Supplementary Table 1. Herbal compositions of ANPCD.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Latin Name | English Name | ChineseName | Part Used | Quantity(Dry Weight) |
| *Os Draconis* | Mastodi Ossis Fossilia  | LongGu | Fossil | 30g |
| *Ostrea gigas* Thunberg | Ostreae Concha  | MuLi | Shell | 30g |
| *Cyathula officinalis* K.C.Kuan | Cyathulae Radix | Chuan NiuXi | Dried roots | 15g |
| *Tribulus terrestris* L. | Tribuli Fructus  | BaiJiLi | Dried ripe fruit | 12g |
| *Uncaria* *rhynchophylla*(Miq.) Miq. ex Havil. | Uncariae Ramulus Cum Uncis | GouTeng | Dried hooked stem and branch | 12g |
| *Alisma**plantago-aquatica*L. | Alismatis Rhizoma | ZeXie | Dried tuber | 12g |
| *Paeonia**lactiflora*Pall. | Paeoniae Radix Alba Cruda | BaiShao | Dried roots | 12g |
| *Gardenia jasminoides* J.Ellis | Gardeniae Fructus | Zhizi | Dried ripe fruit | 12g |
| *Paeonia ×**suffruticosa*Andr. | Moutan Cortex | MuDanPi | Dried roots bark | 12g |
| *Scutellaria baicalensis* Georgi | Scutellariae Radix | HuangQin | Dried roots | 12g |
| *Rheum palmatum* L. | Rhei Radix et Rhubarb | DaHuang | Dried roots and rhizomes | 9g |
| *Glycyrrhiza uralensis* Fisch . | Glycyrrhizea Radix | GanCao | Dried roots and rhizomes | 6g |

Supplementary Table 2. Modified Neurological Severity Score.

|  |  |
| --- | --- |
|  | Points |
| Motor tests | 6 |
| Raising rat by the tail | 3 |
| Flexion of forelimb | 1 |
| Flexion of hindlimb | 1 |
| Head moved > 10° to vertical axis within 30 s | 1 |
| Placing rat on the floor (normal = 0; maximum = 3) | 3 |
| Normal walk | 0 |
| Inability to walk straight | 1 |
| Circling toward the paretic side | 2 |
| Fall down to the paretic side | 3 |
| Sensory tests  | 2 |
| Placing test (visual and tactile test) | 1 |
| Proprioceptive test (deep sensation, pushing the paw against the table edge to stimulate limb muscles) | 1 |
| Beam balance tests (normal = 0; maximum = 6)  | 6 |
| Balances with steady posture | 0 |
| Grasps side of beam | 1 |
| Hugs the beam and one limb falls down from the beam | 2 |
| Hugs the beam and two limbs fall down from the beam, or spins on beam(> 60 s) | 3 |
| Attempts to balance on the beam but falls off (> 40 s) | 4 |
| Attempts to balance on the beam but falls off (> 20 s) | 5 |
| Falls off: No attempt to balance or hang on to the beam (< 20 s) | 6 |
| Reflexes absent and abnormal movements | 4 |
| Pinna reflex (head shake when touching the auditory meatus) | 1 |
| Corneal reflex (eye blink when lightly touching the cornea with cotton) | 1 |
| Startle reflex (motor response to a brief noise from snapping a clipboardpaper) | 1 |
| Seizures, myoclonus, myodystony | 1 |
| Maximum points  | 18 |

Supplementary Table 3. A comprehensive list of ANPCD compounds that enter the bloodstream

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Peak ID | RT  | Theoretical Exact mass  | Error (ppm)  | MFG Molecular Formula  | Identification  | Compositional Attribution |
| 1 | 5.50  | 404.0956  | 1.74 | C17H24O11 | kingiside | Gardeniae Fructus |
| 2 | 5.682  | 346.1624  | 1.2  | C16H26O8  | Picrocrocinic acid | Gardeniae Fructus |
| 3 | 6.12 | 204.0899 | 2.34 | C11H12N2O2 | Tryptophan | Baical Skullcap Root |
| 4 | 8.71 | 550.1903 | -0.91 | C23H34O15 | Genipin-1-β-D-gentiobioside | Gardeniae Fructus |
| 5 | 10.30 | 386.1215 | -1.34 | C17H24O10 | Geniposide | Gardeniae Fructus |
| 6 | 11.083 | 642.2169 | -0.16 | C29H38O16 | bruceoside F | Radix Cyathulae |
| 7 | 11.487  | 480.1634  | -0.46  | C23H28O11  | Alibiflorin | Radix Paeoniae Alba |
| 8 | 11.653  | 330.1679 | -0.79 | C16H26O7 | Picrocrocin | Gardeniae Fructus |
| 9 | 12.466  | 480.1638 | 2.31 | C23H28O11 | Paeoniflorin | Radix Paeoniae Alba |
| 10 | 13.69  | 578.1639 | 2.14 | C27H30O14 | Kaempferitrin | Fructus Tribuli / Glycyrrhizea Radix |
| 11 | 14.627  | 548.1537  | -1.23  | C26H28O13  | Puerarin-xyloside | Glycyrrhizea Radix |
| 12 | 14.982  | 544.2055  | 0.42 | C27H32N2O10 | Cadambine | Ramulus Uncariae Cum Uncis |
| 13 | 15.264 | 548.1536  | -1.03  | C26H28O13  | Rubiadin | Gardeniae Fructus |
| 14 | 15.73  | 546.2215  | -0.35  | C27H34N2O10  | 3α-dihydrocadambine | Ramulus Uncariae Cum Uncis |
| 15 | 16.638  | 520.3034  | 0.38  | C29H44O8  | Cyasteron | Radix Cyathulae |
| 16 | 16.973  | 696.2273 | 0.93 | C32H40O17 | Safghanoside A | Gardeniae Fructus |
| 17 | 17.08 | 382.1416 | -1.83 | C22H22O6 | licoricone | Glycyrrhizea Radix |
| 18 | 17.902  | 552.2221  | -2.52  | C27H36O12  | 9-O-butyloxypaeonidanin | Moutan Cortex |
| 19 | 18.288  | 446.085  | -0.27  | C21H18O11  | Baicalin | Baical Skullcap Root |
| 20 | 18.633 | 600.1847 | -0.68 | C30H32O13 | Benzoyloxypaeoniflorin | Radix Paeoniae Alba / Moutan Cortex |
| 21 | 18.772 | 384.2057 | -2.09 | C22H28N2O4 | rhynchophylline | Ramulus Uncariae Cum Uncis |
| 22 | 19.06  | 448.1011 | -1.35 | C21H20O11 | Quercitrin | Fructus Tribuli/ Glycyrrhizea Radix / Ramulus Uncariae Cum Uncis |
| 23 | 19.341  | 446.0821  | -1.77 | C21H18O11 | Baicalein-6- glucuronide | Baical Skullcap Root |
| 24 | 19.459  | 476.0962  | -1.52  | C22H20O12  | Diosmetin7-O-β-D-glucuronide | Fructus Tribuli |
| 25 | 19.684  | 446.1218  | -1.19  | C22H22O10  | Rheochrysin | Rhubarb |
| 26 | 19.867  | 460.1005 | 0.04  | C22H20O11  | Melaleucin glycosides | Baical Skullcap Root |
| 27 | 20.196  | 446.0865  | -3.51  | C21H18O11  | Apigenin-7-glucuronide | Baical Skullcap Root |
| 28 | 20.432 | 460.1013 | -1.57  | C22H20O11  | Wogonoside | Baical Skullcap Root |
| 29 | 20.672  | 490.1113  | -0.34  | C23H22O12  | 2''-O- Acetylquercitrin  | Glycyrrhizea Radix / Ramulus Uncariae Cum Uncis |
| 30 | 20.943  | 330.0740 | -2.54 | C17H14O7 | 3,3'-Dimethylquercetin | Glycyrrhizea Radix |
| 31 | 21.486  | 584.1899 | 0.8 | C30H32O12 | Benzoylpaeoniflorin | Radix Paeoniae Alba / Moutan Cortex |
| 32 | 21.686  | 498.1993  | 1.82  | C26H30N2O8  | Strictosamide  | Ramulus Uncariae Cum Uncis |
| 33 | 22.135  | 366.1964  | 2.12 | C22H26N2O3 | Geissoschizine methyl ether | Ramulus Uncariae Cum Uncis |
| 34 | 22.864  | 368.2122  | -1.97 | C22H28N2O3 | Hirsutine | Ramulus Uncariae Cum Uncis |
| 35 | 22.966  | 634.2633 | -1.22  | C32H42O13  | Rheindiglucosid | Baical Skullcap Root |
| 36 | 23.145  | 838.3992 | -1.57 | C42H62O17 | Glyyunnanprosapogenin D | Glycyrrhizea Radix |
| 37 | 24.168  | 840.4144 | -0.02 | C42H64O17 | Khekadaengoside B | Glycyrrhizea Radix |
| 38 | 24.327  | 822.4056 | -2.59 | C42H62O16 | Glycyrrhizic acid | Glycyrrhizea Radix |
| 39 | 25.262  | 822.4052 | -1.33 | C42H62O16 | Glycyrrhizin | Glycyrrhizea Radix |
| 40 | 25.831  | 368.1265  | -1.38  | C21H20O6  | Glycycoumarin | Glycyrrhizea Radix |
| 41 | 26.997  | 344.09  | -1.27  | C18H16O7  | Eupatorin | Baical Skullcap Root |
| 42 | 27.368  | 284.0685  | -0.19  | C16H12O5  | Wogonin | Baical Skullcap Root |
| 43 | 27.66  | 314.0795  | -1.44  | C17H14O6  | kumatakenin | Baical Skullcap Root |
| 44 | 27.886  | 374.1003  | -0.23  | C19H18O8  | Casticin | Baical Skullcap Root |
| 45 | 28.167  | 284.0687  | -0.82  | C16H12O5  | Oroxylin A | Baical Skullcap Root |
| 46 | 29.162  | 352.0955  | -2.23  | C20H16O6  | Llicoisoflavone B | Glycyrrhizea Radix |
| 47 | 30.464  | 354.1106  | -0.69  | C20H18O6  | Isolicoflavonol | Glycyrrhizea Radix |
| 48 | 33.483  | 490.3658 | -0.22 | C30H50O5 | Alisol A | Alismatis Rhizoma |