

室内灰尘中传统邻苯二甲酸酯及新型替代品的赋存特征、神经毒性风险与潜在机制

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Occurrence characteristics, neurotoxicity risk, and potential mechanisms of traditional phthalate esters and novel alternatives in indoor dust

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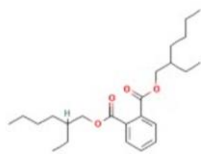
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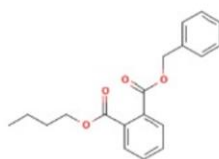
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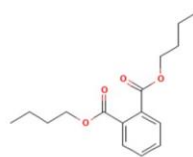
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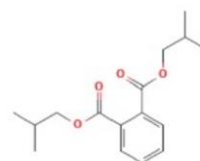
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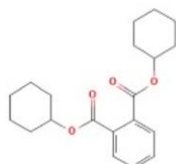
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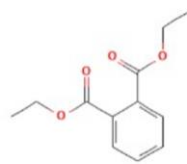
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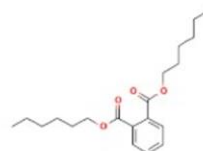
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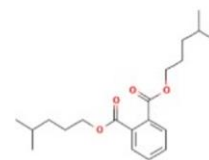
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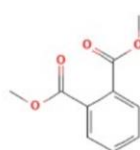
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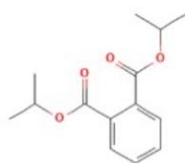
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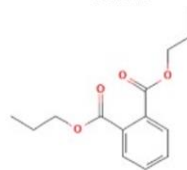
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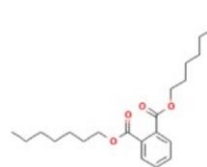
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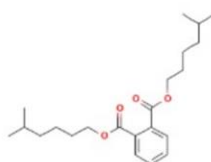
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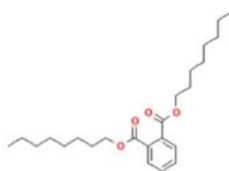
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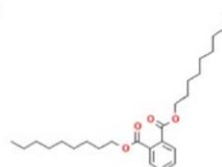
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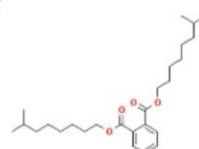
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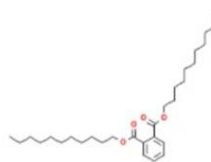
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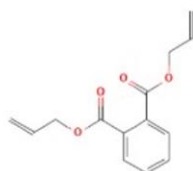
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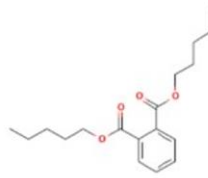
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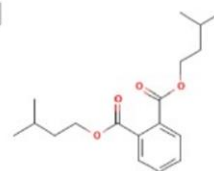
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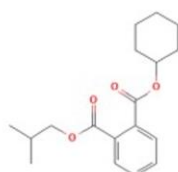
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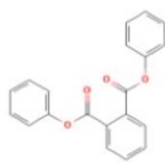
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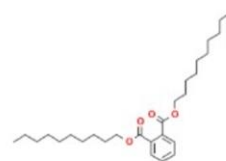
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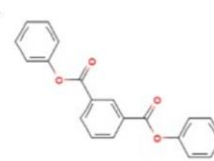
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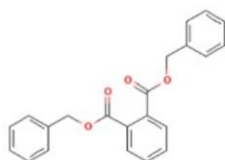
DPhP



DiDP



DPiP



DBzP

PAE alternatives

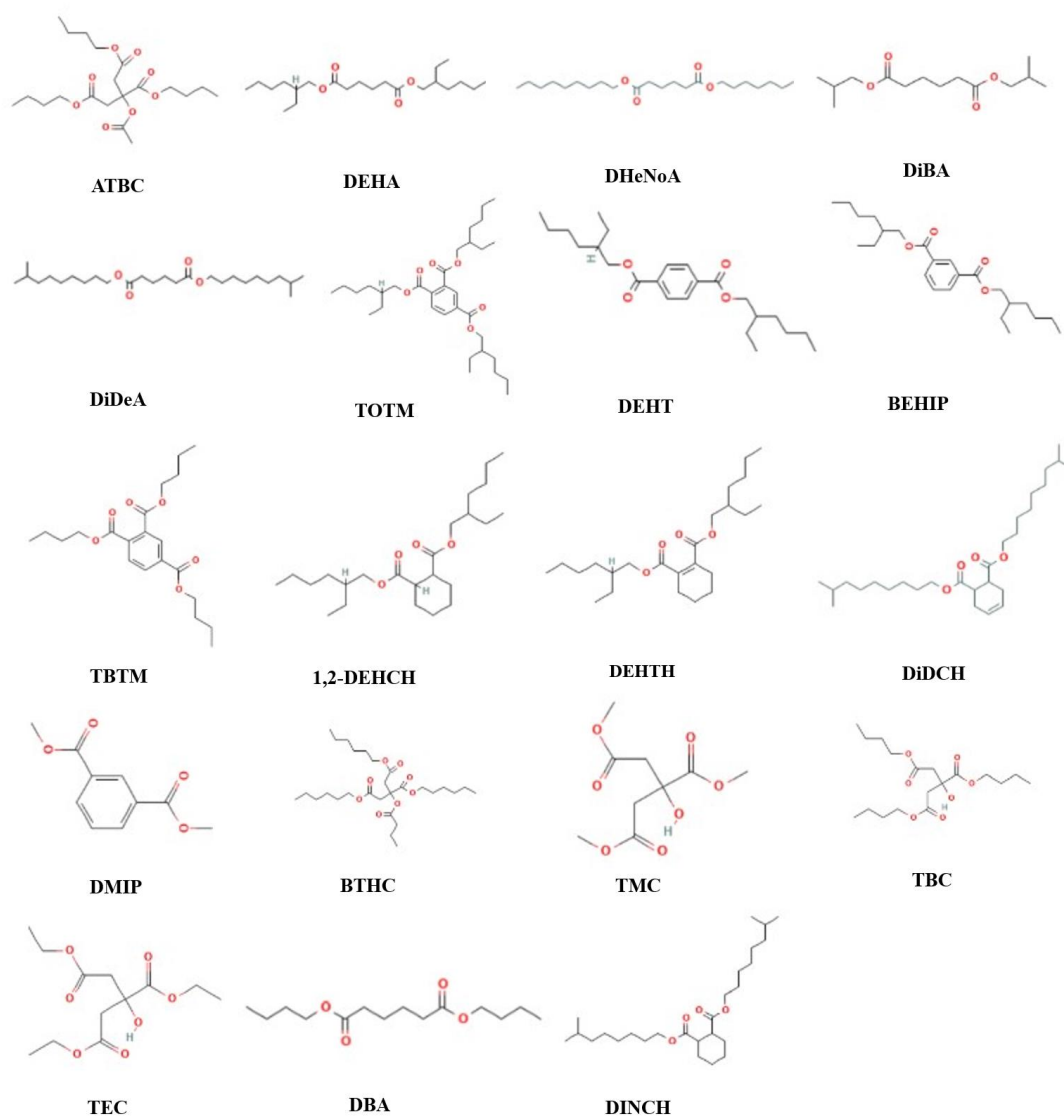


图 S1 25 种 PAEs 和 19 种新型替代品的结构式和缩写

Fig. S1 Structural formulas and abbreviations of 25 PAEs and 19 novel alternatives

表 S1 基于蒙特卡罗模拟 (MCS) 的 PAEs 及其替代品在室内灰尘中的平均含量 ($\mu_{\text{PAE},i}$)和标准偏差 ($\sigma_{\text{PAE},i}$)

Table S1 Average contents ($\mu_{\text{PAE},i}$) and standard deviations ($\sigma_{\text{PAE},i}$) of PAEs and their alternatives in indoor dust based on Monte Carlo simulation (MCS)

Compound	$\mu_{\text{PAE},i}$	$\sigma_{\text{PAE},i}$
DEHP	62.37	39.19
DBP	23.10	16.41
DiBP	17.59	11.66
DCHP	1.54	0.85
DEP	2.04	1.22
DHxP	2.49	1.47
DMP	16.92	9.99
DnOP	5.29	3.17
DiNP	14.70	11.25
DUP	5.32	3.98
DPhP	6.90	3.99
DiDP	8.88	6.52
ATBC	29.05	17.11
DEHA	2.85	1.86
DHeNoA	3.20	2.15
DiBA	0.98	0.54
DiDeA	5.31	4.28
TOTM	23.46	15.67
DEHT	2.72	1.42
DEHTH	45.52	31.63
BTHC	1.93	1.14
TBC	6.05	4.68
DBA	1.52	0.89
DINCH	1.87	1.14

表 S2 评估灰尘中 PAEs 及其替代品每日摄入量（EDI）的暴露参数

Table S2 Exposure parameters for the estimated daily intakes (EDI) of PAEs and their alternatives in dust

Age groups (years) ^a	Gender	BW/(kg) ^b	R _{ing} /(g/day) ^b	R _{inh} /(m ³ /day) ^b	SA/ (cm ²) ^b	EF/(min/day) ^b	ABF ^c	AF ^c	R _{PE} /(m ³ /kg) ^d
0-1	male	8.6	0.030	5.2	1300	1343	0.001	0.20	1.36×10 ⁹
	female	7.9	0.030	4.6	1200	1340	0.001	0.20	1.36×10 ⁹
1-2	male	11.5	0.060	5.9	1500	1283	0.001	0.20	1.36×10 ⁹
	female	10.8	0.060	5.4	1400	1288	0.001	0.20	1.36×10 ⁹
2-3	male	13.7	0.060	6.5	1600	1280	0.001	0.20	1.36×10 ⁹
	female	13.2	0.060	6.0	1500	1277	0.001	0.20	1.36×10 ⁹
3-6	male	17.9	0.076	8.8	1930	1279	0.001	0.20	1.36×10 ⁹
	female	17.3	0.068	8.0	1900	1284	0.001	0.20	1.36×10 ⁹
6-18	male	43.0	0.104	14.0	3050	1295	0.001	0.20	1.36×10 ⁹
	female	39.5	0.087	11.3	2900	1304	0.001	0.20	1.36×10 ⁹
18-45	male	66.7	0.050	18.4	3200	1152	0.001	0.07	1.36×10 ⁹
	female	56.9	0.050	14.6	2900	1183	0.001	0.07	1.36×10 ⁹
45-60	male	66.9	0.050	18.3	3200	1141	0.001	0.07	1.36×10 ⁹
	female	60.0	0.050	14.9	2900	1173	0.001	0.07	1.36×10 ⁹
over 60	male	61.7	0.050	13.4	3200	1188	0.001	0.07	1.36×10 ⁹
	female	54.7	0.050	12.5	2900	1218	0.001	0.07	1.36×10 ⁹

^a The age group intervals are left-closed and right-open (including the lower bound but excluding the upper bound)

^b Cited from Exposure Factors Handbook of Chinese Population ^[1]

^c Cited from Wang et al. ^[2]

^d Cited from Wang et al. ^[2] and Hua et al. ^[3]

表 S3 本研究使用的数据库和对应的网址

Table S3 The database and corresponding website URL used in the present study

Database	Website URL
ADMETlab 3.0	https://admetlab3.scbdd.com/
PubChem	https://pubchem.ncbi.nlm.nih.gov
SwissTargetPrediction	http://www.swisstargetprediction.ch/
GeneCards	https://www.genecards.org/
OMIM	https://www.omim.org/
STRING	https://cn.string-db.org/cgi/help
DAVID	https://david.ncifcrf.gov/tools.jsp
PubChem	https://pubchem.ncbi.nlm.nih.gov/
PDB	http://www.rcsb.org/

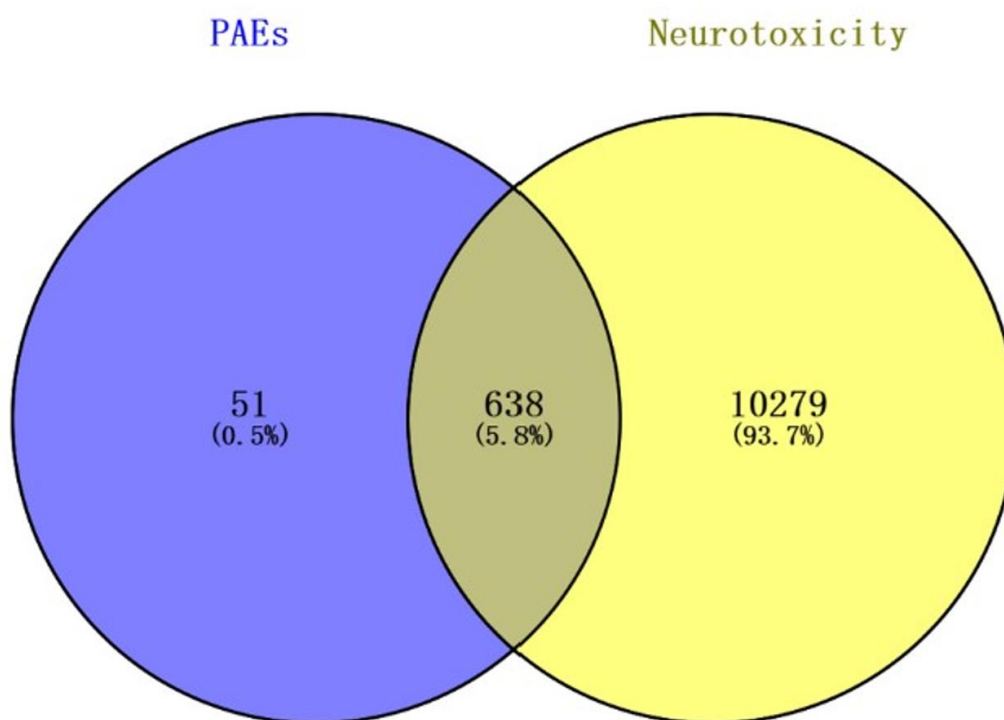


图 S2 PAEs 及其替代品潜在神经毒性靶点的维恩图

Fig. S2 Venn diagram of potential neurotoxicity targets for PAEs and their alternatives.

表 S4 PAEs 及其替代品诱发神经毒性的潜在靶点

Table S4 Potential targets for induced neurotoxicity by PAEs and their alternatives

Potential targets for induced neurotoxicity by PAEs and their alternatives						
SRC	CCND1	MAPK14	ITGB2	RIPK1	CTSB	PSMC3
PIK3R1	PRKCA	RAP1A	BAD	VCP	SLC6A3	CTSS
PIK3CA	PRKCB	GSK3B	AKR1C3	HDAC2	NTRK1	PPP1CA
HSP90AA1	PTPN6	MAPK11	CDK4	CDK7	UGT2B7	TGFBR2
PIK3CD	CDK1	CDC25C	EZH2	SNCA	FGFR1	GSK3A
PIK3CB	PRKCD	CCNB1	PDPK1	LGALS3	HTT	EGLN3
AKT1	ERBB2	MDM2	BTK	SRD5A1	HDAC4	DRD2
STAT3	SYK	PRKCE	CDK5	CYP11B1	ALOX5	LRRK2
ESR1	CASP3	BCL2L1	ALK	CYP2A6	ITGA4	PSMD2
MAPK1	HIF1A	ESR2	PTK2B	CYP11B2	KAT2B	STAT6
KRAS	PRKCG	CDC25B	LCK	CASP8	ITGAL	PARP1
MAPK3	MAP2K1	CDC25A	INSR	GSTP1	PLA2G4A	PSEN1
HSP90AB1	FYN	AR	PTPRC	TRPV4	CACNA1C	CASP1
MAPK8	CDK2	CYP3A4	CYP17A1	EPHX1	TNFRSF1A	MMP9
PTPN11	HDAC1	PLK1	APP	HCK	PSMD4	PPARG
EP300	PGR	PRKCQ	AURKA	SRD5A2	CHRNA3	RORA
JUN	IGF1R	PPP2CA	AURKB	HDAC6	CHRNA4	TRPV1
BCL2	BRAF	PIK3CG	HPGDS	TOP2A	CCNH	MAOB
RAF1	MAPT	IKBKB	HDAC3	RAPGEF3	PSMD14	MPO
LYN	CCNA2	CYP2C9	CYP2C19	PTGS1	CHRNA4	SLC6A4
EGFR	JAK3	KIT	CCND3	PPP1CC	BRD4	CNR1
JAK2	MAPK12	KDR	CCND2	NR3C1	CHRNA2	MAPK9
TLR4	CYP19A1	PTGS2	ABL1	TRPC3		

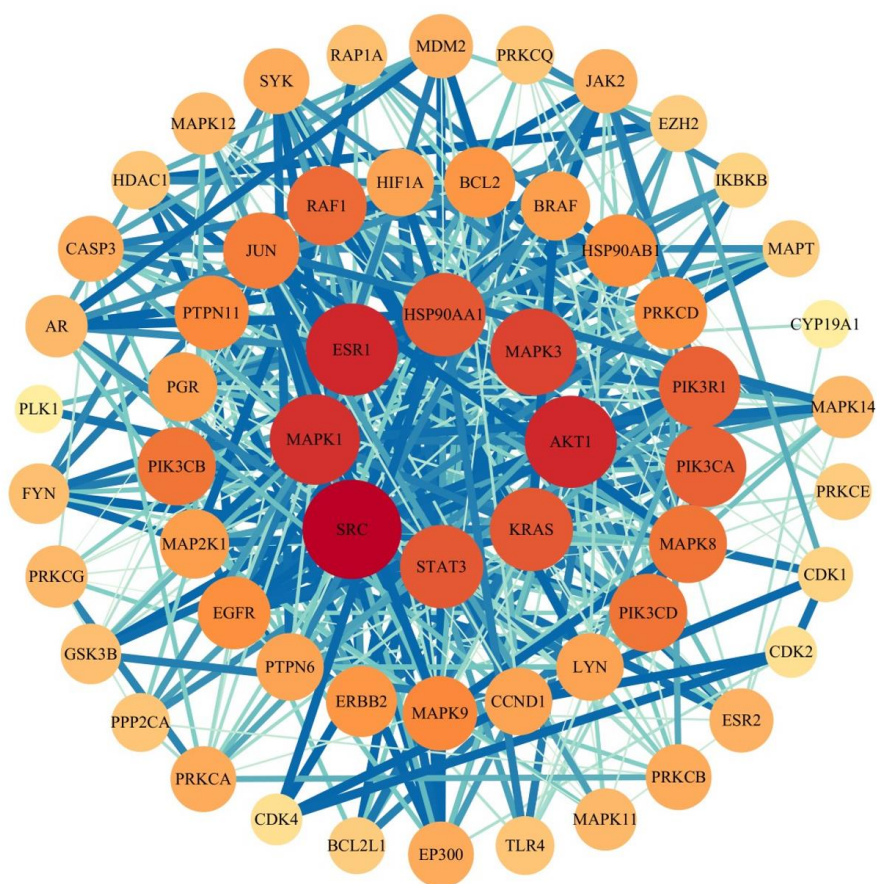


图 S3 核心靶点的 PPI 网络图

Fig. S3 The PPI network of core targets

表 S5 室内灰尘中 PAEs 及其替代品的检出频率(DF, %)、平均含量 (µg/g)和百分比(%)

Table S5 Detection frequencies (DF, %), average contents (µg/g), and percentages (%) of PAEs and their alternatives in indoor dust

Compound	Classroom			Laboratory			Office			Cafeteria			Dormitory		
	DF/%	Mean/ (µg/g)	Proportion/ %	DF/%	Mean/ (µg/g)	Proportion/ %	DF/%	Mean/ (µg/g)	Proportion/ %	DF/%	Mean/ (µg/g)	Proportion/ %	DF/%	Mean/ (µg/g)	Proportion/ %
DEHP	75.00	34.92	15.95	96.36	54.17	20.78	92.86	38.98	17.21	100.00	55.38	24.84	92.65	81.99	23.00
DBP	100.00	8.96	4.09	90.91	22.26	8.54	96.43	20.21	8.92	75.00	15.55	6.98	91.18	27.23	7.64
DiBP	87.50	9.54	4.36	94.55	12.87	4.94	96.43	13.10	5.78	100.00	18.76	8.42	92.65	24.23	6.80
DCHP	87.50	1.21	0.55	94.55	1.36	0.52	96.43	1.76	0.78	100.00	2.27	1.02	95.59	1.58	0.44
DEP	87.50	2.93	1.34	94.55	2.32	0.89	89.29	2.03	0.90	100.00	0.78	0.35	98.53	1.82	0.51
DHxP	87.50	2.20	1.01	83.64	2.47	0.95	82.14	2.88	1.27	50.00	1.80	0.81	85.29	2.42	0.68
DMP	87.50	14.07	6.42	85.45	14.96	5.74	92.86	12.43	5.49	50.00	13.20	5.92	89.71	20.79	5.83
DnOP	87.50	6.19	2.83	90.91	5.37	2.06	85.71	4.95	2.19	100.00	4.80	2.15	80.88	5.28	1.48
DiNP	62.50	6.98	3.19	89.09	12.61	4.84	96.43	12.01	5.31	100.00	20.58	9.23	92.65	17.72	4.97
DUP	87.50	4.49	2.05	92.73	4.74	1.82	92.86	4.11	1.81	50.00	3.49	1.56	80.88	6.60	1.85
DPhP	87.50	5.56	2.54	85.45	7.07	2.71	89.29	6.60	2.91	75.00	3.80	1.70	88.24	7.20	2.02
DiDP	87.50	3.64	1.66	90.91	7.08	2.71	85.71	6.82	3.01	100.00	4.65	2.09	82.35	12.34	3.46
ATBC	75.00	18.66	8.52	85.45	30.87	11.84	82.14	24.13	10.66	100.00	24.70	11.08	92.65	30.75	8.63
DEHA	100.00	3.27	1.49	90.91	2.66	1.02	89.29	3.01	1.33	100.00	1.65	0.74	94.12	2.96	0.83
DHeNoA	87.50	1.68	0.77	87.27	2.54	0.97	82.14	3.00	1.33	75.00	1.71	0.77	98.53	3.97	1.11
DiBA	75.00	1.09	0.50	90.91	0.98	0.38	96.43	1.01	0.45	100.00	0.74	0.33	94.12	0.97	0.27
DiDeA	100.00	4.16	1.90	92.73	4.43	1.70	96.43	3.26	1.44	100.00	3.65	1.64	92.65	7.14	2.00
TOTM	87.50	19.51	8.91	92.73	22.44	8.61	89.29	23.18	10.24	100.00	21.50	9.64	86.76	25.07	7.03
DEHT	75.00	3.04	1.39	90.91	2.58	0.99	85.71	2.30	1.01	75.00	3.14	1.41	89.71	2.94	0.82

表 S5 (续)

Table S5 (Continued)

Compound	Classroom			Laboratory			Office			Cafeteria			Dormitory		
	DF/%	Mean/ ($\mu\text{g/g}$)	Proportion/ %	DF/%	Mean/ ($\mu\text{g/g}$)	Proportion/ %	DF/%	Mean/ ($\mu\text{g/g}$)	Proportion/ %	DF/%	Mean/ ($\mu\text{g/g}$)	Proportion/ %	DF/%	Mean/ ($\mu\text{g/g}$)	Proportion/ %
DEHTH	62.50	59.21	27.04	89.09	36.14	13.86	89.29	31.12	13.74	100.00	15.07	6.76	88.24	60.06	16.85
BTHC	100.00	2.28	1.04	83.64	1.80	0.69	89.29	2.20	0.97	100.00	1.81	0.81	89.71	1.88	0.53
TBC	100.00	2.09	0.95	92.73	5.60	2.15	89.29	4.16	1.84	100.00	1.18	0.53	89.71	8.03	2.25
DBA	62.50	1.50	0.68	98.18	1.66	0.64	89.29	1.35	0.59	75.00	0.50	0.22	92.65	1.52	0.43
DINCH	100.00	1.82	0.83	94.55	1.68	0.64	85.71	1.84	0.81	75.00	2.23	1.00	91.18	2.04	0.57
$\Sigma_{24}\text{PAEs}$	85.42	218.98	100.00	90.76	260.66	100.00	90.03	226.42	100.00	87.50	222.92	100.00	90.44	356.52	100.00

表 S6 室内灰尘中 PAEs 及其替代品的 EDI ($\mu\text{g}/(\text{kg}\cdot\text{day})$)Table S6 EDI ($\mu\text{g}/(\text{kg}\cdot\text{day})$) of PAEs and their alternatives in indoor dust

Groups	Exposure scenarios	DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP	ATBC
Male	median	0.053	0.019	0.023	0.031	0.099	0.010	0.011	0.003	0.019	0.081	0.211	0.009	0.160
0-1	95th	0.111	0.040	0.044	0.065	0.188	0.020	0.022	0.006	0.041	0.165	0.422	0.017	0.326
Female	median	0.058	0.021	0.025	0.034	0.107	0.011	0.012	0.004	0.021	0.088	0.230	0.010	0.174
0-1	95th	0.121	0.043	0.048	0.071	0.204	0.021	0.024	0.007	0.045	0.179	0.459	0.018	0.354
Male	median	0.076	0.027	0.033	0.045	0.141	0.014	0.016	0.005	0.027	0.116	0.301	0.013	0.228
1-2	95th	0.158	0.056	0.063	0.093	0.267	0.028	0.032	0.009	0.059	0.235	0.601	0.024	0.464
Female	median	0.081	0.029	0.036	0.048	0.150	0.015	0.017	0.005	0.029	0.124	0.322	0.014	0.243
1-2	95th	0.169	0.060	0.068	0.100	0.286	0.030	0.034	0.009	0.063	0.251	0.643	0.025	0.496

表 S6 (续)

Table S6 (Continued)

Groups	Exposure scenarios	DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP	ATBC
Male	median	0.063	0.023	0.028	0.037	0.118	0.012	0.013	0.004	0.023	0.097	0.252	0.011	0.191
2-3	95th	0.133	0.047	0.053	0.078	0.224	0.023	0.027	0.007	0.049	0.197	0.504	0.020	0.388
Female	median	0.066	0.023	0.029	0.039	0.122	0.012	0.014	0.004	0.024	0.100	0.261	0.011	0.198
2-3	95th	0.137	0.049	0.055	0.081	0.232	0.024	0.028	0.008	0.051	0.204	0.522	0.021	0.402
Male	median	0.061	0.022	0.027	0.036	0.114	0.011	0.013	0.004	0.022	0.094	0.244	0.010	0.185
3-6	95th	0.128	0.046	0.051	0.076	0.217	0.023	0.026	0.007	0.048	0.191	0.488	0.019	0.376
Female	median	0.057	0.020	0.025	0.034	0.106	0.011	0.012	0.004	0.021	0.087	0.227	0.010	0.172
3-6	95th	0.119	0.043	0.048	0.070	0.202	0.021	0.024	0.007	0.045	0.177	0.454	0.018	0.350
Male	median	0.035	0.013	0.016	0.021	0.066	0.007	0.007	0.002	0.013	0.054	0.141	0.006	0.107
6-18	95th	0.074	0.026	0.030	0.044	0.125	0.013	0.015	0.004	0.028	0.110	0.282	0.011	0.217
Female	median	0.033	0.012	0.014	0.019	0.060	0.006	0.007	0.002	0.012	0.050	0.129	0.006	0.098
6-18	95th	0.068	0.024	0.027	0.040	0.115	0.012	0.014	0.004	0.025	0.101	0.258	0.010	0.199
Male	median	0.010	0.003	0.004	0.006	0.018	0.002	0.002	0.001	0.004	0.015	0.039	0.002	0.029
18-45	95th	0.020	0.007	0.008	0.012	0.034	0.004	0.004	0.001	0.008	0.030	0.078	0.003	0.060
Female	median	0.012	0.004	0.005	0.007	0.022	0.002	0.002	0.001	0.004	0.018	0.047	0.002	0.035
18-45	95th	0.025	0.009	0.010	0.014	0.041	0.004	0.005	0.001	0.009	0.036	0.093	0.004	0.072
Male	median	0.010	0.003	0.004	0.006	0.018	0.002	0.002	0.001	0.003	0.015	0.038	0.002	0.029
45-60	95th	0.020	0.007	0.008	0.012	0.034	0.004	0.004	0.001	0.008	0.030	0.077	0.003	0.059
Female	median	0.011	0.004	0.005	0.007	0.021	0.002	0.002	0.001	0.004	0.017	0.044	0.002	0.033
45-60	95th	0.023	0.008	0.009	0.014	0.039	0.004	0.005	0.001	0.009	0.034	0.088	0.003	0.068

表 S6 (续)

Table S6 (Continued)

Groups	Exposure scenarios	DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP	ATBC
Male	median	0.011	0.004	0.005	0.006	0.020	0.002	0.002	0.001	0.004	0.017	0.043	0.002	0.033
≥60	95th	0.023	0.008	0.009	0.013	0.038	0.004	0.005	0.001	0.008	0.034	0.086	0.003	0.067
Female	median	0.013	0.004	0.006	0.007	0.023	0.002	0.003	0.001	0.005	0.019	0.050	0.002	0.038
≥60	95th	0.026	0.009	0.011	0.015	0.044	0.005	0.005	0.001	0.010	0.039	0.100	0.004	0.077

表 S6 (续)

Table S6 (Continued)

Groups	Exposure scenarios	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH	ΣPAEs
Male	median	0.007	0.022	0.005	0.006	0.081	0.062	0.005	0.007	0.009	0.058	0.018	1.010
0-1	95th	0.013	0.046	0.010	0.012	0.166	0.122	0.010	0.013	0.016	0.110	0.035	2.020
Female	median	0.007	0.024	0.006	0.007	0.088	0.067	0.006	0.007	0.009	0.062	0.019	1.096
0-1	95th	0.014	0.050	0.011	0.013	0.180	0.132	0.011	0.014	0.018	0.119	0.038	2.193
Male	median	0.009	0.031	0.007	0.009	0.115	0.088	0.007	0.010	0.012	0.082	0.025	1.437
1-2	95th	0.018	0.066	0.014	0.018	0.236	0.173	0.014	0.019	0.023	0.156	0.050	2.876
Female	median	0.010	0.033	0.008	0.010	0.123	0.094	0.008	0.010	0.013	0.088	0.027	1.536
1-2	95th	0.019	0.070	0.015	0.019	0.252	0.185	0.015	0.020	0.025	0.167	0.053	3.073
Male	median	0.008	0.026	0.006	0.008	0.097	0.074	0.006	0.008	0.010	0.069	0.021	1.204
2-3	95th	0.015	0.055	0.012	0.015	0.198	0.145	0.012	0.016	0.019	0.131	0.041	2.409
Female	median	0.008	0.027	0.006	0.008	0.100	0.076	0.006	0.009	0.011	0.071	0.022	1.246
2-3	95th	0.016	0.057	0.012	0.015	0.205	0.150	0.012	0.016	0.020	0.135	0.043	2.494

表 S6 (续)

Table S6 (Continued)

Groups	Exposure scenarios	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH	ΣPAEs
Male	median	0.008	0.025	0.006	0.007	0.094	0.071	0.006	0.008	0.010	0.066	0.021	1.166
3-6	95th	0.015	0.053	0.012	0.014	0.192	0.140	0.011	0.015	0.019	0.127	0.040	2.333
Female	median	0.007	0.023	0.006	0.007	0.087	0.066	0.006	0.007	0.009	0.062	0.019	1.084
3-6	95th	0.014	0.050	0.011	0.013	0.178	0.131	0.010	0.014	0.017	0.118	0.037	2.170
Male	median	0.004	0.015	0.003	0.004	0.054	0.041	0.003	0.005	0.006	0.038	0.012	0.673
6-18	95th	0.008	0.031	0.007	0.008	0.111	0.081	0.006	0.009	0.011	0.073	0.023	1.347
Female	median	0.004	0.013	0.003	0.004	0.050	0.038	0.003	0.004	0.005	0.035	0.011	0.618
6-18	95th	0.008	0.028	0.006	0.008	0.102	0.074	0.006	0.008	0.010	0.067	0.021	1.236
Male	median	0.001	0.004	0.001	0.001	0.015	0.011	0.001	0.001	0.002	0.011	0.003	0.185
18-45	95th	0.002	0.008	0.002	0.002	0.030	0.022	0.002	0.002	0.003	0.020	0.006	0.371
Female	median	0.001	0.005	0.001	0.001	0.018	0.014	0.001	0.002	0.002	0.013	0.004	0.223
18-45	95th	0.003	0.010	0.002	0.003	0.037	0.027	0.002	0.003	0.004	0.024	0.008	0.446
Male	median	0.001	0.004	0.001	0.001	0.015	0.011	0.001	0.001	0.002	0.010	0.003	0.183
45-60	95th	0.002	0.008	0.002	0.002	0.030	0.022	0.002	0.002	0.003	0.020	0.006	0.366
Female	median	0.001	0.005	0.001	0.001	0.017	0.013	0.001	0.001	0.002	0.012	0.004	0.210
45-60	95th	0.003	0.010	0.002	0.003	0.034	0.025	0.002	0.003	0.003	0.023	0.007	0.420
Male	median	0.001	0.004	0.001	0.001	0.017	0.013	0.001	0.001	0.002	0.012	0.004	0.207
≥60	95th	0.003	0.009	0.002	0.003	0.034	0.025	0.002	0.003	0.003	0.022	0.007	0.413
Female	median	0.002	0.005	0.001	0.001	0.019	0.015	0.001	0.002	0.002	0.014	0.004	0.239
≥60	95th	0.003	0.011	0.002	0.003	0.039	0.029	0.002	0.003	0.004	0.026	0.008	0.478

表 S7 PAEs 及其替代品的毒性当量因子（TEF）

Table S7 Toxic equivalency factors (TEF) of PAEs and their alternatives

Compound	Neurotoxicity	NR-ER	SR-ARE	SR-MMP	SR-p53
DEHP	0.163	0.068	0.343	0.090	0.000
DBP	0.063	0.999	0.000	0.000	0.000
DiBP	0.088	1.000	0.000	0.000	0.000
DCHP	0.389	0.016	0.313	0.993	0.029
DEP	0.147	0.000	0.004	0.000	0.000
DHxP	0.069	0.095	0.001	0.007	0.017
DMP	0.472	0.000	0.003	0.007	0.002
DnOP	0.055	0.111	0.006	0.017	0.064
DiNP	0.037	0.020	0.005	0.000	0.003
DUP	0.018	0.187	0.003	0.023	0.014
DPhP	0.629	0.776	0.027	0.805	0.000
DiDP	0.027	0.146	0.004	0.016	0.019
ATBC	0.172	0.750	0.001	0.001	0.000
DEHA	0.174	0.002	0.014	0.003	0.000
DHeNoA	0.048	0.010	0.000	0.000	0.000
DiBA	0.058	0.999	0.000	0.000	0.000
DiDeA	0.023	0.009	0.000	0.000	0.000
TOTM	0.074	0.033	0.058	0.099	0.000
DEHTH	0.176	0.207	0.032	0.025	0.000
DEHT	0.116	0.086	0.801	0.051	0.000
BTHC	0.073	0.031	0.000	0.001	0.000
TBC	0.187	0.999	0.000	0.000	0.000
DBA	0.050	0.282	0.000	0.000	0.000
DINCH	0.043	0.067	0.112	0.001	0.003

表 S8 PAEs 及其替代品的毒性当量 (TEQ, ng TEQ/(kg·day))

Table S8 Toxic equivalent quantities (TEQ, ng TEQ/(kg·day)) of PAEs and their alternatives

Biological effects		DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP
Neurotoxicity													
0-1	male	8.678	1.204	2.059	12.170	14.487	0.680	5.247	0.183	0.706	1.447	133.074	0.242
	female	9.419	1.306	2.235	13.210	15.725	0.738	5.695	0.198	0.766	1.570	144.444	0.262
1-2	male	12.353	1.713	2.931	17.325	20.623	0.968	7.470	0.260	1.005	2.059	189.439	0.344
	female	13.201	1.831	3.132	18.513	22.038	1.034	7.982	0.278	1.074	2.201	202.436	0.367
2-3	male	10.349	1.435	2.455	14.514	17.277	0.811	6.258	0.218	0.842	1.725	158.700	0.288
	female	10.712	1.486	2.542	15.023	17.883	0.839	6.477	0.226	0.872	1.786	164.270	0.298
3-6	male	10.022	1.390	2.378	14.056	16.732	0.785	6.060	0.211	0.816	1.671	153.695	0.279
	female	9.319	1.293	2.211	13.070	15.558	0.730	5.635	0.196	0.758	1.554	142.915	0.259
6-18	male	5.785	0.802	1.373	8.114	9.658	0.453	3.498	0.122	0.471	0.964	88.718	0.161
	female	5.309	0.736	1.260	7.446	8.863	0.416	3.210	0.112	0.432	0.885	81.418	0.148
18-45	male	1.593	0.221	0.378	2.234	2.660	0.125	0.963	0.034	0.130	0.266	24.431	0.044
	female	1.917	0.266	0.455	2.688	3.200	0.150	1.159	0.040	0.156	0.320	29.396	0.053
45-60	male	1.573	0.218	0.373	2.206	2.626	0.123	0.951	0.033	0.128	0.262	24.126	0.044
	female	1.802	0.250	0.428	2.528	3.009	0.141	1.090	0.038	0.147	0.301	27.642	0.050
≥60	male	1.776	0.246	0.421	2.491	2.965	0.139	1.074	0.037	0.145	0.296	27.235	0.049
	female	2.053	0.285	0.487	2.879	3.427	0.161	1.241	0.043	0.167	0.342	31.482	0.057
NR-ER													
0-1	male	3.597	18.958	23.398	0.512	0.017	0.940	0.001	0.367	0.392	15.183	164.096	1.323
	female	3.905	20.578	25.398	0.556	0.019	1.020	0.001	0.398	0.425	16.480	178.117	1.436
1-2	male	5.121	26.988	33.309	0.729	0.024	1.338	0.002	0.522	0.558	21.614	233.600	1.883
	female	5.472	28.839	35.594	0.779	0.026	1.430	0.002	0.558	0.596	23.097	249.626	2.012

表 S8 (续)

Table S8 (Continued)

Biological effects		DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP
NR-ER													
2-3	male	4.290	22.609	27.904	0.610	0.020	1.121	0.002	0.437	0.467	18.107	195.696	1.578
	female	4.441	23.402	28.884	0.632	0.021	1.160	0.002	0.453	0.484	18.742	202.564	1.633
3-6	male	4.155	21.896	27.024	0.591	0.020	1.086	0.002	0.424	0.452	17.536	189.524	1.528
	female	3.863	20.360	25.129	0.550	0.018	1.010	0.001	0.394	0.421	16.306	176.231	1.421
6-18	male	2.398	12.639	15.599	0.341	0.011	0.627	0.001	0.245	0.261	10.122	109.399	0.882
	female	2.201	11.599	14.316	0.313	0.010	0.575	0.001	0.224	0.240	9.289	100.398	0.809
18-45	male	0.660	3.481	4.296	0.094	0.003	0.173	0.000	0.067	0.072	2.787	30.127	0.243
	female	0.795	4.188	5.169	0.113	0.004	0.208	0.000	0.081	0.087	3.354	36.249	0.292
45-60	male	0.652	3.437	4.242	0.093	0.003	0.170	0.000	0.067	0.071	2.753	29.750	0.240
	female	0.747	3.938	4.860	0.106	0.004	0.195	0.000	0.076	0.081	3.154	34.085	0.275
≥60	male	0.736	3.880	4.789	0.105	0.004	0.192	0.000	0.075	0.080	3.107	33.583	0.271
	female	0.851	4.485	5.535	0.121	0.004	0.222	0.000	0.087	0.093	3.592	38.821	0.313
SR-ARE													
0-1	male	18.258	0.001	0.000	9.810	0.425	0.014	0.032	0.021	0.088	0.235	5.792	0.033
	female	19.818	0.001	0.000	10.648	0.461	0.015	0.034	0.023	0.095	0.255	6.287	0.036
1-2	male	25.992	0.001	0.000	13.965	0.605	0.020	0.045	0.030	0.125	0.335	8.246	0.047
	female	27.775	0.001	0.000	14.923	0.647	0.022	0.048	0.032	0.133	0.358	8.812	0.050
2-3	male	21.774	0.001	0.000	11.699	0.507	0.017	0.038	0.025	0.104	0.281	6.908	0.039
	female	22.538	0.001	0.000	12.109	0.525	0.018	0.039	0.026	0.108	0.290	7.150	0.041
3-6	male	21.088	0.001	0.000	11.330	0.491	0.016	0.037	0.024	0.101	0.272	6.690	0.038
	female	19.608	0.001	0.000	10.535	0.456	0.015	0.034	0.022	0.094	0.253	6.221	0.035

表 S8 (续)

Table S8 (Continued)

Biological effects		DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP
SR-ARE													
6-18	male	12.172	0.000	0.000	6.540	0.283	0.010	0.021	0.014	0.058	0.157	3.862	0.022
	female	11.171	0.000	0.000	6.002	0.260	0.009	0.019	0.013	0.054	0.144	3.544	0.020
18-45	male	3.352	0.000	0.000	1.801	0.078	0.003	0.006	0.004	0.016	0.043	1.063	0.006
	female	4.033	0.000	0.000	2.167	0.094	0.003	0.007	0.005	0.019	0.052	1.280	0.007
45-60	male	3.310	0.000	0.000	1.778	0.077	0.003	0.006	0.004	0.016	0.043	1.050	0.006
	female	3.793	0.000	0.000	2.038	0.088	0.003	0.007	0.004	0.018	0.049	1.203	0.007
≥60	male	3.737	0.000	0.000	2.008	0.087	0.003	0.007	0.004	0.018	0.048	1.185	0.007
	female	4.319	0.000	0.000	2.321	0.101	0.003	0.008	0.005	0.021	0.056	1.370	0.008
SR-MMP													
0-1	male	4.778	0.004	0.000	31.079	0.012	0.068	0.083	0.054	0.008	1.872	170.316	0.146
	female	5.186	0.004	0.000	33.734	0.013	0.074	0.090	0.059	0.009	2.032	184.868	0.159
1-2	male	6.802	0.005	0.000	44.242	0.017	0.097	0.118	0.078	0.011	2.665	242.455	0.208
	female	7.269	0.006	0.000	47.278	0.018	0.104	0.126	0.083	0.012	2.848	259.089	0.222
2-3	male	5.698	0.005	0.000	37.064	0.014	0.082	0.099	0.065	0.010	2.233	203.114	0.174
	female	5.898	0.005	0.000	38.364	0.015	0.084	0.103	0.067	0.010	2.311	210.243	0.181
3-6	male	5.519	0.004	0.000	35.895	0.014	0.079	0.096	0.063	0.009	2.163	196.708	0.169
	female	5.132	0.004	0.000	33.377	0.013	0.073	0.089	0.059	0.009	2.011	182.911	0.157
6-18	male	3.186	0.003	0.000	20.720	0.008	0.046	0.055	0.036	0.005	1.248	113.546	0.097
	female	2.923	0.002	0.000	19.015	0.007	0.042	0.051	0.033	0.005	1.146	104.203	0.089
18-45	male	0.877	0.001	0.000	5.706	0.002	0.013	0.015	0.010	0.001	0.344	31.269	0.027
	female	1.055	0.001	0.000	6.865	0.003	0.015	0.018	0.012	0.002	0.414	37.623	0.032

表 S8 (续)

Table S8 (Continued)

Biological effects		DEHP	DBP	DiBP	DCHP	DEP	DHxP	DMP	DnOP	DiNP	DUP	DPhP	DiDP
SR-MMP													
45-60	male	0.866	0.001	0.000	5.634	0.002	0.012	0.015	0.010	0.001	0.339	30.877	0.027
	female	0.993	0.001	0.000	6.456	0.002	0.014	0.017	0.011	0.002	0.389	35.377	0.030
≥60	male	0.978	0.001	0.000	6.360	0.002	0.014	0.017	0.011	0.002	0.383	34.856	0.030
	female	1.130	0.001	0.000	7.352	0.003	0.016	0.020	0.013	0.002	0.443	40.292	0.035
SR-p53													
0-1	male	0.019	0.001	0.000	0.904	0.005	0.166	0.019	0.212	0.056	1.139	0.103	0.172
	female	0.021	0.001	0.000	0.982	0.006	0.180	0.021	0.230	0.061	1.237	0.112	0.187
1-2	male	0.027	0.001	0.000	1.287	0.007	0.236	0.027	0.301	0.079	1.622	0.146	0.245
	female	0.029	0.002	0.000	1.376	0.008	0.252	0.029	0.322	0.085	1.733	0.156	0.262
2-3	male	0.023	0.001	0.000	1.078	0.006	0.198	0.023	0.252	0.067	1.359	0.123	0.205
	female	0.024	0.001	0.000	1.116	0.006	0.205	0.024	0.261	0.069	1.406	0.127	0.212
3-6	male	0.022	0.001	0.000	1.044	0.006	0.192	0.022	0.244	0.064	1.316	0.119	0.199
	female	0.021	0.001	0.000	0.971	0.005	0.178	0.021	0.227	0.060	1.224	0.110	0.185
6-18	male	0.013	0.001	0.000	0.603	0.003	0.111	0.013	0.141	0.037	0.760	0.069	0.115
	female	0.012	0.001	0.000	0.553	0.003	0.101	0.012	0.129	0.034	0.697	0.063	0.105
18-45	male	0.004	0.000	0.000	0.166	0.001	0.030	0.004	0.039	0.010	0.209	0.019	0.032
	female	0.004	0.000	0.000	0.200	0.001	0.037	0.004	0.047	0.012	0.252	0.023	0.038
45-60	male	0.003	0.000	0.000	0.164	0.001	0.030	0.003	0.038	0.010	0.207	0.019	0.031
	female	0.004	0.000	0.000	0.188	0.001	0.034	0.004	0.044	0.012	0.237	0.021	0.036
≥60	male	0.004	0.000	0.000	0.185	0.001	0.034	0.004	0.043	0.011	0.233	0.021	0.035
	female	0.005	0.000	0.000	0.214	0.001	0.039	0.005	0.050	0.013	0.270	0.024	0.041

表 S8 (续)

Table S8 (Continued)

Biological effects		ATBC	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH
Neurotoxicity													
0-1	male	27.575	1.133	1.044	0.300	0.148	5.980	10.854	0.595	0.506	1.592	2.892	0.768
	female	29.931	1.230	1.133	0.326	0.161	6.491	11.782	0.646	0.549	1.728	3.139	0.834
1-2	male	39.255	1.613	1.486	0.427	0.211	8.514	15.452	0.848	0.720	2.266	4.117	1.094
	female	41.948	1.724	1.587	0.456	0.226	9.098	16.512	0.906	0.770	2.422	4.399	1.169
2-3	male	32.886	1.352	1.244	0.358	0.177	7.132	12.945	0.710	0.603	1.899	3.449	0.916
	female	34.040	1.399	1.288	0.370	0.183	7.382	13.399	0.735	0.625	1.965	3.570	0.948
3-6	male	31.848	1.309	1.205	0.346	0.171	6.907	12.536	0.688	0.584	1.839	3.340	0.887
	female	29.615	1.217	1.121	0.322	0.159	6.423	11.657	0.639	0.543	1.710	3.106	0.825
6-18	male	18.384	0.756	0.696	0.200	0.099	3.987	7.236	0.397	0.337	1.061	1.928	0.512
	female	16.871	0.693	0.638	0.184	0.091	3.659	6.641	0.364	0.310	0.974	1.769	0.470
18-45	male	5.063	0.208	0.192	0.055	0.027	1.098	1.993	0.109	0.093	0.292	0.531	0.141
	female	6.091	0.250	0.231	0.066	0.033	1.321	2.398	0.132	0.112	0.352	0.639	0.170
45-60	male	4.999	0.205	0.189	0.054	0.027	1.084	1.968	0.108	0.092	0.289	0.524	0.139
	female	5.728	0.235	0.217	0.062	0.031	1.242	2.255	0.124	0.105	0.331	0.601	0.160
≥60	male	5.643	0.232	0.214	0.061	0.030	1.224	2.221	0.122	0.104	0.326	0.592	0.157
	female	6.524	0.268	0.247	0.071	0.035	1.415	2.568	0.141	0.120	0.377	0.684	0.182
NR-ER													
0-1	male	120.006	0.011	0.210	5.183	0.058	2.659	12.753	0.440	0.212	8.499	16.213	1.205
	female	130.260	0.012	0.228	5.626	0.063	2.886	13.842	0.478	0.230	9.225	17.598	1.308
1-2	male	170.836	0.015	0.298	7.378	0.083	3.785	18.154	0.627	0.301	12.099	23.080	1.716
	female	182.556	0.016	0.319	7.885	0.089	4.045	19.400	0.670	0.322	12.929	24.663	1.833

表 S8 (续)

Table S8 (Continued)

Biological effects		ATBC	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH
NR-ER													
2-3	male	143.116	0.013	0.250	6.181	0.069	3.171	15.209	0.525	0.253	10.135	19.335	1.437
	female	148.139	0.013	0.259	6.398	0.072	3.283	15.742	0.544	0.261	10.491	20.013	1.488
3-6	male	138.602	0.012	0.242	5.986	0.067	3.071	14.729	0.509	0.245	9.816	18.725	1.392
	female	128.881	0.011	0.225	5.566	0.063	2.856	13.696	0.473	0.227	9.127	17.412	1.294
6-18	male	80.005	0.007	0.140	3.455	0.039	1.773	8.502	0.294	0.141	5.666	10.809	0.803
	female	73.423	0.007	0.128	3.171	0.036	1.627	7.802	0.269	0.130	5.200	9.919	0.737
18-45	male	22.032	0.002	0.038	0.952	0.011	0.488	2.341	0.081	0.039	1.560	2.977	0.221
	female	26.509	0.002	0.046	1.145	0.013	0.587	2.817	0.097	0.047	1.877	3.581	0.266
45-60	male	21.757	0.002	0.038	0.940	0.011	0.482	2.312	0.080	0.038	1.541	2.939	0.218
	female	24.927	0.002	0.044	1.077	0.012	0.552	2.649	0.091	0.044	1.765	3.368	0.250
≥60	male	24.560	0.002	0.043	1.061	0.012	0.544	2.610	0.090	0.043	1.739	3.318	0.247
	female	28.390	0.003	0.050	1.226	0.014	0.629	3.017	0.104	0.050	2.011	3.836	0.285
SR-ARE													
0-1	male	0.177	0.094	0.000	0.000	0.000	4.702	1.959	4.113	0.001	0.000	0.000	2.001
	female	0.192	0.102	0.000	0.000	0.000	5.104	2.127	4.465	0.001	0.000	0.000	2.172
1-2	male	0.252	0.134	0.000	0.000	0.000	6.694	2.789	5.855	0.002	0.000	0.000	2.848
	female	0.270	0.143	0.000	0.000	0.000	7.153	2.980	6.257	0.002	0.000	0.000	3.044
2-3	male	0.211	0.112	0.000	0.000	0.000	5.607	2.336	4.905	0.001	0.000	0.000	2.386
	female	0.219	0.116	0.000	0.000	0.000	5.804	2.418	5.077	0.001	0.000	0.000	2.470
3-6	male	0.205	0.108	0.000	0.000	0.000	5.431	2.263	4.751	0.001	0.000	0.000	2.311
	female	0.190	0.101	0.000	0.000	0.000	5.050	2.104	4.417	0.001	0.000	0.000	2.149

表 S8 (续)

Table S8 (Continued)

Biological effects		ATBC	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH
SR-ARE													
6-18	male	0.118	0.063	0.000	0.000	0.000	3.135	1.306	2.742	0.001	0.000	0.000	1.334
	female	0.108	0.057	0.000	0.000	0.000	2.877	1.199	2.517	0.001	0.000	0.000	1.224
18-45	male	0.033	0.017	0.000	0.000	0.000	0.863	0.360	0.755	0.000	0.000	0.000	0.367
	female	0.039	0.021	0.000	0.000	0.000	1.039	0.433	0.909	0.000	0.000	0.000	0.442
45-60	male	0.032	0.017	0.000	0.000	0.000	0.852	0.355	0.746	0.000	0.000	0.000	0.363
	female	0.037	0.019	0.000	0.000	0.000	0.977	0.407	0.854	0.000	0.000	0.000	0.416
≥60	male	0.036	0.019	0.000	0.000	0.000	0.962	0.401	0.842	0.000	0.000	0.000	0.409
	female	0.042	0.022	0.000	0.000	0.000	1.112	0.463	0.973	0.000	0.000	0.000	0.473
SR-MMP													
0-1	male	0.092	0.021	0.003	0.000	0.000	7.994	1.561	0.260	0.005	0.000	0.000	0.013
	female	0.100	0.023	0.003	0.000	0.000	8.677	1.694	0.282	0.005	0.000	0.000	0.014
1-2	male	0.131	0.030	0.004	0.000	0.000	11.380	2.222	0.370	0.007	0.000	0.000	0.018
	female	0.140	0.032	0.004	0.000	0.000	12.161	2.374	0.396	0.007	0.000	0.000	0.019
2-3	male	0.110	0.025	0.003	0.000	0.000	9.534	1.861	0.310	0.006	0.000	0.000	0.015
	female	0.114	0.026	0.003	0.000	0.000	9.868	1.927	0.321	0.006	0.000	0.000	0.016
3-6	male	0.106	0.024	0.003	0.000	0.000	9.233	1.802	0.300	0.006	0.000	0.000	0.015
	female	0.099	0.022	0.003	0.000	0.000	8.585	1.676	0.279	0.005	0.000	0.000	0.014
6-18	male	0.061	0.014	0.002	0.000	0.000	5.330	1.040	0.173	0.003	0.000	0.000	0.008
	female	0.056	0.013	0.002	0.000	0.000	4.891	0.955	0.159	0.003	0.000	0.000	0.008
18-45	male	0.017	0.004	0.001	0.000	0.000	1.468	0.287	0.048	0.001	0.000	0.000	0.002
	female	0.020	0.005	0.001	0.000	0.000	1.766	0.345	0.057	0.001	0.000	0.000	0.003

表 S8 (续)

Table S8 (Continued)

Biological effects		ATBC	DEHA	DHeNoA	DiBA	DiDeA	TOTM	DEHT	DEHTH	BTHC	TBC	DBA	DINCH
SR-MMP													
45-60	male	0.017	0.004	0.001	0.000	0.000	1.449	0.283	0.047	0.001	0.000	0.000	0.002
	female	0.019	0.004	0.001	0.000	0.000	1.661	0.324	0.054	0.001	0.000	0.000	0.003
≥60	male	0.019	0.004	0.001	0.000	0.000	1.636	0.319	0.053	0.001	0.000	0.000	0.003
	female	0.022	0.005	0.001	0.000	0.000	1.891	0.369	0.062	0.001	0.000	0.000	0.003
SR-p53													
0-1	male	0.009	0.001	0.006	0.000	0.000	0.005	0.017	0.000	0.000	0.000	0.001	0.062
	female	0.010	0.001	0.006	0.000	0.000	0.005	0.018	0.000	0.000	0.000	0.001	0.067
1-2	male	0.013	0.002	0.008	0.000	0.000	0.006	0.024	0.000	0.000	0.000	0.001	0.088
	female	0.014	0.002	0.008	0.000	0.000	0.007	0.025	0.000	0.000	0.000	0.001	0.095
2-3	male	0.011	0.002	0.007	0.000	0.000	0.005	0.020	0.000	0.000	0.000	0.001	0.074
	female	0.012	0.002	0.007	0.000	0.000	0.006	0.021	0.000	0.000	0.000	0.001	0.077
3-6	male	0.011	0.002	0.006	0.000	0.000	0.005	0.019	0.000	0.000	0.000	0.001	0.072
	female	0.010	0.001	0.006	0.000	0.000	0.005	0.018	0.000	0.000	0.000	0.001	0.067
6-18	male	0.006	0.001	0.004	0.000	0.000	0.003	0.011	0.000	0.000	0.000	0.000	0.041
	female	0.006	0.001	0.003	0.000	0.000	0.003	0.010	0.000	0.000	0.000	0.000	0.038
18-45	male	0.002	0.000	0.001	0.000	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.011
	female	0.002	0.000	0.001	0.000	0.000	0.001	0.004	0.000	0.000	0.000	0.000	0.014
45-60	male	0.002	0.000	0.001	0.000	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.011
	female	0.002	0.000	0.001	0.000	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.013
≥60	male	0.002	0.000	0.001	0.000	0.000	0.001	0.003	0.000	0.000	0.000	0.000	0.013
	female	0.002	0.000	0.001	0.000	0.000	0.001	0.004	0.000	0.000	0.000	0.000	0.015

表 S9 核心靶标的 GO 功能分析富集表

Table S9 The enrichment table of GO function analysis of core targets

Category	GO term	<i>p</i> -value	Gene count
BP	Phosphorylation	7.21460×10^{-33}	33
	Protein phosphorylation	9.96390×10^{-30}	27
	Intracellular signal transduction	3.41388×10^{-19}	21
	Peptidyl-serine phosphorylation	3.55766×10^{-19}	16
	Signal transduction	7.25170×10^{-19}	29
	Positive regulation of gene expression	1.67649×10^{-16}	20
	Insulin-like growth factor receptor signaling pathway	4.13987×10^{-12}	8
	Negative regulation of apoptotic process	1.23133×10^{-11}	16
	Stress-activated MAPK cascade	6.38136×10^{-11}	7
CC	MAPK cascade	1.08054×10^{-10}	10
	Cytosol	1.53528×10^{-23}	53
	Cytoplasm	7.59460×10^{-22}	52
	Nucleus	4.73326×10^{-18}	50
	Nucleoplasm	1.82316×10^{-14}	39
	Mitochondrion	2.58758×10^{-12}	24
	Plasma membrane	7.49122×10^{-10}	39
	Perinuclear region of cytoplasm	1.47719×10^{-08}	15
	Protein-containing complex	3.09791×10^{-07}	13
MF	Phosphatidylinositol 3-kinase complex, class IA	1.68676×10^{-06}	4
	Membrane raft	1.88803×10^{-06}	8
	Protein serine kinase activity	1.52501×10^{-26}	25
	Protein serine/threonine kinase activity	1.54280×10^{-24}	24
	ATP binding	3.55593×10^{-24}	36
	Enzyme binding	2.74536×10^{-20}	21
	Protein kinase activity	9.98622×10^{-20}	19
	Kinase activity	1.03691×10^{-15}	15
	Protein kinase binding	1.00961×10^{-12}	17
	Phosphotyrosine residue binding	2.41224×10^{-10}	8
	Protein tyrosine kinase activity	8.28387×10^{-10}	9
	Protein binding	1.07411×10^{-09}	58

表 S10 主要靶标蛋白口袋坐标和网格框尺寸

Table S10 Primary target protein pocket coordinates and grid box sizes

Target gene	PDB ID	Protein pocket coordinate	Grid box size
SRC	5UUT	$X = -17.721, Y = 79.322, Z = -19.155$	$X = 62.0, Y = 60.0, Z = 72.0$
AKT1	4EJN	$X = 30.390, Y = 43.900, Z = 17.196$	$X = 54.0, Y = 64.0, Z = 72.0$
ESR1	4XI3	$X = -4.700, Y = -8.100, Z = 31.400$	$X = 22.4, Y = 19.4, Z = 20.4$
MAPK1	3W55	$X = 16.300, Y = 38.700, Z = 44.600$	$X = 21.3, Y = 14.5, Z = 16.9$
MAPK3	6GES	$X = 59.031, Y = 12.930, Z = 10.698$	$X = 64.0, Y = 54.0, Z = 74.0$
HSP90AA1	2QG2	$X = 2.800, Y = 33.200, Z = 24.100$	$X = 20.0, Y = 17.6, Z = 15.6$
KRAS	6GJ5	$X = -16.857, Y = -12.286, Z = -10.487$	$X = 48.0, Y = 44.0, Z = 44.0$

表 S11 PAEs 及其替代品与核心靶标($n = 168$)的结合能Table S11 The binding energy of PAEs and their alternatives with the core targets ($n = 168$)

Compound	Protein affinity/(kcal/mol)						
	SRC	AKT1	ESR1	MAPK1	MAPK3	HSP90AA1	KRAS
DEHP	-7.684	-8.228	-7.925	-5.743	-6.673	-7.620	-6.886
DBP	-6.413	-7.229	-6.844	-6.130	-6.403	-7.590	-6.369
DiBP	-7.099	-7.705	-7.204	-6.783	-6.990	-8.576	-6.793
DCHP	-8.524	-9.551	-9.159	-8.173	-8.112	-9.717	-8.139
DEP	-6.663	-7.049	-6.200	-6.223	-6.476	-7.744	-6.146
DHxP	-6.784	-7.176	-6.700	-6.176	-5.700	-7.538	-6.490
DMP	-6.423	-6.546	-5.889	-6.059	-6.152	-7.349	-6.766
DnOP	-7.580	-7.431	-7.309	-5.695	-6.273	-7.827	-6.446
DiNP	-8.218	-8.040	-7.877	-6.409	-6.521	-8.044	-6.822
DUP	-7.884	-6.856	-7.689	-5.897	-6.084	-7.599	-6.022
DPhP	-8.569	-9.685	-8.826	-8.530	-7.761	-10.263	-9.295
DiDP	-8.148	-7.321	-7.586	-6.075	-6.735	-7.704	-6.973
ATBC	-6.138	-6.663	-6.404	-5.342	-5.453	-6.289	-6.236
DEHA	-6.668	-6.665	-6.425	-5.837	-6.204	-6.842	-6.184
DHeNoA	-7.171	-6.177	-6.608	-5.355	-5.670	-6.513	-6.049
DiBA	-6.208	-6.043	-6.056	-5.863	-5.923	-6.449	-6.327
DiDeA	-7.174	-6.892	-7.112	-5.750	-5.783	-7.073	-6.126
TOTM	-7.785	-8.330	-8.142	-6.494	-7.130	-8.338	-6.684
DEHT	-7.481	-7.525	-7.799	-6.459	-6.807	-7.260	-6.689
DEHTH	-7.970	-7.495	-8.011	-6.243	-6.828	-8.248	-6.758
BTHC	-6.399	-7.159	-6.607	-5.925	-6.202	-6.396	-5.472
TBC	-5.926	-6.571	-6.355	-5.677	-5.716	-6.257	-6.763
DBA	-6.868	-6.030	-5.716	-5.077	-5.398	-6.042	-6.216
DINCH	-7.819	-7.710	-7.914	-6.177	-6.656	-7.337	-7.019

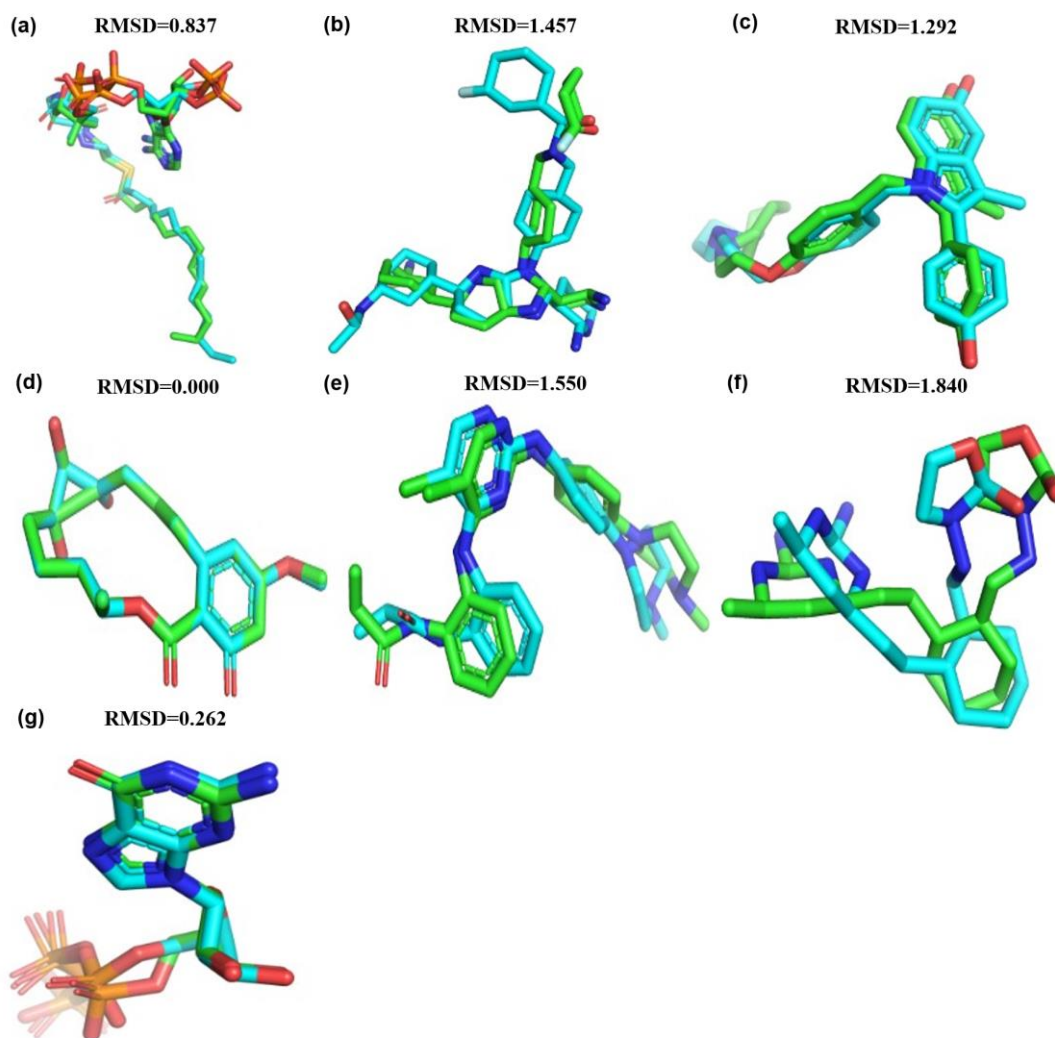


图 S4 重新对接构象（绿色）与原始构象（蓝色）的叠加图像及 RMSD

Fig. S4 Overlapping images and the root-mean-square deviation (RMSD) values of redocking conformation (green) and original conformation (blue)

a: oncogene, non-receptor tyrosine kinase (SRC); b: serine/threonine kinase 1 (AKT1); c: estrogen receptor 1 (ESR1); d: mitogen-activated protein kinase 1 (MAPK1); e: mitogen-activated protein kinase 3 (MAPK3); f: heat shock protein 90 alpha family class a member 1 (HSP90AA1); g: kirsten rat sarcoma viral oncogene homolog (KRAS).

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