

Acetaminophen Prodrug: Microwave-Assisted Synthesis and *in vitro* Metabolism Evaluation by Mass Spectrometry

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Spectroscopy information

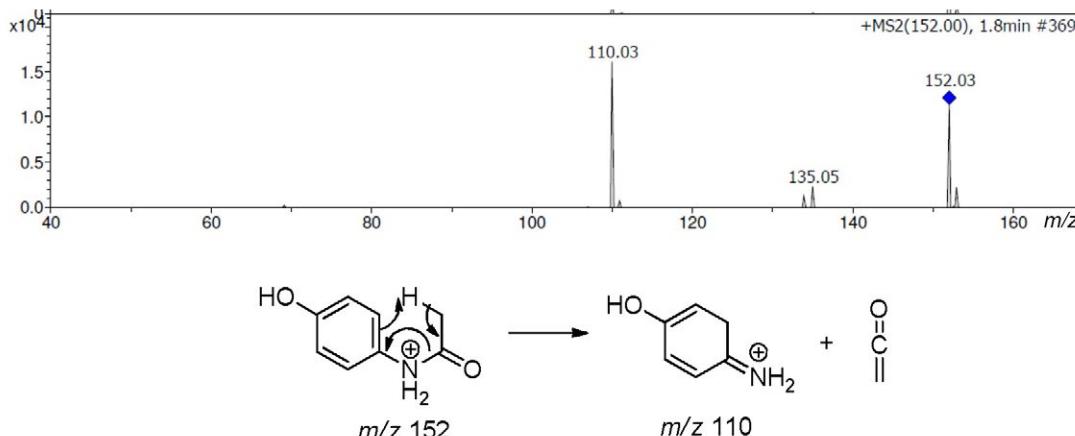


Figure S1. Mass spectrum of acetaminophen.

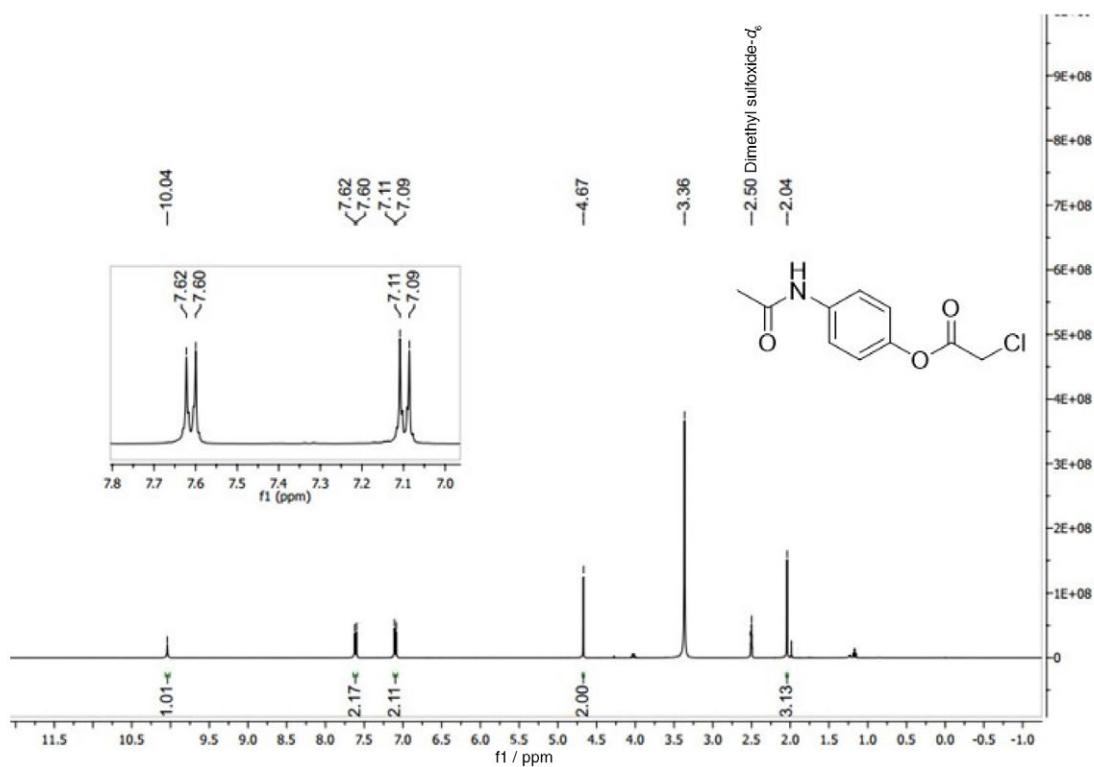


Figure S2. ¹H NMR spectrum (400 MHz, DMSO- d_6) of compound 4.

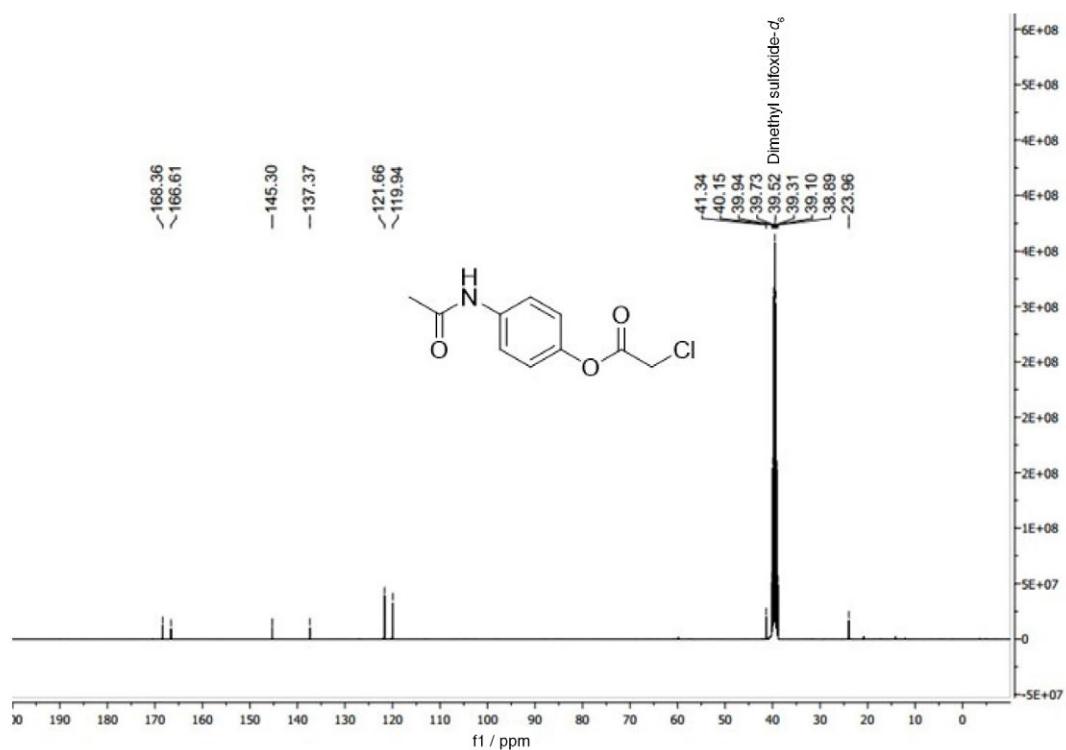
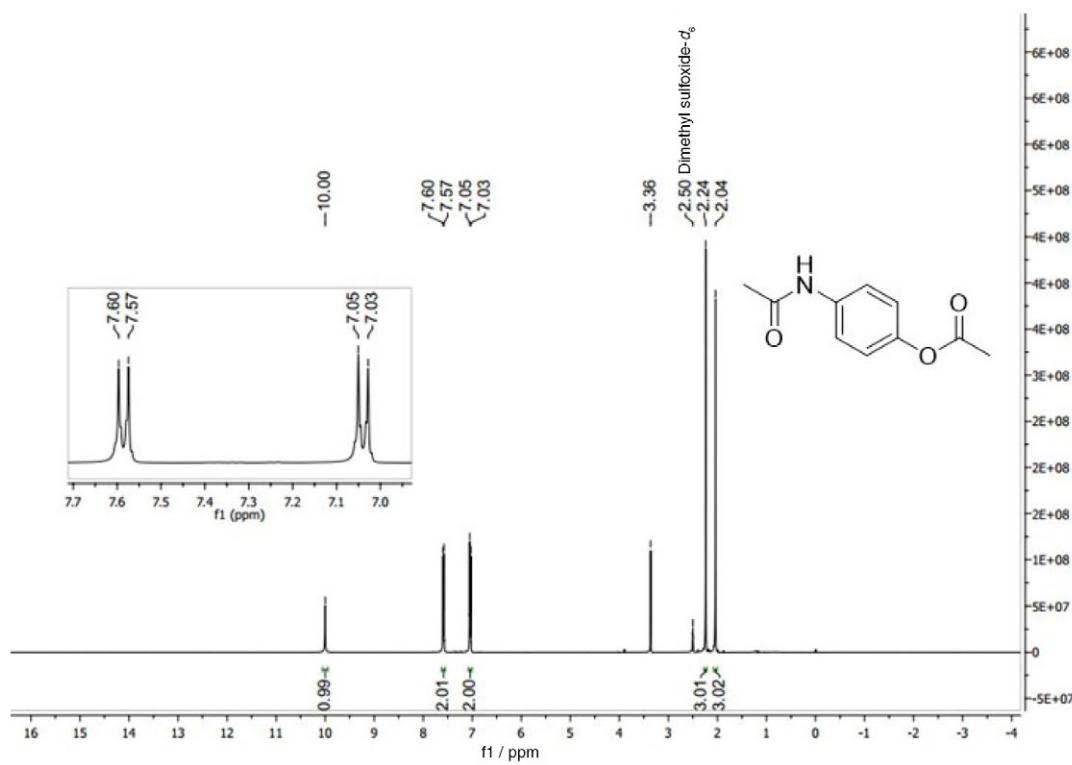
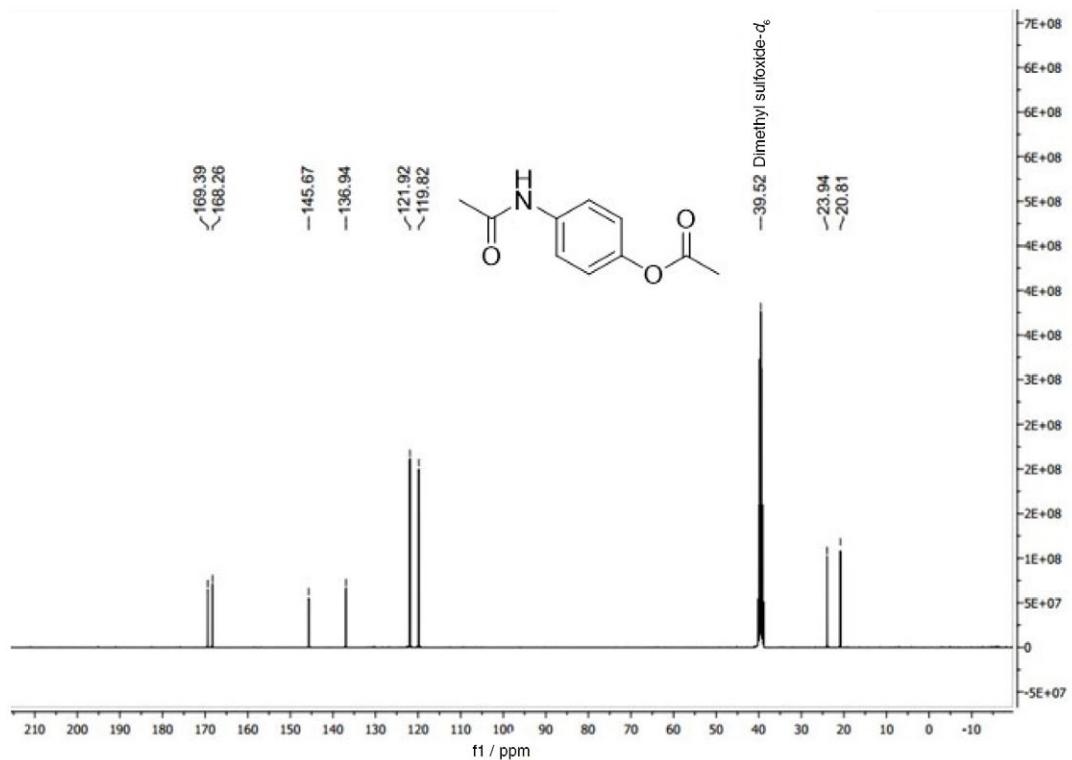


Figure S3. ¹³C NMR spectrum (100 MHz, DMSO- d_6) of compound 4.

**Figure S4.** ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of compound 7.**Figure S5.** ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) of compound 7.

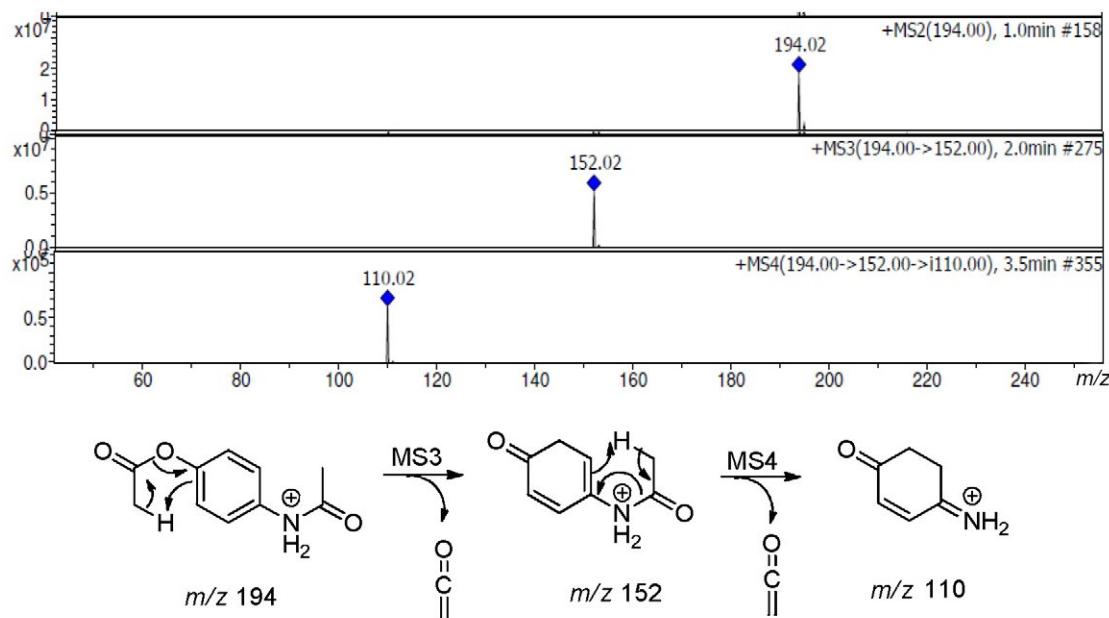


Figure S6. Mass spectrum of 4-acetamidophenyl acetate (**7**).

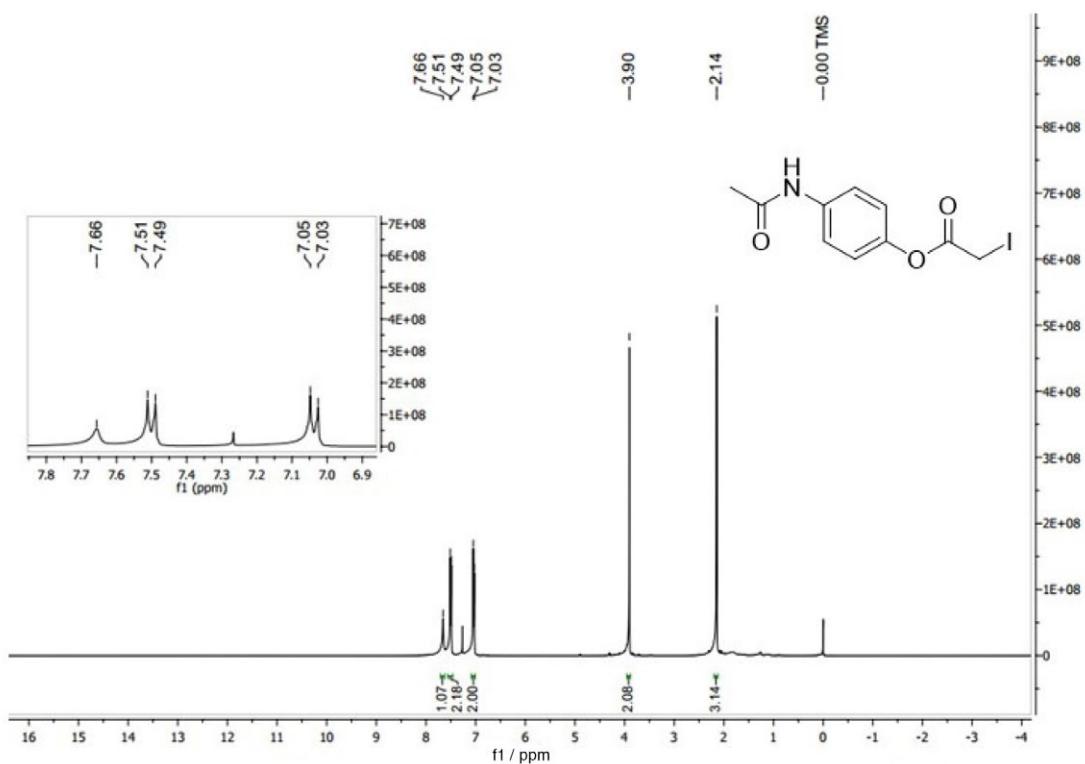


Figure S7. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **6**.

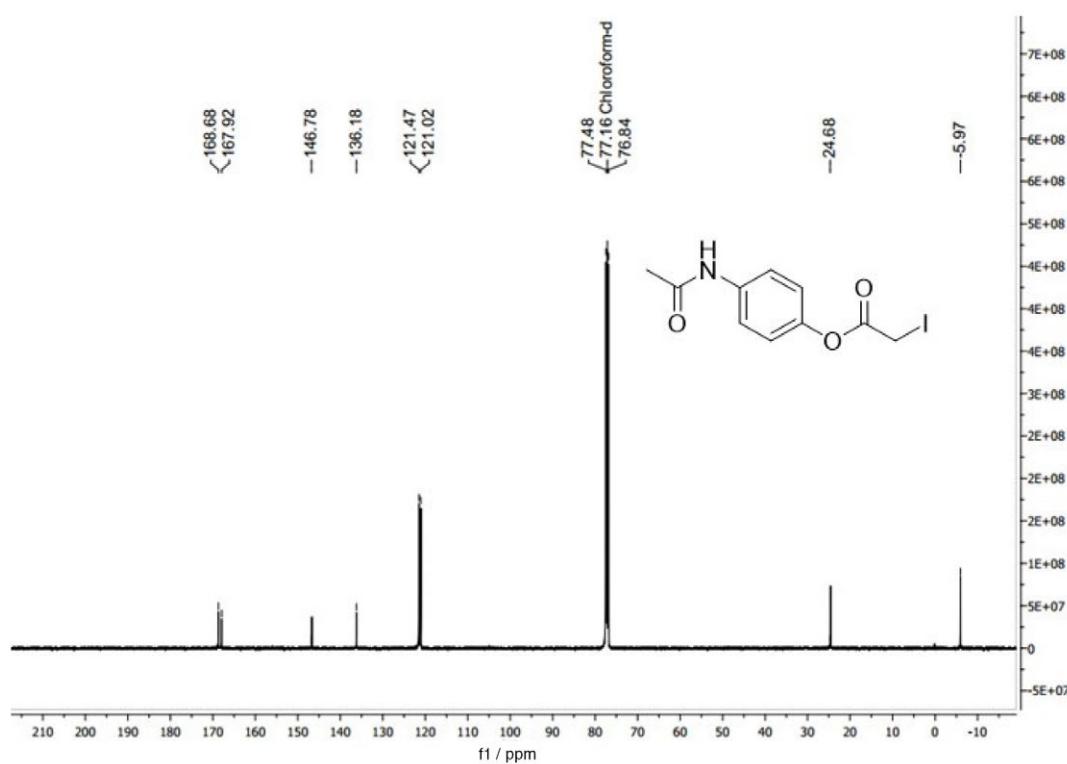


Figure S8. ¹³C NMR spectrum (100 MHz, CDCl₃) of compound 6.

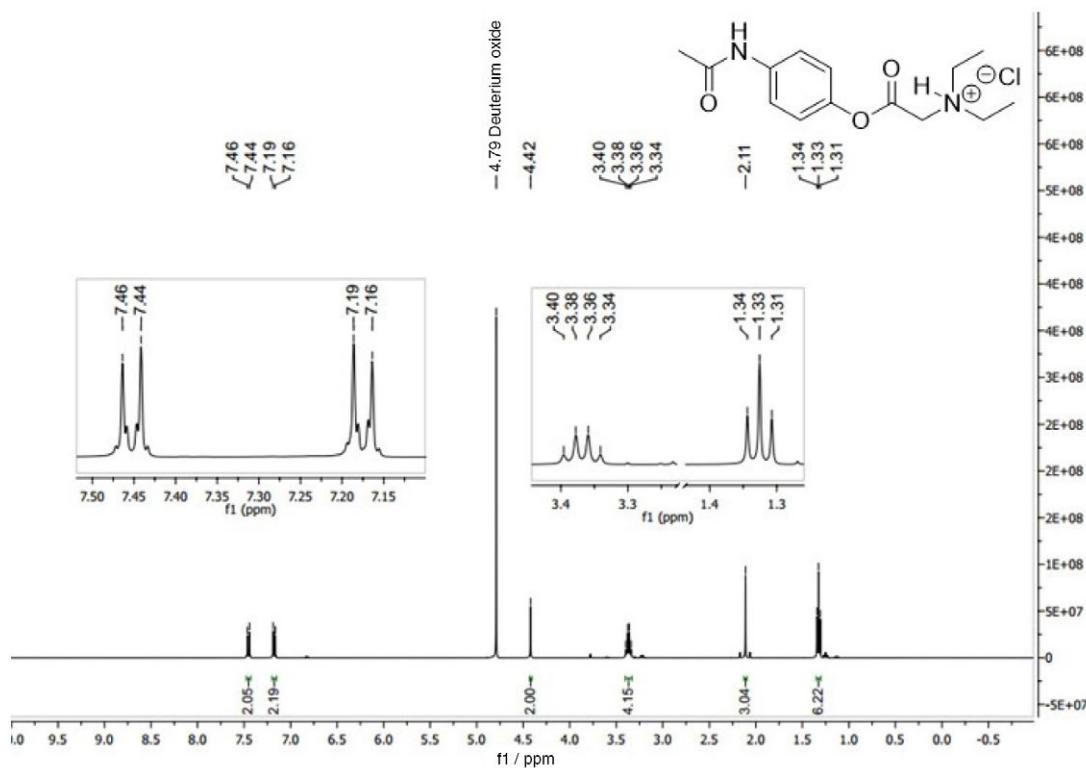


Figure S9. ¹H NMR spectrum (400 MHz, D₂O) of compound 2.

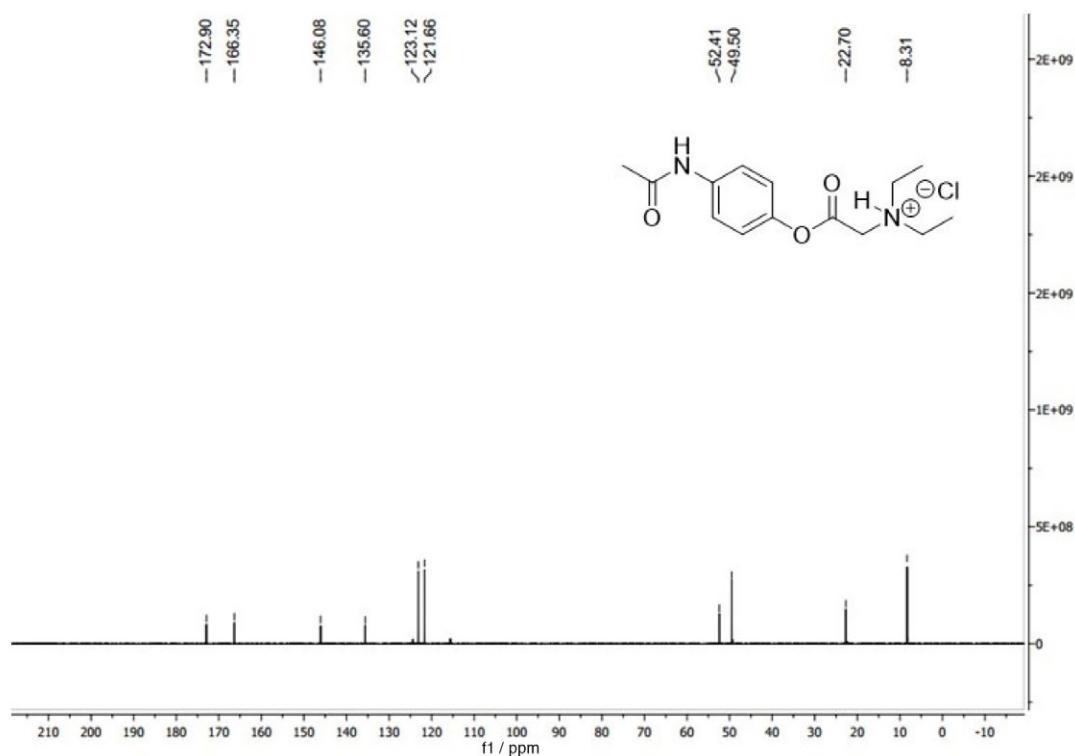


Figure S10. ¹³C NMR spectrum (400 MHz, D₂O) of compound 2.

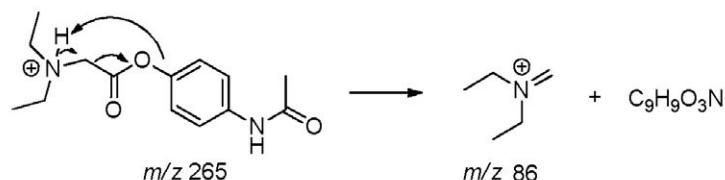
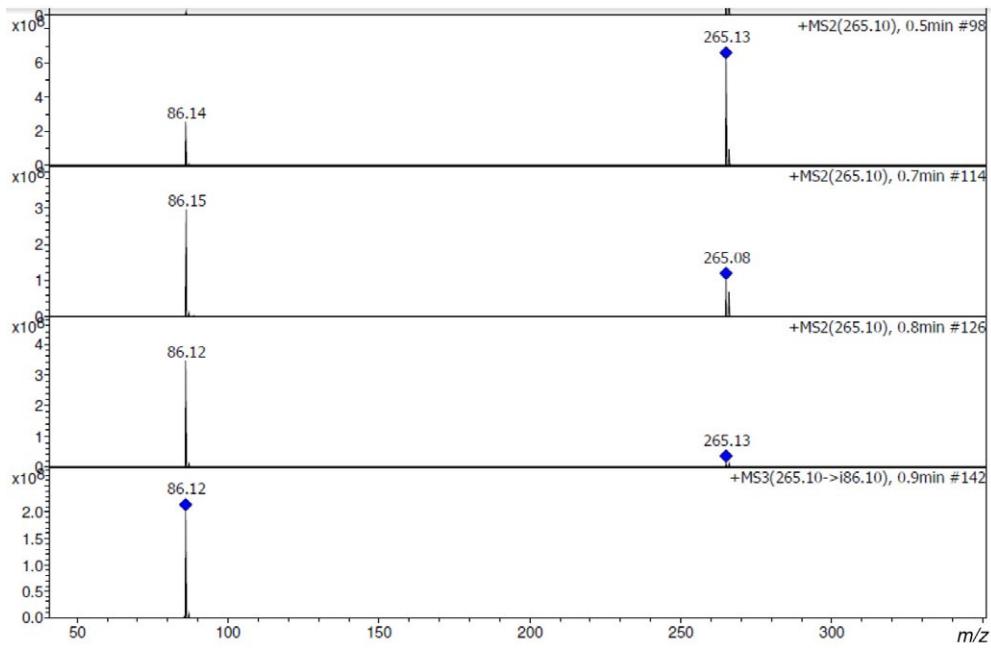


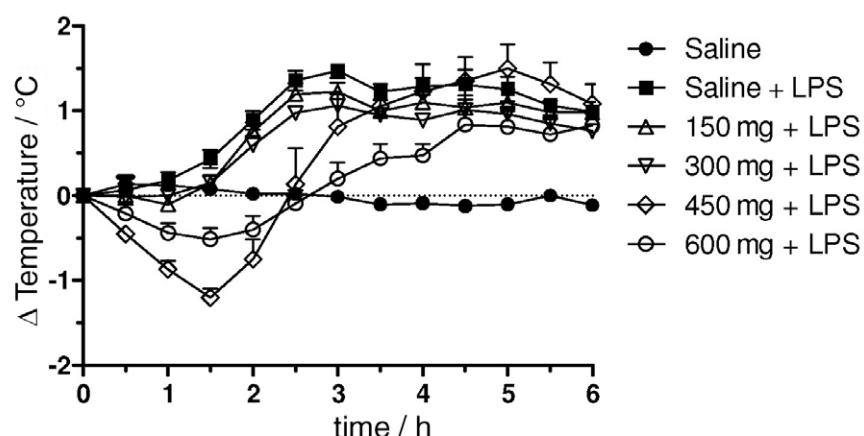
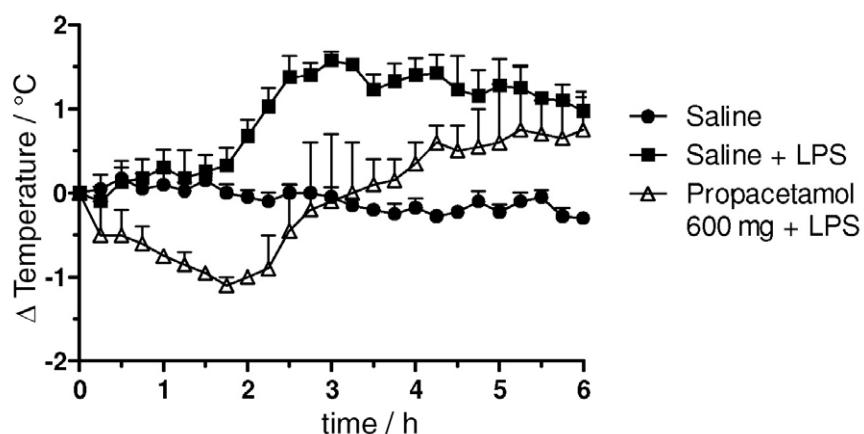
Figure S11. Mass spectrum of propacetamol hydrochloride (2).

Antipyretic assay information

Table S1. Animal groups in relation to administrated drug

Group	Administration solution
1	saline
2	saline + LPS
3	propacetamol 150 mg + LPS
4	propacetamol 300 mg + LPS
5	propacetamol 450 mg + LPS
6	propacetamol 600 mg + LPS
7	paracetamol 300 mg + LPS

LPS: lipopolysaccharide.

**Figure S12.** Comparison of body temperature variation in function of time of different dosages of propacetamol.**Figure S13.** Body temperature variation in function of time of propacetamol (600 mg kg^{-1}).

Information of *in vitro* metabolism evaluation by ion trap tandem mass spectrometry

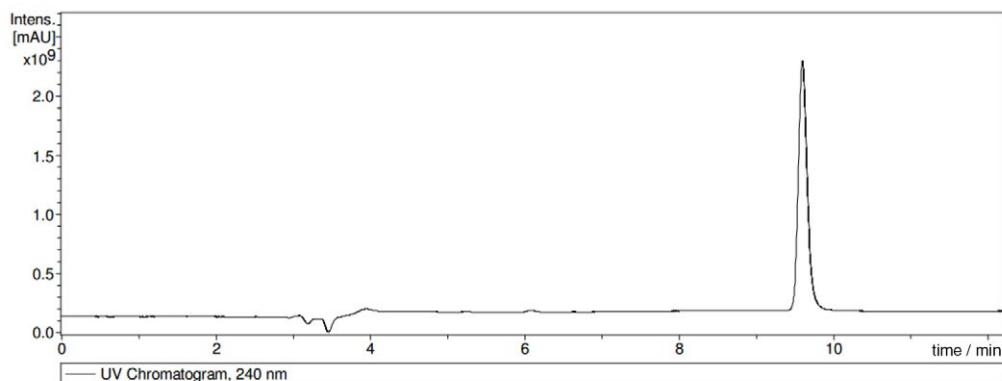


Figure S14. Chromatogram of control tube of 4-acetamidophenyl acetate.

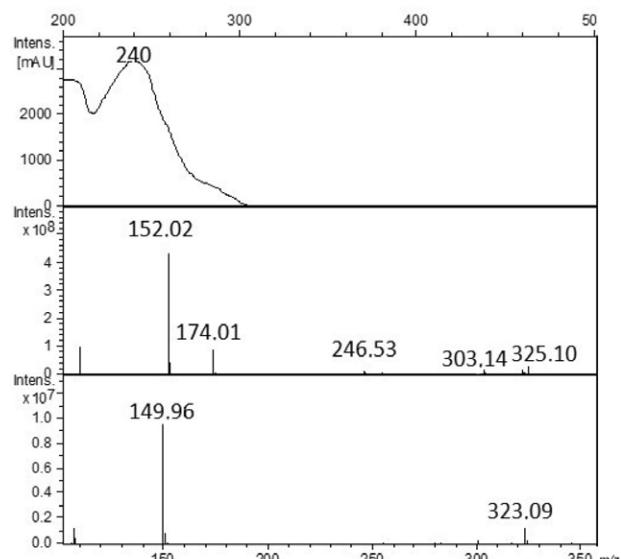


Figure S15. UV and mass spectra of signal in Rt = 9.8 min of control tube of 4-acetamidophenyl acetate.

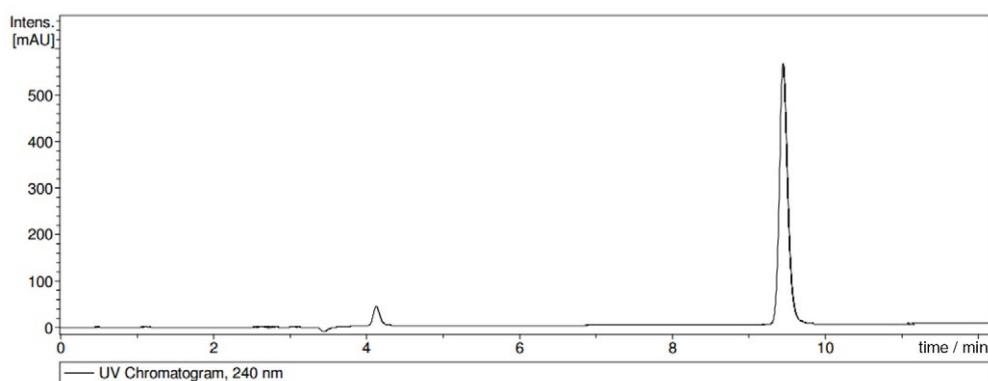


Figure S16. Chromatogram of test tube of 4-acetamidophenyl acetate.

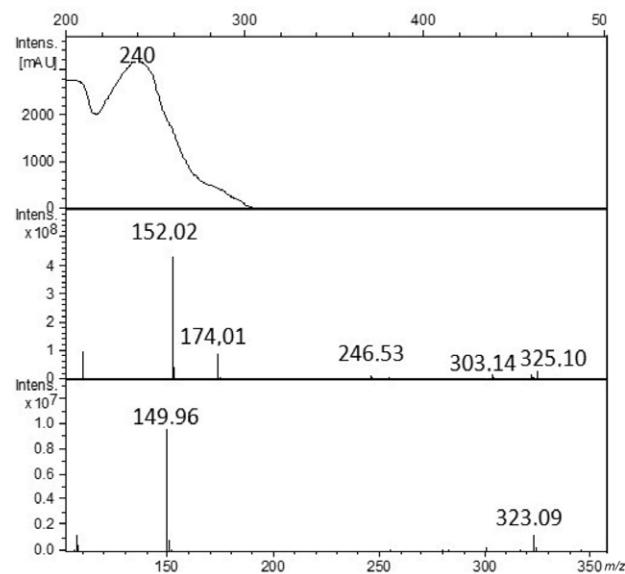


Figure S17. UV and mass spectra of signal in $R_t = 9.8$ min of test tube of 4-acetamidophenyl acetate.

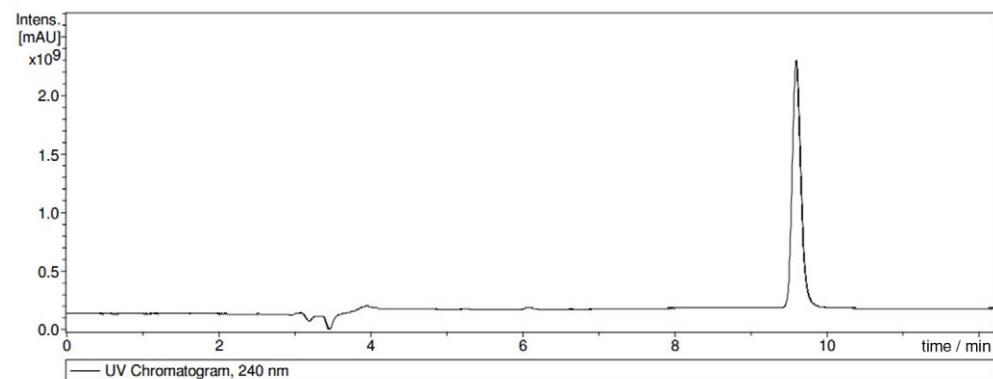


Figure S18. Chromatogram of control tube of acetaminophen.

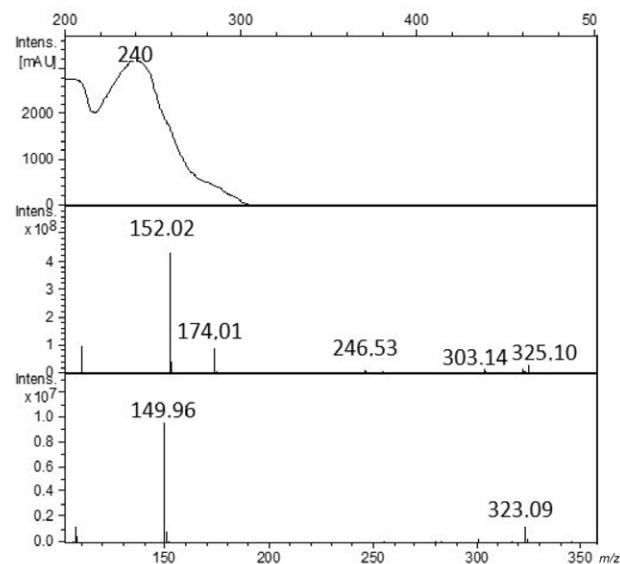


Figure S19. UV and mass spectra of signal in $R_t = 9.8$ min of control tube of acetaminophen.

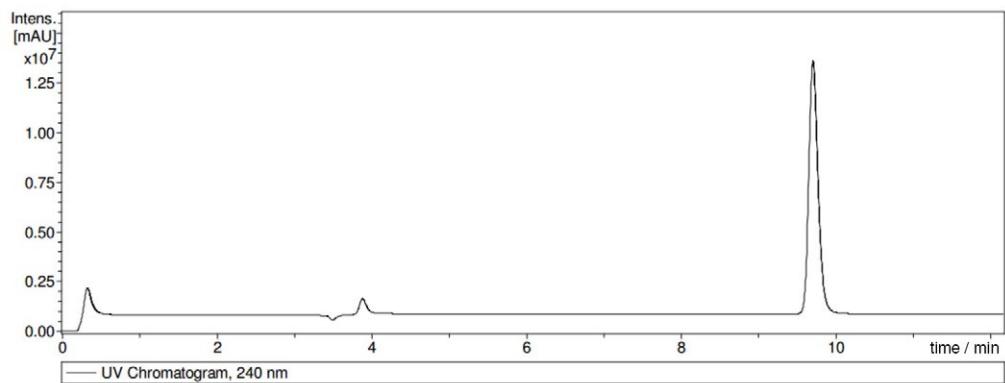


Figure S20. Chromatogram of test tube of acetaminophen.

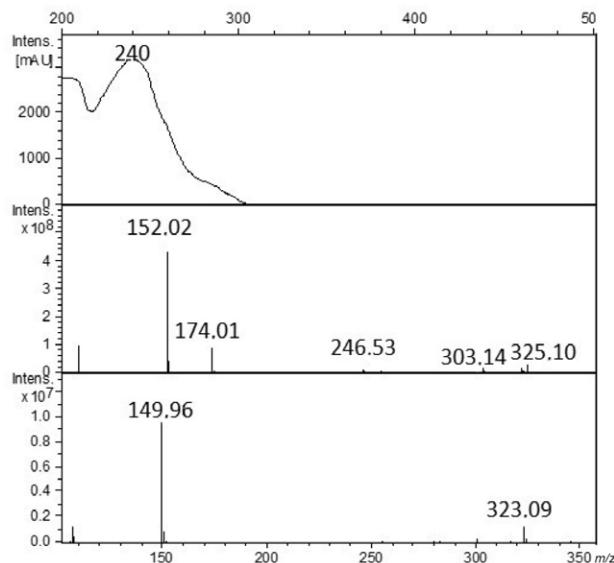


Figure S21. UV and mass spectra of signal in Rt = 9.8 min of test tube of acetaminophen.

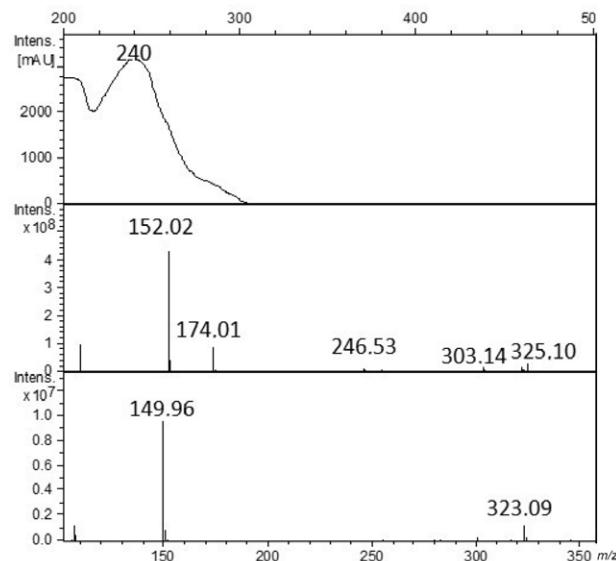


Figure S22. UV and mass spectra of signal in $R_t = 9.8$ min of control tube of propacetamol hydrochloride (showed in Figure 3b, see article).

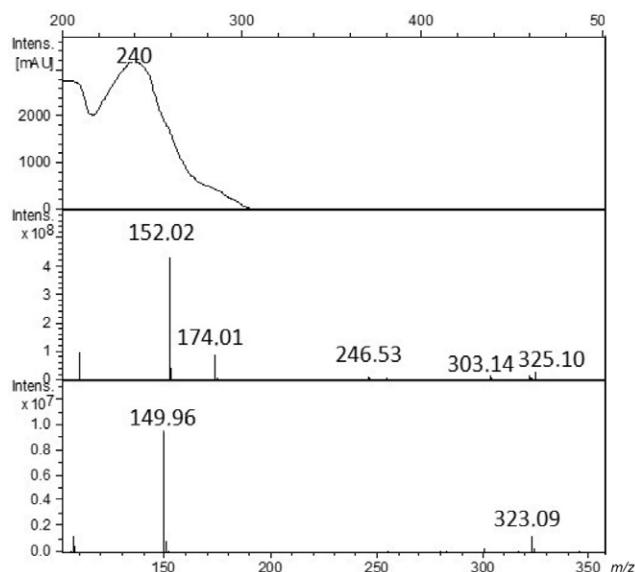


Figure S23. UV and mass spectra of signal in $R_t = 9.8$ min of test tube of propacetamol hydrochloride (showed in Figure 3c, see article).