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Novel Hybrids of 6-Amino-3-n-butylphthalide and Neuroprotective Groups against Ischemic

Stroke<sup>†</sup>

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<sup>1</sup>H NMR, MS, HRMS and HPLC for final compounds of representative compounds

HPLC analysis conditions Column Details:

Column Details:	WondaSil C18 Superb (4.6mm×150mm, 5µm)	
Column Temperature:	30 °C	
Flow Rate:	1 mL/min	
Detector Wavelength:	254 nm	
Injection volume:	20 µl	

Solvent A: acetonitrile; Solvent B: water. Method: 40 % to 80 % of A and 20 % to 60 % of B



**Fig.1** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **NBP (A2)**.



Fig.2 MS of compound NBP (A2).







**Fig.4** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **A4**.



Fig.5 MS of compound A4.



Fig.6 <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>) of compound ABP1.



Fig.7 MS of compound ABP1.



Fig.8 HRMS of compound ABP1.



Fig.9 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound ABP2.



Fig.10 MS of compound ABP2.



Fig.11 HRMS of compound ABP2.



Fig.12 <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound ABP3.



## Fig.13 MS of compound ABP3.





Fig.14 HRMS of compound ABP3.



Fig.15 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound ABP4.



Fig.16 MS of compound ABP4.







Fig.18 MS of compound A7.



Fig.19 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound A8.



Fig.21 MS of compound A9.



**Fig.23** <sup>1</sup>HNMR (400 MHz, DMSO- $d_{\delta}$ ) of compound **ABP5**.



Fig.24 MS of compound ABP5.



Fig.25 MS of compound A11.



Fig.26 <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **ABP6**.



Fig.27 MS of compound ABP6.







**Fig.29** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **ABP7**.



Fig.31 HRMS of compound ABP7.



**Fig.32** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **ABP8**.



Fig.33 MS of compound ABP8.



Fig.34 HRMS of compound ABP8.



**Fig.35** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **B2**.



Fig.36 MS of compound B2.







Fig.38 <sup>1</sup>HNMR (400 MHz, DMSO-*d6*) of compound ABP9.



Fig.39 MS of compound ABP9.



Fig.40 HRMS of compound ABP9.



Fig.41 <sup>1</sup>HNMR (400 MHz, DMSO-*d6*) of compound ABP12.



Fig.42 MS of compound ABP12.



Fig.43 HRMS of compound ABP12.



Fig.44 MS of compound B3.



Fig.45 MS of compound B4.



Fig.46 MS of compound B5.



Fig.47 <sup>1</sup>HNMR (400 MHz, DMSO-*d6*) of compound ABP11.



Fig.48 MS of compound ABP11.



Fig.49 HRMS of compound ABP11.



Fig.50 <sup>1</sup>HNMR (400 MHz, DMSO- $d_{\delta}$ ) of compound **ABP10**.



Fig.51 MS of compound ABP10.



Fig.52 HRMS of compound ABP10.



Fig.53 <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>) of compound ABP13.



Fig.54 MS of compound ABP13.



Fig.55 HRMS of compound ABP13.



Fig.56 <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>) of compound ABP14.







Fig.58 HRMS of compound ABP14.





Fig.60 MS of compound ABP15.







Fig.62 MS of compound A12.



Fig.63 <sup>1</sup>HNMR (400 MHz, DMSO-*d6*) of compound ABP16.



Fig.65 HRMS of compound ABP16.



**Fig.66** <sup>1</sup>HNMR (400 MHz, DMSO- $d_6$ ) of compound **ABP17**.



Fig.67 MS of compound ABP17.







Fig.69 <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>) of compound ABP18.



Fig.70 MS of compound ABP18.











Fig.73 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound ABP19.



Fig.74 MS of compound ABP19.



Fig.75 HRMS of compound ABP19.



Fig.76 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound ABP20.



Fig.77 MS of compound ABP20.



Fig.78 HRMS of compound ABP20.



Fig.79 <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) of compound ABP21.





Fig.81 HRMS of compound ABP21.





Peak Results

peak	time	Area	height	Area %	height %
1	1.095	15030	2479	0.900	1.659
2	3.803	2671	221	0.160	0.148
3	4.255	3891	394	0.233	0.264
4	4.512	36664	4267	2.196	2.855
5	6.231	1611535	142073	96.511	95.074
total		1669790	149433	100.000	100.000

Table 1 peak results of ABP1



Fig.83 HPLC for compound ABP2

## Peak Results

peak	time	Area	height	Area %	height %
1	1.075	9850	1616	0. 592	0.930
2	4.291	2544	271	0.153	0.156
3	4.512	29048	3350	1.745	1.927
4	4.987	1577568	165721	94.787	95.340
5	5.945	9722	821	0.584	0.472
6	6.226	5169	474	0.311	0.273
7	9.879	3518	222	0.211	0.127
8	10.735	6854	382	0.412	0.220
9	12.292	1459	84	0.088	0.048
10	12.767	18604	882	1.118	0.507
tota	1	1664335	173822	100.000	100.000

Table 2 peak results of ABP2



Fig.84 HPLC for compound ABP3

peak	time(min)	Area	height	Area %	height %
1	1.147	28399	3964	0.996	1.637
2	1.743	40756	4009	1.429	1.656
3	2.060	14919	751	0.523	0.310
4	2.969	5114	243	0.179	0.101
5	3.778	2758881	232787	96.739	96.139
6	4.293	1249	146	0.044	0.060
7	4.872	2557	234	0.090	0.097
total		2851875	242135	100.000	100.000

Table 3 peak results of ABP3



Fig.85 HPLC	C for com	pound ABP4
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peak	time(min)	Area	height	Area %	height %
1	1.121	19140	4855	1.669	4.229
2	4.415	1127374	109955	98.331	95.771
total		1146514	114810	100.000	100.000

Table 4 peak results of ABP4



Fig.86 HPLC for compound ABP5

Peak Results

peak	time(min)	Area	height	Area %	height %
1	1.077	11553	1727	0.291	0.563
2	1.298	2336	247	0.059	0.080
3	1.623	2264	209	0.057	0.068
4	2.050	8945	446	0.225	0.145
5	2.578	3771	490	0.095	0.160
6	2.884	2818	292	0.071	0.095
7	3.139	4449	469	0.112	0.153
8	3.665	1506	131	0.038	0.043
9	3.843	1435	147	0.036	0.048
10	4.514	32471	3625	0.817	1.182
11	5.234	4516	418	0.114	0.136
12	5.958	6592	613	0.166	0.200
13	6.267	1862	147	0.047	0.048
14	6.752	1434	108	0.036	0.035
15	7.646	3886659	297561	97.836	97.042
total		3972612	306630	100.000	100.000

Table 5 peak results of ABP5



Fig.87 HPLC for compound ABP6

peak	time(min)	Area	height	Area %	height %
1	1.094	18871	2900	0.967	0.920
2	1.312	2040	233	0.104	0.074
3	1.740	20530	2839	1.052	0.901
4	1.883	7906	1069	0.405	0.339
5	2.028	14647	1081	0.750	0.343
6	2.416	2261	352	0.116	0.112
7	2.673	1831488	300665	93.807	95.374
8	3.140	5674	594	0.291	0.188
9	4. 520	34865	4190	1.786	1.329
10	5.241	4343	455	0.222	0.144
11	5.965	8462	767	0.433	0.243
12	6.782	1312	103	0.067	0.033
total		1952400	315248	100.000	100.000

Table 6 peak results of ABP6



Fig.88 HPLC for compound ABP7

peak	time(min)	Area	height	Area %	height %
1	1.108	30888	3740	1.519	2.575
2	1.845	15965	1752	0.785	1.206
3	4.598	1968993	138659	96.828	95.470
4	6.173	17643	1088	0.868	0.749
total		2033489	145239	100.000	100.000

# Table 7 peak results of ABP7



Fig.89 HPLC for compound ABP8

#### Peak Results

peak	time(min)	Area	height	Area%	height %
1	0.200	1555	118	0.004	0.008
2	1.082	2314	265	0.005	0.018
3	1.634	8805	369	0.020	0.026
4	2.933	8924	461	0.020	0.032
5	3.217	6060	317	0.014	0.022
6	4.489	63277	2654	0.145	0.184
7	5.998	4587	183	0.011	0.013
8	8.159	43435812	1436345	99.781	99.697
total		43531334	1440711	100.000	100.000

Table 8 peak results of ABP8



Fig.90 HPLC for compound ABP9

peak	time(min)	Area	height	Area %	height %
1	1.054	19721	3353	0.070	0.114
2	1.605	5656	1210	0.020	0.041
3	1.738	13080	2059	0.047	0.070
4	1.906	246159	38813	0.876	1.322
5	2.301	95267	8220	0.339	0.280
6	2.485	54360	7012	0.193	0.239
7	2.650	117128	14771	0.417	0.503
8	3.013	30017	2130	0.107	0.073
9	3.339	5366	644	0.019	0.022
10	4.089	7299	1039	0.026	0.035
11	4.299	76384	6914	0.272	0.235
12	4.744	27411072	2848312	97.518	97.010
13	6.805	5061	321	0.018	0.011
14	7.884	8082	500	0.029	0.017
15	8.250	1219	117	0.004	0.004
16	8.798	12966	679	0.046	0.023
total	a construction of the	28108837	2936094	100.000	100.000

Table 9 peak results of ABP9



Fig.91 HPLC for compound ABP10

Peak Results

peak	time(min)	Area	height	Area %	height %
1	1.087	6325	468	0.011	0.012
2	1.403	4394	292	0.008	0.007
3	1.942	4818	280	0.008	0.007
4	2.296	33801	3590	0.059	0.089
5	2.598	183355	17835	0.319	0.440
6	3.492	56779935	3999997	98.831	98.660
7	4.747	84773	6721	0.148	0.166
8	5.400	2212	205	0.004	0.005
9	5.687	38429	3215	0.067	0.079
10	6.212	1062	121	0.002	0.003
11	6.610	295446	20529	0.514	0.506
12	7.194	3767	251	0.007	0.006
13	7.694	3971	192	0.007	0.005
14	8.226	9375	633	0.016	0.016
total		57451661	4054328	100.000	100.000

Table 10 peak results of ABP10



Fig.92 HPLC for compound ABP11

Peak Results

peak	time(min)	Area	height	Area %	height %
1	0.546	65366	2772	0.182	0.101
2	1.188	12999	1445	0.036	0.053
3	1.280	7858	1588	0.022	0.058
4	1.417	22910	2296	0.064	0.083
5	1.663	26601	4385	0.074	0.159
6	1.832	4582	789	0.013	0.029
7	1.931	5598	1234	0.016	0.045
8	2.141	36090	1661	0.100	0.060
9	2.484	37759	1655	0.105	0.060
10	3. 583	35278353	2717146	98.075	98.788
11	5.050	17583	531	0.049	0.019
12	5.922	63816	3713	0.177	0.135
13	6.753	68994	2194	0.192	0.080
14	7.409	17936	932	0.050	0.034
15	9.229	178622	4971	0.497	0.181
16	10.468	125778	3173	0.350	0.115
total		35970844	2750485	100.000	100.000

Table 11 peak results of ABP11



Fig.93 HPLC for compound ABP12

Peak Results

peak	time(min)	Area	height	Area %	height %
1	0.708	3330	232	0.063	0.038
2	0.899	3213	391	0.061	0.064
3	1.000	1369	449	0.026	0.074
4	1.105	9409	533	0.177	0.087
5	1.415	7158	744	0.135	0.122
6	1.550	7283	869	0.137	0.143
7	1.728	20792	3378	0.392	0.554
8	2.102	14574	646	0.275	0.106
9	2.342	1444	236	0.027	0.039
10	4.320	2250	223	0.042	0.037
11	5.175	3730	306	0.070	0.050
12	5.400	4561	382	0.086	0.063
13	6.533	82445	2219	1.554	0.364
14	7.431	236115	2438	4.451	0.400
15	8.595	27255	2610	0.514	0.428
16	8.850	4780084	590887	90.105	96.895
17	10.541	6182	130	0.117	0.021
18	11.608	15957	455	0.301	0.075
19	11.853	29199	822	0.550	0.135
20	14.392	32401	757	0.611	0.124
21	14.727	10357	519	0.195	0.085
22	14.875	2962	377	0.056	0.062
23	15.033	2929	222	0.055	0.036
total		5305001	609825	100.000	100.000

 Table 12 peak results of ABP12



Fig.94 HPLC for compound ABP13

peak	time(min)	Area	height	Area %	height %
1	1.084	13724	2013	0.252	0.453
2	1.304	1521	191	0.028	0.043
3	1.627	3181	321	0.058	0.072
4	2.050	8807	398	0.162	0.089
5	2.579	1826	200	0.033	0.045
6	2.867	1222	138	0.022	0.031
7	3.128	5854	469	0.107	0.105
8	3.704	2054	191	0.038	0.043
9	4.513	28181	3268	0.517	0.735
10	5.234	3326	358	0.061	0.081
11	5.953	7540	600	0.138	0.135
12	6.167	1012	139	0.019	0.031
13	7.019	5372456	436318	98.564	98.137
total		5450703	444603	100.000	100.000

Table 13 peak results of ABP13



Fig.95 HPLC for compound ABP14

peak	time(min)	Area	height	Area %	height %
1	1.090	16488	2585	0.163	0.193
2	1.307	2093	233	0.021	0.017
3	1.629	2254	261	0.022	0.019
4	2.069	7208	379	0.071	0.028
5	2.390	1606	183	0.016	0.014
6	3.143	3486	419	0.035	0.031
7	3.720	9995171	1331427	99.037	99.189
8	4.516	33041	3949	0.327	0.294
9	4.880	13933	1539	0.138	0.115
10	5.236	3690	405	0.037	0.030
11	5.960	8973	754	0.089	0.056
12	6.755	4376	174	0.043	0.013
total		10092318	1342308	100.000	100.000

Table 14 peak results of ABP14



# Fig.96 HPLC for compound ABP15

## Peak Results

peak	time(min)	Area	height	Area %	height %
1	2.114	1414	144	0.039	0.070
2	2.554	269	35	0.007	0.017
3	4.034	3659147	205554	99.901	99.890
4	7.853	1942	48	0.053	0.023
total		3662772	205780	100.000	100.000

## Table 15 peak results of ABP15





## Peak Results

peak	time(min)	Area	height	Area %	height %
1	1.112	11143	1253	0.454	0.562
2	3.455	51840	6688	2.112	3.000
3	4.572	1187	103	0.048	0.046
4	5.649	2368685	214192	96. 521	96.063
5	8.367	2070	99	0.084	0.044
6	8.928	10040	289	0.409	0.130
7	9.472	9102	347	0.371	0.156
total		2454067	222971	100.000	100.000

Table 16 peak results of ABP16



Fig.98 HPLC for compound ABP17

Peak Results

peak	time(min)	Area	height	Area %	height %
1	2.049	1373	156	0.037	0.082
2	2.362	782	76	0.021	0.040
3	3.657	3660496	189901	99.941	99.878
total		3662652	190133	100.000	100.000

Table 17 peak results of ABP17



Fig.99 HPLC for compound ABP18

peak	time(min)	Area	height	Area %	height %
1	0.217	453	64	0.017	0.042
2	1.113	20352	3124	0.752	2.038
3	4.653	307	46	0.011	0.030
4	5.000	74334	7796	2.746	5.085
5	6.803	6602	532	0.244	0.347
6	9.858	1499	87	0.055	0.057
7	10.904	2603091	141656	96.174	92.401
tota	1	2706638	153305	100.000	100.000

Table 18 peak results of ABP18



Fig.100 HPLC for compound ABP19

peak	time(min)	Area	height	Area %	height %
1	1.142	61172	8183	0.382	0.466
2	1.638	3092	418	0.019	0.024
3	2.036	13206	639	0.082	0.036
4	2.367	1888	284	0.012	0.016
5	2.583	13552	761	0.085	0.043
6	3.146	9349	686	0.058	0.039
7	3.443	65731	5333	0.410	0.304
8	4.261	15614298	1727701	97.461	98.408
9	4.818	9548	974	0.060	0.056
10	5.231	2449	295	0.015	0.017
11	5.671	1338	124	0.008	0.007
12	5.978	12114	1033	0.076	0.059
13	6.201	2720	399	0.017	0.023
14	6.428	15267	736	0.095	0.042
15	7.451	114687	5235	0.716	0.298
16	8.367	21018	821	0.131	0.047
17	9.150	5546	232	0.035	0.013
18	9.533	5726	302	0.036	0.017
19	9.977	32072	823	0.200	0.047
20	10.874	5858	293	0.037	0.017
21	12.241	8295	292	0.052	0.017
22	13.244	2070	91	0.013	0.005
total		16020997	1755653	100.000	100.000

Table 19 peak results of ABP19



Fig.101 HPLC for compound ABP20

peak	time(min)	Area	height	Area %	height %
1	1.642	2429	659	0.034	0.085
2	2.330	143742	12588	2.027	1.620
3	2.572	15995	2418	0.226	0.311
4	2.852	8144	705	0.115	0.091
5	3.643	61534	6618	0.868	0.852
6	4.299	6832785	751973	96.350	96.768
7	4.807	3874	515	0.055	0.066
8	5.228	4348	519	0.061	0.067
9	6.508	8771	543	0.124	0.070
10	7.346	1724	113	0.024	0.015
11	7.747	2669	108	0.038	0.014
12	9.092	4170	251	0.059	0.032
13	9.624	1479	77	0.021	0.010
total		7091664	777087	100.000	100.000





Figure.102 HPLC for compound ABP21

peak	time(min)	Area	height	Area %	height %
1	1.100	28993	3328	0.140	0.144
2	1.635	2595	312	0.013	0.013
3	2.051	14284	726	0.069	0.031
4	2.579	11374	755	0.055	0.033
5	2.828	5764	437	0.028	0.019
6	3.331	152802	10526	0.736	0.455
7	4.131	20503964	2295493	98.797	99.122
8	4.503	15958	2482	0.077	0.107
9	4.762	1113	170	0.005	0.007
10	5.229	3642	426	0.018	0.018
11	5.952	8131	789	0.039	0.034
12	6.183	1009	109	0.005	0.005
13	6.697	3009	213	0.014	0.009
14	7.453	1066	68	0.005	0.003
total		20753705	2315834	100.000	100.000

 Table 21 peak results of ABP21