

Integrated Proteomics and Lipidomics Investigation of the Mechanism Underlying the Neuroprotective Effect of N-benzylhexadecanamide

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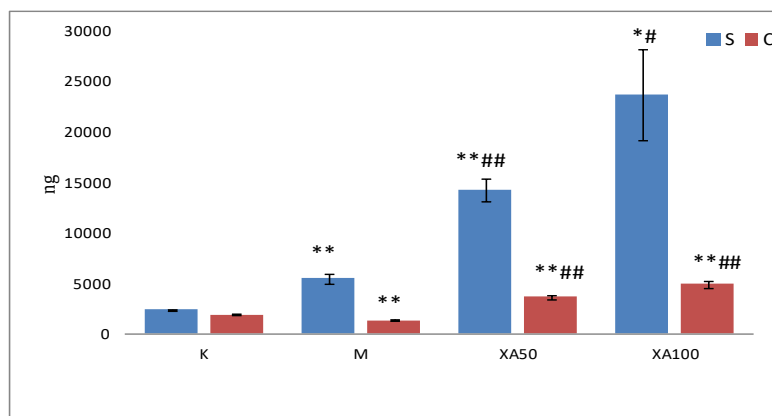
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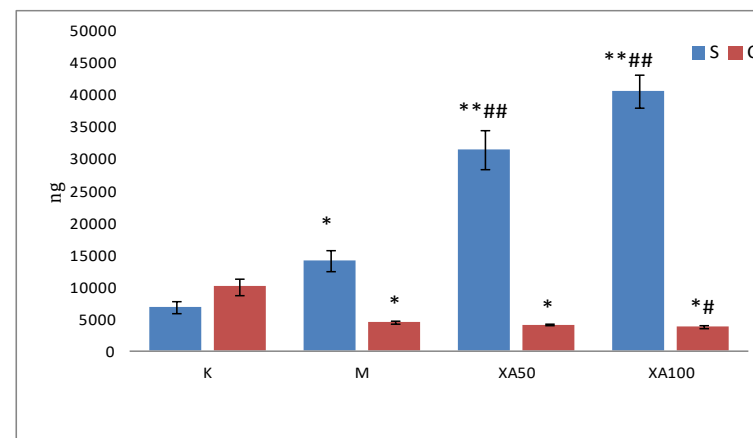
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Table S1. The results of precision, repeatability and stability

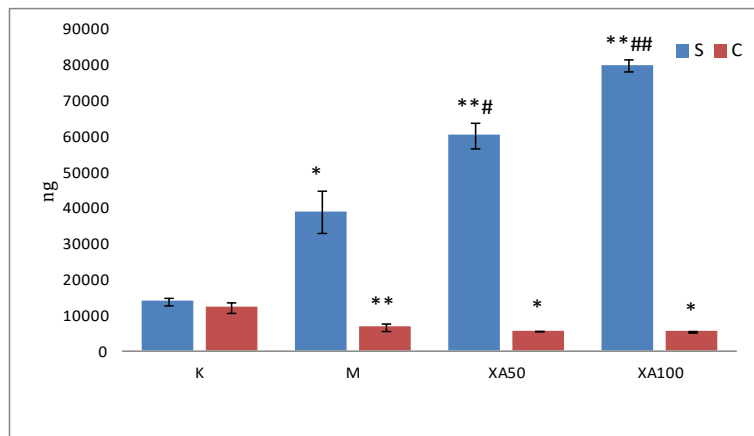
Analyte	precision (RSD%, n=6)	repeatability (RSD%, n=5)	stability (RSD%, n=6)
aspartic acid	2.46	4.23	6.43
asparagine	1.35	4.21	1.51
serine	1.31	4.51	6.73
taurine	3.10	2.02	6.97
tyrosine	1.41	3.29	3.96
noradrenaline	2.05	4.68	5.32
Homovanillic acid	2.75	5.40	3.84
choline	0.70	5.58	3.74
acetylcholine	0.45	4.06	2.36
butyrylcholine	1.07	5.91	4.63



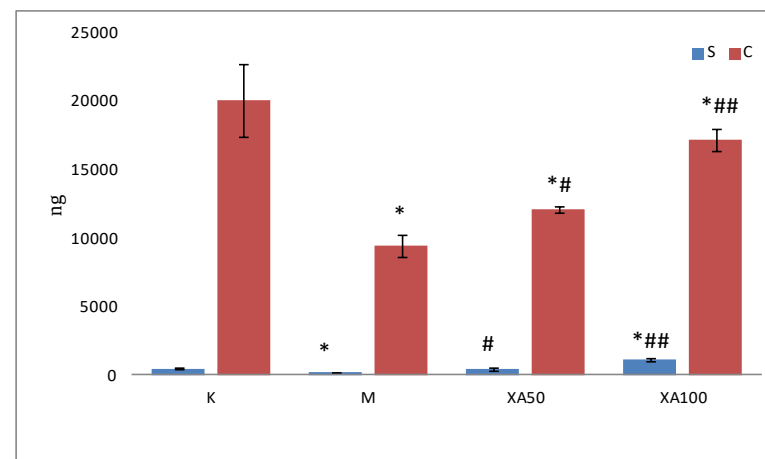
aspartic acid



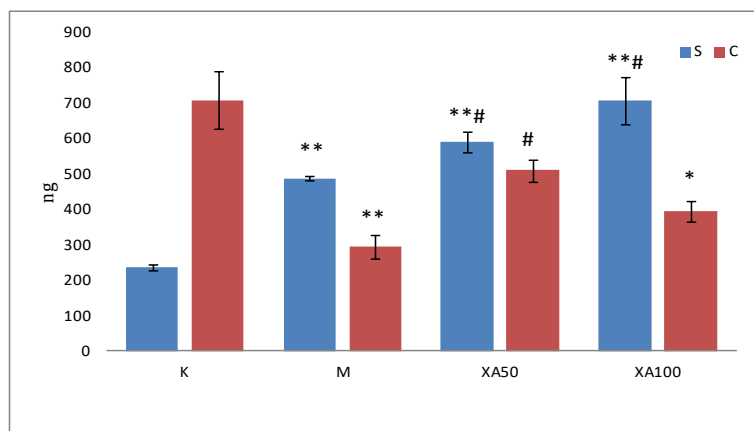
glutamine



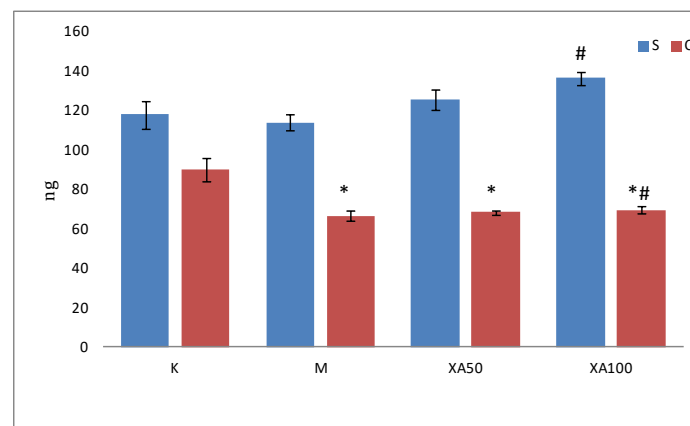
serine



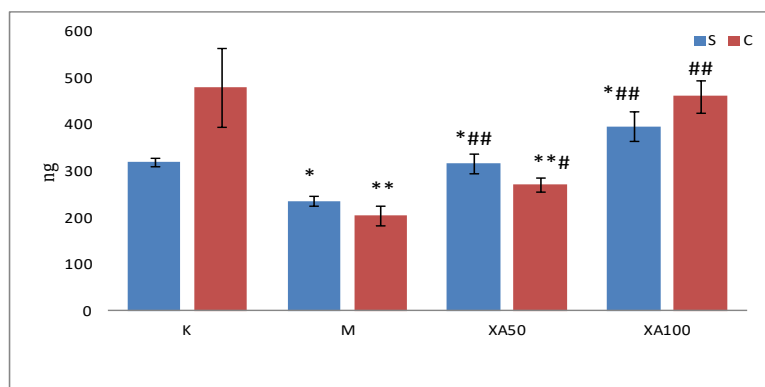
taurine



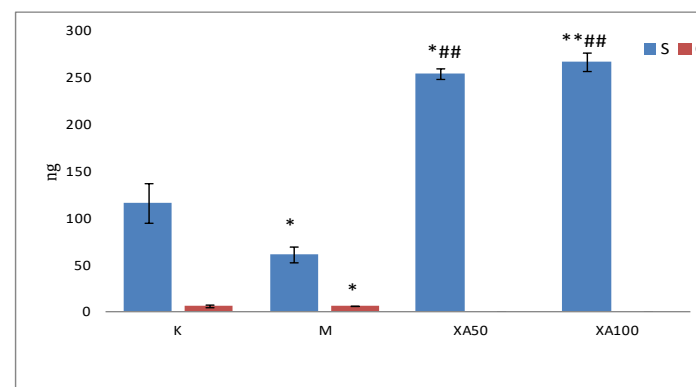
tyrosine



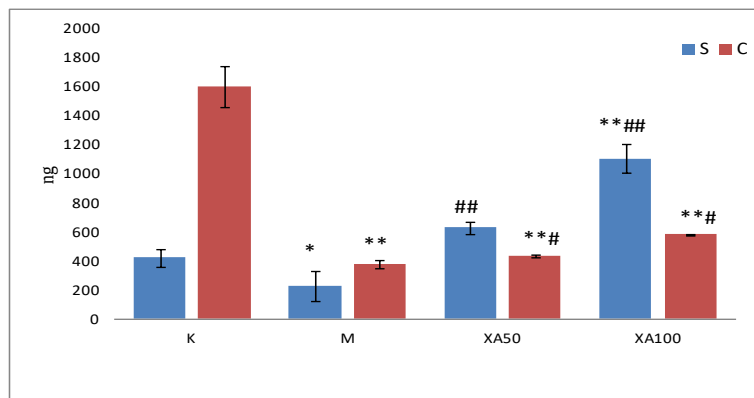
noradrenaline



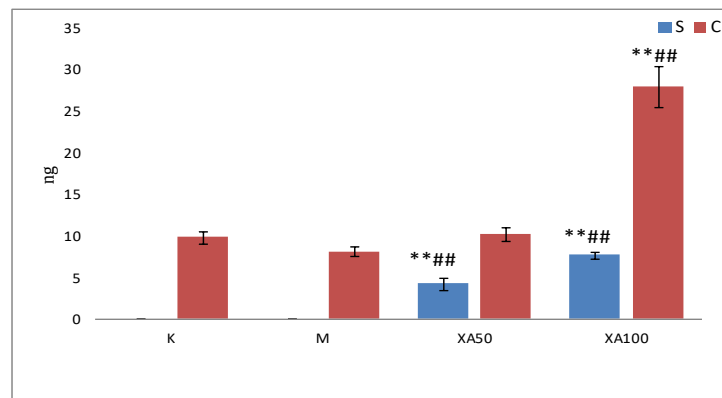
Homovanillic acid



choline

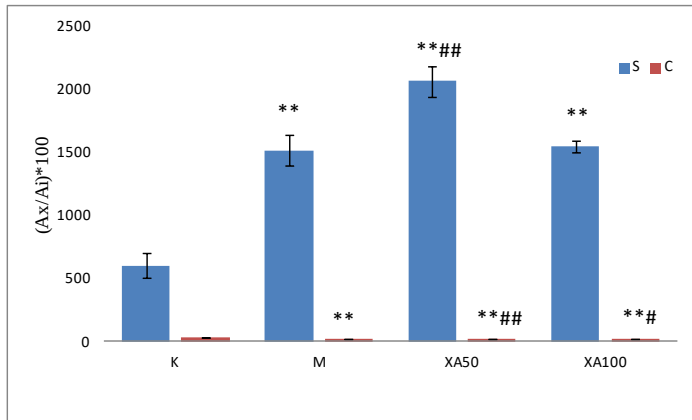


acetylcholine

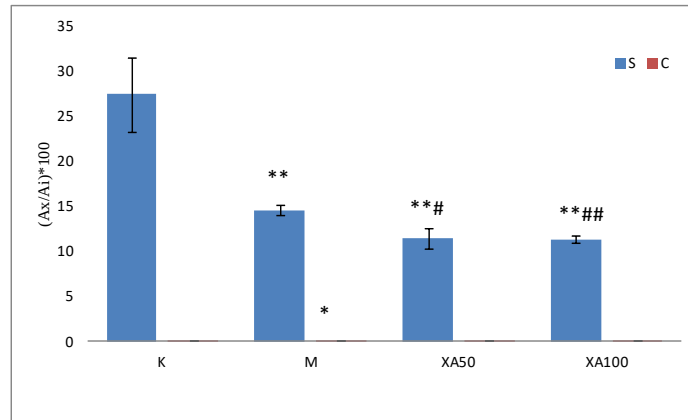


butyrylcholine

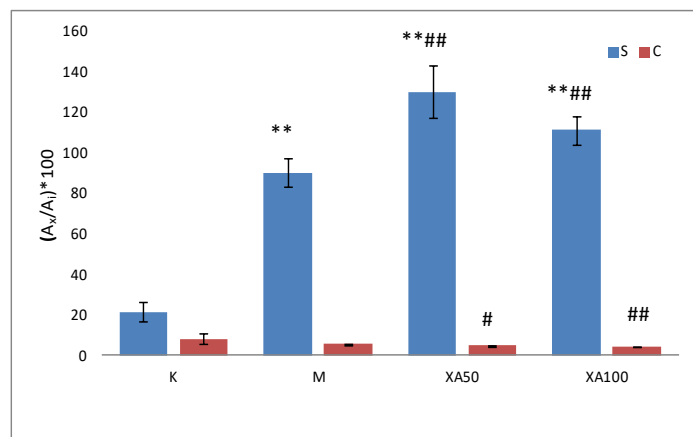
Fig. S1 The absolute quantification results of neurotransmitters (Ax/Ai) $\times 100$, n=3, *P<0.05, **P<0.01: VS control group; #P<0.05, ##P<0.01: VS model group)



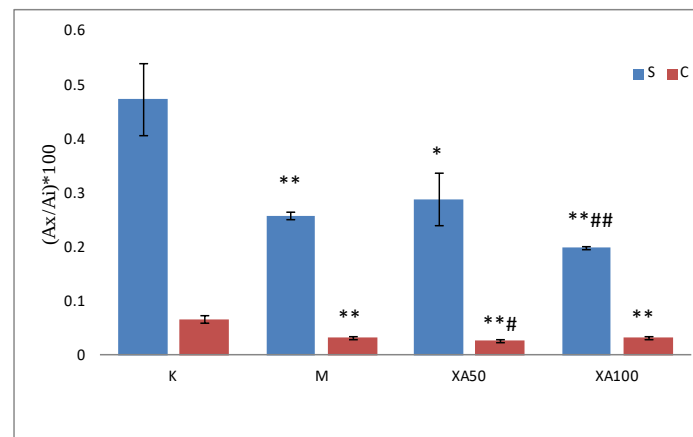
ornithine



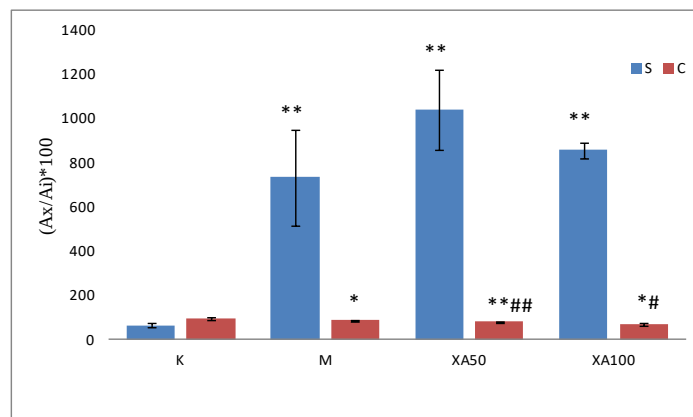
lysine



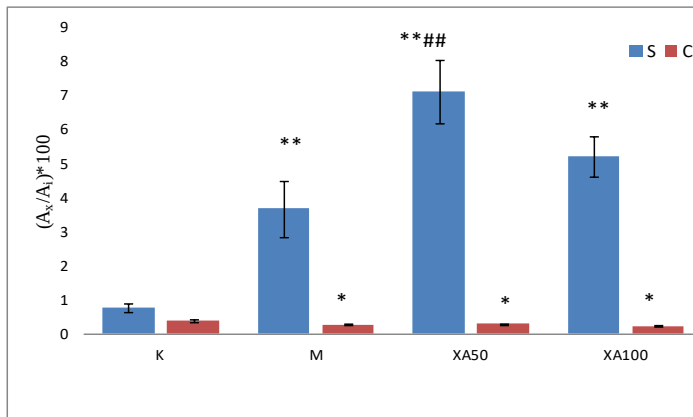
phenylalanine



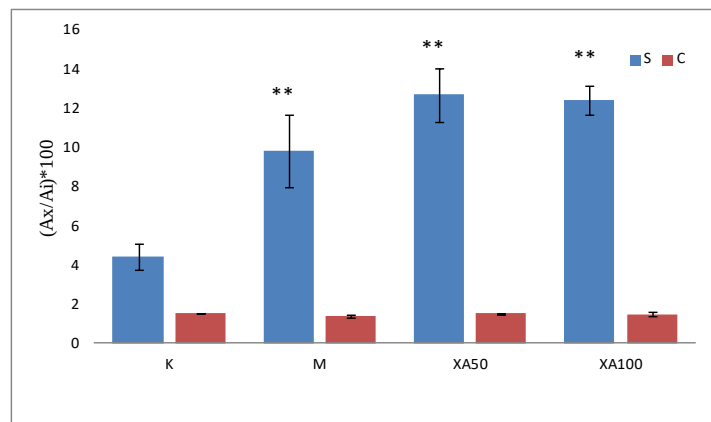
tryptophan



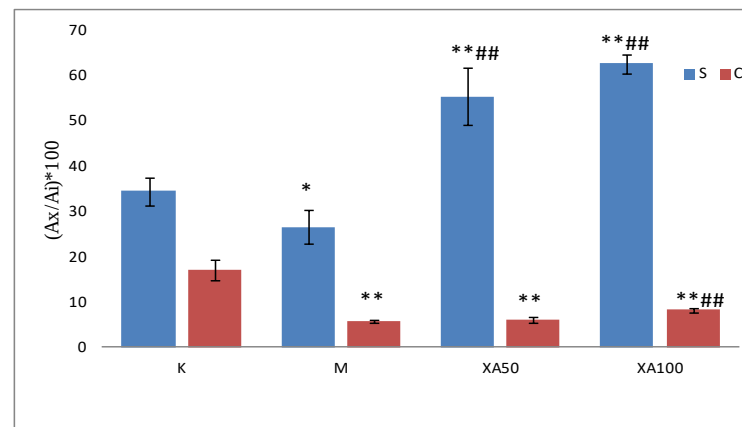
L-leucine



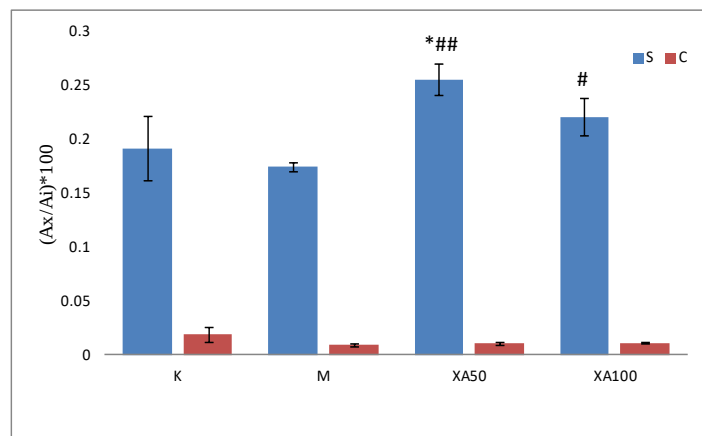
methionine



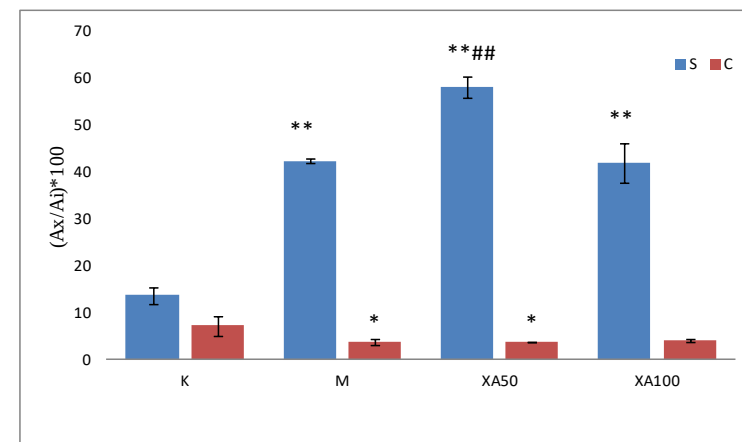
dimethylglycine



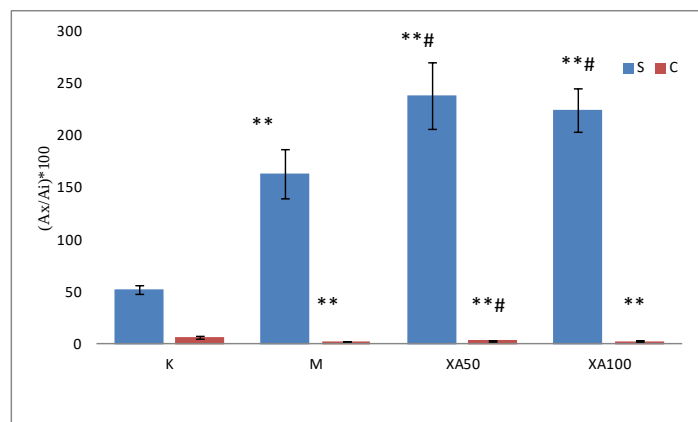
proline



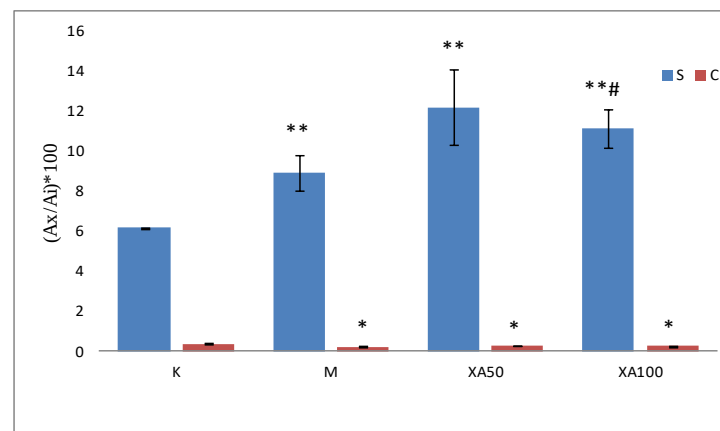
histamine



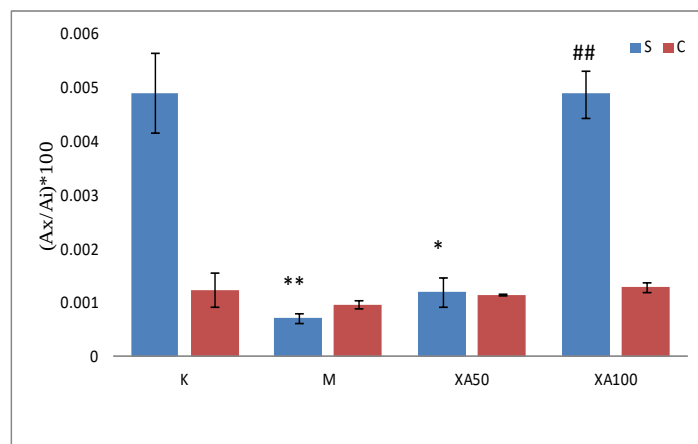
threonine



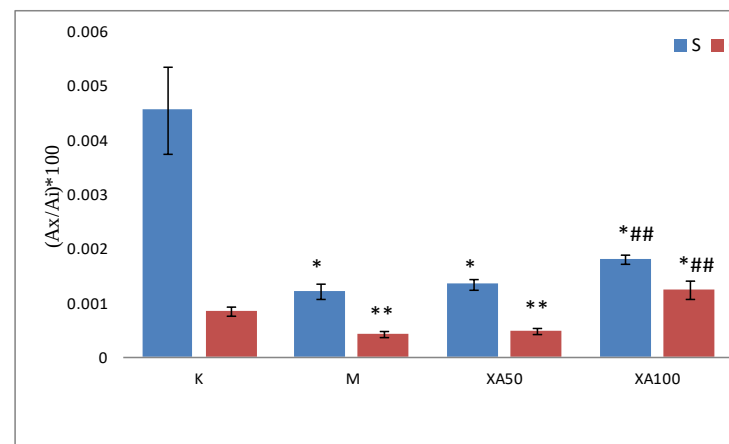
citrulline



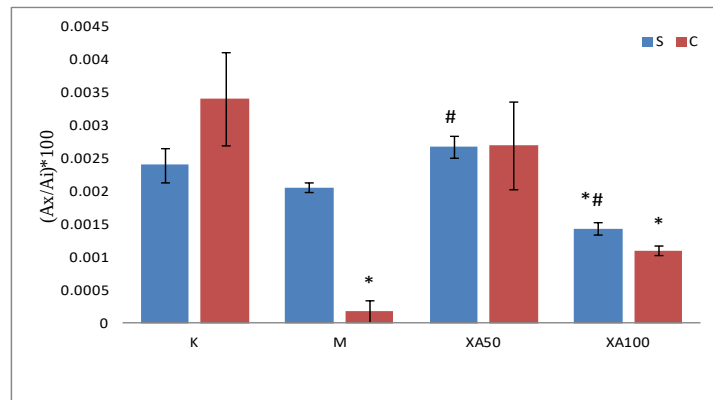
arginine



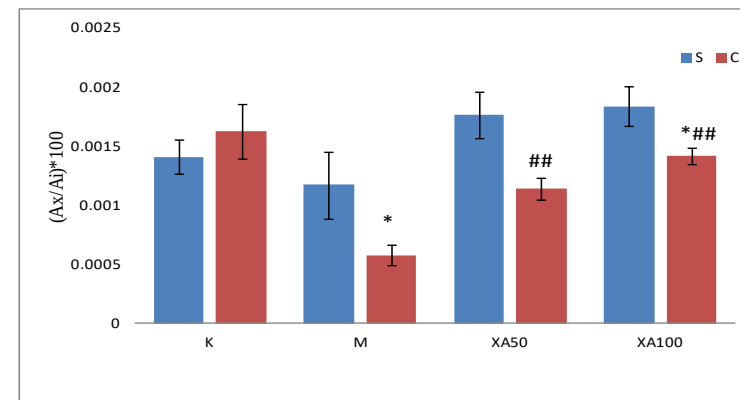
serotonin



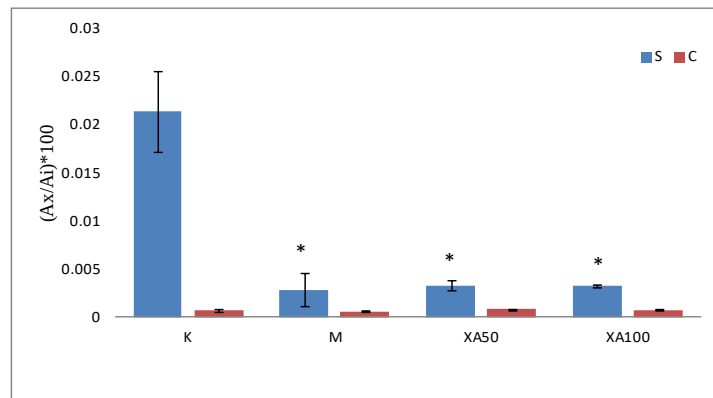
adrenaline



dopamine



levodopa



γ -aminobutyric acid

Fig. S2 The relative quantification results of neurotransmitters ((Ax/Ai)*100, n=3, *P<0.05, **P<0.01: VS control group; #P<0.05, ##P<0.01: VS model group)

Y-axis: (Ax/Ai) $\times$ 100

Table S2. 142 were upregulated and 209 were downregulated after XA treatment

<u>142 proteins upregulated after XA treatment</u>	<u>209 proteins downregulated after XA treatment</u>
<u>SMNDC1</u>	<u>NTPCR</u>
<u>MISMATCH</u>	<u>SLC12A7</u>
<u>DNAJC10</u>	<u>BNIP2</u>
<u>NUP50</u>	<u>GM7244</u>
<u>ASPH</u>	<u>HIRIP3</u>
<u>NUB1</u>	<u>ATPIF1</u>
<u>MISMATCH</u>	<u>LSR</u>
<u>OPA1</u>	<u>TUSC3</u>
<u>NFU1</u>	<u>HNRNPD</u>
<u>POLDIP3</u>	<u>HIF1AN</u>
<u>CNOT1</u>	<u>MAPKAPK2</u>
<u>DHX29</u>	<u>MISMATCH</u>
<u>PKN2</u>	<u>BPHL</u>
<u>PBX3</u>	<u>DIEXF</u>
<u>BAX</u>	<u>PTP4A2</u>
<u>RCOR1</u>	<u>KNTC1</u>
<u>HEATR1</u>	<u>HDAC6</u>
<u>NFIC</u>	<u>TTC9C</u>
<u>FMR1</u>	<u>AMFR</u>
<u>PLCB3</u>	<u>FRYL</u>
<u>YTHDF2</u>	<u>SAT2</u>
<u>COX15</u>	<u>CDC27</u>
<u>D1BWG0212E</u>	<u>1700067P10RIK</u>
<u>AK1</u>	<u>CRTC3</u>
<u>SDF4</u>	<u>RFK</u>
<u>ANAPC4</u>	<u>CSTF2T</u>
<u>ALDOC</u>	<u>SAFB2</u>
<u>CIAPIN1</u>	<u>INSR</u>
<u>PPP4C</u>	<u>MKL2</u>
<u>TOP2B</u>	<u>RUFY3</u>
<u>NDUFB9</u>	<u>ORMDL2</u>

<u>ZC3H14</u>	<u>MTMR6</u>
<u>DHFR</u>	<u>AGFG2</u>
<u>UBQLN2</u>	<u>PDE6A</u>
<u>SCCPDH</u>	<u>LY6G5B</u>
<u>POGZ</u>	<u>OSBPL10</u>
<u>TTC39B</u>	<u>SLC11A2</u>
<u>DDX50</u>	<u>KCTD10</u>
<u>SCARB2</u>	<u>ZFP639</u>
<u>5730455P16RIK</u>	<u>4933407C03RIK</u>
<u>VWF</u>	<u>SETDB1</u>
<u>NPC2</u>	<u>DEF6</u>
<u>ATP5D</u>	<u>PI4KB</u>
<u>EPB4.1L2</u>	<u>A1480653</u>
<u>PRPS2</u>	<u>DDX52</u>
<u>PNMA2</u>	<u>GTF3C4</u>
<u>ATAD3A</u>	<u>MID1IP1</u>
<u>LPCAT1</u>	<u>SUGP2</u>
<u>XRCC6</u>	<u>EVI5L</u>
<u>MFAP1A</u>	<u>MRPL50</u>
<u>CSTB</u>	<u>FGFR1OP</u>
<u>RPS27L</u>	<u>GM4557</u>
<u>CDKN2AIP</u>	<u>SYNGR3</u>
<u>VPS25</u>	<u>BLOC1S1</u>
<u>FAR1</u>	<u>POLE3</u>
<u>DHCR7</u>	<u>PMM1</u>
<u>H2-K1</u>	<u>EPHB3</u>
<u>POLR1C</u>	<u>VPS11</u>
<u>CIRBP</u>	<u>GLE1</u>
<u>PROSC</u>	<u>BIRC5</u>
<u>SRSF9</u>	<u>GTF2H4</u>
<u>CCDC88A</u>	<u>PRL7D1</u>
<u>CPT2</u>	<u>HLTF</u>
<u>EIF4E2</u>	<u>RFX4</u>
<u>PSMD10</u>	<u>HERC2</u>

<u>RAB9</u>	<u>NFIA</u>
<u>KBTBD2</u>	<u>KANK2</u>
<u>YARS2</u>	<u>NUDT9</u>
<u>TRMT6</u>	<u>LLGL1</u>
<u>BCKDHB</u>	<u>ECE1</u>
<u>PPP4R2</u>	<u>ITM2B</u>
<u>WWC2</u>	<u>PRRC2B</u>
<u>MFN2</u>	<u>POLR1D</u>
<u>NDUFAF4</u>	<u>FRMD8</u>
<u>GM15800</u>	<u>RB1CC1</u>
<u>ACYP2</u>	<u>HSDL2</u>
<u>PCM1</u>	<u>ILKAP</u>
<u>TBC1D2B</u>	<u>HSPB6</u>
<u>SLC1A5</u>	<u>SNAPIN</u>
<u>C030046E11RIK</u>	<u>PDLIM4</u>
<u>NDUFA7</u>	<u>SARM1</u>
<u>PCOLCE</u>	<u>RFNG</u>
<u>CYLD</u>	<u>WFS1</u>
<u>IMPA2</u>	<u>9130011E15RIK</u>
<u>SIN3A</u>	<u>HSPA1A</u>
<u>PPP2R5A</u>	<u>MFGE8</u>
<u>SIPA1L1</u>	<u>GNL3L</u>
<u>MACF1</u>	<u>PSTPIP2</u>
<u>TTN</u>	<u>BCL2L1</u>
<u>GOLGA4</u>	<u>MRPS34</u>
<u>DOCK1</u>	<u>BRD3</u>
<u>EED</u>	<u>RABGGTA</u>
<u>LAMP1</u>	<u>ECT2</u>
<u>LUC7L</u>	<u>HMOX1</u>
<u>SMARCD1</u>	<u>BCS1L</u>
<u>FHL3</u>	<u>MOBKL1A</u>
<u>N6AMT2</u>	<u>SSSCA1</u>
<u>UBP1</u>	<u>LSM6</u>
<u>GM14535</u>	<u>4831426I19RIK</u>

<u>LDLRAP1</u>	<u>WDR62</u>
<u>SRSF4</u>	<u>FRK</u>
<u>PIIP5K2</u>	<u>CSTF3</u>
<u>MRPS9</u>	<u>PHLDB1</u>
<u>TBP</u>	<u>MISMATCH</u>
<u>EIF1B</u>	<u>ANKHD1</u>
<u>CCDC92</u>	<u>PARP10</u>
<u>TTC39A</u>	<u>MLYCD</u>
<u>ADO</u>	<u>AFAP1</u>
<u>GCFC1</u>	<u>CNIH4</u>
<u>UTP20</u>	<u>TCF25</u>
<u>PRPF38A</u>	<u>NCDN</u>
<u>FAM135A</u>	<u>SV2B</u>
<u>PCF11</u>	<u>CCDC38</u>
<u>LARP4B</u>	<u>ATG7</u>
<u>RBM4B</u>	<u>SIK3</u>
<u>MED11</u>	<u>LSM12</u>
<u>DDX54</u>	<u>SMAP1</u>
<u>MLF2</u>	<u>TOR1B</u>
<u>OS9</u>	<u>NENF</u>
<u>D19BWG1357E</u>	<u>BYSL</u>
<u>MRPL9</u>	<u>RCL1</u>
<u>FAM53C</u>	<u>ABHD6</u>
<u>VTI1B</u>	<u>TSR1</u>
<u>USP8</u>	<u>SDF2</u>
<u>ECI1</u>	<u>UACA</u>
<u>MTDH</u>	<u>FAM3A</u>
<u>EPN1</u>	<u>SLC39A10</u>
<u>MLST8</u>	<u>EXOC7</u>
<u>MISMATCH</u>	<u>FAM40A</u>
<u>RSL24D1</u>	<u>GALM</u>
<u>MISMATCH</u>	<u>EXOSC3</u>
<u>TRPV5</u>	<u>TPRKB</u>
<u>POLA1</u>	<u>FBXO30</u>

<u>FIGF</u>	<u>UBE2E1</u>
<u>CAMK2D</u>	<u>ZFPL1</u>
<u>CCDC50</u>	<u>ND4</u>
<u>IRF3</u>	<u>CORO1B</u>
<u>GNPDA2</u>	<u>EIF2B4</u>
<u>MAD1L1</u>	<u>FAM125A</u>
<u>MRE11A</u>	<u>FUK</u>
<u>IFT20</u>	<u>RAB34</u>
<u>AATF</u>	<u>PNPLA6</u>
	<u>IQGAP3</u>
	<u>TMED9</u>
	<u>EPN2</u>
	<u>MEA1</u>
	<u>IKBK</u>
	<u>CPT1A</u>
	<u>NAA20</u>
	<u>UBE2O</u>
	<u>RRM2</u>
	<u>CTIF</u>
	<u>AVL9</u>
	<u>COX4I2</u>
	<u>EXOC1</u>
	<u>SUPT6H</u>
	<u>PNP</u>
	<u>DTD1</u>
	<u>MYO1C</u>
	<u>FAM96B</u>
	<u>VRK1</u>
	<u>CLASP1</u>
	<u>INTS7</u>
	<u>MYCBP</u>
	<u>KIF1A</u>
	<u>DPY30</u>
	<u>MVD</u>

[NIP7](#)

[PHC2](#)

[WHSC2](#)

[HEATR5A](#)

[NBEA](#)

[PLA2G15](#)

[ACSL5](#)

[APPL1](#)

[PARP12](#)

[DUT](#)

[EDF1](#)

[EIF2A](#)

[EHD4](#)

[PRKAB1](#)

[CSNK2A2](#)

[CPSF2](#)

[GLB1](#)

[PCYOX1](#)

[RPIA](#)

[CLASP2](#)

[LAMTOR3](#)

[LRRC16A](#)

[EXOSC10](#)

[MBOAT7](#)

[SMARCC2](#)

[S100A10](#)

[RNGTT](#)

[SLC25A32](#)

[EHD3](#)

[NRCAM](#)

[TAP2](#)

[COPG2](#)

[ATP6V0A1](#)

[2310036O22RIK](#)

[NBAS](#)

[CFDP1](#)

[PBK](#)

[AGL](#)

[PSMD13](#)

[GLA](#)

[SQRDL](#)

[1190002N15RIK](#)

Table S2S3. Validation of some differential lipids

No.	Biomarkers	K(peak area)	M(peak area)	XA50(peak area)	XA100(peak area)
1	PC(0:0/18:0)	10079.7±1851.2	52795.7±4144.4	41642.0±3285.9	66487.7±4132.3
2	PC(24:0/0:0)	19082.5±1243.80	11338±322.4	8628.5±311.8	13945.67±627.2
3	PC(P-18:0/0:0)	4154.5±133.6	754.0±75.0	832.5±19.1	1101.0±69.3
4	PC(16:1(9Z)/22:4(7Z,10Z,13Z,16Z))	835346.7±80424.9	1178028.0±79122.5	793231.3±24676.6	1094704±105037.4
5	PC(18:1(9Z)/22:4(7Z,10Z,13Z,16Z))	335539.7±15938.2	405038.0±24576.2	284216.3±977.9	397058.5±37887.5
6	LysoPC(O-18:0)	13281.2±1098.8	1028.3±85.6	1416.0±91.9	1785.0±18.4
7	PE(P-16:0/0:0)	15205.7±1033.1	5318.7±34.6	4000.0±284.3	6520.0±179.6

K: Control group; M: Model group; XA50: 50 µM XA; XA100: 100 µM XA

Table S4S4. Validation of 4 differential proteins

No.	Biomarkers	K(ng/mL)	M(ng/mL)	XA50(ng/mL)	XA100(ng/mL)
1	Csnk2a2	0.7096±0.08189	0.8209±0.08527	0.7233±0.05943	0.6632±0.01767
2	Scarb2	266.813±10.887	244.804±19.894	254.403±18.744	289.369±7.504
3	Vti1b	2.741±0.135	2.680±0.0501	2.777±0.0919	2.842±0.0827
4	Bnip2	0.6524±0.0885	1.232±0.0980	0.992±0.0835	0.4984±0.0492

K: Control group; M: Model group; XA50: 50 μ M XA; XA100: 100 μ M XA; Csnk2a2: Casein kinase II subunit alpha; Scarb2: Lysosome membrane protein 2; Vti1b: Vesicle transport through interaction with t-SNAREs homolog 1B; Bnip2: BCL2/adenovirus E1B 19 kDa protein-interacting protein 2