**1. Verification process for the identification of phloretin metabolites in rat urine, plasma and faeces**

**M37**, **M44** and **M49** gave rise to [M-H]− ions at *m/z* 529.06598, *m/z* 529.06586 and *m/z* 529.06586 (C21H21O14S mass error within 3.000 ppm). In their ESI-MS2 spectra, the FFIs at *m/z* 167 [M-H-SO3-GluA]− and fragment ions at *m/z* 449 [M-H-SO3]− and *m/z* 273 [M-H-GluA]− confirmed the loss of glucuronic acid group and SO3 group. According to the above deduction, **M37**, **M44** and **M49** were the isomeric glucuronidation and sulfation metabolites of phloretin

In positive ion mode, **M35**, **M36** and **M39** showed [M+H]+ ions at *m/z* 277.10641, *m/z* 277.10587 and 277.10559 (C15H17O5 mass error -2.310 ppm, -4.259 ppm and -1.460 ppm) with the mass being 2 Da more than that of phloretin, indicating that they could be hydrogenated products. The FFIs at *m/z* 171 [M+H-C7H6O]+ and fragment ion at *m/z* 107 [M+H-C8H10O4]+ provided evidence for our deduction. Thus, **M35**, **M36** and **M39** were tentatively characterized as hydrogenation metabolites of phloretin. **M17** produced [M+H]+ ion at *m/z* 291.08643 (C15H15O6 mass error 0.396 ppm). The FFIs at *m/z* 169 [M+H-C7H6O2]+ proved it was a hydroxylation metabolite of phloretin.

**M38**, **M40**, **M41**, **M45**, **M46** and **M48** were160 Da more massive than phloretin, proving that they could be isomeric disulfation metabolites. The FFIs at *m/z* 167 [M-H-2SO3-C7H6O]− and fragment ions at m/z 353 [M-H-SO3]− and *m/z* 273 [M-H-2SO3]− provided evidence for our deduction. **M10** showed [M-H]− ion at the *m/z* 447.09344 (C21H19O11 mass error 2.801 ppm). The FFIs at *m/z* 119 [M-H-GluA-C7H4O4]− and characteristic ions at *m/z* 271 [M-H-GluA]− and *m/z* 93 [M-H-GluA-C7H4O4-C2H2]− proved that they could be glucuronidation and dehydrogenation metabolites of phloretin.

**M27** gave rise to [M-H]− ion at the *m/z* 301.11130 (C17H17O5 mass error -1.623 ppm) with 28 Da more than that of phloretin, indicating that they could be deduced as dimethylation metabolite of phloretin. In the ESI-MS2 spectra, the FFIs at *m/z* 195 [M-H-C7H6O]−, *m/z* 167 [M-H-C7H6O-2CH2]− and *m/z* 121 [M-H-C9H8O4]− proved it was dimethylation metabolite of phloretin. **M11** was 176 Da more than **M12**, and the product ions at *m/z* 167, *m/z* 135, *m/z* 287 and *m/z* 463 demonstrated that it was glucuronidation and carbonylation metabolite of phloretin. In positive ion mode, **M9** showed [M+H]+ ion at the *m/z* 289.10678 (C16H17O5 mass error -0.934 ppm) with 14 Da more than that of phloretin, suggesting it was a methylation metabolite of phloretin. The FFIs at *m/z* 123 [M+H-CH2-C7H4O4]+ and *m/z* 169 [M+H-CH2-C7H6O]+ confirmed evidence for our deduction.

**2. Verification process for the identification of phlorizin metabolites in rat urine, plasma and faeces**

**P7**, **P8**, and **P12** (C27H29O17 mass error within 3.000 ppm) were 352 Da (2GluA) more than that of phloretin, indicating that they could be isomeric diglucuronidation metabolites of phloretin. **P19** eluted at 4.89 min and showed [M-H]− ion at the *m/z* 435.12994 (C21H23O10 mass error 3.141 ppm) with the same molecular formula as phlorizin. The product ions at m/z 167, m/z 273 and m/z 93 confirmed that it was the prototype of phlorizin. **P29** produced FFIs at *m/z* 167 [M-H-2GluA-C7H6O]− and product ions at *m/z* 449 [M-H-GluA]− and *m/z* 273 [M-H-2GluA]− confirmed that it could be a glucuronidation metabolite of phloretin.

In positive ion mode, **P25** afforded [M+H]+ ion at the *m/z* 451.12283 (C21H23O11 mass error -1.458 ppm), and showing fragment ions similar to **P22**. Therefore, **P25** could be defined as isomeric carbonylation product. **P17** and **P33** showed [M-H]− ions at the *m/z* 479.11996 and *m/z* 479.11993 (C22H23O12 mass error 3.251 ppm and 3.188 ppm) with the mass being 30 Da more than **P22**. The characteristic product ion at *m/z* 303 [M-H-Glu-CH2]− and the FFIs at *m/z* 153 [M-H-Glu-CH2-C8H5O3]− suggested that **P17** and **P33** could be deduced as isomeric carbonylation hydroxylation and methylation metabolites of phlorizin. **P6, P9**, **P15**, **P18** and **P24** were 176 Da more than **P22** and generated [M-H]− ions at the *m/z* 625.14136, *m/z* 625.141 30, *m/z* 625.14117, *m/z* 625.14124 and *m/z* 625.14117 (C27H29O17 mass error 2.294 ppm, 2.198 ppm, 1.990 ppm, 2.102 ppm and 1.990 ppm). They produced fragment ion at *m/z* 449 [M-H-GluA]− with loss of GluA group. Therefore, they could be deduced as isomeric glucuronidation and carbonylation metabolites of phlorizin.

**P42** and **P44** showed [M-H]− ion at *m/z* 369.02881 and *m/z* 369.02878 (C15H13O9S mass error 3.607 ppm and 3.525 ppm), respectively. They were 96 Da more than that of phloretin, proving that they could be isomeric hydroxylation and sulfation metabolites of phloretin. The FFIs at *m/z* 167 [M-H-SO3-C7H6O2]− and fragment ion at *m/z* 289 [M-H-SO3]− suggested that the neturl loss of SO3 group. **P41** was a sulfation metabolite of phloretin, which displayed [M-H]− ion at the *m/z* 353.03381 (C15H13O8S mass error 3.528 ppm). The characteristic product ion at *m/z* 273 was generated by the loss of 80 (SO3) from the ion at *m/z* 353. **P43** was 2 Da more than phloretin that showed [M+H]+ ion at the *m/z* 277.10587 (C15H17O5 mass error -4.259 ppm). The FFIs at *m/z* 171 [M+H-C7H6O]+ deduced it could be a hydrogenation metabolite of phloretin. In negative ion mode, **P45** was 96 Da more than that of phloretin, the characteristic product ion at *m/z* 289 showed the loss of SO3 group. Therefore, **P45** could be hydroxylation and sulfation metabolite of phloretin. **P23** and **P30** generated [M+H]+ ions at the *m/z* 451.12250 and *m/z* 451.12244 (C21H23O11 mass error -2.190 ppm and -2.323 ppm) with the 176 Da more than phloretin. The fragment ion at *m/z* 275 was suggested the loss of GluA group and the FFIs at *m/z* 169 and *m/z* 123 proved that they could be glucuronidation metabolites of phloretin. **P37** afforded [M-H]− ion at the *m/z* 353.03394 (C15H13O8S mass error 3.896 ppm) with the 80 Da more than phloretin. The fragment ions at *m/z* 273, *m/z* 167 and *m/z* 121 proved it was a sulfation metabolite of phloretin.