Supplemental Material

Rotenone, Paraquat and Parkinson's Disease

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Supplemental Material, Table 1: Pesticides Selected for Detailed Study in FAME

Agent	Class	Proposed Mechanism(s)	Number Exposed Before Reference Date
HERBICIDES			
2,4-D	**Chlorphenoxy**	**Alpha-synuclein fibril formation**	**329**
Benomyl	**Benzimidazole**	**Mitochondrial Complex I inhibition**	**22**
Diquat	Bipyridylium	Paraquat analogue	3
Paraquat	**Bipyridylium**	**Alpha-synuclein fibril formation; Oxidative stress**	**72**
Trifluralin	**Dinitroaniline**	**Alpha-synuclein fibril formation**	**192**
Vegedex	Dithiocarbamate	Alpha-synuclein fibril formation	0
FUNGICIDES			
Carbendazim	Benzimidazole	Mitochondrial Complex I inhibition	3
Chloranil	Quinone	Oxidative stress: Pro-oxidant & Glutathione depletion	4
Copper Compounds	**Inorganic**	**Alpha-synuclein fibril formation**	**34**
Ferbam	**Dithiocarbamate**	**Alpha-synuclein fibril formation**	**36**
Mancozeb	**Dithiocarbamate**	**Alpha-synuclein fibril formation**	**17**
Maneb	Dithiocarbamate	Alpha-synuclein fibril formation	6
Mercury Compounds	Inorganic	Oxidative stress: Pro-oxidant	7
Thiabendazole	**Benzimidazole**	**Mitochondrial Complex I inhibition**	**15**
Thiram	Dithiocarbamate	Alpha-synuclein fibril formation	2
Zineb	**Dithiocarbamate**	**Alpha-synuclein fibril formation**	**12**
Ziram	Dithiocarbamate	Alpha-synuclein fibril formation	0
INSECTICIDES			
Acifluorfen (Blazer)	**Nitrophenol ether**	**Mitochondrial aconitase inhibition**	**57**
Aldrin	**Cyclodiene**	**Dieldrin precursor**	**126**
Carbon disulfide	Inorganic	Oxidative stress	5
Cyhalothrin	Pyrethroid	Mitochondrial Complex I inhibition; Oxidative stress: Glutathione depletion	2
Cyanides	**Inorganic**	**Mitochondrial Complex IV inhibition**	**30**
DDT	**Organochlorine**	**Alpha-synuclein fibril formation**	**211**
Dieldrin	**Cyclodiene**	**Alpha-synuclein fibril formation**	**44**
Methyl parathion	**Organophosphate**	**Alpha-synuclein fibril formation**	**16**
Permethrin	**Pyrethroid**	**Mitochondrial Complex I inhibition; Oxidative stress: Glutathione depletion**	**57**
Pyridaben	Pyridazinone	Mitochondrial Complex I inhibition	1
Rotenone	**Botanical**	**Mitochondrial Complex I inhibition; Alpha-synuclein fibril formation**	**51**
MULTIPLE USES			
Dichlone	**Quinone**	**Oxidative stress: Pro-oxidant**	**11**
Metam sodium	Dithiocarbamate	Alpha-synuclein fibril formation	5
SYNERGIST			
Piperonyl butoxide	Benzodioxole	Oxidative stress: Oxidative phosphorylation uncoupling; Glutathione depletion	6

Abbreviations: 2,4-D- 2,4-dichlorophenoxyacetic acid; DDT- Dichlorodiphenyltrichloroethane; FAME- Farming and Movement Evaluation study
Legend: Pesticides are grouped by their main agricultural use(s); chemical classes and mechanisms relevant to PD are identified. Pesticides shown in boldface were reported by at least 10 subjects.

Supplemental Material, Table 2: Association of PD with Ever Use of Pesticides Used by More Than 10 Subjects Before Reference Date

Pesticide	Cases (N=110)		Controls (N=358)		Men and women		Men only	
	Men (n=80)	Women (n=30)	Men (n=265)	Women (n=93)	OR	95% CI	OR	95% CI
2,4-D	72	4	234	19	1.2	0.57-2.4	1.7	0.61-5.0
Acifluorfen	13	0	44	0	1.1	0.54-2.2	1.1	0.54-2.2
Aldrin	26	0	95	5	1.1	0.60-1.9	1.3	0.68-2.3
Benomyl	6	1	15	0	1.9	0.70-5.0	1.6	0.58-4.7
Copper	6	0	26	2	0.8	0.30-1.9	0.8	0.32-2.1
Cyanides	6	0	24	0	0.8	0.33-2.2	0.8	0.32-2.2
DDT	40	7	148	16	1.1	0.65-1.7	0.9	0.52-1.6
Dichlone	3	0	8	0	1.6	0.40-6.2	1.6	0.40-6.4
Dieldrin	12	0	30	2	1.6	0.73-3.3	1.8	0.82-4.0
Ferbam	9	0	27	0	1.4	0.60-3.1	1.4	0.62-3.2
Mancozeb	1	0	13	3	0.24	0.03-1.9	0.34	0.04-2.8
Methyl Parathion	6	0	9	1	2.4	0.82-6.8	2.7	0.91-8.1
Paraquat	23	0	49	0	2.5 *	1.4-4.7	2.7 *	1.4-5.1
Permethrin	15	1	40	1	1.5	0.77-2.9	1.4	0.73-2.9
Rotenone	16	3	22	10	2.5 **	1.3-4.7	3.2 *	1.5-6.7
Thiabendazole	3	0	11	1	0.83	0.23-3.1	0.89	0.24-3.4
Trifluralin	44	2	140	6	1.2	0.72-2.1	1.2	0.69-2.2
Zineb	4	0	7	1	1.7	0.5-6.1	2.0	0.56-7.4

Abbreviations: 2,4-D- 2,4-dichlorophenoxyacetic acid; CI- Confidence interval; N- Number; OR- Odds ratio; PD- Parkinson's disease.

Legend: Analyses used logistic regression adjusted for reference age tertile, gender, state, and cigarette smoking. * $p < 0.005$, ** $p < 0.01$

Supplemental Material, Table 3: Association of Cumulative Lifetime Days of Pesticide Use and PD in Men, for Pesticides Endorsed by More Than 30 Men

Agent	Lifetime Days		Unexposed		≤Median duration				>Median duration			
	Median in Controls	Range Cases and Controls	Cases	Controls	Cases	Controls	OR	95%CI	Cases	Controls	OR	95% CI
			N	N	N	N			N	N		
2,4-D	90	1 – 4200	6	27	38	117	1.9	0.63-5.5	27	113	1.4	0.47-4.3
Acifluorfen	10	1 – 156	58	211	5	22	0.7	0.26-2.1	8	21	1.6	0.66-3.9
Aldrin	28	1 – 378	39	161	11	47	1.1	0.48-2.4	10	45	1.0	0.43-2.3
Copper	9	1 – 1110	66	232	0	11	0.2	0-1.5	6	12	1.7	0.49-5.2
DDT	27	1 – 3420	34	106	16	69	0.7	0.36-1.5	16	69	0.8	0.41-1.7
Dieldrin	18	1 – 360	50	209	3	14	1.0	0.25-3.6	8	14	2.5 *	0.94-6.8
Ferbam	14	1 – 264	60	223	2	14	0.6	0.13-2.7	7	13	2.3 *	0.87-6.3
Paraquat	8	1 – 205	47	207	10	23	2.4 **	1.0-5.5	13	23	3.6 #	1.6-8.1
Permethrin	4	1 – 811	57	218	5	21	0.9	0.32-2.6	9	18	2.0	0.83-4.7
Rotenone	14	1 – 142	59	233	10	9	4.9 #	1.9-13	5	12	1.8	0.59-5.4
Trifluralin	42	1 – 1260	30	118	15	70	0.9	0.43-1.9	25	69	1.4	0.72-2.7

Abbreviations: 2,4-D- 2,4-dichlorophenoxyacetic acid; CI- Confidence interval; N- Number; OR- Odds ratio; PD- Parkinson's disease; SD- Standard deviation

Legend: ORs are calculated relative to the unexposed group. Exact ORs are reported for copper.
*p < 0.10; ** p < 0.05; # p < 0.005.