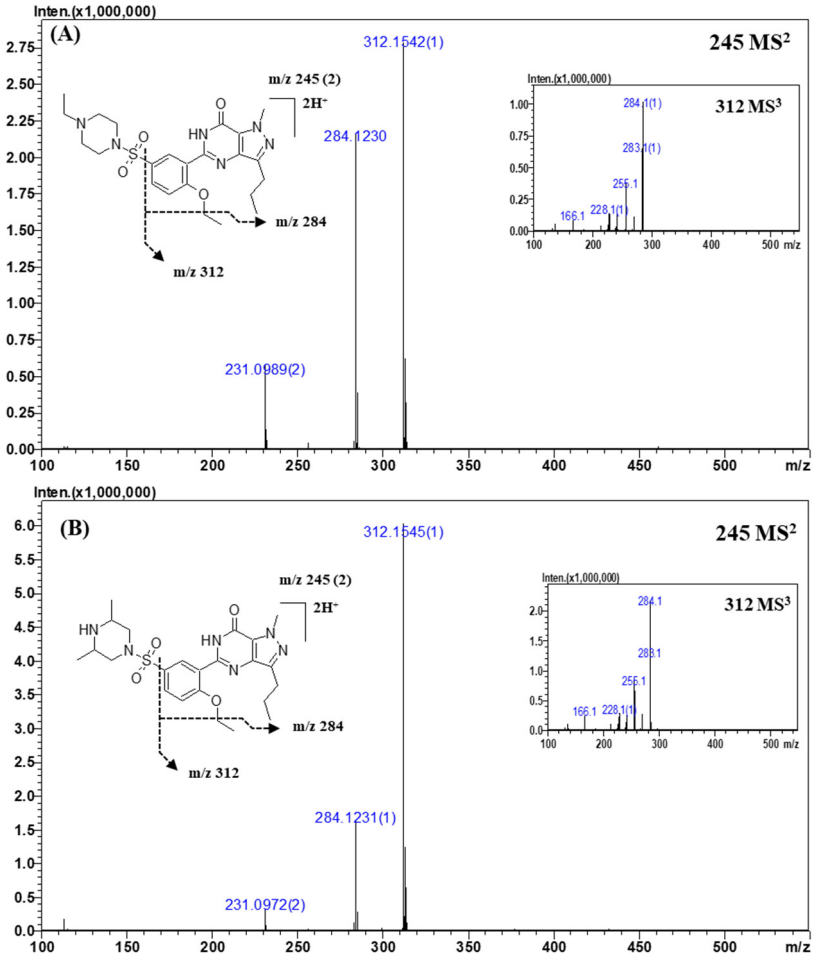
Figure S1. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of



homosildenafil (A) and dimethylsildenafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

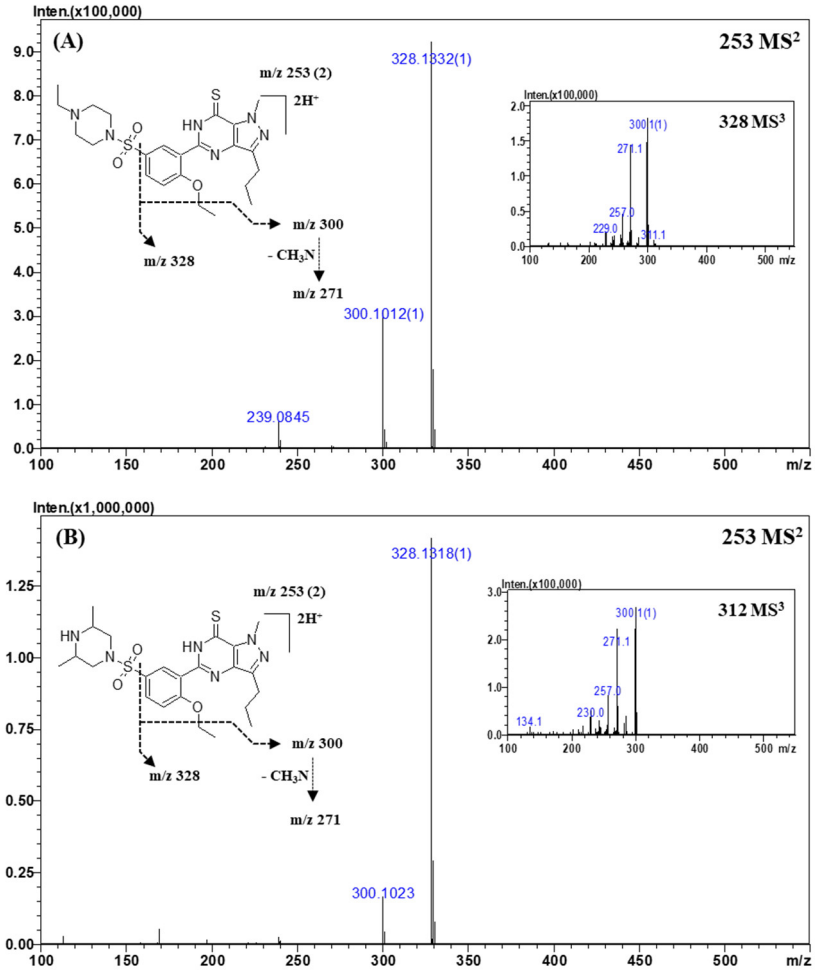


Figure S2. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of thiohomosildenafil (A) and dimethylthiosildenafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

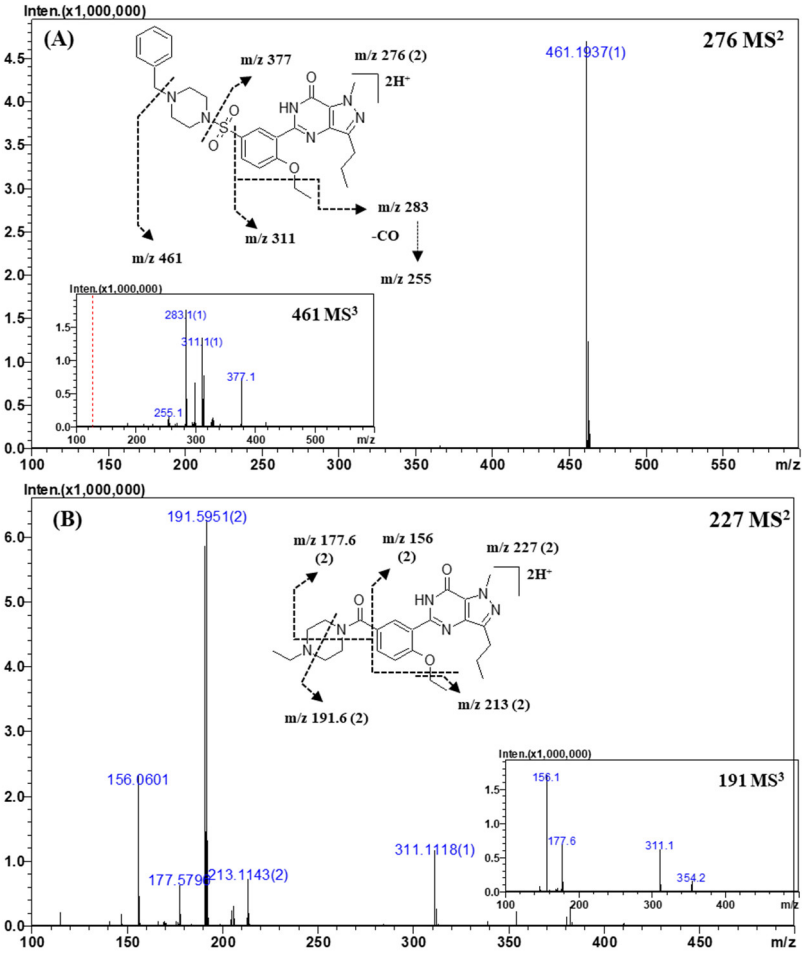


Figure S3. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of benzylsildenafil (A) and carbodenafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

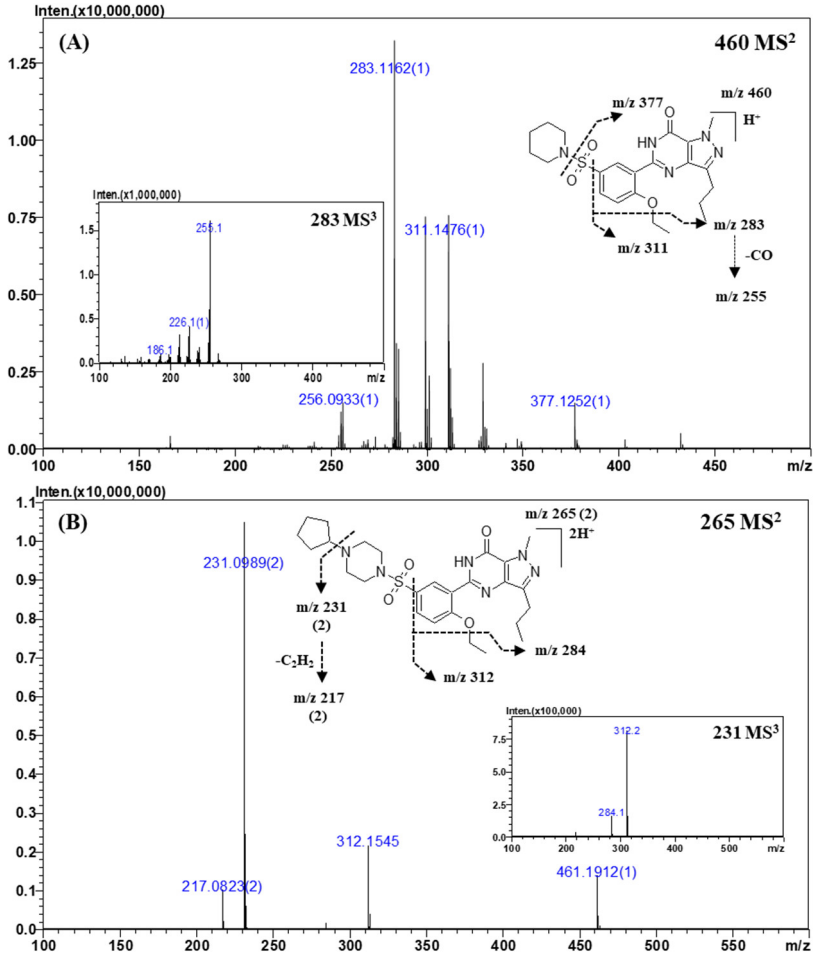


Figure S4. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of norneosildenafil (A) and cyclopentinafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

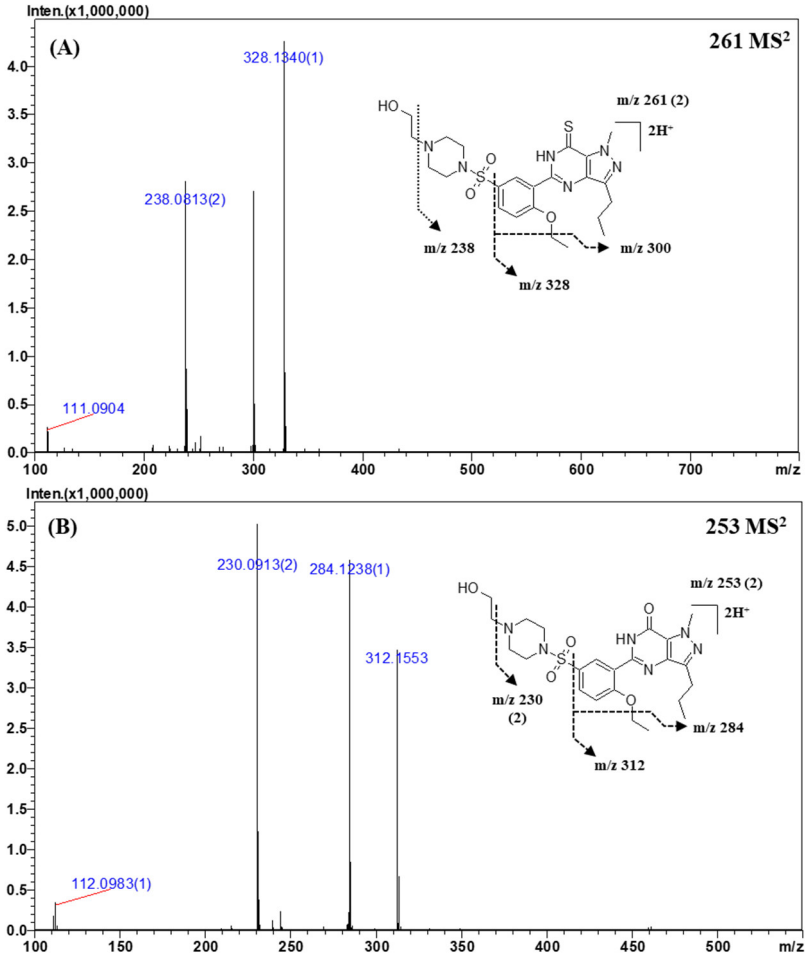


Figure S5. Representative MS^2 spectra and proposed fragmentation mechanisms of hydroxythiohomosildenafil (A) and hydroxyhomosildenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

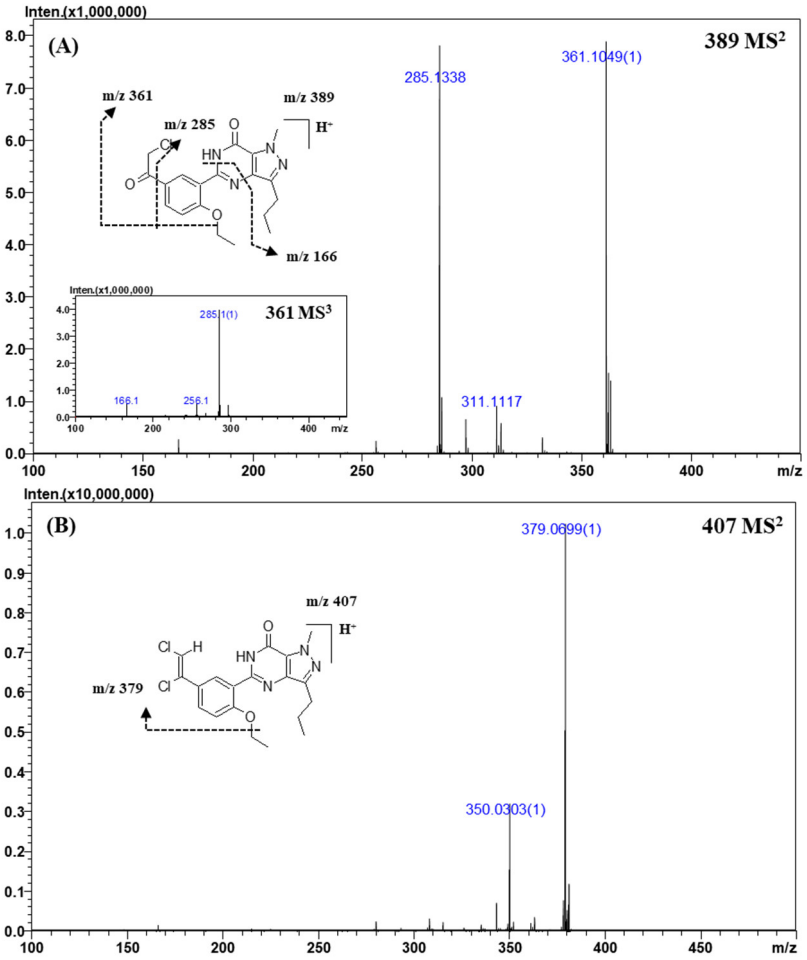


Figure S6. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of chlorodenafil (A) and dichlorodenafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

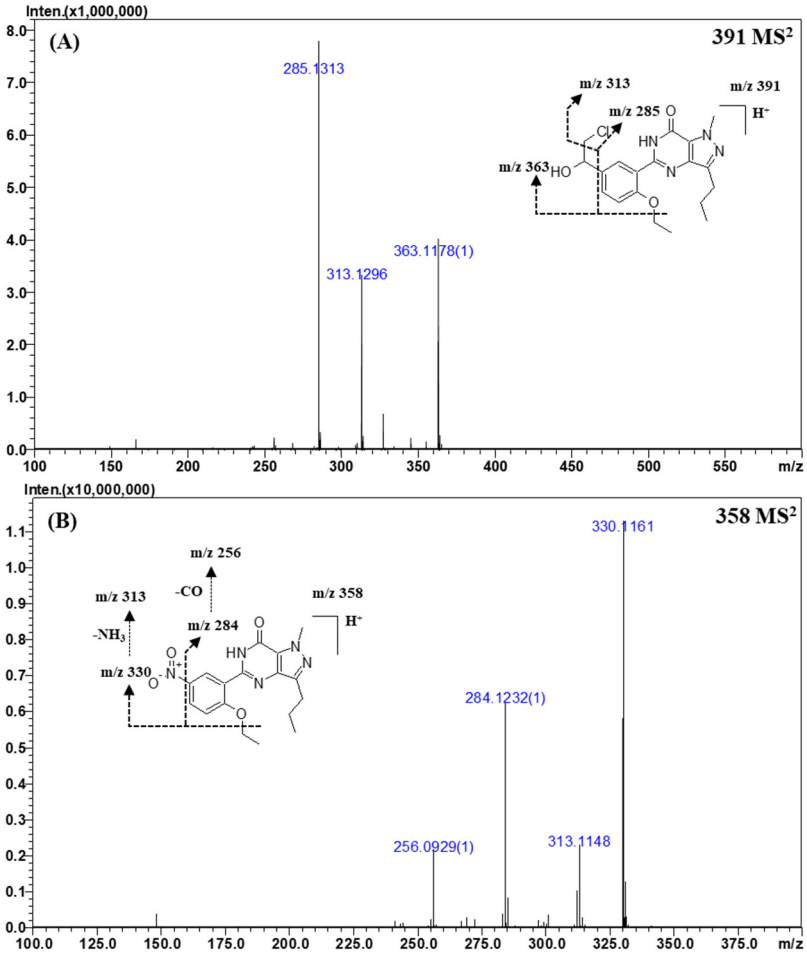


Figure S7. Representative MS^2 spectra and proposed fragmentation mechanisms of hydroxychlorodenafil (A) and nitrodenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

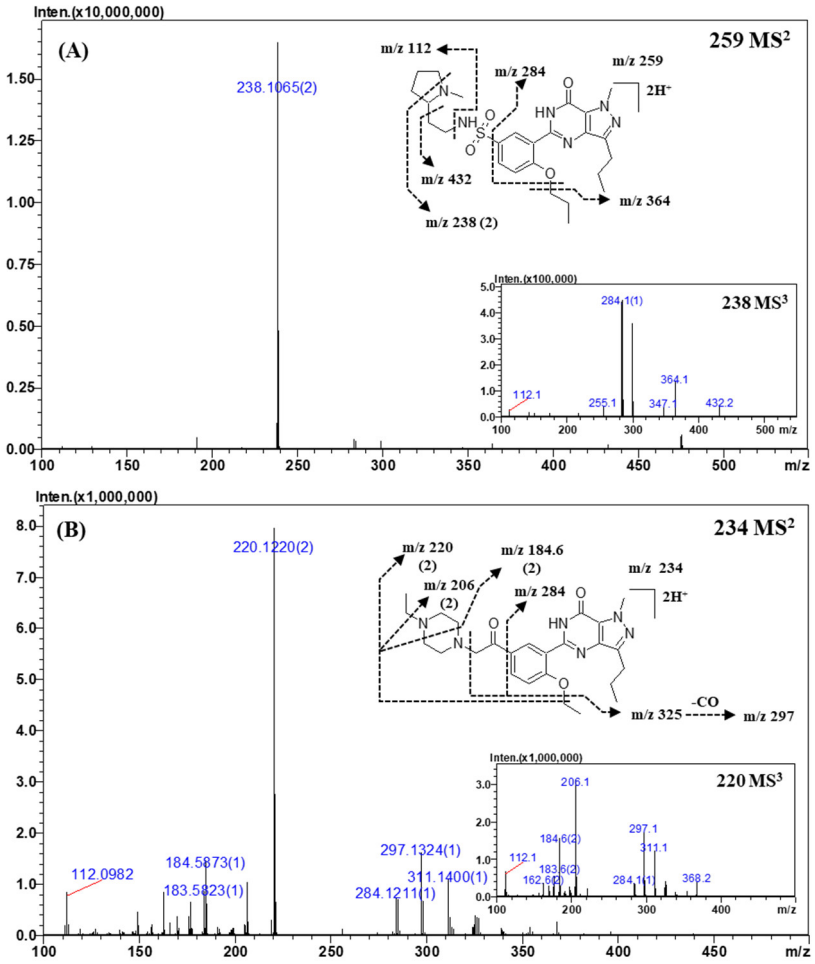


Figure S8. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of udenafil (A) and hongdenafil (B). The bracketed numbers next to the m/z values indicate the charge state of the ions.

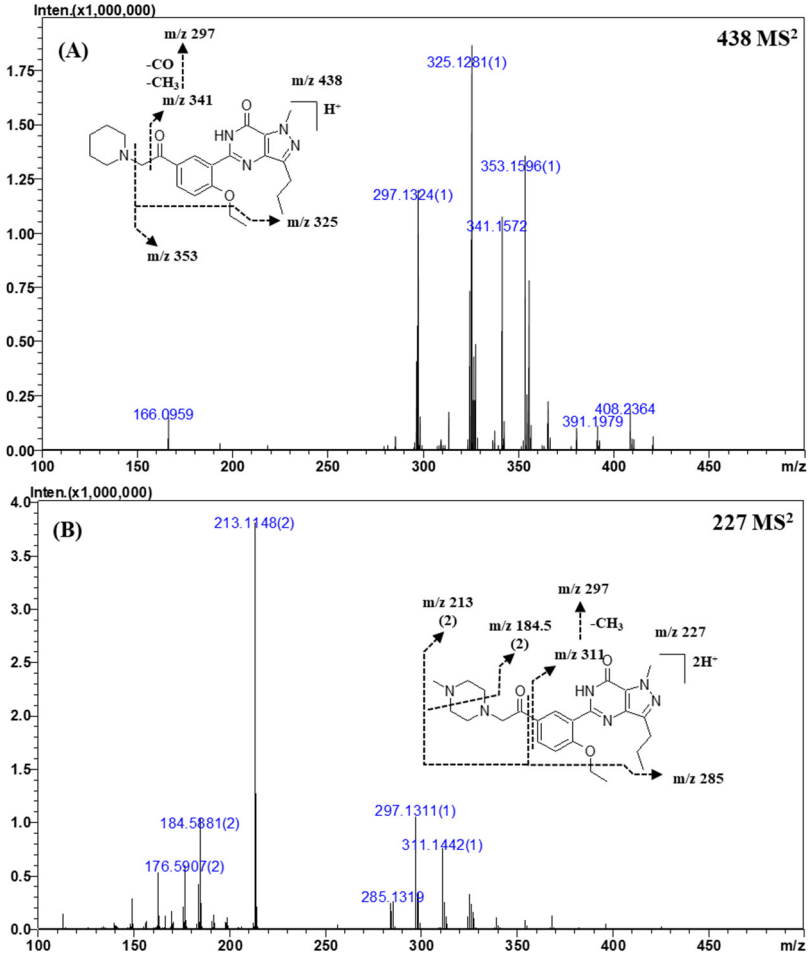


Figure S9. Representative MS^2 and proposed fragmentation mechanisms of piperidinohongdenafil (A) and demethylhongdenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

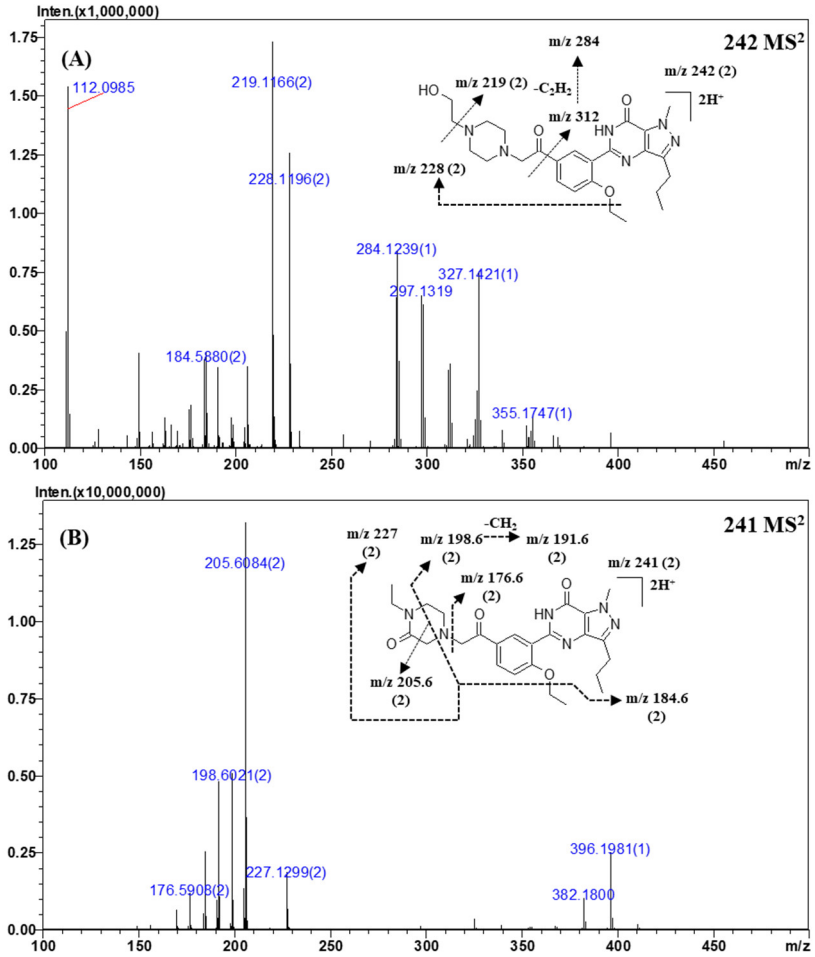


Figure S10. Representative MS^2 spectra and proposed fragmentation mechanisms of hydroxyhongdenafil (A) and oxohongdenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

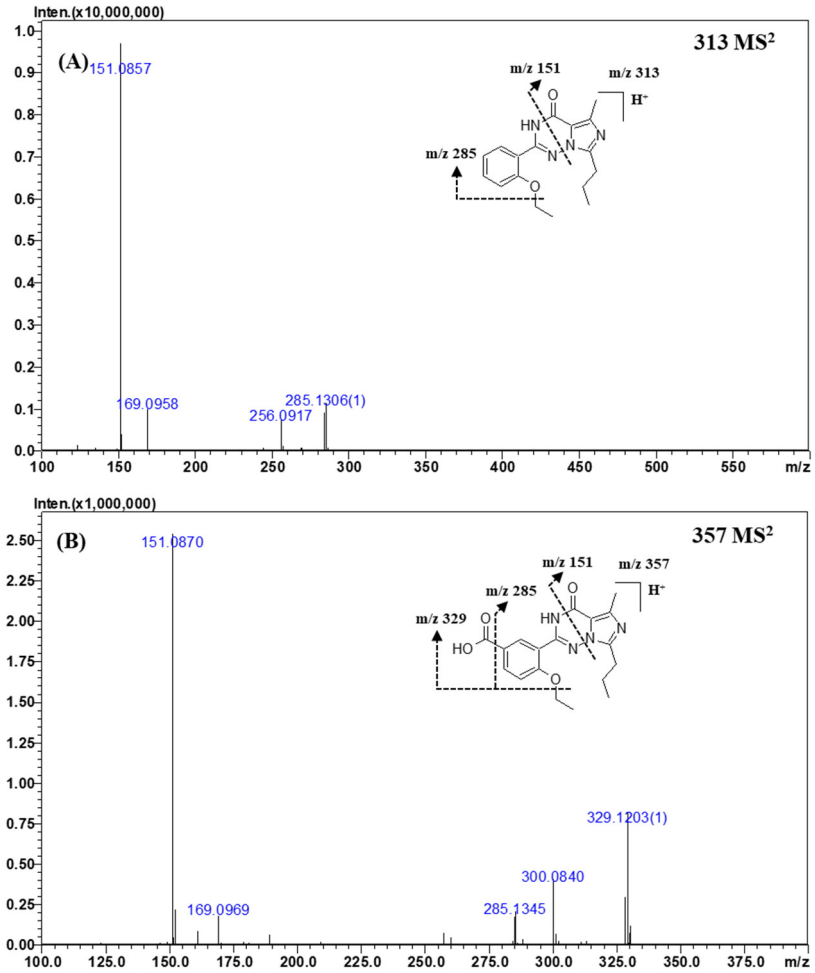


Figure S11. Representative MS^2 spectra and proposed fragmentation mechanisms of desolfovardenafil (A) and nor-neovardenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

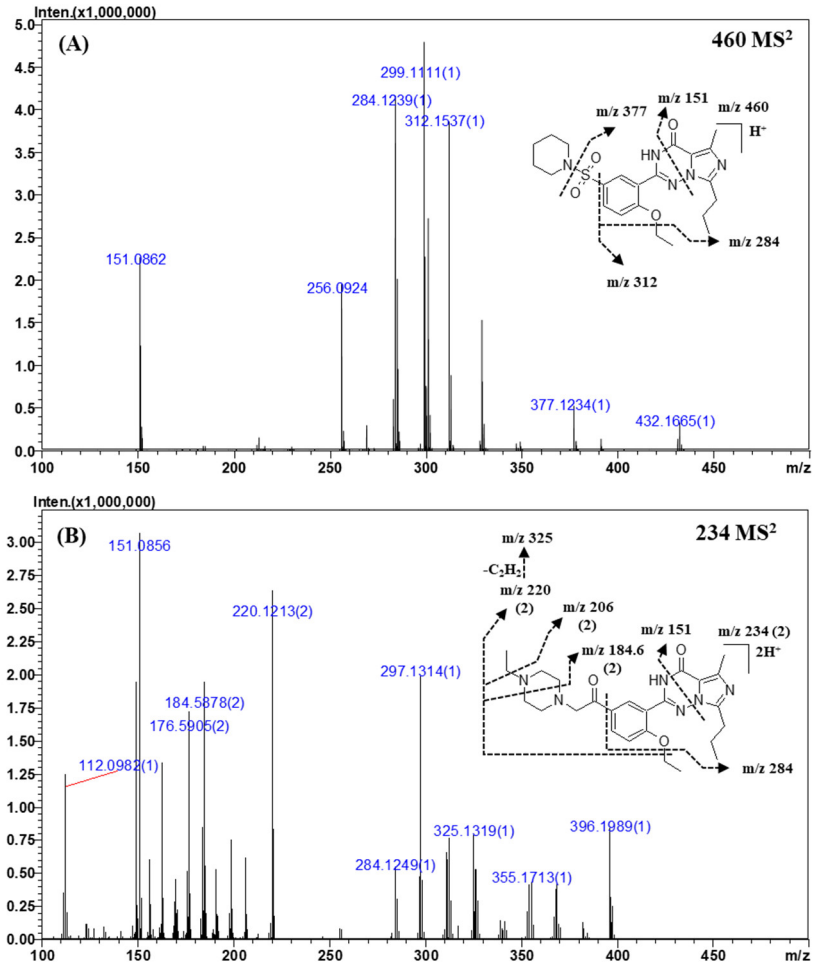


Figure S12. Representative MS^2 spectra and proposed fragmentation mechanisms of pseudovardenafil (A) and acetylvardenafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

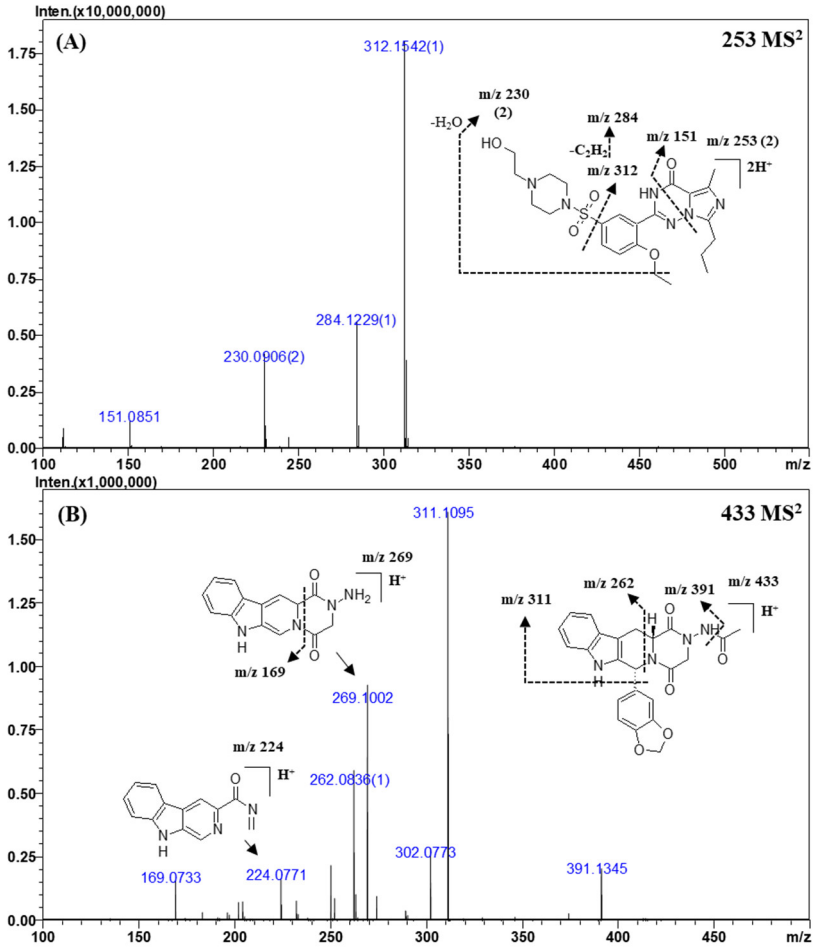


Figure S13. Representative MS^2 spectra and proposed fragmentation mechanisms of hydroxyvardenafil (A) and acetaminotadalafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

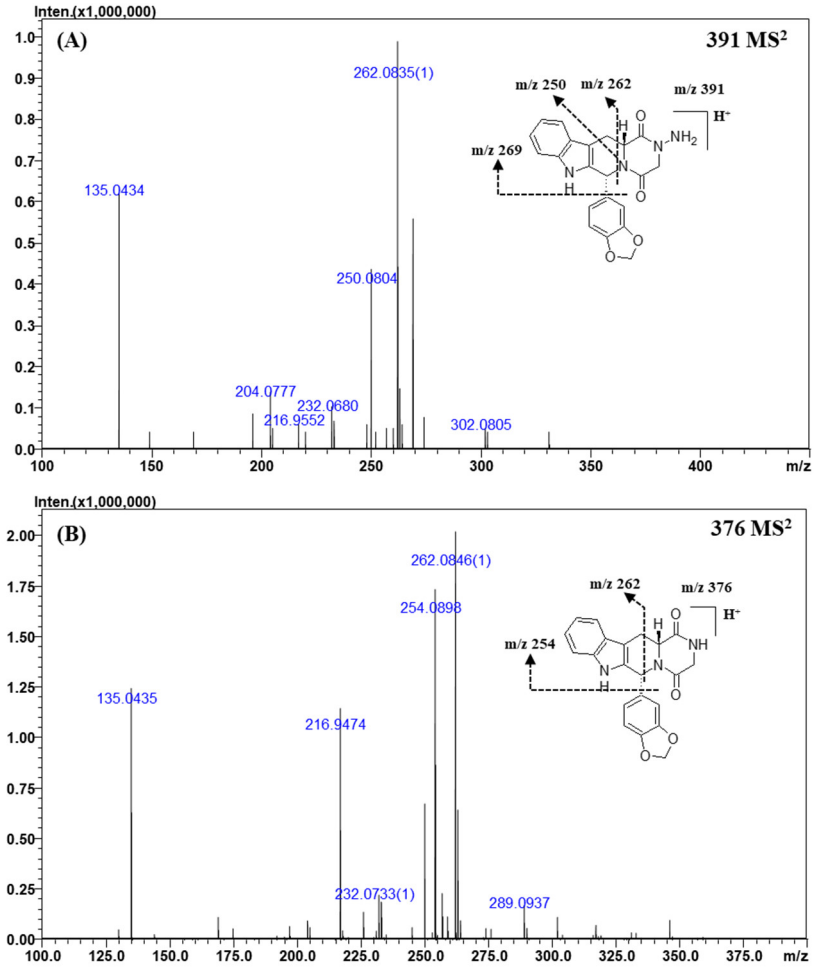


Figure S14. Representative MS^2 spectra and proposed fragmentation mechanisms of aminotadalafil (A) and demethyltadalafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

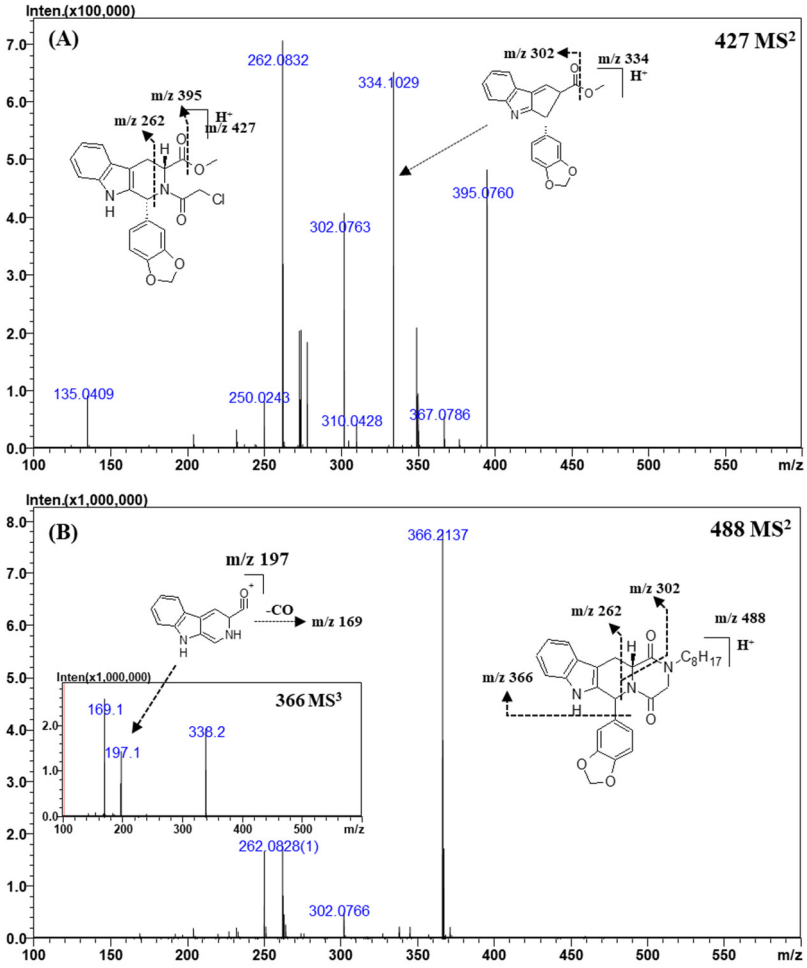


Figure S15. Representative MS^n (n = 2, 3) spectra and proposed fragmentation mechanisms of chloropretadalafil (A) and *N*-octyltadalafil (B). The bracketed numbers next to the *m*/*z* values indicate the charge state of the ions.

Table S1. Accurate masses and mass errors for fragment and precursor ions of PDE-5 inhibitors and their analogs.

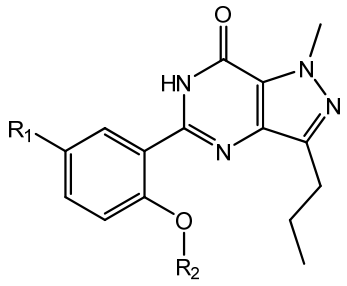
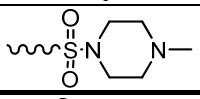
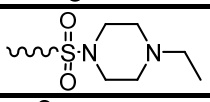
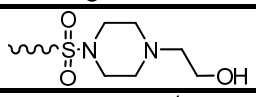
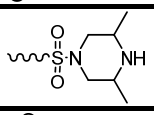
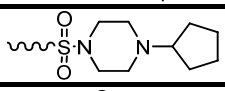
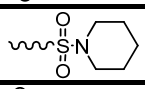
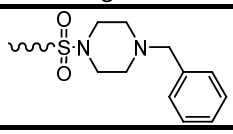
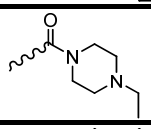
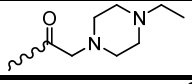
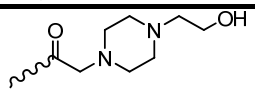
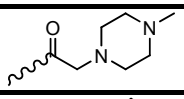
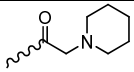
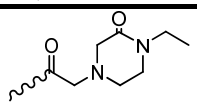
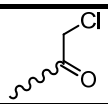
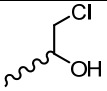
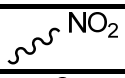
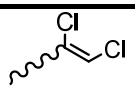
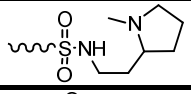
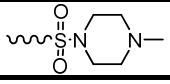
Compound	Elemental composition	Measured mass	Theoretical mass	Δm (mDa)	Error (ppm)
Homosildenafil	$C_{23}H_{32}N_6O_4S$[a]	245.1170[b]	245.1176	–0.6	–2.45
	$C_{17}H_{20}N_4O_2$	312.1576	312.1581	–0.5	–1.60
	$C_{15}H_{16}N_4O_2$	284.1266	284.1268	–0.2	–0.70
Dimethylsildenafil	$C_{23}H_{32}N_6O_4S$[a]	245.1174[b]	245.1176	–0.2	–0.82
	$C_{17}H_{20}N_4O_2$	312.1558	312.1581	–2.3	–7.37
	$C_{15}H_{16}N_4O_2$	284.1243	284.1268	–2.5	–8.80
Thiohomosildenafil	$C_{23}H_{33}N_6O_3S_2$	253.1053[b]	253.1061	–0.8	–3.32
	$C_{17}H_{19}N_4OS$	328.1364	328.1352	1.2	3.66
	$C_{15}H_{15}N_4OS$	300.1019	300.1039	–2.0	–6.66
	$C_{14}H_{12}N_3O_3$	271.0920	271.0951	–3.1	–11.44
Dimethylthiosildenafil	$C_{23}H_{33}N_6O_3S_2$[a]	253.1060[b]	253.1061	–0.1	–0.56
	$C_{17}H_{19}N_4OS$	328.1336	328.1352	–1.6	–4.88
	$C_{15}H_{15}N_4OS$	300.1046	300.1039	0.7	2.33
	$C_{14}H_{12}N_3O_3$	271.0892	271.0951	–5.9	–21.76
Benzylsildenafil	$C_{28}H_{34}N_6O_4S$[a]	276.1239[b]	276.1254	–1.5	–5.43
	$C_{21}H_{28}N_6O_4S$	461.1970	461.1966	0.4	0.87
	$C_{17}H_{20}N_4O_4S$	377.1272	377.1278	–0.6	–1.59
	$C_{17}H_{18}N_4O_2$	311.1492	311.1503	–1.1	–3.54
	$C_{15}H_{14}N_4O_2$	283.1191	283.1190	0.1	0.35
	$C_{14}H_{14}N_4O$	255.1196	255.1240	–4.4	–17.25
Carbodenafil	$C_{24}H_{32}N_6O_3$[a]	227.1326[b]	227.1341	–1.5	–6.60
	$C_{16}H_{14}N_4O_3$	311.1119	311.1139	–2.0	–6.43
	$C_{22}H_{28}N_6O_3$	213.1164[b]	213.1184	–2.0	–9.38
	$C_{20}H_{23}N_5O_3$	191.5971[b]	191.5973	–0.2	–1.04
	$C_{16}H_{14}N_4O_3$	156.0619[b]	156.0606	1.3	8.33
	$C_{18}H_{19}N_5O_3$	177.5830[b]	177.5817	1.3	7.32
Nor-neosildenafil	$C_{22}H_{29}N_5O_4S$[a]	460.2011	460.2013	–0.2	–0.43
	$C_{20}H_{25}N_5O_4S$	432.1686	432.1700	–1.4	–3.24
	$C_{17}H_{20}N_4O_4S$	377.1267	377.1278	–1.1	–2.92
	$C_{17}H_{18}N_4O_2$	311.1487	311.1503	–1.6	–5.14
	$C_{15}H_{14}N_4O_2$	283.1180	283.1190	–1.0	–3.53
	$C_{14}H_{14}N_4O$	255.1226	255.1240	–1.4	–5.49
Cyclopentinafil	$C_{26}H_{36}N_6O_4S$[a]	265.1322[b]	265.1332	–1.0	–3.77
	$C_{21}H_{28}N_6O_4S$	231.1009[b]	231.1019	–1.0	–4.33
	$C_{21}H_{28}N_6O_4S$	461.1951	461.1966	–1.5	–3.25
	$C_{17}H_{20}N_4O_2$	312.1581	312.1581	0.0	0.00
	$C_{19}H_{24}N_6O_4S$	217.0846[b]	217.0863	–1.7	–7.83
	$C_{15}H_{16}N_4O_2$	284.1225	284.1268	–4.3	–15.13
Hydroxythiohomosildenafil	$C_{23}H_{32}N_6O_4S_2$[a]	261.1011[b]	261.1036	–2.5	–9.57
	$C_{17}H_{20}N_4OS$	328.1340	328.1352	–1.2	–3.76
	$C_{21}H_{25}N_6O_3S_2$	238.0813[b]	238.0827	–1.4	–5.74
	$C_{15}H_{16}N_4OS$	300.1028	300.1039	–1.1	–3.78
Hydroxyhomosildenafil	$C_{23}H_{32}N_6O_5S$[a]	253.1163[b]	253.1150	1.3	5.14
	$C_{17}H_{19}N_4O_2$	312.1576	312.1581	–0.5	–1.60
	$C_{15}H_{15}N_4O_2$	284.1257	284.1268	–1.1	–3.87
	$C_{21}H_{26}N_6O_4S$	230.0933[b]	230.0941	–0.8	–3.48
Chlorodenafil	$C_{19}H_{21}N_4O_3Cl$[a]	389.1370	389.1375	–0.5	–1.28
	$C_{17}H_{17}N_4O_3Cl$	361.1066	361.1062	0.4	1.11
	$C_{15}H_{16}N_4O_2$	285.1339	285.1346	–0.7	–2.45
Dichlorodenafil	$C_{19}H_{20}N_4O_2Cl_2$[a]	407.1034	407.1036	–0.2	–0.49
	$C_{17}H_{16}N_4O_2Cl_2$	379.0719	379.0723	–0.4	–1.08

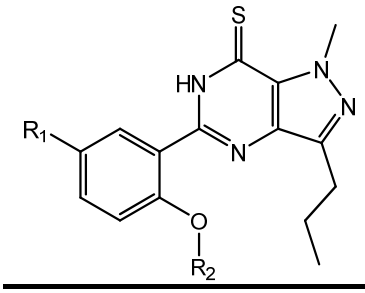
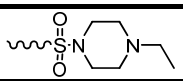
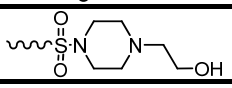
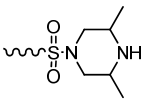
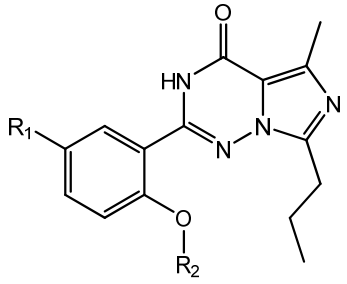
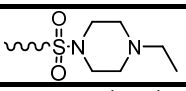
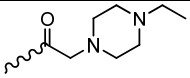
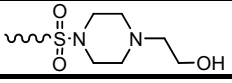
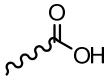
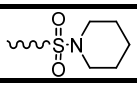
Hydroxychlorodenafil	$C_{19}H_{23}N_4O_3Cl$[a]	391.1538	391.1531	0.7	1.79
	$C_{17}H_{19}N_4O_3Cl$	363.1217	363.1218	–0.1	–0.28
	$C_{16}H_{16}N_4O_3$	313.1326	313.1295	3.1	9.90
	$C_{15}H_{16}N_4O_2$	285.1346	285.1346	0.0	0.00
Nitrodenafil	$C_{17}H_{19}N_5O_4$[a]	358.1506	358.1510	–0.4	–1.12
	$C_{15}H_{15}N_5O_4$	330.1189	330.1197	–0.8	–2.42
Udenafil	$C_{25}H_{36}N_6O_4S$[a]	259.1304[b]	259.1332	–2.8	–10.81
	$C_{22}H_{30}N_6O_4S$	238.1087[b]	238.1097	–1.0	–4.20
	$C_{15}H_{17}N_5O_4S$	364.1026	364.1074	–4.8	–13.18
	$C_{15}H_{14}N_4O_3$	299.1133	299.1139	–0.6	–2.01
	$C_{15}H_{14}N_4O_2$	283.1194	283.1190	0.4	1.41
Hongdenafil	$C_{25}H_{34}N_6O_3$[a]	234.1398[b]	234.1419	–2.1	–8.97
	$C_{23}H_{30}N_6O_3$	220.1223[b]	220.1262	–3.9	–17.72
	$C_{21}H_{26}N_6O_3$	206.1049[b]	206.1106	–5.7	–27.66
	$C_{17}H_{16}N_4O_3$	325.1335	325.1295	4.0	12.30
	$C_{17}H_{18}N_4O_2$	311.1454	311.1503	–4.9	–15.75
	$C_{16}H_{16}N_4O_2$	297.1330	297.1346	–1.6	–5.38
Piperidinohongdenafil	$C_{24}H_{31}N_5O_3$[a]	438.2501	438.2500	0.1	0.23
	$C_{19}H_{20}N_4O_3$	353.1601	353.1608	–0.7	–1.98
	$C_{18}H_{20}N_4O_3$	341.1592	341.1608	–1.6	–4.69
	$C_{17}H_{16}N_4O_3$	325.1293	325.1295	–0.2	–0.62
Demethylhongdenafil	$C_{24}H_{32}N_6O_3$[a]	227.1331[b]	227.1341	–1.0	–4.40
	$C_{22}H_{28}N_6O_3$	213.1165[b]	213.1184	–1.9	–8.92
	$C_{17}H_{18}N_4O_2$	311.1455	311.1503	–4.8	–15.43
	$C_{16}H_{16}N_4O_2$	297.1330	297.1346	–1.6	–5.38
	$C_{22}H_{28}N_6O_3$	213.1165[b]	213.1184	–1.9	–8.92
	$C_{19}H_{21}N_5O_3$	184.5896	184.5895	0.1	0.54
Hydroxyhongdenafil	$C_{25}H_{34}N_6O_4$[a]	242.1372[b]	242.1394	–2.2	–9.09
	$C_{23}H_{30}N_6O_4$	228.1228[b]	228.1237	–0.9	–3.95
	$C_{23}H_{28}N_6O_3$	219.1171[b]	219.1184	–1.3	–5.93
	$C_{17}H_{18}N_4O_3$	327.1440	327.1452	–1.2	–3.67
	$C_{17}H_{20}N_4O_2$	312.1558	312.1581	–2.3	–7.37
	$C_{15}H_{16}N_4O_2$	284.1243	284.1268	–2.5	–8.80
Oxohongdenafil	$C_{25}H_{32}N_6O_4$[a]	241.1306[b]	241.1315	–0.9	–3.73
	$C_{22}H_{27}N_5O_3$	205.6100[b]	205.6130	–3.0	–14.59
	$C_{21}H_{25}N_5O_3$	198.6032[b]	198.6051	–1.9	–9.57
	$C_{20}H_{23}N_5O_3$	191.5963[b]	191.5973	–1.0	–5.22
	$C_{19}H_{21}N_5O_3$	184.5892[b]	184.5895	–0.3	–1.63
Desulfovardenafil	$C_{17}H_{20}N_4O_2$[a]	313.1648	313.1659	–1.1	–3.51
	$C_{15}H_{16}N_4O_2$	285.1348	285.1346	0.2	0.70
	$C_8H_{10}N_2O$	151.0876	151.0866	1.0	6.62
Nor-neovardenafil	$C_{18}H_{20}N_4O_4$[a]	357.1546	357.1557	–1.1	–3.08
	$C_{16}H_{16}N_4O_4$	329.1237	329.1244	–0.7	–2.13
	$C_8H_{10}N_2O$	151.0877	151.0866	1.1	7.28
	$C_{15}H_{16}N_4O_2$	285.1339	285.1346	–0.7	–2.45
Pseudovardenafil	$C_{22}H_{29}N_5O_4S$[a]	460.2016	460.2013	0.3	0.65
	$C_{20}H_{25}N_5O_4S$	432.1722	432.1700	2.2	5.09
	$C_{17}H_{20}N_4O_4S$	377.1273	377.1278	–0.5	–1.33
	$C_{17}H_{20}N_4O_2$	312.1564	312.1581	–1.7	–5.45
	$C_{15}H_{16}N_4O_2$	284.1255	284.1268	–1.3	–4.58
	$C_8H_{10}N_2O$	151.0870	151.0866	0.4	2.65
Acetylvardenafil	$C_{25}H_{34}N_6O_3$[a]	234.1407[b]	234.1419	–1.2	–5.13
	$C_{23}H_{30}N_6O_3$	220.1226[b]	220.1262	–3.6	–16.35
	$C_{21}H_{26}N_6O_3$	206.1135[b]	206.1106	2.9	14.07
	$C_{19}H_{21}N_5O_3$	184.5904[b]	184.5895	0.9	4.88

	$C_{15}H_{16}N_4O_2$	284.1256	284.1268	–1.2	–4.14
	$C_{17}H_{16}N_4O_3$	325.1332	325.1295	3.7	11.38
	$C_{16}H_{16}N_4O_2$	297.1333	297.1346	–1.3	–4.38
	$C_8H_{10}N_2O$	151.0876	151.0866	1.0	6.62
Hydroxyvardenafil	$C_{23}H_{32}N_6O_5S$[a]	253.1159[b]	253.1150	0.9	3.56
	$C_{17}H_{19}N_4O_2$	312.1575	312.1581	–0.6	–1.92
	$C_{15}H_{15}N_4O_2$	284.1265	284.1268	–0.3	–1.06
	$C_{21}H_{26}N_6O_4S$	230.0938[b]	230.0941	–0.3	–1.30
	$C_8H_{10}N_2O$	151.0866	151.0866	0.0	0.00
Acetaminotadalafil	$C_{23}H_{20}N_4O_5$[a]	433.1496	433.1506	–1.0	–2.31
	$C_{21}H_{18}N_4O_4$	391.1433	391.1401	3.2	8.18
	$C_{16}H_{14}N_4O_3$	311.1121	311.1139	–1.8	–5.79
	$C_{14}H_{12}N_4O_2$	269.1029	269.1033	–0.4	–1.49
	$C_{17}H_{11}NO_2$	262.0864	262.0863	0.1	0.38
	$C_{13}H_9N_3O$	224.0781	224.0818	–3.7	–16.51
	$C_{11}H_8N_2$	169.0780	169.0760	2.0	11.83
Aminotadalafil	$C_{21}H_{18}N_4O_4$[a]	391.1399	391.1401	–0.2	–0.51
	$C_{14}H_{12}N_4O_2$	269.1017	269.1033	–1.6	–5.95
	$C_{17}H_{11}NO_2$	262.0859	262.0863	–0.4	–1.53
	$C_{16}H_{11}NO_2$	250.0849	250.0863	–1.4	–5.60
	$C_{11}H_8N_2$	169.0771	169.0760	1.1	6.51
	$C_8H_6O_2$	135.0451	135.0441	1.0	7.40
Demethyltadalafil	$C_{21}H_{17}N_3O_4$[a]	376.1287	376.1292	–0.5	–1.33
	$C_{17}H_{11}NO_2$	262.0856	262.0863	–0.7	–2.67
	$C_{14}H_{11}N3O_2$	254.0912	254.0924	–1.2	–4.72
	$C_{16}H_9NO$	232.0744	232.0757	–1.3	–5.60
	$C_{15}H_9N$	204.0797	204.0808	–1.1	–5.39
	$C_{11}H_8N_2$	169.0751	169.0760	–0.9	–5.32
	$C_8H_6O_2$	135.0449	135.0441	0.8	5.92
Chloropretadalafil	$C_{22}H_{19}N_2O_5Cl$[a]	427.1039	427.1055	–1.6	–3.75
	$C_{21}H_{15}N_2O_4Cl$	395.0788	395.0793	–0.5	–1.27
	$C_{20}H_{16}N_2O_4$	349.1168	349.1183	–1.5	–4.30
	$C_{20}H_{15}NO_4$	334.1063	334.1074	–1.1	–3.29
	$C_{19}H_{11}NO_3$	302.0812	302.0812	0.0	0.00
	$C_{17}H_{11}NO_2$	262.0849	262.0863	–1.4	–5.34
N-Octyltadalafil	$C_{29}H_{33}N_3O_4$[a]	488.2540	488.2544	–0.4	–0.82
	$C_{22}H_{27}N_3O_2$	366.2170	366.2176	–0.6	–1.64
	$C_{19}H_{11}NO_3$	302.0778	302.0812	–3.4	–11.26
	$C_{17}H_{11}NO_2$	262.0878	262.0863	1.5	5.72
	$C_{21}H_{27}N_3O$	338.2207	338.2227	–2.0	–5.91
	$C_{12}H_8N_2O$	197.0710	197.0709	0.1	0.51
	$C_{11}H_8N_2$	169.0770	169.0760	1.0	5.91

[a] Precursor ion; [b] Multiple charged protonated ion $[M+2H]^{2+}$.

Table S2. The structures of PDE-5 inhibitors and their analogues.

Backbone of the structure	Name of compound	R_1	R_2
	Sildenafil		
	Homosildenafil		
	Hydroxyhomosildenafil		
	Dimethylsildenafil		
	Cyclopentinafil		
	Norneosildenafil		
	Benzylsildenafil		
	Carbodenafil		
	Hondenafil		C_2H_5
	Hydroxyhongdenafil		
	Demethylhongdenafil		
	Piperidinohongdenafil		
	Oxohongdenafil		
	Chlorodenafil		
	Hydroxychlorodenafil		
	Nitrodenafil		
	Dichlorodenafil		
	Udenafil		C_3H_7
	Thiosildenafil		C_2H_5

	Thiohomosildenafil		
	Hydroxythiohomosildenafil		
	Dimethylthiosildenafil		
	Vardenafil		C_2H_5
	Acetylvardenafil		
	Hydroxyvardenafil		
	norneovardenafil		
	Pseudovardenafil		
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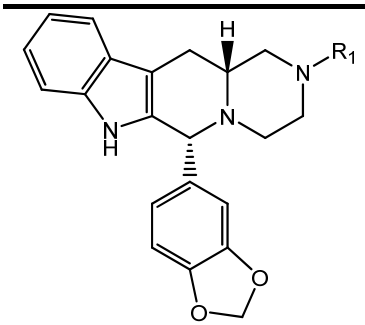
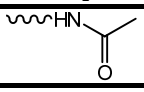
	Tadalafil	CH_3	-
	Aminotaldalfil	NH_2	
	Acetaminotadalafil		
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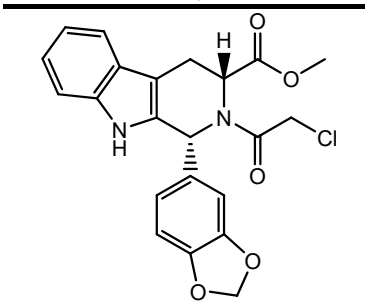
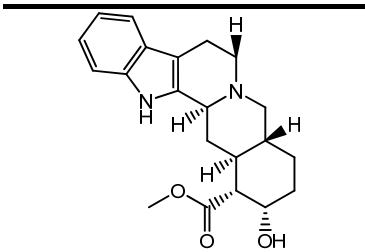
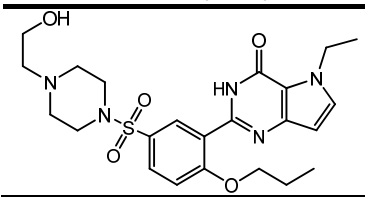
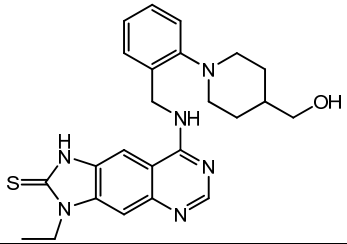
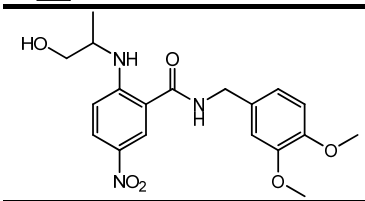
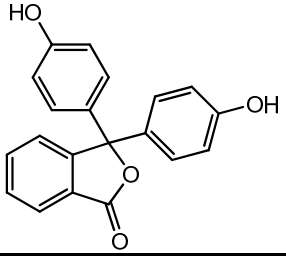
	N-octyltadalafil	C_8H_{17}	
	Chloropretadalafil	-	
	Yohimbine	-	-
	Mirodenafil	-	-

	Thioquinapiperifil	-	-
	Xanthoanthrafil		
	Phenolphtalein (IS)	-	-

*All analytes contain guanosine like structure as a pharmacophore.