Screening and evaluation of antioxidant activity of phosphoroselenoates and derivates

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INTRODUCTION

Compounds containing phosphorus are known as powerful herbicides and anti-fungicide(1,2). However, more studies are necessary to expand other applications of these compounds with different groups, such as selenium.

Thus, this study aims to evaluate the antioxidant activity of five phosphoroselenoates that could lead to new potential drugs capable of restoring the redox system equilibrium of an organism.

MATERIALS AND METHODS

The phosphoroselenoates were synthesized by Laboratório de Sintese Orgânica Limpa (LASOL) of UFPel.

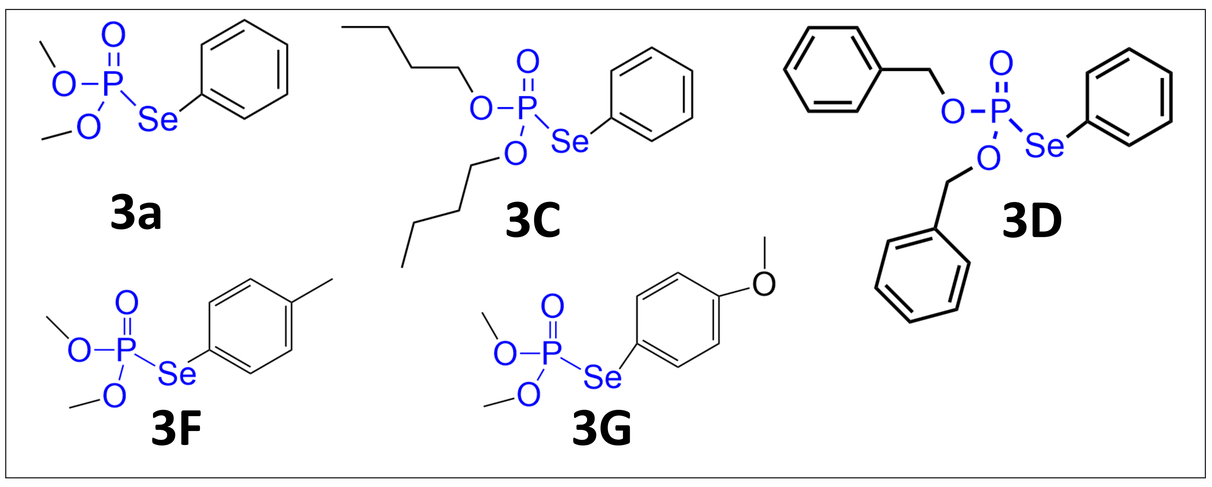
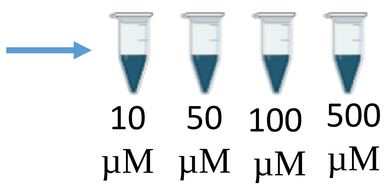


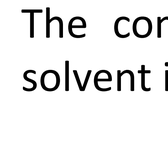
Figure 1. Chemical structure of O,O-Dimethyl Se-phenyl phosphoroselenoate (**3a**), O,O-Dibutyl Se-phenyl phosphoroselenoate (**3c**), O,O-Dibenzyl Se-phenyl phosphoroselenoate (**3d**), O,O-Dimethyl Se-(p-tolyl) phosphoroselenoate (**3f**), Se-(4-Methoxyphenyl) O,O-dimethyl phosphoroselenoate (**3g**).

The compounds were diluted using dimethyl sulfoxide as a solvent in a concentration curve:



Assays to evaluate the antioxidant activity:

- Free radical scavenging activity of 2-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) (3,4).
- Ferric ion reducing antioxidant power (FRAP) (5).
- Inhibition of reactive oxygen species (ROS) formation and thiobarbituric acid reactive species (TBARS) on cerebral tissue of mice (CEEA-13008-2020), induced by azide and sodium nitroprusside, respectively (6,7).



Statistical analysis : One-way ANOVA followed by Tukey's test, using the software GraphPad prism 7.

RESULTS

The results indicate that the phosphoroselenoates have different levels of antioxidant activity in the assays.

All compounds, except **3a**, were effective in protecting against lipid peroxidation on TBARS and present antioxidant power on reducing ferric ion. **3a, 3c, 3d,** and **3g** also prevented the ROS levels when compared by the induced group. The phosphoroselenoates had their scavenging activity in synthetic radicals on ABTS and DPPH assays tested. From them, **3a** and **3g** were effective on both assays, and **3f** was only able to scavenge free radicals on ABTS.

	Compound concentration			
	10µM	50µM	100µM	500µM
Phosphoroselenoates effect on TBARS assay in cerebral tissue of mice.				
3a	84.69 ± 8.41	80.59 ± 11.5	85.89 ± 7.34	79.77 ± 4.97
3c	79.35 ± 4.97	83.79 ± 5.83	90.36 ± 3.05	57.02 ± 13.05 **
3d	59.51 ± 14.15 *	-	-	-
3f	73.00 ± 0.69 *	-	-	-
3g	87.64 ± 2.42	78.64 ± 2.68	78.11 ± 0.72	57.96 ± 8.95 ***
Phosphoroselenoates effect on ROS assay in the cerebral cortex of mice.				
3a	71.50 ± 13.00 *	-	-	-
3c	98.30 ± 7.15	76.10 ± 7.90 *	61.40 ± 2.76 **	-
3d	61.70 ± 15.00 *	-	-	-
3f	70.30 ± 18.90	84.90 ± 13.40	70.10 ± 17.50	62.7±12.3
3g	94.00 ± 11.10	94.10 ± 3.92	67.20 ± 15.80 *	-
Phosphoroselenoates effect on the FRAP assay				
3a	0.11 ± 0.02	0.12 ± 0.01	0.12 ± 0.02	0.16 ± 0.01
3c	0.11 ± 0.02	0.15 ± 0.01	0.15 ± 0.01	0.3 ± 0.01 ***
3d	0.16 ± 0.01	0.23 ± 0.04	0.40 ± 0.03	1.02 ± 0.18 ***
3f	0.14 ± 0.01	0.17 ± 0.016	0.17 ± 0.04	0.29 ± 0.04 *
3g	0.16 ± 0.01	0.16 ± 0.01	0.19 ± 0.03	0.26 ± 0.02 **
Phosphoroselenoates effect on DPPH radical scavenging assay.				
3a	5.53 ± 3.67	7.83 ± 4.09	4.68 ± 2.39	21.93 ± 0.88 *
3c	6.14 ± 6.14	18.38 ± 7.49	12.21 ± 6.20	7.38 ± 4.18
3d	2.19 ± 2.19	3.94 ± 3.94	3.72 ± 3.72	5.04 ±5.04
3f	12.20 ± 6.48	6.83 ± 2.93	9.87 ± 9.87	3.62 ± 3.62
3g	3.72 ± 3.72	6.95 ± 3.81	11.92 ± 4.69	19.06 ± 3.60 *
Phosphoroselenoates effect on $ABTS^{+}$ radical scavenging assay.				
3a	5.02 ± 3.19	10.35 ± 1.09 *	-	-
3c	1.92 ±1.92	8.76 ± 0.79	3.84 ± 3.14	2.34 ± 2.34
3d	3.85 ± 3.85	3.06 ± 3.06	1.86 ± 0.93	12.40 ± 6.53
3f	11.50 ± 1.22	12.50 ± 2.64	29.90 ± 1.92 ***	-
3g	6.76 ± 2.59	8.60 ± 2.43	6.91 ± 3.29	19.80 ± 2.57 **

no effect | effect | unable to evaluate

Figure 2. Antioxidant activity of the compounds in different assays.
TBARS: Data are expressed as mean ± SEM (n = 3) of % of lipid peroxidation in cerebral tissue, vehicle 33.5 ± 5.65, induced 100; **ROS:** Data are expressed as mean ± SDM (n = 3) of units of fluorescence, vehicle 82.10 ± 0.05, induced 139 ± 26.8; **FRAP:** Data are expressed as mean ± SDM (n = 3) of units of fluorescence, vehicle 0.11 ± 0.02. **DPPH and ABTS:** Data expressed mean ± SDM (n=3) percentage of scavenging activity, veichle 0.00 ± 0.00. The asterisks represent significant difference (** p<0.05 **p<0.01 ***p<0.001*) when compared with vehicle/induced group. One-way ANOVA followed by Tukey's test.

CONCLUSION

In conclusion, the study suggests the antioxidant effects of the compounds in *in vitro assays*. On this group of molecules, the **3g** appears to have the most promising effect, which will be used on *in vivo* assays in the future studies.

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