Supplementary Table 1. Herbal compositions of ANPCD.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Latin Name | English Name | Chinese  Name | 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 clipboard  paper) | 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 |