



K-picO

Fig. 2A Asymmetric unit of K-picO

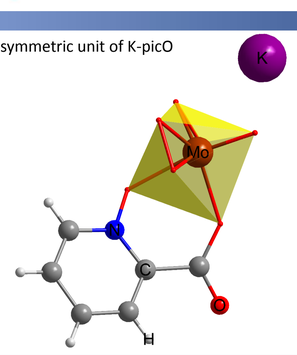
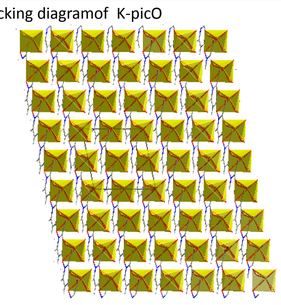



Fig. 2B Packing diagramof K-picO



Na-picO

Fig. 3A Asymmetric unit of Na-picO

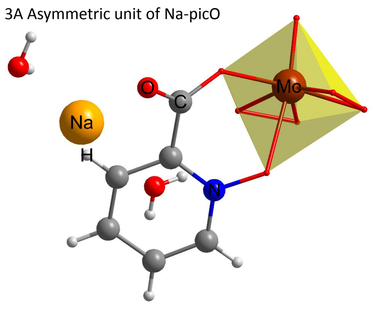



Fig. 3B Packing diagram of Na-picO

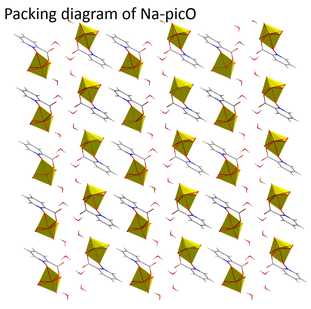


Fig. 4A LDH

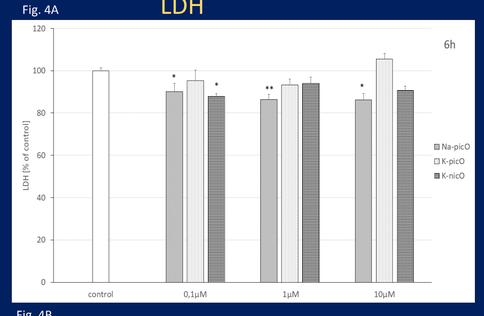



Fig. 4B

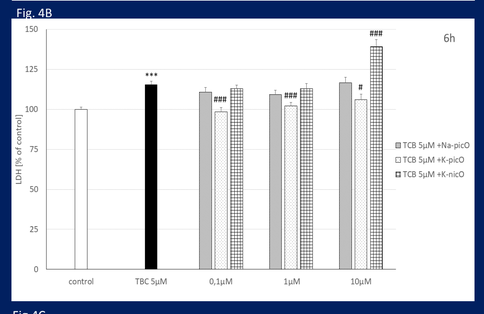



Fig.4C

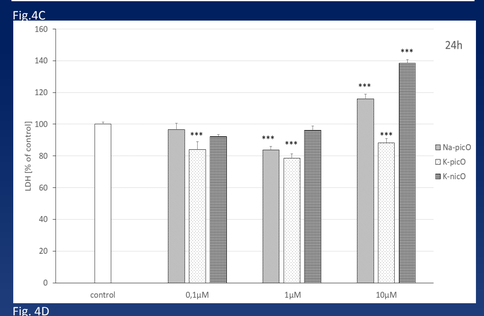



Fig. 4D

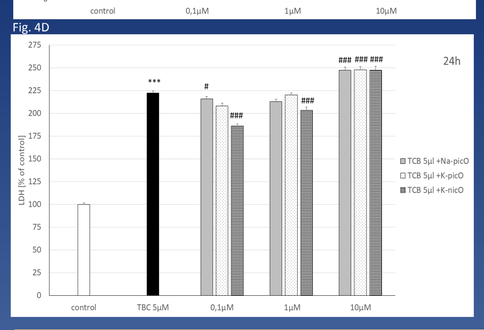



Fig. 5A CASPASE-3

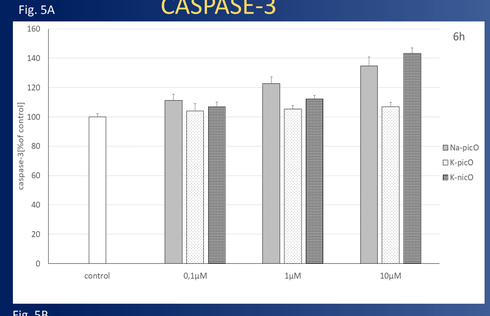



Fig. 5B

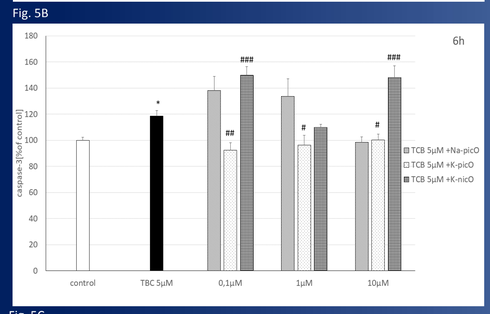



Fig. 5C

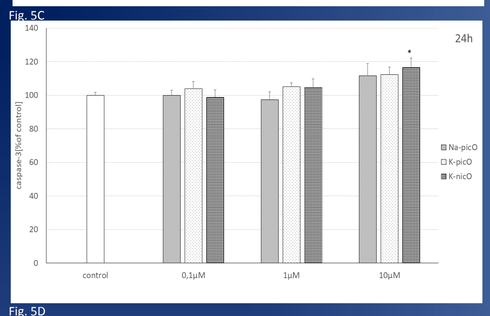



Fig. 5D

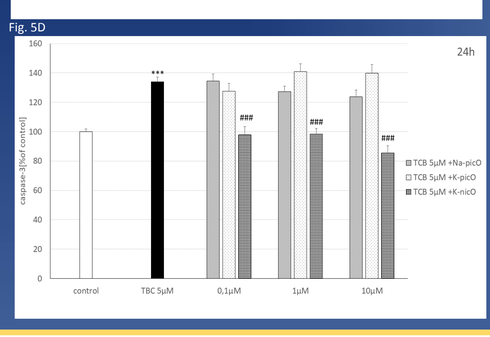



Fig. 6A

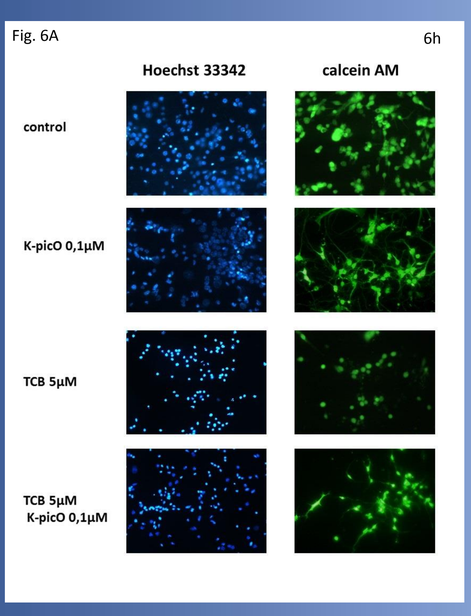
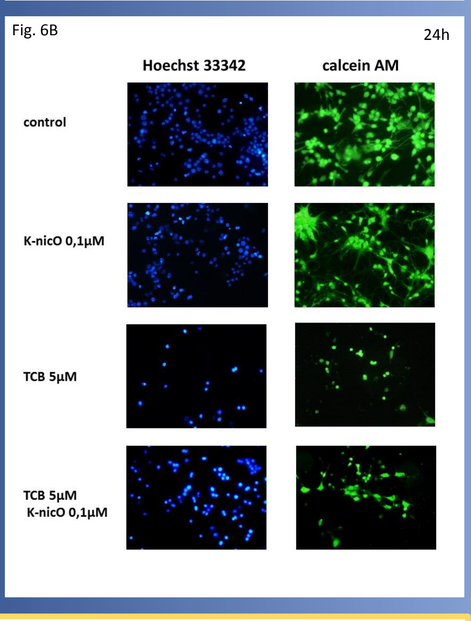



Fig. 6B




## Summary and Conclusion

We have examined the neurobiological activity of new peroxomolybdate hybrid compounds (inorganic-organic) on primary neuronal cell cultures originating from Swiss mouse embryonic brains. Present study confirmed the lack of toxic effects of the tested compounds in a concentration range of 0.1 and 1 μM, except for Na-picO. K-picO and K-nicO did not change the control levels of caspase-3 and lactate dehydrogenase activities in neocortical cultures at 7 day *in vitro*. Furthermore, the compounds exerted neuroprotective properties by inhibiting the effects of triclocarban (TCB), both in respect to LDH and caspase-3. The K-picO (0.1 and 1 μM) decreased the levels of TCB-induced LDH release and caspase-3 activity at 6 h of exposure, whereas the K-nicO (0.1 and 1 μM) was effective at 24 h of exposure. Although the effects of K-picO ranged from 20 to 27%, the effects of K-nicO were more profound and reached the level of approximately 40% of the control value.

***These data strongly point to neuroprotective capacities of peroxocompounds, including their anti-apoptotic potential in mammalian brain neurons.***

## References

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