For ***Arabian Journal of Chemistry***

**Comprehensive chemical profiling and quantification of Shexiang Xintongning Tablets by integrating liquid chromatography-mass spectrometry and gas chromatography-mass spectrometry**

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Table S1. Information on seven batches of commercially available SXXTN.

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Batch | Pharmaceutical factory | Production Dates |
| B1 | 190501 | Shandong Hongjitang Pharmaceutical | 2019.05.10 |
| B2 | 190502 | Shandong Hongjitang Pharmaceutical | 2019.05.10 |
| B3 | 190503 | Shandong Hongjitang Pharmaceutical | 2019.05.22 |
| B4 | 190504 | Shandong Hongjitang Pharmaceutical | 2019.05.21 |
| B5 | 190601 | Shandong Hongjitang Pharmaceutical | 2019.06.05 |
| B6 | 190602 | Shandong Hongjitang Pharmaceutical | 2019.06.05 |
| B7 | 190603 | Shandong Hongjitang Pharmaceutical | 2019.06.15 |

Table S2. Information of standard references

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Standard references | Batch. No. | Manufacturers |
| 2 | Malic acid | M109342 | Shanghai Aladdin Biochemical Technology Co., Ltd. |
| 3 | Succinic acid | B20534 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 4 | *DL*-Pipecolinic acid | PS2456 | Chengdu Push Bio-Technology Co. Ltd. |
| 5 | Phenylalanine | PS2477 | Chengdu Push Bio-Technology Co. Ltd. |
| 6 | Tetramethylpyrazine | MUST-190503110 | Chengdu Must Biotechnology Co., Ltd. |
| 7 | Neochlorogenic acid | PS1134 | Chengdu Push Bio-Technology Co. Ltd. |
| 8 | 4-Hydroxybenzoic acid | PS1219 | Chengdu Push Bio-Technology Co. Ltd. |
| 10 | Chlorogenic acid | PS0100 | Chengdu Push Bio-Technology Co. Ltd. |
| 11 | Vanillic acid | PS010559 | Chengdu Push Bio-Technology Co. Ltd. |
| 12 | Caffeic acid | PS010522 | Chengdu Push Bio-Technology Co. Ltd. |
| 14 | Benzoic acid | PS010411 | Chengdu Push Bio-Technology Co. Ltd. |
| 16 | Reticuline | PS010321 | Chengdu Push Bio-Technology Co. Ltd. |
| 21 | Scoulerine | PS210524-01 | Chengdu Push Bio-Technology Co. Ltd. |
| 23 | Isocorydine | PS010325 | Chengdu Push Bio-Technology Co. Ltd. |
| 26 | Ferulic acid | PS012244 | Chengdu Push Bio-Technology Co. Ltd. |
| 28 | Corydalmine | PS210526-01 | Chengdu Push Bio-Technology Co. Ltd. |
| 29 | Tetrahydrocolumbamine | PS210509 | Chengdu Push Bio-Technology Co. Ltd. |
| 31 | Berberrubine | PS210501 | Chengdu Push Bio-Technology Co. Ltd. |
| 33 | Corypalmine | B20541 | Shanghai Shidande Bio-Technology Co. Ltd. |
| 36 | Corydinine | PS210506 | Chengdu Push Bio-Technology Co. Ltd. |
| 37 | Demethyleneberberine | PS020303 | Chengdu Push Bio-Technology Co. Ltd. |
| 43 | Norglaucine | B20566 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 44 | Allocryptopine | PS020453 | Chengdu Push Bio-Technology Co. Ltd. |
| 46 | Glaucine | PS011395 | Chengdu Push Bio-Technology Co. Ltd. |
| 47 | Tetrahydrocoptisine | PS020568 | Chengdu Push Bio-Technology Co. Ltd. |
| 48 | Tetrahydropalmatine | PS020570 | Chengdu Push Bio-Technology Co. Ltd. |
| 50 | Yuanhunine | PS020577 | Chengdu Push Bio-Technology Co. Ltd. |
| 52 | Coptisin | PS13121901 | Chengdu Push Bio-Technology Co. Ltd. |
| 53 | Columbamine | PS012621 | Chengdu Push Bio-Technology Co. Ltd. |
| 55 | Jatrorrhizine | PS010630 | Chengdu Push Bio-Technology Co. Ltd. |
| 57 | Trimethoxycinnamic acid | PS010621 | Chengdu Push Bio-Technology Co. Ltd. |
| 58 | Canadine | PS011145 | Chengdu Push Bio-Technology Co. Ltd. |
| 60 | Corydaline | PS020572 | Chengdu Push Bio-Technology Co. Ltd. |
| 63 | 20-*O*-glucoginsenoside Rf | PS012331 | Chengdu Push Bio-Technology Co. Ltd. |
| 64 | Worenine | PS210524-02 | Chengdu Push Bio-Technology Co. Ltd. |
| 66 | Cinnamic acid | PS012432 | Chengdu Push Bio-Technology Co. Ltd. |
| 67 | Notoginsenoside R1 | PS012523 | Chengdu Push Bio-Technology Co. Ltd. |
| 68 | Ethylparaben | B20332 | Chengdu Push Bio-Technology Co. Ltd. |
| 69 | Muramine | PS012541 | Chengdu Push Bio-Technology Co. Ltd. |
| 70 | Berberine | B139120 | Chengdu Push Bio-Technology Co. Ltd. |
| 71 | Palmatine | PS012545 | Chengdu Push Bio-Technology Co. Ltd. |
| 73 | Ginsenoside Rg1 | PS010153 | Chengdu Push Bio-Technology Co. Ltd. |
| 74 | Ginsenoside Re | PS011693 | Chengdu Push Bio-Technology Co. Ltd. |
| 75 | Dehydrocorydaline | PS020572 | Chengdu Push Bio-Technology Co. Ltd. |
| 76 | 13-Methylberberine | B28312 | Chengdu Push Bio-Technology Co. Ltd. |
| 80 | Ginsenoside Rf | PS010759 | Chengdu Push Bio-Technology Co. Ltd. |
| 81 | Notoginsenoside R4 | PS011699 | Chengdu Push Bio-Technology Co. Ltd. |
| 82 | Notoginsenoside R2 | PS011843 | Chengdu Push Bio-Technology Co. Ltd. |
| 83 | 20(*S*)-Ginsenoside Rg2 | PS011811 | Chengdu Push Bio-Technology Co. Ltd. |
| 84 | Ginsenoside Ra2 | PS011761 | Chengdu Push Bio-Technology Co. Ltd. |
| 85 | Ginsenoside Ra3 | PS011620 | Chengdu Push Bio-Technology Co. Ltd. |
| 86 | Ginsenoside Rb1 | B21050 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 88 | Ginsenoside Rc | PS011017 | Chengdu Push Bio-Technology Co. Ltd. |
| 89 | Ginsenoside Ra1 | B22040 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 90 | Ginsenoside Ro | B21068 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 93 | Ginsenoside Rb2 | PS020391 | Chengdu Push Bio-Technology Co. Ltd. |
| 94 | Ginsenoside Rb3 | PS010922 | Chengdu Push Bio-Technology Co. Ltd. |
| 96 | Pseudoginsenoside RT1 | PS020421 | Chengdu Push Bio-Technology Co. Ltd. |
| 99 | Corynoline | PSP2P511 | Chengdu Push Bio-Technology Co. Ltd. |
| 101 | Ginsenoside Rd | B21054 | Chengdu Push Bio-Technology Co. Ltd. |
| 102 | Ginsenoside RS2 | PS020530 | Chengdu Push Bio-Technology Co. Ltd. |
| 106 | Gypenoside VXII | PS020531 | Chengdu Push Bio-Technology Co. Ltd. |
| 107 | 8-Oxycoptisine | PS020569 | Chengdu Push Bio-Technology Co. Ltd. |
| 108 | Senkyunolide A | PS2132 | Chengdu Push Bio-Technology Co. Ltd. |
| 110 | Butylphthalide | PS2342 | Chengdu Push Bio-Technology Co. Ltd. |
| 111 | (*E*)-Ligustilide | B20492 | Chengdu Push Bio-Technology Co. Ltd. |
| 113 | Sedanolide | PS020520 | Chengdu Push Bio-Technology Co. Ltd. |
| 114 | Zingibroside R1 | PS020502 | Chengdu Push Bio-Technology Co. Ltd. |
| 115 | (*Z*)-Ligustilide | PS020510 | Chengdu Push Bio-Technology Co. Ltd. |
| 116 | 20(*S*)-ginsenoside Rg3 | PS020527 | Chengdu Push Bio-Technology Co. Ltd. |
| 118 | 20(*R*)-ginsenoside Rg3 | B21759 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 120 | Dihydrochelerythrine | PS020581 | Chengdu Push Bio-Technology Co. Ltd. |
| 123 | Dihydrosanguinarine | PS020570 | Chengdu Push Bio-Technology Co. Ltd. |
| 126 | Tokinolide B | PS011217 | Chengdu Push Bio-Technology Co. Ltd. |
| 128 | Angelicide | B22821 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 130 | Oleanonic acid | PS020531 | Chengdu Push Bio-Technology Co. Ltd. |
| 132 | linoleic acid | B21421 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 138 | Palmitic acid | A0604 | Chengdu Must Biotechnology Co., Ltd. |
| 139 | Oleic acid | B21592 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 140 | Octadecanoic acid | B25060 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 144 | Fenchol | B22257 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 145 | Camphor | B25328 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 146 | Isoborneol | Z111512 | National Institutes for Food and Drug Control |
| 147 | Phenol, 4-ethyl- | PS011318 | Chengdu Push Bio-Technology Co. Ltd. |
| 148 | Borneol | Z110881 | National Institutes for Food and Drug Control |
| 150 | 3-Phenylpropanol | B29870 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 151 | Cinnamyl alcohol | PS0254 | Chengdu Push Bio-Technology Co. Ltd. |
| 152 | 2-Methoxy-4-vinylphenol | B24361 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 153 | Hydrocinnamic acid | B24333 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 155 | Caryophyllene | B24256 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 156 | (*Z*)-Ethyl Cinnamate | B24211 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 157 | 2,4-Di-tert-butylphenol | B25388 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 160 | *Z*-Butylidenephthalide | B25378 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 162 | Neocnidilide | B25390 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 163 | Muscone | A0128 | Chengdu Must Biotechnology Co., Ltd. |
| 169 | Benzyl cinnamate | B25438 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 171 | Borny cinnamate | B27809 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| 175 | Prasterone | 2113 | Shanghai Shidande Biotechnology Co., Ltd |
| 176 | Androsterone | D1302001 | Shanghai Yuanye Bio-Technology Co. Ltd. |
| IS1 | Nitidine chloride | B20783 | Chengdu Push Bio-Technology Co. Ltd. |
| IS2 | Saikosaponin C | PS0432 | Chengdu Push Bio-Technology Co. Ltd. |
| IS3 | Naphthalene | ZDR-C20905000 | Shanghai Zhenzhun Biotechnology Co., Ltd. |

Table S3 Multi-reaction monitoring conditions of target analytes in Group A by HPLC-QQQ MS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **tR**  **(min)** | **ESI ion polarity** | **Precursor Ion**  **(*m/z*)** | **Product Ion (*m/z*)** | **Q1 Pre Bias (V)** | **CE (eV)** | **Q3 Pre Bias (V)** |
| 6 | 1.66 | + | 137.10 | 55.00 | -30 | -23 | -23 |
| 21 | 2.35 | + | 328.00 | 178.05 | -30 | -30 | -30 |
| 23 | 2.83 | + | 342.15 | 278.95 | -30 | -25 | -30 |
| 28 | 2.90 | + | 342.00 | 192.00 | -30 | -35 | -30 |
| 29 | 3.76 | + | 342.00 | 163.00 | -30 | -50 | -30 |
| 33 | 4.28 | + | 342.05 | 178.05 | -30 | -35 | -30 |
| 36 | 5.11 | + | 354.00 | 189.00 | -30 | -35 | -30 |
| 37 | 4.17 | + | 324.00 | 307.95 | -30 | -35 | -30 |
| 43 | 6.35 | + | 342.10 | 325.05 | -19 | -12 | -22 |
| 44 | 6.62 | + | 369.95 | 188.00 | -30 | -30 | -30 |
| 46 | 6.64 | + | 356.00 | 294.00 | -30 | -25 | -30 |
| 48 | 7.11 | + | 356.00 | 192.00 | -30 | -35 | -30 |
| 52 | 8.01 | + | 319.95 | 292.00 | -30 | -28 | -20 |
| 53 | 7.26 | + | 338.00 | 322.00 | -30 | -35 | -30 |
| 55 | 8.39 | + | 338.00 | 294.00 | -30 | -31 | -30 |
| 58 | 9.48 | + | 340.00 | 176.00 | -30 | -35 | -30 |
| 60 | 10.34 | + | 370.05 | 192.05 | -30 | -35 | -30 |
| 70 | 14.14 | + | 335.95 | 292.00 | -30 | -35 | -30 |
| 71 | 14.20 | + | 352.05 | 336.00 | -30 | -35 | -30 |
| 75 | 14.93 | + | 366.00 | 350.05 | -30 | -35 | -30 |
| 76 | 15.08 | + | 350.00 | 334.00 | -30 | -35 | -30 |
| 107 | 16.38 | + | 335.95 | 307.95 | -30 | -30 | -30 |
| 120 | 17.49 | + | 335.95 | 303.95 | -30 | -23 | -14 |
| 123 | 17.39 | + | 350.05 | 334.00 | -30 | -28 | -23 |
| IS1 | 14.90 | + | 348.00 | 331.95 | -30 | -28 | -24 |

Table S4 Multi-reaction monitoring conditions of target analytes in Group B by HPLC-QQQ MS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **NO.** | **tR**  **(min)** | **ESI ion polarity** | **Precursor Ion (*m/z*)** | **Product Ion (*m/z*)** | **Q1 Pre Bias (V)** | **CE (eV)** | **Q3 Pre Bias (V)** |
| 5 | 1.36 | - | 164.20 | 147.05 | 17 | 15 | 15 |
| 66 | 5.76 | - | 977.30 | 637.25 | 36 | 44 | 22 |
| 67 | 8.27 | - | 147.05 | 103.05 | 30 | 13 | 20 |
| 73 | 5.99 | - | 845.30 | 799.25 | 30 | 26 | 40 |
| 74 | 5.94 | - | 991.55 | 799.20 | 36 | 36 | 28 |
| 80 | 9.15 | - | 799.35 | 475.25 | 28 | 41 | 22 |
| 83 | 10.97 | - | 829.35 | 783.30 | 30 | 23 | 38 |
| 84 | 10.76 | - | 1209.45 | 191.10 | 34 | 55 | 19 |
| 85 | 11.01 | - | 1239.65 | 1107.40 | 34 | 51 | 40 |
| 86 | 11.10 | - | 1107.35 | 179.25 | 40 | 53 | 18 |
| 88 | 12.13 | - | 1077.40 | 783.45 | 38 | 50 | 38 |
| 89 | 12.20 | - | 1209.45 | 1077.05 | 34 | 50 | 38 |
| 93 | 13.22 | - | 1077.40 | 944.95 | 30 | 46 | 34 |
| 94 | 13.38 | - | 1077.35 | 149.25 | 30 | 52 | 29 |
| 101 | 15.62 | - | 991.30 | 783.15 | 36 | 44 | 38 |
| 116 | 16.76 | - | 829.50 | 783.30 | 30 | 21 | 38 |
| IS2 | 11.68 | - | 971.50 | 925.50 | 34 | 28 | 34 |

Table S5 Multi-reaction monitoring conditions of target analytes of Group C by GC-QQQ MS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **Rt (min)** | **Analytes** | **Precursor Ion** | **Product Ion** | **CE (V)** |
| 144 | 6.80 | Fenchol | 80.6 | 79.07 | 10 |
| 145 | 7.78 | Camphor | 107.6 | 93.3 | 8 |
| 147 | 8.24 | 4-Ethylphenol | 107.0 | 77.06 | 18 |
| 150 | 10.60 | 3-Phenylpropanol | 117.5 | 91.15 | 24 |
| 151 | 12.24 | Cinnamyl alcohol | 133.6 | 91.1 | 24 |
| 155 | 14.25 | Caryophyllene | 92.6 | 77.07 | 10 |
| 110 | 18.25 | Butylphthalide | 132.5 | 51.07 | 36 |
| 160 | 18.62 | *Z*-Buthlidenephthalide | 159.0 | 77.03 | 34 |
| 108 | 19.55 | Senkyunolide A | 106.6 | 77.1 | 16 |
| 162 | 19.67 | Neocnidilide | 108.0 | 79.07 | 14 |
| 111 | 19.84 | (*E*)-Ligustilide | 147.5 | 77.04 | 34 |
| 163 | 21.61 | Muscone | 84.6 | 43.22 | 16 |
| 169 | 24.07 | Benzyl cinnamate | 192.4 | 191.03 | 20 |
| IS3 | 9.16 | Naphthalene | 127.5 | 77.07 | 22 |

Table S6 Multi-reaction monitoring conditions of target analytes of Group D by GC-QQQ MS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **Rt (min)** | **Analytes** | **Precursor Ion** | **Product Ion** | **CE (V)** |
| 146 | 4.63 | Isoborneol | 94.6 | 67.05 | 8 |
| 148 | 4.72 | Borneol | 94.6 | 55.06 | 16 |
| 173 | 9.70 | 3-Phenylpropyl cinnamate | 117.5 | 91.06 | 26 |
| 174 | 10.11 | Cinnamyl cinnamate | 130.5 | 77.03 | 26 |
| IS3 | 4.96 | Naphthalene | 127.5 | 77.07 | 22 |

Table S7 Calibration curves, LODs and LOQs of 40 analytes in SXXTN by LC-QQQ MS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **Calibration curves** | ***R2*** | **Linearuty range**  **(μg/ml)** | **LODs**  **(ng/ml)** | **LOQs**  **(ng/ml)** |
| 5 | Y=0.4237X+0.1499 | 0.9900 | 0.0202-10.100 | 0.112 | 0.224 |
| 6 | Y=0.3444X-0.0000 | 0.9916 | 0.0037-0.4575 | 0.092 | 0.458 |
| 21 | Y=3.8646X+0.0346 | 0.9925 | 0.0276-5.5200 | 0.005 | 0.007 |
| 23 | Y=2.5382X+0.0015 | 0.9973 | 0.0131-2.6200 | 0.001 | 0.002 |
| 28 | Y=3.1684X+0.0050 | 0.9996 | 0.0109-2.1840 | 0.007 | 0.027 |
| 29 | Y=1.7437X+0.0032 | 0.9992 | 0.0310-6.2100 | 0.016 | 0.031 |
| 33 | Y=1.7164X+0.0006 | 0.9989 | 0.0277-5.5440 | 0.007 | 0.014 |
| 36 | Y=0.7667X+0.0538 | 0.9969 | 0.1185-23.700 | 0.037 | 0.099 |
| 37 | Y=1.4258X-0.0008 | 0.9958 | 0.0041-0.2575 | 0.001 | 0.003 |
| 43 | Y=0.1483X-0.0002 | 0.9975 | 0.1200-7.5000 | 6.000 | 40.00 |
| 44 | Y=1.5695X+0.0090 | 0.9998 | 0.0832-16.640 | 0.007 | 0.042 |
| 46 | Y=3.8004X+0.0212 | 0.9970 | 0.0129-2.5800 | 0.008 | 0.011 |
| 48 | Y=6.2111X-0.0047 | 0.9945 | 0.0058-1.1640 | 0.001 | 0.002 |
| 52 | Y=1.2003X+0.0138 | 0.9990 | 0.0918-18.368 | 0.015 | 0.077 |
| 53 | Y=1.3303X+0.0107 | 0.9997 | 0.0845-16.896 | 0.026 | 0.042 |
| 55 | Y=2.9055X-0.0022 | 0.9928 | 0.0059-0.0371 | 0.004 | 0.588 |
| 58 | Y=6.8046X-0.0080 | 0.9935 | 0.0092-0.5780 | 0.002 | 0.009 |
| 60 | Y=3.4744X-0.0098 | 0.9915 | 0.0180-2.2500 | 0.005 | 0.011 |
| 66 | Y=1.6136X+0.1300 | 0.9975 | 0.0202-10.100 | 2.020 | 5.050 |
| 67 | Y=0.1020X+0.0066 | 0.9977 | 0.0106-5.3250 | 0.710 | 1.065 |
| 70 | Y=1.9193X+0.0003 | 0.9993 | 0.0294-5.8800 | 0.002 | 0.005 |
| 71 | Y=1.7779X+0.0066 | 0.9993 | 0.0449-8.9760 | 0.002 | 0.005 |
| 73 | Y=0.7581X+0.0939 | 0.9913 | 0.0243-6.0750 | 0.304 | 0.405 |
| 74 | Y=0.0113X+0.0019 | 0.9904 | 0.0325-8.1375 | 8.138 | 16.275 |
| 75 | Y=2.6862X-0.0056 | 0.9960 | 0.0177-2.2162 | 0.003 | 0.009 |
| 76 | Y=3.1255X+0.0101 | 0.9919 | 0.0077-0.4812 | 0.001 | 0.002 |
| 80 | Y=0.4813X+0.1733 | 0.9907 | 0.0260-13.000 | 0.578 | 0.650 |
| 83 | Y=2.7252X+0.2390 | 0.9933 | 0.0093-4.6500 | 0.155 | 0.207 |
| 84 | Y=0.1542X-0.0113 | 0.9980 | 0.0406-10.150 | 3.383 | 25.375 |
| 85 | Y=0.0510X+0.0076 | 0.9911 | 0.0436-8.7200 | 13.625 | 27.250 |
| 86 | Y=0.0985X+0.0192 | 0.9936 | 0.0308-12.320 | 15.400 | 30.800 |
| 88 | Y=0.0733X+0.0082 | 0.9940 | 0.0190-4.7375 | 7.106 | 14.213 |
| 89 | Y=0.0892X+0.0113 | 0.9923 | 0.0212-10.600 | 7.950 | 15.900 |
| 93 | Y=0.2675X-0.0132 | 0.9982 | 0.0235-2.9375 | 8.813 | 17.625 |
| 94 | Y=0.2391X+0.0084 | 0.9978 | 0.0092-4.5900 | 6.885 | 13.770 |
| 101 | Y=0.0962X+0.0150 | 0.9910 | 0.0220-4.4000 | 8.250 | 16.500 |
| 107 | Y=1.9118X+0.0050 | 0.9994 | 0.0124-2.4720 | 0.002 | 0.003 |
| 116 | Y=1.8332X-0.0625 | 0.9937 | 0.0045-1.1200 | 0.280 | 0.560 |
| 120 | Y=20.466X-0.0156 | 0.9960 | 0.0068-0.4256 | 0.002 | 0.017 |
| 123 | Y=5.3325X-0.0037 | 0.9955 | 0.0146-1.8300 | 0.002 | 0.004 |

Table S8 Precision, repeatability, stability and accuracy of analytes in SXXTN by LC-QQQ MS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Intra-day precision**  **(RSD, n = 6, %)** | **Inter-day precision**  **(RSD, n = 9, %)** | **Repeatability**  **(RSD, n = 6, %)** | **Stability**  **(RSD, n = 6, %)** | **Accuracy**  **(n = 6, %)** | |
| **Recovery** | **RSD** |
| 5 | 2.83 | 9.43 | 4.79 | 5.73 | 96.09 | 12.61 |
| 6 | 2.23 | 3.28 | 3.28 | 1.23 | 94.88 | 6.48 |
| 21 | 2.04 | 3.31 | 1.80 | 0.83 | 102.18 | 10.98 |
| 23 | 2.49 | 3.26 | 2.64 | 1.36 | 98.54 | 9.16 |
| 28 | 1.43 | 4.52 | 2.51 | 1.77 | 101.27 | 8.54 |
| 29 | 4.84 | 5.16 | 2.19 | 1.59 | 108.63 | 8.34 |
| 33 | 1.19 | 4.81 | 2.33 | 2.68 | 106.37 | 2.38 |
| 36 | 1.77 | 2.74 | 2.68 | 1.76 | 99.62 | 8.41 |
| 37 | 1.16 | 2.96 | 2.11 | 1.62 | 110.06 | 6.93 |
| 43 | 2.94 | 4.93 | 2.34 | 3.61 | 99.03 | 9.02 |
| 44 | 1.39 | 3.88 | 2.87 | 1.25 | 103.04 | 6.95 |
| 46 | 2.88 | 3.41 | 2.45 | 2.22 | 89.13 | 9.16 |
| 48 | 2.66 | 3.74 | 2.54 | 1.47 | 110.77 | 6.13 |
| 52 | 2.00 | 2.06 | 0.67 | 1.53 | 104.37 | 6.66 |
| 53 | 2.16 | 2.43 | 0.64 | 1.38 | 107.94 | 6.54 |
| 55 | 2.08 | 4.83 | 2.80 | 2.60 | 104.40 | 6.07 |
| 58 | 1.71 | 3.29 | 2.46 | 1.75 | 110.05 | 6.87 |
| 60 | 1.72 | 4.50 | 2.61 | 1.44 | 114.20 | 7.38 |
| 66 | 1.54 | 7.36 | 1.55 | 3.52 | 116.83 | 11.62 |
| 67 | 2.40 | 5.27 | 1.70 | 2.96 | 103.61 | 7.84 |
| 70 | 1.66 | 2.06 | 2.22 | 1.02 | 102.28 | 4.02 |
| 71 | 1.48 | 1.18 | 1.50 | 1.16 | 105.65 | 5.45 |
| 73 | 2.02 | 3.32 | 1.92 | 2.27 | 110.19 | 4.80 |
| 74 | 4.79 | 4.53 | 1.38 | 2.60 | 100.04 | 7.49 |
| 75 | 1.07 | 3.13 | 2.23 | 0.6 | 117.57 | 5.36 |
| 76 | 1.42 | 2.14 | 2.15 | 0.95 | 100.48 | 5.52 |
| 80 | 1.32 | 5.60 | 1.30 | 4.62 | 108.63 | 10.04 |
| 83 | 1.24 | 4.44 | 1.33 | 4.14 | 104.03 | 4.05 |
| 84 | 2.30 | 5.82 | 1.84 | 6.14 | 80.96 | 4.46 |
| 85 | 1.19 | 2.73 | 5.91 | 4.29 | 101.17 | 10.68 |
| 86 | 2.43 | 5.84 | 3.13 | 5.95 | 116.49 | 5.46 |
| 88 | 2.38 | 5.45 | 2.06 | 5.04 | 117.13 | 6.31 |
| 89 | 1.93 | 3.57 | 1.31 | 2.51 | 115.78 | 8.34 |
| 93 | 4.87 | 7.46 | 2.64 | 5.38 | 90.52 | 9.34 |
| 94 | 5.41 | 7.84 | 2.58 | 5.29 | 90.64 | 8.10 |
| 101 | 3.55 | 4.42 | 3.33 | 4.78 | 104.48 | 3.50 |
| 107 | 1.41 | 1.30 | 2.12 | 1.62 | 102.66 | 9.37 |
| 116 | 3.56 | 3.44 | 2.62 | 5.26 | 80.36 | 6.45 |
| 120 | 1.29 | 5.75 | 1.27 | 1.74 | 99.36 | 8.50 |
| 123 | 1.70 | 3.61 | 3.43 | 0.73 | 102.26 | 7.00 |

Table S9 Calibration curves, LODs and LOQs of 17 analytes in SXXTN by GC-QQQ MS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **Calibration curves** | ***R2*** | **Linearity range (μg/ml）** | **LODs (μg/ml)** | **LOQs (μg/ml)** |
| 144 | Y=1.0381x+0.0045 | 0.9986 | 0.1500-7.5000 | 0.005 | 0.015 |  |
| 145 | Y=0.4938x+0.0017 | 0.9955 | 0.1030-5.1500 | 0.005 | 0.013 |  |
| 146 | Y=0.5635x+0.0139 | 0.9976 | 0.8138-81.375 | 0.018 | 0.054 |  |
| 147 | Y=2.3087x-0.1334 | 0.9965 | 1.2175-12.175 | 0.097 | 0.122 |  |
| 148 | Y=0.8043x+0.0100 | 0.9985 | 1.0000-100.00 | 0.008 | 0.020 |  |
| 150 | Y=1.2172x-0.1702 | 0.9976 | 2.9040-29.040 | 0.581 | 1.162 |  |
| 151 | Y=0.3903x-0.2382 | 0.9935 | 9.9060-99.060 | 2.642 | 5.283 |  |
| 155 | Y=0.5161x-0.0041 | 0.9990 | 0.1515-7.5750 | 0.008 | 0.019 |  |
| 110 | Y=3.7624x-0.2920 | 0.9970 | 1.9300-24.125 | 0.241 | 0.965 |  |
| 160 | Y=0.3858x-0.0443 | 0.9954 | 1.4000-35.000 | 0.350 | 1.400 |  |
| 108 | Y=2.2567x-0.5197 | 0.9904 | 2.0700-51.800 | 1.035 | 2.070 |  |
| 162 | Y=5.5589x-0.3427 | 0.9976 | 1.1700-14.625 | 0.146 | 1.170 |  |
| 111 | Y=0.4468x-0.1676 | 0.9990 | 8.3160-83.160 | 2.218 | 6.653 |  |
| 163 | Y=0.2721x-0.0230 | 0.9990 | 1.0725-53.600 | 0.250 | 0.500 |  |
| 169 | Y=1.6498x-0.6952 | 0.9927 | 7.4280-74.280 | 0.743 | 1.733 |  |
| 173 | Y=2.6254x-0.5582 | 0.9921 | 0.7725-77.250 | 0.640 | 0.774 |  |
| 174 | Y=2.1513x-1.0933 | 0.9907 | 8.0800-101.00 | 2.020 | 4.040 |  |

Table S10 Precision, repeatability, stability and accuracy of analytes in SXXTN by GC-QQQ MS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Intra-day**  **precision**  **(RSD, n = 6, %)** | **Inter-day**  **precision**  **(RSD, n = 9, %)** | **Repeatability**  **(RSD,**  **n = 6, %)** | **Stability**  **(RSD,**  **n = 6, %)** | **Accuracy**  **(n = 6, %)** | |
| **Recovery** | **RSD** |
| 144 | 0.69 | 1.91 | 4.40 | 1.24 | 99.02 | 2.76 |
| 145 | 0.65 | 2.65 | 4.96 | 1.34 | 98.37 | 2.24 |
| 146 | 0.70 | 0.80 | 2.58 | 1.44 | 103.44 | 4.71 |
| 147 | 5.47 | 5.19 | 7.52 | 3.15 | 90.20 | 9.59 |
| 148 | 0.68 | 0.83 | 1.63 | 1.54 | 100.98 | 5.31 |
| 150 | 4.70 | 4.66 | 9.66 | 5.63 | 94.24 | 10.67 |
| 151 | 5.44 | 6.5 | 8.37 | 7.97 | 99.47 | 8.64 |
| 155 | 0.44 | 1.88 | 4.64 | 1.14 | 104.98 | 1.70 |
| 110 | 0.54 | 1.78 | 6.05 | 2.51 | 104.87 | 1.96 |
| 160 | 1.56 | 2.86 | 7.34 | 3.50 | 114.51 | 2.60 |
| 108 | 3.11 | 2.14 | 9.47 | 6.00 | 106.78 | 4.88 |
| 162 | 0.67 | 1.69 | 6.61 | 3.94 | 102.21 | 5.01 |
| 111 | 0.77 | 1.57 | 5.96 | 2.59 | 104.65 | 2.33 |
| 163 | 0.95 | 1.90 | 5.23 | 1.61 | 105.21 | 2.32 |
| 169 | 0.99 | 8.06 | 5.79 | 3.28 | 104.11 | 1.48 |
| 173 | 5.53 | 3.05 | 5.27 | 7.97 | 123.51 | 7.15 |
| 174 | 9.06 | 5.04 | 8.12 | 6.99 | 116.50 | 11.95 |



Fig S1 The characteristic MS/MS spectra of representative compounds in SXXTN.

A: Tetrahydropalmatine, B: Berberine, C: Protopine, D: Glaucine, E: Ginsenoside Rd,

F: Ginsenoside Rg1, G: Ginsenoside Ro, H: Ginsenoside Rb2, I: Ferulic acid, J: Cinnamic acid,

K: Senkyunolide A, L: Angelicide



Fig S2 The fragmentation pathways of representative compounds in SXXTN.

A: Tetrahydropalmatine, B: Berberine, C: Protopine, D: Glaucine, E: Ginsenoside Rd,

F: Ginsenoside Rg1, G: Ginsenoside Ro, H: Ferulic acid, I: Senkyunolide A

Fig S3 The multi-reaction monitoring chromatograms of SXXTN in Group A (A) and Group B (B) by HPLC-QQQ MS



Fig S4 The multi-reaction monitoring chromatograms of SXXTN in Group C (A) and Group D (B) by GC-QQQ MS