**Supporting information**

**Table lists**

Table S1 The detailed information of prototypes detected in bio-samples after dosed GXB and GXB-dePRP.

Table S2 The detailed information of metabolites characterized in bio-samples after dosed GXB and GXB-dePRP.

Table S3 The linear ranges and regression equations for 5 quantitative components (n=3)

Table S4 The LLOQs of 5 analytes in rat plasma (n=6)

Table S5 The accuracies and inter/intra-day precisions of 5 analytes in rat plasma (n=6)

Table S6 The matrix effects and extraction recoveries of 5 analytes and IS in rat plasma (n=6)

Table S7 Stabilities of 5 quantitative components in three different conditions

Table S8 Linear ranges and regression equations for 15 quantitative components (n=3)

Table S9 The LLOQs of 15 analytes in rat intestine content (n=6)

Table S10 Accuracies and inter/intra-day precisions of 15 analytes in rat intestine content (n=6)

Table S11 The matrix effects and extraction recoveries of 15 analytes and IS in rat intestine content (n=6)

Table S12 Stabilities of 15 quantitative components in rat intestine content

**Figure captions**

Fig. S1 The extract ion chromatogram (EIC) of prototypes characterized in rat bio-samples

Fig. S2 Specificity for 5 quantitative components and IS in rat plasma

Fig. S3 Carryover for 5 quantitative components and IS

Fig. S4 Specificity for 15 quantitative components and IS in rat intestine content

Fig. S5 Carryover for 15 quantitative components and IS in rat intestine content

Table S1 The detailed information of prototypes detected in bio-samples after dosed GXB and GXB-dePRP.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NO.** | **t*R*** | **selected ion** | **Mass error** | **Elemental composition** | **Calculated mass** | **Measured Mass** | **Fragmentation** | **Identification** | **Source** | **P** | **U** | **B** | **F** | **I** |
| **1\*** | 0.66 | [M+H]+ | -1.0 | C11H15N5O4S | 314.0923 | 314.092 | 314.0920,268.1044,136.0624 | 5'-deoxy-5'-β-methylsulphinyl-adenosine | TP/AMB |  | + |  | +# | +# |
| **2\*** | 0.94 | [M+H]+ | 0.0 | C11H15N5O4S | 314.0923 | 314.0923 | 314.0920,268.1044,136.0624 | 5'-deoxy-5'-α-methylsulphinyl-adenosine | TP/AMB |  | + |  | +# | +# |
| **3** | 1.49 | [M+H]+ | 0.5 | C9H14N2O3 | 199.1083 | 199.1084 | 181.0985 | Pedatisectine D | PRP | + | +# |  |  |  |
| **4** | 2.14 | [M-H]\_ | -0.7 | C7H6O4 | 153.0188 | 153.0187 | 137.0242,109.0295 | 3,4-dihydroxybenzoic acid | TP/AMB |  |  |  | +# |  |
| **5** | 2.34 | [M-H]- | 3.0 | C11H12N2O2 | 203.0821 | 203.0827 | 186.0554,159.0950,142.0668,116.0490 | *L*-tryptophan | PRP |  | + | + |  |  |
| **6** | 2.66 | [M+H]+ | 0.7 | C15H29NO4 | 288.2175 | 288.2177 | 270.2073,210.1853 | N-Lauroyl-*L*-serine | PRP |  | + |  | + | + |
| **7\*** | 3.02 | [M+H]+ | -0.5 | C12H12N2O2 | 217.0977 | 217.0976 | 156.0802,144.0819 | 2,3,4,9-Tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid | AMB | +# | + |  | + | +# |
| **8** | 3.22 | [M+H]+ | -1.3 | C13H14N2O2 | 231.1134 | 231.1131 | 214.0870 | (1*S*,3*S*)-2,3,4,9-Tetrahydro-1methyl-1*H*-pyrido [3,4-b]indole-3-carboxylic acid | AMB |  | +# |  | +# | +# |
| **9** | 3.27 | [M-H]- | 2.9 | C27H30O15 | 593.1506 | 593.1529 | 503.1199,473.1098,413.0868,383.0765, 353.0652 | Apigenin 6,8-di-C-D-glucoside | TP |  | +# |  | +# | +# |
| **10** | 3.43 | [M+H]+ | 3.5 | C13H14N2O2 | 231.1134 | 231.1142 | 214.0860, | (1*R*,3*S*)-2,3,4,9-Tetrahydro-1methyl-1*H*-pyrido[3,4-b]indole-3-carboxylic acid | AMB |  | +# |  | +# | +# |
| **11\*** | 3.80 | a[M+H]+ | 1.0 | C45H74O20 | 917.4746 | 917.4746 | 917.4755,755.4253,737.4100,593.3722, 431.3127,413.3055,395.2946,377.2846, 289.2165, 271.2065,253.1932 | Macrostemonoside G | AMB |  | +# |  | # | +# |
| **12\*** | 3.90 | a[M+H]+ | -3.1 | C45H76O20 | 919.4903 | 919.4903 | 919.4902,757.4385,595.3811,433.3310, 415.3285,397.3098,289.2167,271.2056, 253.1939 | Elephanoside E | AMB |  | + |  | # | +# |
| **13** | 4.08 | [M-H]- | -0.5 | C27H30O14 | 577.1557 | 577.1554 | 577.1568,549.1580,503.1219, 457.1149, 383.0782, 353.0640 | Violanthin | PRP |  | + |  | + | + |
| **14** | 4.12 | [M-H]- | 1.1 | C26H30O13 | 549.1608 | 549.1614 | 549.1614,255.0662,135.0083,119.0504 | Liquiritin-7-*O*-*β*-D-apiofuranoside 4'-*O*-*β*-D glucopyranoside | PRP |  | + |  |  | + |
| **15** | 4.16 | [M-H]- | 0.6 | C18H28O10 | 403.1604 | 403.1609 | 385.1869,223.0981,179.1089 | (2*E*,4*E*)-8-(*β*-D-glucopyranosyloxy)-2,7-dimethyl-2,4-decadiendioic acid | TP |  |  |  |  | + |
| **16** | 4.16 | [M+H]+ | 0.0 | C15H29NO3 | 272.2226 | 272.2226 | 254.2112 | Tridecanoylglycine | TP |  | + |  | + |  |
| **17\*** | 4.18 | [M-H]- | 0.8 | C27H30O16 | 611.1610 | 611.1611 | 301.0328,300.0267,271.0244,255.0296, 243.0302,178.9977,151.0037 | Rutin | TP |  | + |  | + | +# |
| **18** | 4.24 | [M-H]- | -1.1 | C26H30O13 | 549.1608 | 549.1602 | 549.1602,417.1181,255.0659,135.0085, 119.0508 | Liquiritin apioside | PRP |  | + |  | + | + |
| **19** | 4.26 | [M-H]- | -1.2 | C9H10O3 | 165.0552 | 165.0550 | 147.0442,119.0496 | 3-methoxy-4-methylbenzoic acid | TP/AMB |  | + |  | +# |  |
| **20** | 4.36 | [M-H]- | 2.2 | C21H22O9 | 417.1186 | 417.1195 | 255.0662,135.0092, 119.0506,91.0195 | Liquiritin | PRP |  |  |  |  | + |
| **21** | 4.37 | [M-H]- | 2.9 | C27H30O15 | 593.1506 | 593.1529 | 447.0918,285.0389,284.0311,255.0291,  151.0037 | Kaempferol-3-*O*-*β*-rutinoside | TP |  |  |  | # | +# |
| **22\*** | 4.38 | a[M+H]+ | -2.2 | C45H72O20 | 915.459 | 915.459 | 915.4570,753.4048,591.3512,573.3460,  431.3113,429.2999,411.2888,397.2771,  375.2660,357.2435,339.2343,287.1998, 269.1908 | Macrostemonoside I | AMB |  | +# |  |  | +# |
| **23\*** | 4.40 | [M-H]- | 1.3 | C21H20O12 | 463.0877 | 463.0883 | 447.0931,301.0313,300.0257,285.0384,  284.0294,271.0238,255.0282,178.9951,  151.0037 | Quercetin-3-*O*-glucoside | TP |  |  |  |  | +# |
| **24\*** | 4.43 | [M-H]- | -0.4 | C21H20O11 | 447.0927 | 447.0925 | 285.0398,284.0317,255.0285,199.0370, 151.0048,133.0311 | Luteolin-7-*O*-*β*-glucoside | TP |  |  |  |  | +# |
| **25\*** | 4.50 | a[M+H]+ | -2.8 | C45H74O20 | 917.4746 | 917.4746 | 917.4720,755.4193,593.3663,431.3172,  413.3044,395.2911,299.2355,281.2253,  287.1992, 269.1908 | (25*R*)-Macrostemonoside I | AMB |  | + |  | # | +# |
| **26\*** | 4.57 | a[M+H]+ | -2.3 | C45H76O20 | 919.4903 | 919.4903 | 919.4882,757.4399,595.3828,433.3286, 415.3195,397.3090,379.3001,271.2056,  253.1945 | (25*R*)-12*α*-OH-Timosaponin B II | AMB |  | # |  | +# | +# |
| **27\*** | 4.61 | a[M+H]+ | 0.3 | C33H54O12 | 625.3588 | 625.3590 | 665.3480,625.3571,463.3041,321.2083, 303.1940,285.1839, 267.1730 | Macrostemonoside N | AMB |  |  |  |  | +# |
| **28** | 4.69 | a[M+H]+ | -0.3 | C33H56O12 | 627.3735 | 627.3742 | 627.3742,465.3233,321.2109, 303.1904, 285.1834,267.1748 | Macrostemonoside M isomer | AMB |  |  |  |  | +# |
| **29** | 4.70 | [M-H]- | 1.2 | C20H18O11 | 433.0771 | 433.0776 | 301.0300,300.0274,271.0263,255.0308, 243.0313,151.0023 | Quercetin-3-*O*-arabinofuranoside | TP |  |  |  |  | +# |
| **30** | 4.72 | [M-H]- | 2.4 | C28H32O16 | 623.1612 | 623.1617 | 315.0494,299.0197,283.0834,271.0256, 255.0288,243.0299 | Isorhamnetin-3-*O*-rutinoside | TP |  |  |  | # | +# |
| **31\*** | 4.75 | a[M+H]+ | 0.0 | C33H56O12 | 627.3735 | 627.3735 | 627.3735,465.3233,321.2110, 303.1999, 285.1878,267.1728 | Macrostemonoside M | AMB |  |  |  | # | +# |
| **32** | 4.85 | [M-H]- | 1.2 | C28H36O13 | 579.2078 | 579.2085 | 417.1551,387.1068,181.0514,166.0267, 151.0041 | Syringaresinol-4'-*O*-*β*-D-glucoside | TP |  |  |  |  | + |
| **32** | 4.86 | [M-H]- | -2.4 | C27H30O14 | 577.1557 | 577.1543 | 549.1580,503.1219,457.1149,383.0782, 353.0640 | Apigenin-7-*O*-*β*-D-neohesperidoside | TP |  |  | + | + | +# |
| **33\*** | 4.91 | [M+H]+ | 0.0 | C11H16O3 | 197.1178 | 197.1178 | 179.1088,137.0626,120.0810 | (-)-Loliolide | TP | +# | +# | +# | +# | +# |
| **34** | 4.92 | a[M+H]+ | -2.0 | C45H74O20 | 917.4746 | 917.4728 | 917.4728,755.4143,593.3713,431.3161, 413.3074,271.2043, 253.1954, | 25(27)-ene-Macrostemonoside J | AMB |  |  |  |  | +# |
| **35** | 4.93 | a[M+H]+ | -1.9 | C57H94O30 | 1241.5803 | 1241.5830 | 1241.5779,1079.5314,917.4791,755.4188,593.3698,431.3124,289.2156,271.2057,253.2949 | 25(27)-ene-12-*β*-OH-Macrostemonoside B | AMB |  |  |  |  | +# |
| **36** | 4.94 | a[M+H]+ | -0.3 | C45H76O20 | 919.4903 | 919.4900 | 919.4906,757.4345,595.3799,433.3292, 289.2155,271.2062,253.1988, | Macrostemonoside J | AMB |  |  |  |  | +# |
| **37** | 5.00 | [M-H]- | -0.2 | C21H20O10 | 431.0978 | 431.0977 | 269.0457,268.0363,241.0506,240.0432, 211.0399,151.0035 | Galangin-3-*O*-*β*-D-glucoside | TP |  |  |  |  | +# |
| **38** | 5.05 | a[M+H]+ | 1.3 | C57H96O30 | 1243.5959 | 1243.5975 | 1081.5387,919.4858,757.4314,595.3856,433.3302,415.3194,271.2043,253.1956 | Macrostemonoside R | AMB |  |  |  |  | +# |
| **39** | 5.15 | a[M+H]+ | -1.3 | C45H76O20 | 919.4903 | 919.4891 | 919.4891,757.4399,595.3802,433.3288, 289.2154,271.2079,253.1937, | Macrostemonoside J isomer 1 | AMB |  |  |  |  | + |
| **40** | 5.16 | [M+H]+ | -0.8 | C45H72O19 | 917.4746 | 917.4739 | 917.4730,755.4209,593.3719,431.3131, 289.2168,271.2056,253.1957 | 20(22)-ene-Macrostemonoside G | AMB |  |  |  |  | +# |
| **41** | 5.17 | [M-H]- | -1.4 | C22H22O11 | 461.1084 | 461.1070 | 446.0851,299.0499,298.0474,284.0304, 283.0251,255.0309 | Chrysoeriol-7-*O*-glucoside | TP |  |  |  |  | +# |
| **42** | 5.29 | [M-H]- | -2.7 | C21H20O11 | 447.0927 | 447.0915 | 285.0396,284.0309,255.0301, 151.0027 | Kampferol-3-*O*-β-glucoside | TP |  | + |  |  |  |
| **43** | 5.55 | [M+H]+ | -2.5 | C17H17NO3 | 284.1287 | 284.128 |  | N-(*p-cis*-Coumaroyl)tyramine | AMB |  | + |  |  |  |
| **44** | 5.59 | [M-H]- | 2.9 | C7H6O3 | 137.0239 | 137.0243 | 109.0297 | Protocatechuic aldehyde isomer | TP/PRP |  |  |  | # |  |
| **45** | 5.68 | [M+H]+ | 1.9 | C45H70O19 | 915.4590 | 915.4607 | 915.4607,753.4059,591.3531,429.3010, 411.2896,287.1993, 269.1927, | 20(22)-ene-Macrostemonoside I | AMB |  |  |  |  | +# |
| **46** | 5.73 | a[M+H]+ | -1.3 | C45H76O20 | 919.4903 | 919.4892 | 919.4891,757.4399,595.3802,433.3288, 289.2154,271.2079, 253.1937, | Macrostemonoside P | AMB |  |  |  |  | +# |
| **47** | 5.73 | [M+H]+ | 0.1 | C45H74O19 | 919.4903 | 919.4904 | 919.4902,757.4398,595.3824,433.3324, 415.3226,289.2189,271.2058 | Macrostemonoside L | AMB |  |  |  |  | +# |
| **48** | 5.83 | [M+H]+ | 0.0 | C18H19NO4 | 314.1392 | 314.1392 |  | N-*cis*-Feruloyltyramine | AMB |  | + |  |  |  |
| **49** | 5.85 | a[M+H]+ | -0.7 | C45H74O19 | 901.4797 | 901.4791 | 739.4226,577.3725,415.3222,397.3115, 273.2209, 255.2110 | Macrostemonoside O | AMB |  |  |  |  | +# |
| **50\*** | 5.98 | [M+H]+ | -0.7 | C45H76O19 | 903.4947 | 903.4953 | 903.4947,741.4410,579.3912,435.2781, 417.3378,399.3282, 273.2213,255.2109 | Timosaponin BII | AMB |  | +# | + |  | +# |
| **51** | 6.00 | [M+H]+ | -1.4 | C17H17NO3 | 284.1287 | 284.1283 |  | N-(*p*-*trans*-Coumaroyl)tyramine | AMB |  | +# |  |  |  |
| **52\*** | 6.04 | a[M+H]+ | 0.2 | C45H76O19 | 903.4955 | 903.4955 | 903.4955,741.4413,579.3900,435.2719, 417.3378,273.2211, 255.2111 | (25*R*)-Timosaponin BII | AMB | +# | +# | +# | +# | +# |
| **53** | 6.07 | [M+H]+ | -3.8 | C45H72O19 | 917.4746 | 917.4911 | 755.4209,593.3719,431.3131,289.2168, 271.2056, 253.1957 | 25(27)-ene-2*β*-OH-Timosaponin A III+ glc | AMB |  |  |  |  | +# |
| **54** | 6.08 | a[M+H]+ | 0.9 | C57H94O29 | 1225.5853 | 1225.5853 | 1225.5864,1063.5314,901.4785,739.4252,577.3750,415.3214,397.3106,271.2060, 253.1959 | 25S-5(6)-ene-Macrostemonoside B | AMB |  | + |  |  | +# |
| **55\*** | 6.18 | a[M+H]+ | 0.3 | C57H96O29 | 1227.601 | 1227.601 | 1227.6014,1065.5542,903.4886,741.4418,579.3904,435.2749,417.3369,273.2221, 255.2115 | (25*S*)-Macrostemonoside B | AMB |  | +# |  |  | +# |
| **56\*** | 6.22 | a[M+H]+ | 0.3 | C57H96O29 | 1227.601 | 1227.601 | 1227.6014,1065.5542,903.4886,741.4418, 579.3904,435.2749,417.3369,273.2221, 255.2115 | Macrostemonoside B | AMB | +# | # |  |  | +# |
| **57** | 6.27 | [M-H]- | 0.8 | C12H17NO4 | 238.1079 | 238.1081 | 194.1174,164.1078 | 5-ethoxymethyl-1-carboxyl  propyl-1*H*-pyrrole-2-carbaldehyde | TP |  | +# |  | +# | + |
| **58** | 6.30 | [M+H]+ | 2.2 | C18H19NO4 | 314.1392 | 314.1399 |  | N-*trans*-Feruloyltyramine | AMB |  | +# | + |  |  |
| **59** | 6.37 | [M+H]+ | 1.1 | C51H84O23 | 1065.5482 | 1065.5494 | 903.4972,741.4409,579.3926,435.2789, 417.3370,399.3245,273.2225,255.2105 | Macrostemonoside A | AMB |  | + |  |  | +# |
| **60\*** | 6.50 | [M-H]- | 2.7 | C15H12O4 | 255.0657 | 255.0664 | 135.0079,119.0502,91.0193 | Liquiritigenin | TP |  | + |  | + | + |
| **61** | 6.74 | a[M+H]+ | -2.4 | C45H76O19 | 903.4953 | 903.4931 | 903.4931,741.4417,579.3902,417.3345, 273.2190,255.2113 | 25*S*-Macrostemonoside B-2glc | AMB |  | + |  |  | +# |
| **62\*** | 6.81 | [M-H]- | -1.4 | C15H10O6 | 285.0399 | 285.0395 | 133.0290, | Luteolin | TP |  | +# |  | +# | +# |
| **63** | 6.94 | [M+H]+ | -2.8 | C39H64O13 | 741.4425 | 741.4404 | 763.4183,741.4393,579.3889,417.3363, 399.3253,273.2218, 255.2110 | (3*β*,5*β*,25*S*)-26-Hydroxy-5-furost-20(22)-en-3-yl-2-*O*-*β*-D-glucopyranosyl-*β*-D-galactopyranoside | AMB |  |  |  |  | + |
| **64** | 7.12 | a[M+H]+ | 1.8 | C59H96O30 | 1267.5959 | 1267.5982 | 903.5028,739.4268,577.3722,415.3195, 271.2070, 253.1952 | 5(6)-ene-Macrostemonoside B+Ac | AMB |  |  |  |  | +# |
| **66** | 7.19 | [M-H]- | 1.2 | C21H24O9 | 419.1342 | 419.1347 | 839.2783,257.0818,136.0166,135.0084, 91.0173 | Davidigenin-glucoside | PRP |  |  |  |  | + |
| **67** | 7.21 | [M-H]- | 1.2 | C38H56O13 | 719.3643 | 719.3655 | 765.3688,719.3655,661.3564,575.2871, 499.3073,413.2327,165.0920 | Arvenin I | TP |  |  |  |  | + |
| **68** | 7.23 | a[M+H]+ | -0.4 | C59H98O30 | 1269.6116 | 1269.6111 | 1309.6035,1269.6111,1107.5753,903.4974, 741.4407,579.3884,435.2724,417.3361, 273.2204,255.2103 | Macrostemonoside B+Ac | AMB |  |  |  |  | +# |
| **69** | 7.98 | a[M+H]+ | -2.9 | C45H74O19 | 901.4797 | 901.4771 | 739.4247,577.3738,415.3172,273.2204, 255.2101 | 25(27)-ene-Macrostemonoside F | AMB |  |  |  |  | +# |
| **70** | 8.17 | [M+H]+ | -4.1 | C16H14O4 | 271.0970 | 271.0959 | 229.0866,177.0566,134.0364 | Medicarpin | PRP |  | + |  |  | + |
| **71\*** | 8.19 | [M-H]- | 0.4 | C15H10O5 | 269.0450 | 269.0451 | 225.0559 | Apigenin | TP |  | # |  | +# | +# |
| **72\*** | 8.44 | [M+H]+ | -1.5 | C45H74O18 | 903.4953 | 903.4953 | 903.4939,741.4401,579.3881, 417.3370,399.3248,273.2213,255.2107 | Timosaponin B III | AMB |  | +# | + |  | +# |
| **73** | 8.55 | a[M+H]+ | 1.1 | C45H76O19 | 903.4953 | 903.4953 | 925.4745,903.4963,741.4426,579.3903, 417.3380,399.3237, 273.2205,255.2107 | Macrostemonoside F | AMB |  |  |  |  | + |
| **74** | 8.57 | [M-H]- | -0.3 | C16H12O6 | 299.0556 | 299.0555 | 299.0555,284.0321,256.0370,255.0311, 227.0337 | Chrysoeriol | TP |  | +# |  | +# | +# |
| **75** | 8.76 | [M+H]+ | -1.5 | C57H94O28 | 1227.6010 | 1227.5991 | 1249.5847,1227.5991,1065.5457,903.4961, 741.4396,579.3899,435.2769,417.3360, 273.2213,255.2105 | 25*S*-Macrostemonoside E | AMB |  |  |  |  | +# |
| **76** | 8.81 | [M+H]+ | -3.3 | C42H62O17 | 839.4065 | 839.4037 | 663.3666,487.3366,469.3301,451.3246, | Licorice-saponin G2 | PRP |  | + |  | + | + |
| **77** | 8.92 | [M+H]+ | 0.9 | C57H94O28 | 1227.6010 | 1227.6021 | 1065.5436,903.4890,741.4409,579.3918, 435.2769,417.3373,273.2218,255.2123 | Macrostemonoside E | AMB |  |  |  |  | +# |
| **78** | 9.22 | [M+H]+ | -1.7 | C39H62O14 | 755.4218 | 755.4205 | 777.4086,755.4205,593.3707,431.3156, 413.3099,289.2182, 271.2072,253.1914 | Macrostemonoside S | AMB |  | +# | + | +# | +# |
| **79** | 9.32 | [M-H]- | -0.4 | C32H46O8 | 557.3114 | 557.3112 | 603.3151,557.3112,539.2996,515.3012, 497.2895,479.2788,443.2293,385.2383, 375.1836,327.2154 | Cucurbitacin B+COOH | TP |  | +# |  | +# |  |
| **80\*** | 9.42 | [M-H]- | 2.4 | C15H12O4 | 255.0657 | 255.0663 | 135.0086,119.0510,91.0185 | Isoliquiritigenin | PRP |  | + | + | + |  |
| **81** | 9.47 | [M+H]+ | -1.3 | C42H62O17 | 839.4065 | 839.4054 | 663.3761,487.3425,469.3314,451.3195 | Licorice-saponin G2 | PRP |  | + |  | + |  |
| **82** | 9.48 | [M+H]+ | -0.3 | C39H64O14 | 757.4374 | 757.4372 | 757.4372,595.3870,433.3331,415.3220, 271.2049,253.1948 | (25*R*)-12*β*-OH-Timosaponin A III | AMB |  | +# |  | +# | +# |
| **83** | 9.48 | [M+H]+ | 0.5 | C33H54O9 | 595.3846 | 595.3849 | 595.3849,577.3775,433.3314,415.3220, 271.2068,253.1952 | (25*S*)-Funkioside B | AMB |  | +# | + | +# | +# |
| **84** | 9.51 | [M-H]- | 0.7 | C32H46O8 | 557.3114 | 557.3118 | 603.3129,557.3118,539.3046,515.3024, 497.2901,479.2768,439.2500,351.0573, 239.1645 | Cucurbitacin B+COOH | TP |  | +# |  | + |  |
| **85** | 9.52 | [M-H]- | -0.8 | C18H32SO6 | 375.1841 | 375.1838 | 357.1743,295.2273,277.2180,263.0942, 195.1389,191.0742,183.1385,171.1025, 132.9963,79.9572 | unknown | PRP |  | + |  | + |  |
| **86** | 9.75 | [M+H]+ | -1.9 | C42H62O17 | 839.4065 | 839.4049 | 487.3439,469.3333,451.3217 | Licorice-saponin G2 | PRP |  | + |  | + |  |
| **86** | 10.05 | [M+H]+ | -0.1 | C42H62O17 | 839.4065 | 839.4064 | 487.3428,469.3316,451.3214 | Licorice-saponin G2 | PRP |  | + |  | + | + |
| **87** | 10.09 | a[M+H]+ | -2.4 | C33H56O9 | 579.3897 | 579.3882 | 619.3861,579.3883,417.3335,273.2228, 255.2112, | Asparagoside B | AMB |  |  | +# |  | +# |
| **88\*** | 10.14 | [M+H]+ | 0.1 | C42H62O16 | 823.4116 | 823.4117 | 647.3809,471.3470,453.3363,435.3272, 407.3307,389.3200 | 18 *β*-glycyrrhizic acid | PRP |  | + |  | + | + |
| **89** | 10.18 | [M+H]+ | -0.3 | C39H64O14 | 757.4374 | 757.4372 | 757.4372,595.3870,433.3331,415.3220, 271.2049,253.1948 | (25*R*)-2-OH-Timosaponin A III | AMB |  | +# |  | +# | +# |
| **90\*** | 10.95 | [M+H]+ | 1.3 | C42H62O16 | 823.4116 | 823.4127 | 845.4031,647.3775,453.3355,435.3266, 407.3294, | Uralasaponin B | PRP |  | + |  | + | + |
| **91** | 11.07 | [M-H]- | 2.7 | C15H14O4 | 257.0814 | 257.0820 | 257.0821,151.0396,135.0087 | Davidigenin | PRP |  | + | + | + | + |
| **92** | 11.12 | [M-H]- | -1.0 | C34H48O9 | 599.3220 | 599.3214 | 557.3115,539.3024,497.2876,411.2130 | Cucurbitacin B+Ac | TP |  |  | +# | +# |  |
| **93** | 11.24 | [M+H]+ | 0.0 | C42H62O16 | 823.4116 | 823.4116 | 453.3376,435.3271,407.3376 | Glycyrrhizic acid/Licorice-saponin H2 | PRP |  | + |  | + | + |
| **94** | 11.39 | [M-H]- | 0.7 | C34H48O9 | 599.3220 | 599.3224 | 645.3270,599.3224,557.3105,539.3000, 497.2898,479.2788,411.2164 | Cucurbitacin B+Ac | TP |  | +# | +# | +# |  |
| **95** | 11.78 | [M-H]- | 2.3 | C34H48O9 | 599.3220 | 599.3234 | 645.3295,599.3234,539.3011,497.2902, 479.2874,411.2180 | Cucurbitacin B+Ac | TP |  |  | +# | +# | +# |
| **96** | 11.95 | [M-H]- | 0.0 | C34H48O9 | 599.3220 | 599.3220 | 645.3234,599.3220,539.3023,497.2876, 479.2880,449.2370,411.2168 | Cucurbitacin B+Ac | TP |  |  |  | +# |  |
| **97\*** | 11.99 | b[M-H]- | -0.7 | C32H46O8 | 603.3169 | 603.3169 | 603.3165,557.3123,539.2966,497.2906, 479.2755,437.2649,411.2138,301.1462, 165.0934 | Cucurbitacin B | TP |  | +# | # | +# | +# |
| **98** | 13.08 | [M-H]- | -0.7 | C18H35NO2 | 298.2746 | 298.2744 | 280.2645 | Sphingadienine | PRP |  |  |  | + | + |
| **99** | 13.33 | [M-H]- | 3.0 | C18H35NO2 | 298.2746 | 298.2755 | 280.2647 | 4,8-Sphingadienine | PRP |  |  |  | + | + |
| **100\*** | 13.52 | [M+H]+ | 1.9 | C39H64O13 | 741.4425 | 741.4393 | 763.4183,741.4393,579.3889,417.3363, 399.3253,273.2218,255.2110 | (25*S*)-Timosaponin A III | AMB |  | + | + | + | +# |
| **101** | 13.52 | [M+H]+ | -1.7 | C33H54O8 | 579.3897 | 579.3887 | 417.3338,273.2225,255.2102 | Capsicoside A2 | AMB | + | +# | +# | +# | +# |
| **102\*** | 13.54 | [M+H]+ | -2.9 | C39H64O13 | 741.4425 | 741.4393 | 763.4183,741.4393,579.3889,417.3363, 399.3253,273.2218,255.2110 | (25*R*)-Timosaponin A III | AMB |  | + | + | +# | +# |
| **103\*** | 15.56 | [M+H]+ | -1.9 | C30H46O4 | 471.3474 | 471.3466 | 941.6872,493.3282,453.3376,319.2246, 235.1697,217.1590, 189.1632,175.1479, | Glycyrrhetic acid | PRP | + | + | + | + | + |

Note: a[M+H]+ meant [M+H-H2O]+; b[M-H]- meant [M-H+HCOOH]+; P, U, B, F, I meant plasma, urine, bile acid, feces and intestinal content, respectively; + meant prototypes detected in biological samples after orally administration of GXB; # meant prototypes detected in biological samples after orally administration of GXB-dePRP.

Table S2 The detailed information of metabolites characterized in bio-samples after dosed GXB and GXB-dePRP.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NO.** | **t*R*** | **selected ion** | **Mass error** | **Elemental composition** | **Calculated mass** | **Measured Mass** | **Fragmentation** | **Identification** | **Source** | **P** | **U** | **B** | **F** | **I** |
| **M1** | 1.88 | [M+H]+ | 0.5 | C10H16N2O3 | 213.1239 | 213.1240 | 195.1143,177.1010,165.1028,149.1074,135.0930 | Pedatisectine D+CH2 | PRP | **+#** |  |  |  | **+** |
| **M2** | 2.68 | [M-H]- | 3.4 | C16H14O7S | 349.0382 | 349.0394 | 269.0823,255.0662,135.0084,119.0510 | Liquirligenin+CH2+SO3 | PRP |  |  |  | **+** |  |
| **M3** | 3.51 | [M-H]- | 1.8 | C15H14O7S | 337.0382 | 337.0388 | 255.0660,135.0083,119.0494 | Liquirtigenin+2H+SO3 | PRP |  | **+** |  | **+** |  |
| **M4** | 3.93 | [M-H]- | 3.3 | C15H14O7S | 337.0382 | 337.0392 | 383.0430,257.0827,239.0712,137.0232,119.0501,91.0184 | Galangin+4H+SO3-O | PRP |  | **+** |  |  |  |
| **M5** | 4.14 | [M-H]- | -2.3 | C16H14O7S | 349.0382 | 349.0374 | 269.0836,267.0659,255.0664,135.0090,133.0647,119.0497 | Liquirligenin+CH2(B) +SO3 | PRP |  |  |  | **+** |  |
| **M6** | 4.33 | [M-H]- | -3.2 | C21H20O10 | 431.0966 | 431.0978 | 255.0651,135.0081,119.0496 | Liquirtigenin-7-O-gluA | PRP | **+** |  |  |  | **+** |
| **M7** | 4.42 | [M-H]- | -0.9 | C21H20O10 | 431.0966 | 431.0974 | 255.0651,135.0095,119.0502 | Liquirtigenin-4'-O-gluA | PRP | **+** | **+** |  |  |  |
| **M8** | 4.81 | [M-H]- | 1.6 | C15H10O9S | 364.9967 | 364.9976 | 285.0406,151.0050, | Kaempferol+SO3 | TP |  |  |  | **+#** | **+#** |
| **M9** | 4.88 | [M-H]- | -1.2 | C15H12O7S | 335.0225 | 335.0221 | 255.0659,135.0076,119.0503,91.0183 | Liquirtigenin+SO3 | PRP |  | **+** |  |  | **+** |
| **M10** | 5.04 | [M-H]- | 0.2 | C21H18O11 | 445.0771 | 445.0773 | 891.1609,269.0448 | Apigenin-7-O-GluA | TP |  |  | **+#** |  | **+#** |
| **M11** | 5.07 | [M-H]- | 3.6 | C15H12O7S | 335.0225 | 335.0237 | 255.0669,135.0098,119.0509 | Liquirtigenin+SO3 | PRP |  |  | **+** |  | **+#** |
| **M12** | 5.13 | [M-H]- | -2.7 | C15H12O7S | 335.0225 | 335.0216 | 255.0652,135.0094,119.0509,91.0194 | Liquirtigenin+SO3 | PRP |  | **+** |  |  |  |
| **M13** | 5.30 | [M-H]- | 3.0 | C21H18O12 | 461.0720 | 461.0734 | 285.0410 | Luteoline-3’-O-gluA | TP |  | **+#** |  |  | **+#** |
| **M14** | 5.40 | [M-H]- | 0.3 | C15H10O9S | 364.9967 | 364.9968 | 285.0402 | Luteolin+SO3 | TP |  | **+#** |  |  |  |
| **M15** | 5.48 | [M-H]- | 0.4 | C16H14O5 | 285.0763 | 285.0763 | 267.0658,255.0666,135.0093,119.0506 | Liquirligenin+OCH2 | PRP |  | **+#** |  |  |  |
| **M16** | 5.84 | [M-H]- | 0.9 | C15H16O6S | 323.0589 | 323.0592 | 243.1005,119.0506 | Galangin+SO3+4H-2O | PRP |  |  |  | **+** |  |
| **M17** | 5.84 | [M-H]- | -1.4 | C21H22O10 | 433.1135 | 433.1129 | 257.0811,151.0380 | Liquirtigenin+2H+gluA | PRP | **+** |  |  |  |  |
| **M18** | 5.96 | [M-H]- | -1.6 | C15H10O4 | 253.0501 | 253.0497 | 225.0533,197.0610,135.0098,117.0335 | Luteoline-2O(A,B) | TP |  | **+#** |  | **+** |  |
| **M19** | 5.97 | [M-H]- | -1.8 | C21H22O10 | 433.1135 | 433.1127 | 257.0801,151.0361,135.0074,119.0493 | Liquirtigenin+2H+gluA | PRP | **+** | **+** |  |  |  |
| **M20** | 6.03 | a[M+H]+ | 3.1 | C39H64O14 | 739.4269 | 739.4233 | 739.4233,577.3741,415.3203,271.2051,253.1950 | Timosaponin B II-glc-2H | AMB |  |  |  |  | **+#** |
| **M21** | 6.09 | [M-H]- | -0.7 | C21H20O10 | 431.0966 | 431.0975 | 255.0663,135.0061,119.0507 | Liquirtigenin+gluA | PRP | **+** |  |  |  |  |
| **M22** | 6.11 | [M-H]- | -1.1 | C15H10O9S | 364.9992 | 364.9988 | 285.0399,253.0508,225.0552,135.0083,133.0293,119.0491 | Luteoline+SO3 | TP |  | **+#** |  |  |  |
| **M23** | 6.27 | [M-H]- | -1.2 | C15H14O7S | 337.0382 | 337.0378 | 257.0816,151.0393,135.0082 | Davidigenin+SO3 | PRP |  |  |  | **+#** |  |
| **M24** | 6.30 | [M-H]- | -1.6 | C16H14O9S | 381.0280 | 381.0274 | 301.0712,151.0022,149.0601 | Cherysoeriol+2H+SO3 | TP |  | **+#** |  |  |  |
| **M25** | 6.31 | [M-H]- | -1.8 | C16H12O9S | 379.0124 | 379.0117 | 299.0555,284.0318,256.0375 | Chrysoeriol+SO3 | TP |  |  |  | **+#** |  |
| **M26** | 6.44 | [M-H]- | -0.3 | C15H14O7S | 337.0382 | 337.0381 | 257.0801,151.0392,135.0085,119.0505,91.0178 | Isoliquiritigenin+2H  +SO3 | PRP |  | **+** |  |  |  |
| **M27** | 6.50 | [M-H]- | 1.3 | C16H12O9S | 379.0124 | 379.0129 | 299.0550,284.0320,255.0668,227.0332 | Chrysoeriol+SO3 | TP |  | **+#** |  |  |  |
| **M28** | 6.62 | [M-H]- | -1.5 | C15H14O7S | 337.0382 | 337.0378 | 257.0817,151.0392 | Liquirligenin+2H+SO3 | PRP |  |  |  | **+** |  |
| **M29** | 6.64 | [M-H]- | -2.9 | C32H50O8 | 561.3427 | 561.3411 | 607.3401,501.3229, | Cucurbitacin B+2H2 | TP |  |  |  | **+#** | **+** |
| **M30** | 7.30 | [M-H]- | 0.2 | C21H22O10 | 433.1135 | 433.1136 | 257.0823,135.0095,121.0658 | Liquirtigenin+2H+gluA | PRP |  |  | **+** |  | **+** |
| **M31** | 7.35 | [M-H]- | -1.4 | C21H22O10 | 433.1135 | 433.1129 | 257.0811,151.0380 | Liquirtigenin+2H+gluA | PRP | **+** |  |  |  |  |
| **M32** | 7.38 | [M+H]+ | -0.3 | C39H60O14 | 753.4061 | 753.4069 | 591.3518,429.3005,411.2880,299.2380,287.2018,269.1922 | 25(27)-ene  -elephanoside H | AMB |  |  |  | **+#** | **+#** |
| **M33** | 7.53 | [M-H]- | 1.2 | C14H12O4 | 243.0657 | 243.0660 | 227.0557,199.0762,149.0240,135.0085 | Galangin+2H-CO | PRP |  | **+** |  |  |  |
| **M34** | 7.54 | [M+H]+ | -1.8 | C39H62O13 | 739.4269 | 739.4256 | 577.3730,415.3172,273.2219,255.2097 | Timosaponin BII-H2O  -glc-2H | AMB |  |  |  | **+#** | **+#** |
| **M35** | 7.83 | [M-H]- | 0.7 | C32H50O8 | 561.3427 | 561.3431 | 607.3495,501.3207,483.3122,165.0916 | Cucurbitacin B+2H2 | TP |  | **+#** |  | **+#** | **+#** |
| **M36** | 8.05 | [M+H]+ | -3.2 | C30H46O8S | 567.2992 | 567.2974 | 487.3438,469.3340, | Glycyrrhetic acid+O  +SO3 | RPR |  |  |  | **+** |  |
| **M37** | 8.09 | [M-H]- | -1.4 | C32H48O9 | 575.3220 | 575.3212 | 621.3274,557.3129,515.2982,497.2916,411.2128,165.0925 | Cucurbitacin B+H2O | TP |  | **+#** |  | **+#** |  |
| **M38** | 8.09 | [M-H]- | 3.7 | C15H12O5 | 271.0606 | 271.0616 | 151.0045,119.0484, | Liquirligenin+O(A) | PRP |  | **+** |  |  |  |
| **M39** | 8.14 | [M-H]- | 1.8 | C15H14O5 | 273.0763 | 273.0768 | 258.0533,135.0086 | Naringenin+2H | PRP |  | **+** |  |  |  |
| **M40** | 8.39 | [M+H]+ | -1.6 | C39H64O14 | 757.4374 | 757.4362 | 585.3055,433.3346,289.2177,271.2062,253.1951, | 25R-12β-OH  -timosaponin AIII | AMB |  |  |  | **+#** |  |
| **M41** | 8.43 | [M-H]- | 1.4 | C32H46O11S | 637.2683 | 637.2692 | 577.2462,557.3090,497.2917,479.2754,411.2141,165.0936 | Cucurbitacin B+SO3 | AMB |  |  |  | **+#** |  |
| **M42** | 8.73 | [M+H]+ | 1.0 | C30H46O9S | 583.2941 | 583.2947 | 503.3381,485.3253,467.3139 | Glycyrrhetic acid+2O  +SO3 | PRP |  |  |  | **+** |  |
| **M43** | 8.75 | [M+H]+ | 1.7 | C27H44O6 | 465.3224 | 465.3216 | 433.3318,289.2175,271.2013,253.1962 | Smilagenin+3O | AMB |  |  |  | **+#** |  |
| **M44** | 8.81 | [M-H]- | 0.6 | C16H12O7 | 315.0505 | 315.0507 | 299.0567,151.0045 | Quercetin +CH2 | TP |  | **+#** |  |  |  |
| **M45** | 8.84 | [M-H]- | -2.5 | C32H46O11S | 637.2683 | 637.2667 | 577.2460,557.3124,497.2927,479.2758,411.2145,165.0933 | Cucurbitacin B+SO3 | TP |  |  |  | **+#** |  |
| **M46** | 8.97 | [M-H]- | -0.3 | C32H46O11S | 637.2683 | 637.2681 | 577.2485,557.3114,497.2910,479.2753 | Cucurbitacin B+SO3 | TP |  |  |  | **+#** |  |
| **M47** | 9.00 | [M+H]+ | 1.7 | C27H44O6 | 465.3216 | 465.3224 |  | Smilagenin+3O | AMB |  |  |  | **+#** |  |
| **M48** | 9.10 | [M-H]- | 2.7 | C15H14O4 | 257.0814 | 257.0814 | 257.0821,151.0396,135.0087 | Davidigenin isomer | PRP |  | **+** |  | **+** |  |
| **M49** | 9.28 | [M-H]- | -1.0 | C38H54O14 | 733.3435 | 733.3428 | 557.3115,497.2909,479.2788,411.2147,165.0930 | Cucurbitacin B+gluA | TP |  | **+#** |  |  | **+#** |
| **M50** | 9.38 | [M+H]+ | -3.0 | C27H44O6 | 465.3216 | 465.3202 | 447.3113,433.3306,429.2999,415.3203,271.2064,253.1961 | Smilagenin+3O | AMB |  |  |  | **+#** |  |
| **M51** | 9.45 | [M+H]+ | -1.8 | C36H54O11 | 663.3744 | 663.3732 | 487.3403, | Glycyrrhetic acid+O +gluA | PRP |  |  | **+** |  | **+** |
| **M52** | 9.64 | [M+H]+ | -3.3 | C39H64O14 | 757.4374 | 757.4349 | 595.3857,433.3319,415.3203,397.3115,379.3008,271.2055,253.1953 | 25R-12β-OH  -timosaponin AIII | AMB |  |  |  | **+#** | **+#** |
| **M53** | 9.67 | [M+H]+ | -1.8 | C36H54O11 | 663.3744 | 663.3732 | 487.3404, | Glycyrrhetic acid+O +gluA | PRP |  |  | **+** |  | **+** |
| **M54** | 9.88 | [M+H]+ | 3.0 | C30H46O8S | 567.2992 | 567.3009 |  | Glycyrrheticacid+O+SO3 | PRP |  |  |  | **+** |  |
| **M55** | 10.01 | [M-H]- | 1.1 | C15H12O5 | 271.0606 | 271.0609 | 256.0361,243.0643,227.0706,135.0081 | Liquirligenin+O(B) | PRP |  | **+** |  |  |  |
| **M56** | 10.04 | [M+H]+ | 0.0 | C39H62O14 | 755.4218 | 755.4218 | 777.4044,593.3691,431.3130,413.30547,395.2971,289.2156,271.2055,253.1937 | Macrostemonoside G  -H2O-glc | AMB |  |  |  | **+#** |  |
| **M57** | 10.10 | [M-H]- | 1.1 | C32H46O8 | 557.3114 | 557.3120 | 601.3171,539.2952,515.2989,497.2911,479.2777, | Cucurbitacin B isomer | TP |  |  |  | **+#** |  |
| **M58** | 10.10 | [M+H]+ | 0.0 | C33H50O9 | 591.3533 | 591.3533 | 591.3526,429.2997,411.2884,269.1903,251.1790 | 25(27)-ene  -Elephanoside H-glc | AMB |  |  |  | **+#** | **+#** |
| **M59** | 10.14 | [M-H]- | -0.2 | C32H44O8 | 555.2958 | 555.2957 | 537.2857,513.2863,495.2761,477.2633,453.2578,437.2344,411.2159,163.0750 | Cucurbitacin B-H2(A) | TP |  |  |  | **+** |  |
| **M60** | 10.21 | [M+H]+ | -2.0 | C39H64O14 | 757.4374 | 757.4359 | 595.3842,433.3311,415.3206,271.2070,253.1950 | 25R-12β-OH-Timosaponin AIII | AMB |  |  |  | **+#** | **+#** |
| **M61** | 10.33 | [M+H]+ | 0.2 | C33H52O10 | 609.3639 | 609.3640 |  | Timosaponin BII-2glc-gal-2H+gluA | AMB |  |  |  |  | **+#** |
| **M62** | 10.33 | [M+H]+ | -2.4 | C33H52O11 | 625.3588 | 625.3573 | 647.3405,625.3573,607.3453,589.3362,449.3264,431.3148,413.3043,271.2071,253.1960 | Timosaponin BII-2glc-gal-2H+OH+gluA | AMB |  |  | **+#** |  | **+#** |
| **M63** | 10.36 | a[M+H]+ | -0.4 | C27H46SO7 | 497.2935 | 497.2935 | 515.3049,497.2935,479.2827,417.3352,399.3265,271.2079,253.1971 | Smilagenin+SO3 | AMB |  |  | **+** |  |  |
| **M64** | 10.40 | [M+H]+ | -0.4 | C30H46O8S | 567.2992 | 567.2990 | 589.2829,487.3417,441.3376 | Glycyrrhetic acid+O  +SO3 | PRP |  |  |  | **+** | **+** |
| **M65** | 10.41 | [M+H]+ | 0.6 | C36H54O11 | 663.3744 | 663.3748 | 685.3568,487.3414,469.3320,441.3358,423.3276,405.3162, | Glycyrrhetic acid+O +gluA | PRP |  |  | **+** |  | **+** |
| **M66** | 10.47 | [M+H]+ | 2.3 | C30H46O8S | 567.2992 | 567.3005 |  | Glycyrrhetic acid+O +SO3 | PRP |  | **+** |  |  | **+** |
| **M67** | 10.50 | [M+H]+ | 0.6 | C27H44O6 | 465.3216 | 465.3219 | 447.3109,429.2995,411.2893,393.2799,375.2687,271.2067,253.1981, | Smilagenin+3O | AMB |  |  |  | **+#** | **+** |
| **M68** | 10.58 | [M+H]+ | -3.7 | C30H46O8S | 567.2992 | 567.2971 | 487.3401,469.3339,441.3381,405.3149 | Glycyrrhetic acid+O +SO3 | PRP |  |  |  | **+** |  |
| **M70** | 10.63 | [M+H]+ | 3.0 | C30H46O8S | 567.2992 | 567.3009 | 487.3401,469.3339,441.3381,405.3149 | Glycyrrhetic acid+O +SO3 | PRP |  | **+** |  |  |  |
| **M71** | 10.69 | [M+H]+ | 8.0 | C30H46O6 | 503.3373 | 503.3373 | 485.3272,469.3326,467.3153,457.3335,449.3036 | Glycyrrhetic acid+2O | PRP |  |  | **+** | **+** | **+** |
| **M72** | 10.87 | [M+H]+ | -1.0 | C39H64O15 | 773.4323 | 773.4315 | 795.4267,773.4315,611.3808,449.3283,431.3155,413.3053,287.1989,269.1931 | 25R-macrostemonoside I-glc | AMB |  |  |  | **+#** | **+#** |
| **M73** | 10.88 | a[M+H]+ | -0.4 | C39H64O14 | 739.4269 | 739.4269 | 779.4202,739.4268,577.3735,415.3243,271.2139,253.1904 | Timosaponin BII -glc-2H | AMB |  |  |  | **+#** | **+#** |
| **M74** | 11.14 | [M-H]- | 1.8 | C16H12O5 | 285.0763 | 285.0768 |  | Galangin+CH2 | PRP |  |  |  | **+** |  |
| **M75** | 11.27 | [M+H]+ | -1.2 | C27H44SO7 | 513.2886 | 513.2880 | 495.2770,433.3348,353.1787, 273.2234,255.2103 | Smilagenin+OH+SO3 | AMB |  |  | **+** |  | **+** |
| **M76** | 11.30 | [M+H]+ | -1.1 | C27H44O6 | 465.3216 | 465.3211 | 447.3105,429.2994,411.2891,271.2005,253.1909 | Smilagenin+3O | AMB |  |  |  | **+#** | **#** |
| **M77** | 11.31 | [M+H]+ | -2.4 | C33H52O11 | 625.3588 | 625.3573 | 647.3389,607.3489,589.3369,571.3248,449.3243,431.3177,413.3044,271.2055,253.1948 | Timosaponin BII-2glc-gal-2H+OH+gluA | AMB |  |  | **+#** |  | **+#** |
| **M78** | 11.40 | [M+H]+ | 3.1 | C30H46O8S | 567.2992 | 567.2985 | 487.3409 | Glycyrrhetic acid+O  +SO3 | PRP |  |  |  | **+** | **+** |
| **M79** | 11.54 | [M+H]+ | 1.5 | C36H52O11 | 661.3588 | 661.3598 | 683.3588,485.3274,467.3162,439.3222,421.2112,217.1594 | Glycyrrhetic acid+O  -2H+gluA | PRP |  |  | **+** |  | **+** |
| **M80** | 11.75 | [M+H]+ | 0.9 | C51H82O24 | 1079.5274 | 1079.5284 | 1101.5101,917.4727,755.4224,593.3675,  431.3163,413.3078,289.2168,271.2064 | Borivilianoside G | AMB |  |  |  | **+** | **+** |
| **M81** | 11.75 | [M+H]+ | 0.2 | C30H46O5 | 487.3423 | 487.3424 | 441.3354,423.3270, | Glycyrrhetic acid+O | PRP |  |  | **+** | **+** | **+** |
| **M82** | 12.01 | [M+H]+ | 1.4 | C36H54O11 | 663.3744 | 663.3753 | 487.3412,441.3388,423.3289,405.3163 | Glycyrrhetic acid+O +gluA | PRP |  |  | **+** |  | **+** |
| **M83** | 12.16 | [M+H]+ | -0.6 | C27H44SO6 | 497.2934 | 497.2935 | 417.3368,399.3259 | Smilagenin+SO3 | AMB |  |  | **+** |  |  |
| **M84** | 12.19 | [M+H]+ | -2.7 | C27H44SO7 | 513.2872 | 513.2886 | 433.3311,417.3380 | Smilagenin+O+SO3 | AMB |  |  | **+** |  | **+#** |
| **M85** | 12.22 | [M+H]+ | -3.7 | C51H84O24 | 1081.5431 | 1081.5391 | 1103.5238,919.4918,757.4353,595.3833,433.3319,415.3210,289.2166,271.2054,253.1995, | 2α-OH-Macrostemonoside A | AMB |  |  |  | **+#** | **+#** |
| **M86** | 12.37 | [M+H]+ | -0.5 | C39H64O14 | 757.4374 | 757.4370 | 779.4086,757.4370,595.3770,431.3141,415.3201,289.2123, 271.2054,253.1995 | 25R-12-OH-timosaponin AIII isomer | AMB |  |  |  | **+#** | **+#** |
| **M87** | 12.38 | [M+H]+ | -2.3 | C33H52O10 | 609.3639 | 609.3625 | 433.3209, | Timosaponin BII-2glc-gal-2H+gluA | AMB |  |  | **#** |  | **+#** |
| **M88** | 12.47 | [M-H]- | 3.5 | C34H48O9 | 599.3220 | 599.3241 | 645.3270,581.3129,557.3137,539.3017,479.2776, | Cucurbitacin B+C2H2O | TP |  |  |  | **+#** |  |
| **M89** | 12.51 | [M+H]+ | -2.9 | C27H44SO7 | 513.2871 | 513.2880 | 271.2052,253.1973 | Smilagenin+OH+SO3 | AMB |  |  | **+#** |  | **+** |
| **M90** | 12.53 | [M+H]+ | 0.2 | C45H74O19 | 919.4903 | 919.4905 | 941.4702,919.4893,757.4398, 595.3868,433.3305,415.3224,289.2166,271.2068, 253.1965 | 2α-OH-Macrostemonoside A-glc | AMB |  |  |  | **+#** | **+#** |
| **M91** | 12.53 | [M+H]+ | 1.0 | C33H52O10 | 609.3645 | 609.3625 | 591.3524,449.2560,415.3130,397.3036,273.2218, 255.2099 | Timosaponin BII-2glc-gal-2H+gluA | AMB |  |  | **#** |  | **+#** |
| **M92** | 12.70 | [M+H]+ | -3.1 | C33H50O10 | 607.3482 | 607.3463 | 431.3165,413.3065,289.2113, 271.2055 | Macrostemonoside G-H2O-2glc-gal+gluA | AMB |  |  | **+#** |  | **+#** |
| **M93** | 12.88 | [M+H]+ | -0.1 | C39H64O13 | 741.4425 | 741.4424 | 763.4240,741.4407,579.3887,417.3368,399.3277,273.2240,255.2112 | Timosaponin BII-H2O-glc | AMB |  |  | **+** | **+#** | **+#** |
| **M94** | 12.93 | [M+H]+ | -1.6 | C39H62O13 | 739.4269 | 739.4257 | 761.4083,577.3745,415.3192,397.3088,273.2221,255.2109 | Timosaponin BII -glc-2H | AMB |  |  |  | **+#** | **+#** |
| **M95** | 12.93 | a[M+H]+ | 0.8 | C63H106O34 | 1389.6549 | 1389.6549 | 1411.6337,1065.5466,903.4935,741.4400,  579.3906,417.3333,273.2229,255.2112 | Capsicoside G | AMB |  |  |  | **+#** | **+#** |
| **M96** | 12.95 | a[M+H]+ | 0.5 | C27H46O6 | 449.3267 | 449.3269 | 471.3068,431.3164,413.3027,271.2069,253.1953 | Macrostemonoside G-2glc-gal | AMB | **+#** |  |  |  | **+#** |
| **M97** | 12.97 | [M+H]+ | 2.7 | C30H46O5 | 487.3423 | 487.3436 | 441.3345,423.3282, | Glycyrrhetic acid+O | PRP |  |  | **+** | **+** | **+** |
| **M98** | 13.00 | [M+H]+ | -2.7 | C27H44O5 | 449.3267 | 449.3255 | 433.3310,417.3392,399.3284,273.2218,255.2103 | Smilagenin+2O | AMB |  |  |  | **+#** |  |
| **M99** | 13.06 | [M+H]+ | 0.0 | C30H44O5 | 485.3267 | 485.3267 | 467.3190,421.3102 | Glycyrrhetic acid+O-H2 | PRP |  |  | **+** |  |  |
| **M100** | 13.24 | [M+H]+ | -1.4 | C36H54O10 | 647.3795 | 647.3786 | 669.3600,471.3449,453.3349 | Glycyrrhetic acid+gluA | PRP |  |  |  | **+** | **+** |
| **M101** | 13.42 | a[M+H]+ | -3.5 | C27H46O6 | 449.3267 | 449.3251 | 271.2051,253.1953 | Macrostemonoside G-2glc-gal-2 | AMB | **+#** |  |  |  | **+#** |
| **M102** | 13.42 | [M+H]+ | -2.5 | C36H54O10 | 647.3795 | 647.3779 | 1293.7510,669.3607,471.3473,425.3413,407.3319,389.3219,217.1596, | Glycyrrhetic acid+gluA | PRP | **+** |  | **+** |  |  |
| **M103** | 13.45 | [M+H]+ | 0.5 | C39H64O13 | 741.4425 | 741.4429 | 579.3874,417.3372,273.2241,255.2111 | Macrostemonoside B-H2O-3glc | AMB |  |  |  | **+#** | **+#** |
| **M104** | 13.47 | a[M+H]+ | 2.0 | C27H46O6 | 449.3267 | 449.3276 | 271.2074,253.1966 | Macrostemonoside G-2glc-gal-3 | AMB | **+#** |  |  | **+#** | **+#** |
| **M105** | 13.72 | [M+H]+ | -1.0 | C33H52O10 | 609.3645 | 609.3633 |  | Timosaponin BII-2glc-gal-2H+gluA | AMB |  |  | **#** |  | **+#** |
| **M106** | 13.84 | [M+H]+ | 0.0 | C36H54O10 | 647.3795 | 647.3795 | 1293.7588,669.3602,471.3495,407.3331 | Glycyrrhetic acid+gluA | PRP |  |  | **+** |  | **+** |
| **M107** | 13.88 | [M+H]+ | 2.9 | C30H46O5 | 487.3423 | 487.3437 | 469.3312,441.3372,373.2743,317.2481,217.1594,189.1276 | Glycyrrhetic acid+O(A) | PRP | **+** |  |  | **+** | **+** |
| **M108** | 14.06 | [M+H]+ | 2.2 | C33H54O8 | 579.3897 | 579.3910 | 417.3374,399.3267,273.2221,255.2139 | Capsicoside A2 | AMB |  |  |  | **+** |  |
| **M109** | 14.20 | [M+H]+ | 3.1 | C30H46O5 | 487.3423 | 487.3438 | 469.3328,451.3232,441.3372,423.3227,315.2324,233.1535,215.1443,189.1640 | Glycyrrhetic acid+O(B) | PRP | **+** |  | **+** | **+** | **+** |
| **M110** | 14.21 | [M+H]+ | -2.6 | C33H54O8 | 579.3897 | 579.3892 | 417.3358,399.3246,273.2226,255.2129 | Smilagenin+glc/gal | AMB |  |  |  | **+** |  |
| **M111** | 14.39 | [M+H]+ | 2.7 | C30H46O7S | 551.3042 | 551.3057 |  | Glycyrrhetic acid+SO3 | PRP |  |  |  | **+** |  |
| **M112** | 14.41 | [M+H]+ | -2.3 | C39H64O13 | 741.4425 | 741.4408 | 763.4225,741.4412,579.3898,417.3367,399.3264,273.2218,255.2113 | Smilagenin+gal+glc | AMB |  |  |  | **+#** |  |
| **M113** | 14.68 | [M+H]+ | 1.9 | C30H44O5 | 485.3267 | 485.3276 | 467.3169,449.3066 | Glycyrrhetic acid+O-H2 | PRP |  |  |  | **+** | **+** |
| **M114** | 14.82 | [M+H]+ | 2.1 | C39H64O13 | 741.4425 | 741.4408 | 763.4225,741.4412,579.3898,417.3367,399.3264,273.2218,255.2113 | Smilagenin+glc+gal | AMB |  |  |  | **+#** | **+#** |
| **M115** | 15.12 | [M+H]+ | -1.5 | C30H44O4 | 469.3318 | 469.3311 |  | Glycyrrhetic acid-2H | PRP |  |  |  | **+** |  |
| **M116** | 15.23 | [M+H]+ | -2.8 | C27H44O4 | 433.3318 | 433.3306 |  | Smilagenin+O | AMB |  |  |  | **+#** |  |
| **M117** | 15.40 | [M+H]+ | 2.9 | C33H54O8 | 579.3897 | 579.3914 | 601.3690,561.3758,417.3363,399.3266,273.2202,255.2129 | Smilagenin+glc/gal | AMB |  |  | **+#** | **+#** | **+#** |

Note: P, U, B, F, I meant the metabolites detected in rat plasma, urine, bile, feces, intestine content, respectively. +, # meant the metabolites observed in rat bio-samples after dosed GXB, GXB-dePRP, respectively. (A), (B) meant the adduct moiety was preliminarily supposed to be in A ring or B ring. gal, glc, gluA meant galactose, glucose, glucuronic acid, respectively.

Table S3 The linear ranges and regression equations for 5 quantitative components (n=3)

|  |  |  |  |
| --- | --- | --- | --- |
| Analytes | Range (ng/mL) | Linear regression (n=3) | Coefficient (r) |
| Lol | 0.05 ~ 18.00 | y=4.876880x + 0.14715000 | 0.9978 |
| Tpica | 0.22 ~ 70.00 | y=0.418601x + 0.04475530 | 0.9981 |
| TB II | 0.22 ~ 69.60 | y=0.199752x - 0.00659660 | 0.9982 |
| MB | 1.47 ~ 471.20 | y=0.025086x - 0.03047190 | 0.9960 |
| Gly | 0.50 ~ 158.62 | y=0.112137x + 0.00296832 | 0.9980 |

Note：Lol- (-)-loliolide；Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid；TB II- (25R)-timosaponin B II；MB-macrostemonoside B；Gly-glycyrrhetic acid.

Table S4 The LLOQs of 5 analytes in rat plasma (n=6)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Analytes | Con.  (ng/mL) | Detected Con.  (ng/mL, mean ± SD) | RSD (%) | RE (%) |
| Lol | 0.05 | 0.05 ± 0.01 | 15.1 | -0.9 |
| Tpica | 0.22 | 0.20 ± 0.02 | 12.1 | -9.0 |
| TB II | 0.22 | 0.25 ± 0.02 | 8.6 | 12.9 |
| MB | 1.47 | 1.50 ± 0.13 | 8.0 | 2.3 |
| Gly | 0.50 | 0.51 ± 0.09 | 17.2 | 1.1 |

Note: Lol- (-)-loliolide; Tpica-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid; TB II-(25R)-timosaponin B II; MB-macrostemonoside B; Gly-glycyrrhetic acid.

Table S5 The accuracies and inter/intra-day precisions of 5 analytes in rat plasma (n=6)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analytes | Spiked.  (ng/mL) | Inter-day (n=18) | | |  | Intra-day (n=6) | | |
| Calculated Con.(ng/mL) | Precision (RSD, %) | Accuracy (RE, %) |  | Calculated Con. (ng/mL) | Precision (RSD, %) | Accuracy (RE, %) |
| Lol | 0.05 | 0.05 ± 0.01 | 16.2 | -15.8 |  | 0.05 ± 0.01 | 14.8 | -6.1 |
|  | 0.11 | 0.11 ± 0.01 | 10.3 | -1.8 |  | 0.11 ± 0.05 | 9.9 | -0.6 |
|  | 7.20 | 6.35 ± 0.51 | 8.1 | -11.8 |  | 6.30 ± 0.49 | 7.8 | -12.5 |
|  | 14.40 | 12.20 ± 0.80 | 6.6 | -15.0 |  | 13.28 ± 1.30 | 9.8 | -7.7 |
| Tpica | 0.22 | 0.22 ± 0.03 | 15.6 | 1.1 |  | 0.21 ± 0.03 | 14.8 | -3.3 |
|  | 0.44 | 0.39 ± 0.04 | 11.0 | -10.5 |  | 0.39 ± 0.06 | 14.5 | -11.9 |
|  | 28.00 | 24.06 ± 1.92 | 8.0 | -14.1 |  | 24.15 ± 1.75 | 7.3 | -13.7 |
|  | 56.00 | 48.22 ± 1.29 | 2.7 | 13.9 |  | 51.48 ± 4.52 | 8.8 | -8.1 |
| TBII | 0.22 | 0.21 ± 0.02 | 11.2 | -2.1 |  | 0.24 ± 0.03 | 14.2 | 10.9 |
|  | 0.44 | 0.42 ± 0.06 | 14.8 | -4.4 |  | 0.47 ± 0.07 | 14.9 | 7.3 |
|  | 27.84 | 24.26 ± 1.59 | 6.6 | -13.2 |  | 25.09 ± 2.04 | 8.1 | -9.9 |
|  | 55.68 | 49.87 ± 4.11 | 8.3 | -10.4 |  | 51.6 ± 4.38 | 8.5 | -7.3 |
| MB | 1.47 | 1.53 ± 0.15 | 10.0 | 3.6 |  | 1.45 ± 0.21 | 14.4 | -1.4 |
|  | 2.94 | 3.11± 0.33 | 10.5 | 5.7 |  | 3.25 ± 0.42 | 12.9 | 10.6 |
|  | 188.48 | 173.28 ± 15.25 | 8.8 | -8.1 |  | 171.49 ± 13.16 | 7.7 | -9.0 |
|  | 376.96 | 372.59 ± 29.47 | 7.9 | -1.2 |  | 360.88 ± 25.57 | 7.1 | -4.3 |
| Gly | 0.50 | 0.44 ± 0.08 | 17.2 | -11.1 |  | 0.53 ± 0.09 | 17.8 | 7.3 |
|  | 0.99 | 1.03 ± 0.41 | 13.4 | 4.2 |  | 1.06 ± 0.13 | 12.1 | 6.7 |
|  | 63.45 | 64.04 ± 4.53 | 7.1 | 0.9 |  | 62.33 ± 4.48 | 7.2 | -1.8 |
|  | 126.90 | 109.35 ± 8.69 | 7.9 | -13.8 |  | 109.25 ± 13.97 | 12.8 | -13.9 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; TB II-(25*R*)-timosaponin B II; MB-macrostemonoside B; Gly-glycyrrhetic acid.

Table S6 The matrix effects and extraction recoveries of 5 analytes and IS in rat plasma (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Analytes | Con.  (ng/mL) | Matrix effect | | Recovery | |
| Average (%) | RSD (%) | Average (%) | RSD (%) |
| Lol | 0.11 | 109.7 | 12.3 | 98.3 | 12.3 |
|  | 7.20 | 88.6 | 6.6 | 73.9 | 6.0 |
|  | 14.4 | 87.5 | 11.6 | 78.2 | 9.2 |
| Tpica | 0.44 | 112.3 | 13.9 | 96.6 | 11.0 |
|  | 28.00 | 86.6 | 3.4 | 78.7 | 11.2 |
|  | 56.00 | 87.4 | 5.9 | 73.8 | 11.9 |
| TB II | 0.44 | 99.8 | 5.6 | 89.5 | 11.7 |
|  | 27.84 | 95.0 | 10.2 | 83.0 | 8.9 |
|  | 55.68 | 93.6 | 11.0 | 79.9 | 7.7 |
| MB | 2.94 | 97.1 | 6.4 | 83.1 | 10.1 |
|  | 188.48 | 94.4 | 9.2 | 78.6 | 7.0 |
|  | 376.96 | 99.6 | 9.1 | 72.9 | 10.4 |
| Gly | 0.99 | 87.2 | 12.5 | 28.5 | 12.3 |
|  | 63.45 | 91.3 | 10.0 | 50.4 | 9.7 |
|  | 126.90 | 88.5 | 8.2 | 49.9 | 12.0 |
| DSMS(IS) | 100.00 | 87.1 | 8.4 | 89.1 | 5.8 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid; TB II-(25R)-timosaponin B II; MB-macrostemonoside B; Gly-glycyrrhetic acid.

Table S7 Stabilities of 5 quantitative components in three different conditions

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analytes | Spiked.  (ng/mL) | Room temperature for 12 h (n=6) | | |  | Three freeze-thaw cycle (n=6) | | |  | -80 °C for a month (n=6) | | |
| Calculated Con.  (ng/mL) | Precision  (RSD, %) | Accuracy  (RE, %) |  | Calculated Con. (ng/mL) | Precision  (RSD, %) | Accuracy  (RE, %) |  | Calculated Con.  (ng/mL) | Precision  (RSD, %) | Accuracy  (RE, %) | |
| Lol | 0.11 | 0.12 ± 0.02 | 13.3 | 6.5 |  | 0.12 ± 0.02 | 13.0 | 8.5 |  | 0.12 ± 0.01 | 9.4 | 4.8 | |
|  | 7.20 | 7.80 ± 1.01 | 12.9 | 8.3 |  | 7.76 ± 0.51 | 6.5 | 7.8 |  | 7.10 ± 0.78 | 11.0 | -1.4 |
|  | 14.40 | 15.00 ±1.40 | 9.4 | 4.2 |  | 15.40 ± 1.57 | 10.2 | 6.9 |  | 15.80 ± 0.77 | 4.9 | 9.7 |
| Tpica | 0.44 | 0.48 ± 0.03 | 5.9 | 8.9 |  | 0.41 ± 0.04 | 8.8 | -6.0 |  | 0.40 ± 0.04 | 9.9 | -9.2 |
|  | 28.00 | 29.00 ± 3.69 | 12.7 | 3.6 |  | 31.20 ± 3.75 | 12.0 | 11.4 |  | 29.40 ± 3.34 | 11.4 | 5.0 |
|  | 56.00 | 59.02 ± 5.65 | 9.6 | 5.4 |  | 60.00 ± 5.70 | 9.5 | 7.1 |  | 59.20 ± 3.80 | 6.4 | 5.7 |
| TBII | 0.435 | 0.48 ± 0.04 | 7.6 | 11.0 |  | 0.49 ± 0.06 | 12.1 | 13.8 |  | 0.41 ± 0.05 | 11.8 | -5.6 |
|  | 27.84 | 26.04 ± 3.36 | 12.9 | -6.4 |  | 26.64 ± 3.05 | 11.4 | -4.3 |  | 26.24 ± 3.46 | 13.2 | -5.7 |
|  | 55.68 | 60.08 ± 6.56 | 10.9 | 7.9 |  | 50.68 ± 7.20 | 14.2 | -9.0 |  | 61.28 ± 5.57 | 9.1 | 10.0 |
| MB | 2.94 | 3.14 ± 0.22 | 6.9 | 6.8 |  | 3.12 ± 0.17 | 5.4 | 6.1 |  | 3.10 ± 0.26 | 8.5 | 5.2 |
|  | 188.48 | 204.48 ± 21.69 | 10.6 | 8.5 |  | 178.90 ± 5.31 | 5.3 | 11.9 |  | 198.48 ± 20.01 | 10.1 | 5.3 |
|  | 376.96 | 401.56 ± 56.78 | 14.1 | 6.5 |  | 352.16 ± 28.53 | 8.1 | -6.5 |  | 400.16 ± 47.35 | 11.8 | 6.2 |
| Gly | 0.99 | 0.91 ± 0.21 | 10.1 | 7.3 |  | 0.93 ± 0.10 | 10.8 | -6.0 |  | 1.10 ± 0.13 | 12.3 | 10.5 |
|  | 63.45 | 64.45 ± 5.39 | 8.8 | 1.6 |  | 69.05 ± 8.23 | 11.9 | 8.8 |  | 71.65 ± 4.21 | 5.9 | 12.9 |
|  | 126.90 | 122.90 ± 10.58 | 8.6 | -3.2 |  | 120.90 ± 12.45 | 10.3 | -4.7 |  | 145.30 ± 8.61 | 7.2 | 14.5 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; TB II-(25*R*)-timosaponin B II; MB-macrostemonoside B; Gly-glycyrrhetic acid.

Table S8 Linear ranges and regression equations for 15 quantitative components (n=3)

|  |  |  |  |
| --- | --- | --- | --- |
| Analytes | Range  (ng/mL) | Linear regression  (n=3) | Coefficient  (r) |
| Lol | 0.17~21.60 | y=0.497708x + 0.14358500 | 0.9973 |
| Tpica | 0.10~100.00 | y=0.088360x + 0.01530400 | 0.9980 |
| Luteo | 0.10~98.10 | y=0.463501x + 0.00325239 | 0.9993 |
| Rutin | 0.06~112.50 | y=0.109972x + 0.08330180 | 0.9962 |
| MM | 0.13~267.50 | y=0.202745x + 0.00111710 | 0.9974 |
| MI | 0.51~1022.00 | y=0.034936x + 0.00237870 | 0.9983 |
| MG | 0.81~808.50 | y=0.011080x + 0.00864807 | 0.9979 |
| NTBII | 0.58~582.00 | y=0.030771x + 0.00384513 | 0.9976 |
| Gly | 0.35~700.00 | y=0.078484x + 0.01855250 | 0.9980 |
| 25TAIII | 3.05~3048.00 | y=0.004290x - 0.00489259 | 0.9958 |
| GS | 0.35~704.00 | y=0.135297x + 0.01230660 | 0.9952 |
| TB II | 1.58~3160.00 | y=0.046660x - 0.01592520 | 0.9977 |
| TB III | 1.76~1760.00 | y=0.008911x - 0.00274193 | 0.9966 |
| MB | 2.18~4360.00 | y=0.005004x - 0.00394468 | 0.9914 |
| 56MB | 1.09~2180.00 | y=0.014107x + 0.00181388 | 0.9973 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; Luteo- luteolin-7-*O-β*-glucoside; MM-macrostemonoside M; MI-macrostemonoside I; MG-macrostemonoside G; NTB II-(25*R*)-12*α*-OH-timosaponin B II; Gly-glycyrrhetic acid; 25TA III-(25R)-timosaponin A III; GS-18 *β*-glycyrrhizic acid; TB II-(25*R*)-timosaponin B II; TB III-timosaponin B III; MB-macrostemonoside B; 56MB-5(6)-ene-macrostemonoside B.

Table S9 The LLOQs of 15 analytes in rat intestine content (n=6)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Analytes | Con.  (ng/mL) | Detected Con.  (ng/mL, mean ± SD) | RSD (%) | RE (%) |
| Lol | 0.02 | 0.02 ± 0.01 | 10.2 | -3.8 |
| Tpica | 0.10 | 0.10 ± 0.01 | 6.9 | -3.5 |
| Luteo | 0.10 | 0.11 ± 0.00 | 1.9 | 15.9 |
| Rutin | 0.06 | 0.05 ± 0.01 | 19.5 | -3.9 |
| MM | 0.13 | 0.15 ± 0.01 | 6.6 | 12.8 |
| MI | 0.51 | 0.56 ± 0.05 | 8.4 | 8.7 |
| MG | 0.81 | 0.74 ± 0.12 | 16.0 | -7.7 |
| NTBII | 0.58 | 0.68 ± 0.07 | 10.5 | 17.4 |
| Gly | 0.35 | 0.41 ± 0.03 | 7.6 | 17.3 |
| 25TAIII | 3.05 | 3.39 ± 0.45 | 13.4 | 11.3 |
| GS | 0.35 | 0.41 ± 0.02 | 4.1 | 16.2 |
| TB II | 1.58 | 1.86 ± 0.10 | 5.4 | 12.6 |
| TB III | 1.76 | 1.99 ± 0.13 | 6.7 | 13.1 |
| 56MB | 1.09 | 1.24 ± 0.17 | 13.7 | 13.5 |
| MB | 2.18 | 2.44 ± 0.24 | 9.9 | 11.7 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; Luteo- luteolin-7-*O-β*-glucoside; MM-macrostemonoside M; MI-macrostemonoside I; MG-macrostemonoside G; NTB II-(25*R*)-12*α*-OH-timosaponin B II; Gly-glycyrrhetic acid; 25TA III-(25R)-timosaponin A III; GS-18 *β*-glycyrrhizic acid; TB II-(25*R*)-timosaponin B II; TB III-timosaponin B III; MB-macrostemonoside B; 56MB-5(6)-ene-macrostemonoside B.

Table S10 Accuracies and inter/intra-day precisions of 15 analytes in rat intestine content (n=6)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analytes | Spiked.  (ng/mL) | Inter-day (n=18) | | |  | Intra-day (n=6) | | |
| Calculated Con. (ng/mL) | Precision (RSD, %) | Accuracy (RE, %) |  | Calculated Con.(ng/mL) | Precision (RSD, %) | Accuracy (RE, %) |
| Lol | 0.02 | 0.02 ± 0.00 | 19.1 | 13.0 |  | 0.02 ± 0.00 | 19.5 | 10.3 |
|  | 0.04 | 0.04 ± 0.01 | 12.6 | 1.1 |  | 0.04 ± 0.01 | 12.8 | -0.5 |
|  | 8.64 | 9.36 ± 0.29 | 3.1 | 8.4 |  | 9.36 ± 0.29 | 3.2 | 8.3 |
|  | 17.28 | 16.27 ± 0.24 | 1.5 | -5.9 |  | 16.29 ± 0.24 | 1.5 | -5.7 |
| 2349 | 0.10 | 0.11 ± 0.01 | 8.0 | 8.6 |  | 0.11 ± 0.01 | 7.6 | 14.8 |
|  | 0.20 | 0.21 ± 0.02 | 10.4 | 6.2 |  | 0.22 ± 0.02 | 9.9 | 12.1 |
|  | 40.00 | 44.29 ± 1.25 | 2.8 | 10.7 |  | 44.27 ± 1.25 | 2.8 | 10.7 |
|  | 80.00 | 78.05 ± 4.71 | 6.0 | -2.4 |  | 80.42 ± 4.71 | 5.9 | 0.5 |
| Luteo | 0.10 | 0.11 ± 0.01 | 6.7 | 11.2 |  | 0.11 ± 0.01 | 6.8 | 0.1 |
|  | 0.20 | 0.20 ± 0.01 | 6.1 | 2.9 |  | 0.19 ± 0.01 | 6.4 | -1.7 |
|  | 39.24 | 44.45 ± 1.61 | 3.6 | 13.3 |  | 44.31 ± 1.61 | 3.6 | 12.9 |
|  | 78.48 | 74.67 ± 2.58 | 3.4 | -4.9 |  | 75.70 ± 2.58 | 3.4 | -3.5 |
| Rutin | 0.06 | 0.06 ± 0.01 | 16.5 | 9.3 |  | 0.06 ± 0.01 | 17.5 | 12.2 |
|  | 0.11 | 0.12 ± 0.01 | 8.2 | 7.8 |  | 0.13 ± 0.01 | 7.7 | 13.8 |
|  | 45.00 | 50.61 ± 1.38 | 5.7 | 12.5 |  | 48.99 ± 1.38 | 2.8 | 8.9 |
|  | 90.00 | 83.78 ± 2.69 | 3.9 | -6.9 |  | 84.21 ± 2.69 | 3.2 | -6.4 |
| MM | 0.13 | 0.16 ± 0.01 | 8.4 | 18.7 |  | 0.16 ± 0.01 | 8.4 | 18.7 |
|  | 0.27 | 0.28 ± 0.02 | 6.2 | 6.4 |  | 0.28 ± 0.02 | 6.4 | 3.2 |
|  | 107.00 | 120.00 ± 3.91 | 6.3 | 12.1 |  | 119.80 ± 3.91 | 3.3 | 12.0 |
|  | 214.00 | 212.39 ± 8.18 | 3.9 | -0.8 |  | 214.72 ± 8.18 | 3.8 | 0.3 |
| MI | 0.51 | 0.61 ± 0.12 | 19.6 | 18.8 |  | 0.61 ± 0.12 | 19.6 | 18.9 |
|  | 1.02 | 1.10 ± 0.13 | 11.8 | 7.3 |  | 1.21 ± 0.13 | 10.7 | 14.7 |
|  | 408.80 | 452.97 ± 15.32 | 3.4 | 10.8 |  | 444.52 ± 15.32 | 3.5 | 8.7 |
|  | 817.60 | 772.27 ± 25.27 | 3.3 | -5.5 |  | 762.88 ± 25.27 | 3.3 | -6.7 |
| MG | 0.81 | 0.82 ± 0.08 | 9.5 | 1.2 |  | 0.89 ± 0.08 | 8.8 | 9.6 |
|  | 1.62 | 1.73 ± 0.24 | 13.7 | 6.9 |  | 1.69 ± 0.24 | 14.0 | 4.3 |
|  | 323.80 | 358.36 ± 21.28 | 5.9 | 10.8 |  | 354.97 ± 21.28 | 6.0 | 9.8 |
|  | 646.80 | 627.35 ± 22.72 | 3.6 | -3.0 |  | 637.92 ± 22.72 | 3.6 | -1.4 |
| NTBII | 0.58 | 0.55 ± 0.06 | 10.4 | -5.3 |  | 0.48 ± 0.06 | 11.8 | -16.7 |
|  | 1.16 | 1.07 ± 0.13 | 12.6 | -8.2 |  | 1.00 ± 0.13 | 13.5 | -13.9 |
|  | 232.80 | 263.55 ± 9.25 | 3.5 | 13.2 |  | 267.03 ± 9.25 | 3.5 | 14.7 |
|  | 465.60 | 472.24 ± 17.33 | 3.7 | 1.4 |  | 486.86 ± 17.33 | 3.6 | 4.6 |
| Gly | 0.35 | 0.37 ± 0.06 | 15.9 | 4.4 |  | 0.37 ± 0.06 | 15.9 | 4.6 |
|  | 0.70 | 0.75 ± 0.06 | 7.7 | 7.1 |  | 0.69 ± 0.06 | 8.5 | -2.2 |
|  | 280.72 | 295.55 ± 7.71 | 2.6 | 5.3 |  | 265.43 ± 7.71 | 2.9 | -5.5 |
|  | 561.44 | 542.34 ± 38.27 | 7.1 | -3.4 |  | 492.71 ± 38.27 | 7.8 | -12.2 |
| 25TAIII | 3.41 | 2.91 ± 0.45 | 15.5 | -4.6 |  | 2.78 ± 0.45 | 16.3 | -8.9 |
|  | 6.10 | 5.45 ± 0.47 | 8.5 | -10.5 |  | 5.27 ± 0.47 | 8.8 | -13.5 |
|  | 1219.20 | 1349.43 ± 64.14 | 4.8 | 10.7 |  | 1328.77 ± 64.14 | 4.8 | 9.0 |
|  | 2438.40 | 2388.38 ± 90.53 | 3.8 | -2.0 |  | 2385.15 ± 90.53 | 3.8 | -2.2 |
| GS | 0.35 | 0.30 ± 0.05 | 17.6 | -15.9 |  | 0.30 ± 0.05 | 17.2 | -13.5 |
|  | 0.70 | 0.70 ± 0.10 | 13.6 | -0.2 |  | 0.65 ± 0.10 | 14.7 | -8.2 |
|  | 281.60 | 307.24 ± 28.23 | 9.2 | 9.1 |  | 301.32 ± 28.23 | 9.4 | 7.0 |
|  | 563.20 | 528.55 ± 21.38 | 4.0 | -6.2 |  | 530.58 ± 21.38 | 4.0 | -5.8 |
| TB II | 1.58 | 1.54 ± 0.20 | 12.8 | -2.6 |  | 1.54 ± 0.20 | 13.5 | -3.2 |
|  | 3.16 | 3.07 ± 0.39 | 12.8 | -2.9 |  | 3.07 ± 0.39 | 12.8 | -2.6 |
|  | 1264.00 | 1364.24 ± 62.21 | 4.6 | 7.9 |  | 1308.15 ± 62.21 | 4.8 | 3.5 |
|  | 2528.00 | 2520.21 ± 71.30 | 2.8 | -0.3 |  | 2597.85 ± 71.30 | 2.9 | -1.2 |
| TB III | 1.76 | 2.10 ± 0.21 | 10.0 | 19.4 |  | 2.05 ± 0.25 | 12.2 | 16.5 |
|  | 3.52 | 3.77 ± 0.26 | 6.9 | 7.2 |  | 4.02 ± 0.26 | 6.4 | 14.3 |
|  | 704.00 | 805.87 ± 45.76 | 5.7 | 14.5 |  | 810.67 ± 20.70 | 2.6 | 14.3 |
|  | 1408.00 | 1470.31 ± 57.83 | 3.9 | 4.4 |  | 1515.01 ± 57.83 | 3.8 | 7.6 |
| 56MB | 1.09 | 1.21 ± 0.17 | 14.0 | 10.9 |  | 1.21 ± 0.17 | 13.2 | 10.0 |
|  | 2.18 | 2.27 ± 0.45 | 12.7 | 4.2 |  | 2.18 ± 0.33 | 15.1 | 0.0 |
|  | 872.00 | 1003.08 ± 42.75 | 4.2 | 14.3 |  | 1020.30 ± 42.75 | 4.2 | 12.0 |
|  | 1744.00 | 1727.26 ± 87.36 | 5.1 | -0.9 |  | 1756.63 ± 87.36 | 5.0 | 0.7 |
| MB | 2.18 | 2.52 ± 0.45 | 17.7 | 15.5 |  | 2.52 ± 0.45 | 17.0 | 14.9 |
|  | 4.36 | 4.07 ± 0.72 | 12.8 | -6.7 |  | 4.03 ± 0.72 | 13.9 | -7.6 |
|  | 1744.00 | 1888.10 ± 180.70 | 9.6 | 8.2 |  | 1860.20 ± 180.70 | 9.7 | 6.7 |
|  | 3488.00 | 3383.06 ± 168.42 | 5.0 | -3.0 |  | 3240.45 ± 168.42 | 5.2 | -7.1 |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; Luteo- luteolin-7-*O-β*-glucoside; MM-macrostemonoside M; MI-macrostemonoside I; MG-macrostemonoside G; NTB II-(25*R*)-12*α*-OH-timosaponin B II; Gly-glycyrrhetic acid; 25TA III-(25R)-timosaponin A III; GS-18 *β*-glycyrrhizic acid; TB II-(25*R*)-timosaponin B II; TB III-timosaponin B III; MB-macrostemonoside B; 56MB-5(6)-ene-macrostemonoside B.

Table S11 The matrix effects and extraction recoveries of 15 analytes and IS in rat intestine content (n=6)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Analytes | Con.  (ng/mL) | Matrix effect | | Recovery | | |
| Average (%) | RSD (%) | Average (%) | RSD (%) | |
| Lol | 0.04 | 87.0 | 13.3 | 98.4 | 8.4 |
|  | 8.64 | 84.9 | 11.3 | 99.3 | 7.3 | |
|  | 17.28 | 95.2 | 12.4 | 102.2 | 10.9 | |
| Tpica | 0.20 | 113.4 | 11.0 | 112.7 | 8.8 | |
|  | 40.00 | 101.6 | 5.6 | 92.0 | 9.5 | |
|  | 80.00 | 94.0 | 3.5 | 92.6 | 7.9 | |
| Luteo | 0.20 | 87.0 | 6.2 | 96.4 | 14.2 | |
|  | 39.24 | 87.0 | 5.7 | 80.2 | 12.0 | |
|  | 78.48 | 86.7 | 8.8 | 88.2 | 14.8 | |
| Rutin | 0.11 | 93.2 | 13.2 | 99.5 | 14.7 | |
|  | 45.00 | 85.5 | 2.8 | 85.2 | 9.4 | |
|  | 90.00 | 86.0 | 3.8 | 98.8 | 14.3 | |
| MM | 0.27 | 105.8 | 10.6 | 93.0 | 10.3 | |
|  | 107.00 | 101.6 | 6.5 | 97.9 | 9.0 | |
|  | 214.00 | 94.3 | 2.9 | 107.8 | 9.8 | |
| MI | 1.02 | 109.6 | 7.4 | 104.4 | 6.7 | |
|  | 408.80 | 101.8 | 5.9 | 95.1 | 10.4 | |
|  | 817.60 | 90.9 | 3.4 | 107.8 | 12.4 | |
| MG | 1.62 | 107.2 | 12.9 | 98.1 | 13.2 | |
|  | 323.40 | 104.5 | 4.2 | 93.9 | 12.9 | |
|  | 646.80 | 96.5 | 6.1 | 109.0 | 14.7 | |
| NTBII | 1.16 | 96.6 | 11.3 | 90.9 | 12.2 | |
|  | 232.80 | 99.4 | 4.4 | 98.1 | 8.7 | |
|  | 465.60 | 93.6 | 3.0 | 106.4 | 12.8 | |
| Gly | 0.70 | 24.3 | 10.0 | 81.5 | 9.8 | |
|  | 280.72 | 91.1 | 12.1 | 79.3 | 11.9 | |
|  | 561.44 | 106.1 | 4.5 | 32.1 | 5.0 | |
| 25TAIII | 6.10 | 91.5 | 13.0 | 97.7 | 12.9 | |
|  | 1219.20 | 87.0 | 8.3 | 98.8 | 7.3 | |
|  | 2438.40 | 85.5 | 2.1 | 104.0 | 3.3 | |
| GS | 0.70 | 52.4 | 10.9 | 59.2 | 10.9 | |
|  | 281.60 | 54.2 | 8.0 | 57.4 | 7.4 | |
|  | 563.20 | 52.3 | 5.0 | 57.6 | 7.2 | |
| TB II | 3.16 | 97.0 | 8.7 | 110.9 | 4.3 | |
|  | 1264.00 | 111.8 | 12.6 | 105.3 | 11.6 | |
|  | 2528.00 | 112.8 | 2.4 | 102.4 | 8.0 | |
| TB III | 3.52 | 34.3 | 9.7 | 112.3 | 10.7 | |
|  | 704.00 | 29.5 | 3.3 | 106.1 | 8.4 | |
|  | 1408.00 | 30.0 | 2.1 | 113.7 | 5.9 | |
| 56MB | 2.18 | 101.8 | 12.3 | 110.2 | 13.7 | |
|  | 872.00 | 90.9 | 5.6 | 100.4 | 11.5 | |
|  | 1744.00 | 87.9 | 3.2 | 102.5 | 7.7 | |
| MB | 4.36 | 89.1 | 10.5 | 72.9 | 8.6 | |
|  | 1744.00 | 87.7 | 12.7 | 68.3 | 3.0 | |
|  | 3488.00 | 85.4 | 4.0 | 71.0 | 6.5 | |
| IS | 13.75 | 85.6 | 9.1 | 83.0 | 12.8 | |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; Luteo- luteolin-7-*O-β*-glucoside; MM-macrostemonoside M; MI-macrostemonoside I; MG-macrostemonoside G; NTB II-(25*R*)-12*α*-OH-timosaponin B II; Gly-glycyrrhetic acid; 25TA III-(25R)-timosaponin A III; GS-18 *β*-glycyrrhizic acid; TB II-(25*R*)-timosaponin B II; TB III-timosaponin B III; MB-macrostemonoside B; 56MB-5(6)-ene-macrostemonoside B.

Table S12 Stabilities of 15 quantitative components in rat intestine content

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analytes | Spiked.  (ng/mL) | Room temperature for 12 h (n=6) | | |  | Three freeze-thaw cycle (n=6) | | |  | -80 °C for a month (n=6) | | | | |
| Calculated Con.  (ng/mL) | Precision  (RSD, %) | Accuracy  (RE, %) |  | Calculated Con.  (ng/mL) | Precision  (RSD, %) | Accuracy  (RE, %) |  | Calculated Con.  (ng/mL) | Precision  (RSD, %) | | Accuracy  (RE, %) |
| Lol | 0.04 | 0.04 ± 0.00 | 9.5 | 3.0 |  | 0.04 ± 0.00 | 11.0 | -3.9 |  | 0.04 ± 0.01 | 11.7 | 0.3 | |
|  | 8.64 | 8.54 ± 0.49 | 5.8 | -1.2 |  | 9.22 ± 0.20 | 2.2 | 6.7 |  | 9.56 ± 0.53 | 5.6 | 10.6 | | |
|  | 17.28 | 18.61 ± 1.44 | 7.8 | 7.7 |  | 18.65 ± 2.53 | 13.6 | 7.9 |  | 19.15 ± 2.08 | 10.9 | 10.8 | | |
| Tpica | 0.20 | 0.22 ± 0.01 | 5.9 | 11.3 |  | 0.22 ± 0.03 | 11.5 | 11.0 |  | 0.22 ± 0.03 | 12.1 | 11.2 | | |
|  | 40.00 | 40.35 ± 2.04 | 5.1 | 0.9 |  | 44.62 ± 1.59 | 3.6 | 11.6 |  | 45.28 ± 3.67 | 8.1 | 13.2 | | |
|  | 80.00 | 85.89 ± 8.99 | 10.5 | 7.4 |  | 87.70 ± 10.98 | 12.5 | 9.6 |  | 90.96 ± 5.45 | 6.0 | 13.7 | | |
| Luteo | 0.20 | 0.21 ± 0.02 | 8.9 | 5.3 |  | 0.21 ± 0.02 | 9.3 | 6.1 |  | 0.21 ± 0.02 | 7.0 | 7.2 | | |
|  | 39.24 | 42.60 ± 2.07 | 4.9 | 8.6 |  | 44.51 ± 2.74 | 6.2 | 13.4 |  | 43.91 ± 2.53 | 5.8 | 11.9 | | |
|  | 78.48 | 90.14 ± 9.15 | 10.2 | 14.7 |  | 89.05 ± 9.04 | 10.2 | 13.5 |  | 87.14 ± 8.70 | 10.0 | 11.0 | | |
| Rutin | 0.11 | 0.10 ± 0.01 | 13.5 | -9.0 |  | 0.12 ± 0.02 | 11.9 | 9.8 |  | 0.11 ± 0.01 | 12.0 | -4.4 | | |
|  | 45.00 | 50.33 ± 2.76 | 5.5 | 11.8 |  | 49.10 ± 3.45 | 7.0 | 9.1 |  | 49.37 ± 5.25 | 10.6 | 9.7 | | |
|  | 90.00 | 101.77 ± 8.21 | 8.1 | 13.1 |  | 96.73 ± 8.75 | 9.1 | 7.5 |  | 100.05 ± 8.69 | 8.7 | 11.2 | | |
| MM | 0.27 | 0.27 ± 0.02 | 8.1 | 1.7 |  | 0.29 ± 0.04 | 12.9 | 8.7 |  | 0.30 ± 0.01 | 12.0 | -4.4 | | |
|  | 107.00 | 120.42 ± 5.17 | 4.3 | 12.5 |  | 117.84 ± 8.34 | 7.1 | 10.1 |  | 116.88 ± 8.21 | 7.0 | 9.2 | | |
|  | 214.00 | 233.66 ± 23.00 | 9.8 | 9.2 |  | 229.27 ± 28.35 | 12.4 | 7.1 |  | 228.56 ± 16.18 | 7.1 | 6.8 | | |
| MI | 1.02 | 1.02 ± 0.10 | 10.1 | -0.5 |  | 0.99 ± 0.10 | 10.6 | -3.5 |  | 1.08 ± 0.13 | 11.7 | 6.0 | | |
|  | 408.80 | 434.35 ± 20.23 | 4.7 | 6.3 |  | 453.73 ± 40.92 | 9.0 | 11.0 |  | 440.38 ± 19.01 | 4.3 | 7.7 | | |
|  | 817.60 | 910.05 ± 88.58 | 9.7 | 11.3 |  | 919.67 ± 86.89 | 9.5 | 12.5 |  | 865.08 ± 78.72 | 9.1 | 5.8 | | |
| MG | 1.62 | 1.63 ± 0.18 | 10.8 | 0.7 |  | 1.65 ± 0.21 | 13.0 | 1.8 |  | 1.70 ± 0.17 | 9.8 | 4.9 | | |
|  | 323.40 | 362.82 ± 19.49 | 5.4 | 12.2 |  | 361.20 ± 37.30 | 10.3 | 11.7 |  | 352.60 ± 26.00 | 7.4 | 9.0 | | |
|  | 646.80 | 732.68 ± 74.83 | 10.2 | 13.3 |  | 714.42 ± 27.96 | 3.9 | 10.5 |  | 691.81 ± 51.58 | 7.5 | 7.0 | | |
| NTBII | 1.16 | 1.24 ± 0.16 | 13.1 | 6.3 |  | 1.26 ± 0.14 | 11.3 | 7.8 |  | 1.03 ± 0.13 | 12.5 | -11.4 | | |
|  | 232.80 | 247.95 ± 16.18 | 6.5 | 6.5 |  | 258.30 ± 14.45 | 5.6 | 11.0 |  | 250.22 ± 14.56 | 5.8 | 7.5 | | |
|  | 465.60 | 517.84 ± 50.18 | 9.7 | 11.2 |  | 510.91 ± 59.30 | 11.6 | 9.7 |  | 511.48 ± 54.27 | 10.6 | 9.9 | | |
| Gly | 0.70 | 0.79 ± 0.10 | 13.1 | 12.2 |  | 0.798 ± 0.10 | 13.0 | 13.7 |  | 0.78 ± 0.07 | 9.5 | 11.2 | | |
|  | 280.72 | 307.12 ± 20.76 | 6.8 | 9.4 |  | 300.73 ± 17.89 | 6.0 | 7.1 |  | 296.64 ± 21.40 | 7.2 | 5.7 | | |
|  | 561.44 | 623.52 ± 53.65 | 8.6 | 11.1 |  | 576.86 ± 75.31 | 13.1 | 2.8 |  | 604.76 ± 63.45 | 10.5 | 7.7 | | |
| 25TAIII | 6.10 | 6.24 ± 0.43 | 6.9 | 2.3 |  | 6.75 ± 0.82 | 12.2 | 10.7 |  | 5.95 ± 0.61 | 10.3 | -2.4 | | |
|  | 1219.20 | 1307.35 ± 90.36 | 6.9 | 7.2 |  | 1364.79 ± 80.51 | 5.9 | 11.9 |  | 1302.51 ± 89.41 | 6.9 | 6.9 | | |
|  | 2438.40 | 2607.29 ± 254.92 | 9.8 | 6.9 |  | 2763.87 ± 267.48 | 9.7 | 13.4 |  | 2391.83 ± 171.45 | 7.2 | -1.9 | | |
| GS | 0.70 | 0.68 ± 0.10 | 14.1 | -3.3 |  | 0.80 ± 0.07 | 9.1 | 13.2 |  | 0.73 ± 0.10 | 14.0 | 3.9 | | |
|  | 281.60 | 299.67 ± 16.53 | 5.5 | 6.4 |  | 303.32 ± 18.15 | 6.0 | 7.7 |  | 293.49 ± 14.56 | 5.0 | 4.2 | | |
|  | 563.20 | 593.87 ± 69.42 | 11.7 | 5.5 |  | 586.82 ± 79.33 | 13.5 | 4.2 |  | 567.83 ± 73.37 | 12.9 | 0.8 | | |
| TB II | 3.16 | 3.39 ± 0.44 | 13.0 | 7.4 |  | 2.74 ± 0.34 | 12.5 | -13.3 |  | 3.15 ± 0.23 | 7.4 | -0.4 | | |
|  | 1264.00 | 1376.03 ± 95.23 | 6.9 | 8.9 |  | 1379.64 ± 163.28 | 11.8 | 9.2 |  | 1435.95 ± 81.21 | 5.7 | 13.6 | | |
|  | 2528.00 | 2660.00 ± 196.81 | 7.4 | 5.3 |  | 2808.42 ± 335.86 | 12.0 | 11.1 |  | 2798.02 ± 257.91 | 9.2 | 10.7 | | |
| TB III | 3.52 | 3.37 ± 0.42 | 12.6 | -4.2 |  | 3.54 ± 0.45 | 12.6 | 0.6 |  | 3.84 ± 0.49 | 12.9 | 9.0 | | |
|  | 704.00 | 789.91 ± 37.08 | 4.7 | 12.2 |  | 784.75 ± 61.90 | 7.9 | 11.5 |  | 787.88 ± 37.24 | 4.7 | 11.9 | | |
|  | 1408.00 | 1545.29 ± 145.83 | 9.4 | 9.8 |  | 1533.75 ± 140.46 | 9.2 | 8.9 |  | 1547.76 ± 156.01 | 10.1 | 9.9 | | |
| 56MB | 2.18 | 2.35 ± 0.20 | 8.5 | 7.9 |  | 1.99 ± 0.21 | 10.6 | -8.9 |  | 2.09 ± 0.16 | 7.5 | -4.1 | | |
|  | 872.00 | 968.25 ± 43.90 | 4.5 | 11.0 |  | 941.67 ± 46.25 | 4.9 | 8.0 |  | 916.23 ± 63.91 | 7.0 | 5.1 | | |
|  | 1744.00 | 1893.26 ± 188.88 | 10.0 | 8.6 |  | 1848.18 ± 86.27 | 4.7 | 6.0 |  | 1911.06 ± 233.37 | 12.2 | 9.6 | | |
| MB | 4.36 | 4.33 ± 0.57 | 13.3 | -0.8 |  | 4.18 ± 0.29 | 6.9 | -4.1 |  | 4.45 ± 0.62 | 14.0 | 2.0 | | |
|  | 1744.00 | 1905.81 ± 127.03 | 6.7 | 9.3 |  | 1925.33 ± 164.26 | 8.5 | 10.4 |  | 1510.70 ± 175.45 | 11.6 | -13.4 | | |
|  | 3488.00 | 3833.75 ± 450.30 | 11.8 | 9.9 |  | 2565.88 ± 125.24 | 3.5 | 2.2 |  | 3366.30 ± 238.58 | 7.1 | -3.5 | | |

Note: Lol-(-)-loliolide; Tpica-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; Luteo- luteolin-7-*O-β*-glucoside; MM-macrostemonoside M; MI-macrostemonoside I; MG-macrostemonoside G; NTB II-(25*R*)-12*α*-OH-timosaponin B II; Gly-glycyrrhetic acid; 25TA III-(25R)-timosaponin A III; GS-18 *β*-glycyrrhizic acid; TB II-(25*R*)-timosaponin B II; TB III-timosaponin B III; MB-macrostemonoside B; 56MB-5(6)-ene-macrostemonoside B.

E:\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\第二篇文章写法-GXB\20210511\图片处理\血浆原型合并.tif

Fig. S1-a

E:\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\第二篇文章写法-GXB\20210511\图片处理\尿液原型合并.tif

Fig. S1-b

E:\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\第二篇文章写法-GXB\20210511\图片处理\胆汁原型合并.tif

Fig. S1-c

E:\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\第二篇文章写法-GXB\20210511\图片处理\粪便原型合并.tif

Fig. S1-d

E:\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\第二篇文章写法-GXB\20210511\图片处理\肠内容物原型合并.tif

Fig. S1-e

Fig. S1 The extract ion chromatogram (EIC) of prototypes characterized in rat bio-samples

( a, b, c, d, e stand for the EIC chromatogram of plasma, urine, bile, feces, intestine content, respectively; GXB, GXB-dePRP mean Gualou-Xiebai-Banxia decoction and GXB deducted PRP, respectively)

J:\2022年4月19日电脑E盘备份\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\3.药动学测试实验\血浆动力学实验数据\专属性图及残留\专属合并all-加指峰.tif

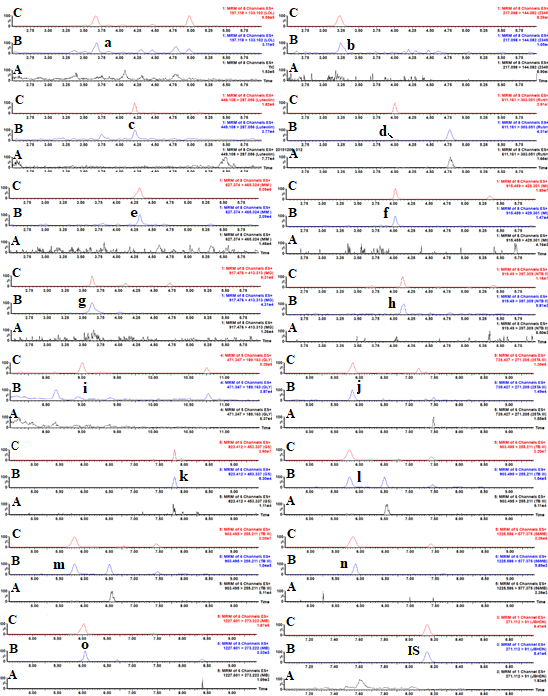
Fig. S2 Specificity for 5 quantitative components and IS in rat plasma

(a-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid, b-(-)-loliolide, c-(25*R*)-timosaponin B II, d-macrostemonoside B, e-glycyrrhetic acid；IS-dexamethasone; red-plasma sample at 2 h; blue-blank plasma spiked with LLOQ; black-blank plasma)

J:\2022年4月19日电脑E盘备份\林培-2018年12月21日之后\博士期间相关\栝楼薤白半夏汤\3.药动学测试实验\血浆动力学实验数据\专属性图及残留\残留all-加峰指.tif

Fig. S3 Carryover for 5 quantitative components and IS

(a-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid, b-(-)-loliolide, c-25 *R*-timosaponin B II, d-macrostemonoside B, e-glycyrrhetic acid; IS-dexamethasone; blue-blank plasma spiked with HLOQ and IS; black-blank plasma; red: blank plasma spiked with LLOQ)

**** Fig. S4 Specificity for 15 quantitative components and IS in rat intestine content

(A-blank plasma; B-blank plasma spiked with LLOQ; C-plasma sample at 2 h; a-(-)-loliolide; b-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; c-luteolin-7-*O*-*β*-glucoside; d-rutin; e-macrostemonoside M; f-macrostemonoside I; g-macrostemonoside G; h-(25*R*)-12*α*-OH-timosaponin B II; i-glycyrrhetic acid; j-(25*R*)-timosaponin A III; k-18 *β*-glycyrrhizic acid; l-(25*R*)-timosaponin B II; m- timosaponin B III; n-5(6)-ene-macrostemonoside B; o-macrostemonoside B; IS-tolbutamide）

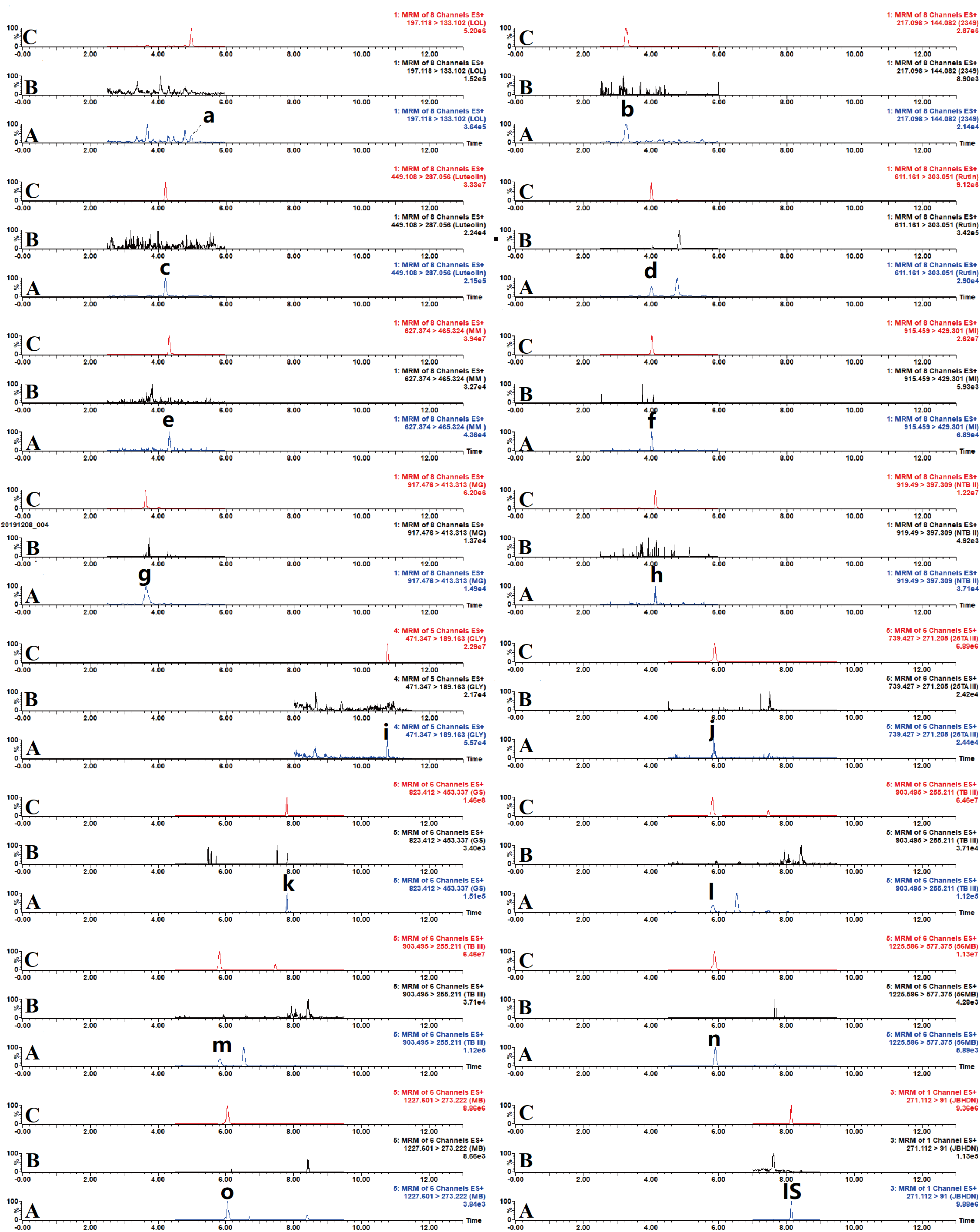


Fig. S5 Carryover for 15 quantitative components and IS in rat intestine content

(A-blank plasma spiked with LLOQ ; B-blank plasma; C-blank plasma spiked with HLOQ and IS; a-(-)-loliolide; b-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole-3-carboxylic acid; c-luteolin-7-*O*-*β*-glucoside; d-rutin; e-macrostemonoside M; f-macrostemonoside I; g-macrostemonoside G; h-(25*R*)-12*α*-OH-timosaponin B II; i-glycyrrhetic acid; j-(25*R*)-timosaponin A III; k-18 *β*-glycyrrhizic acid; l-(25*R*)-timosaponin B II; m- timosaponin B III; n-5(6)-ene-macrostemonoside B; o-macrostemonoside B; IS-tolbutamide）