

1           **Rapid detection of hypnotics using surface-enhanced Raman scattering based on gold**  
2                           **nanoparticle co-aggregation in wet system**

3  
4 Hiroki Segawa<sup>†</sup>, Takao Fukuoka<sup>‡</sup>, Tamitake Itoh<sup>§</sup>, Yuichi Imai<sup>⊥</sup>, Yuko T. Iwata<sup>†</sup>, Tadashi  
5 Yamamuro<sup>†</sup>, Kenji Kuwayama<sup>†</sup>, Kenji Tsujikawa<sup>†</sup>, Tatsuyuki Kanamori<sup>†</sup> and Hiroyuki Inoue<sup>†</sup>

6  
7  
8 <sup>†</sup> Third Department of Forensic Science, National Research Institute of Police Science  
9 6-3-1, Kashiwanoha, Kashiwa, Chiba 277-0882, Japan

10  
11 <sup>‡</sup> Laboratory of Advanced Science and Technology for Industry, University of Hyogo  
12 3-1-2, Kouto, Kamigori-cho, Ako, Hyogo 678-1205, Japan

13  
14 <sup>§</sup> Health Research Institute, National Institute of Advanced Industrial Science and Technology  
15 2217-14, Hayashi-cho, Takamatsu, Kagawa 761-0395, Japan

16  
17 <sup>⊥</sup> STRAWB Inc.  
18 1542-1, Nakahara-cho, Takahashi, Okayama 716-0045, Japan

19  
20  
21   Supporting information

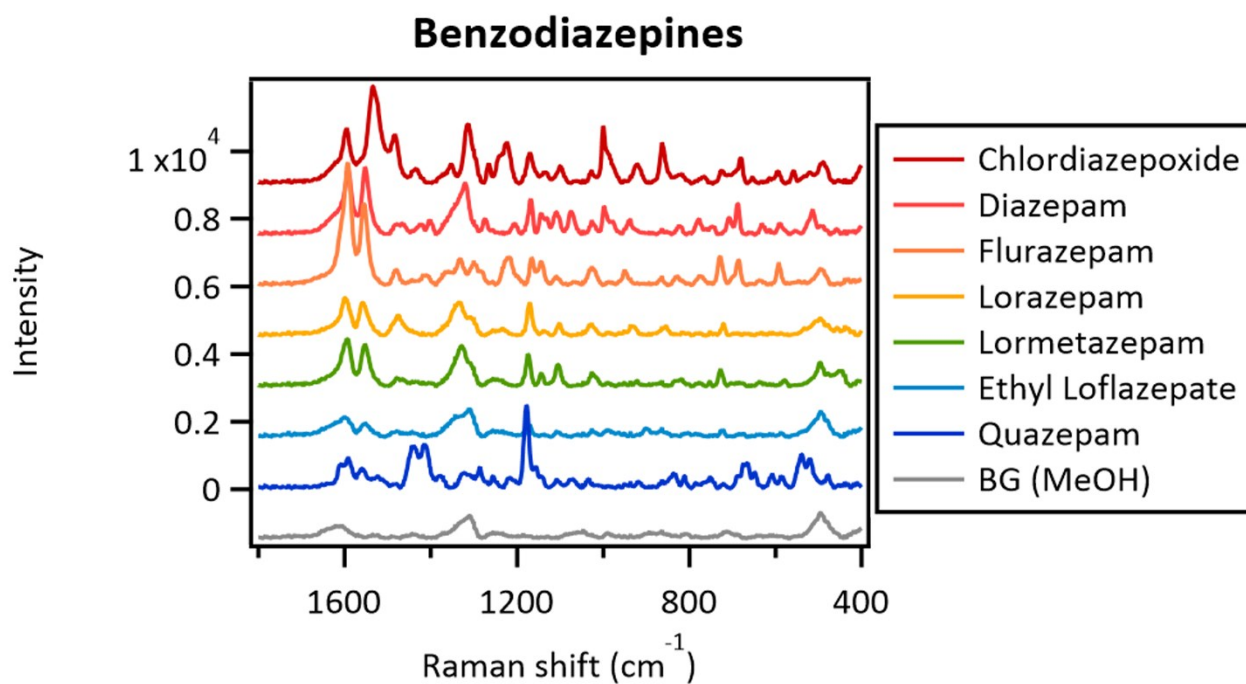
22 S-1 Surface enhanced Raman scattering spectra of hypnotics examined.

23 S-2 Enlarged views of calibration plots in the low concentration region.

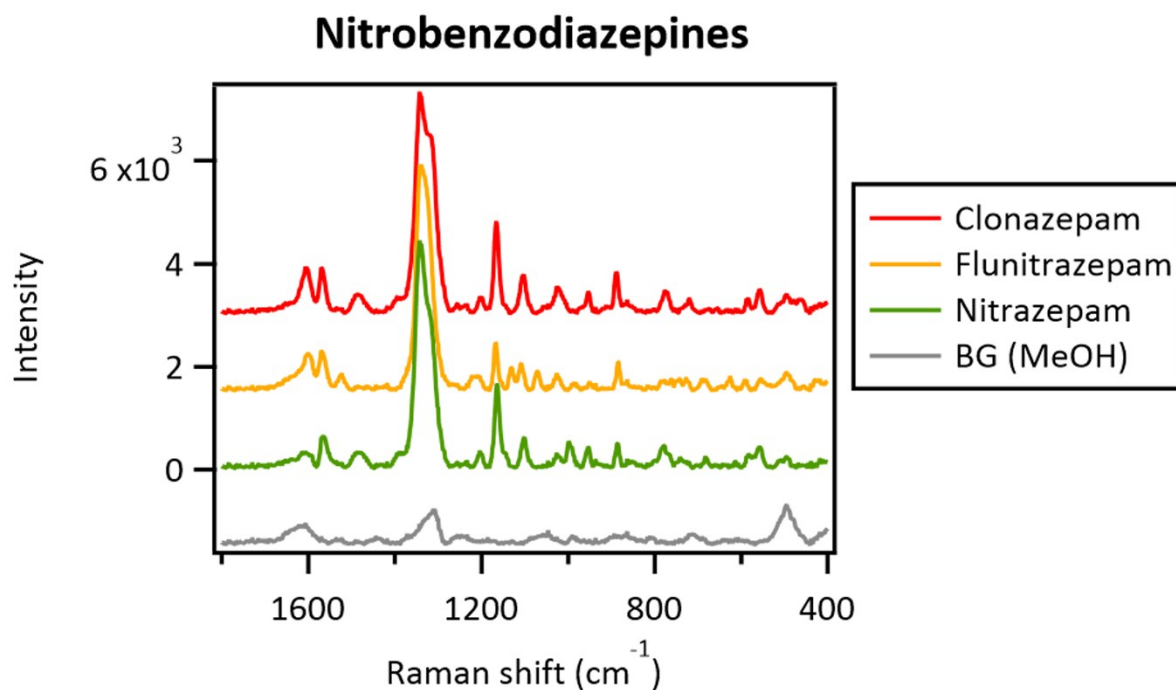
24 S-3 Surface enhanced Raman scattering spectra of hypnotic in apple juice.

25

(a)



(b)



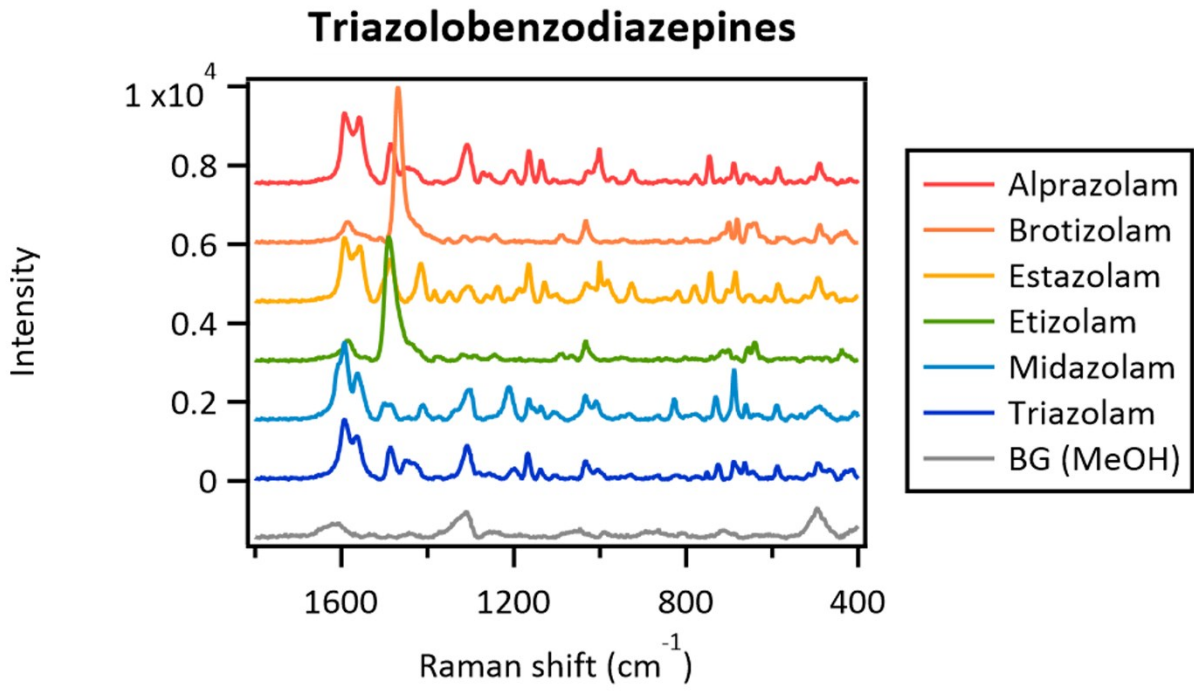
26

27 Figure S-1 Surface enhanced Raman scattering spectra of hypnotics examined in this study. Exposure

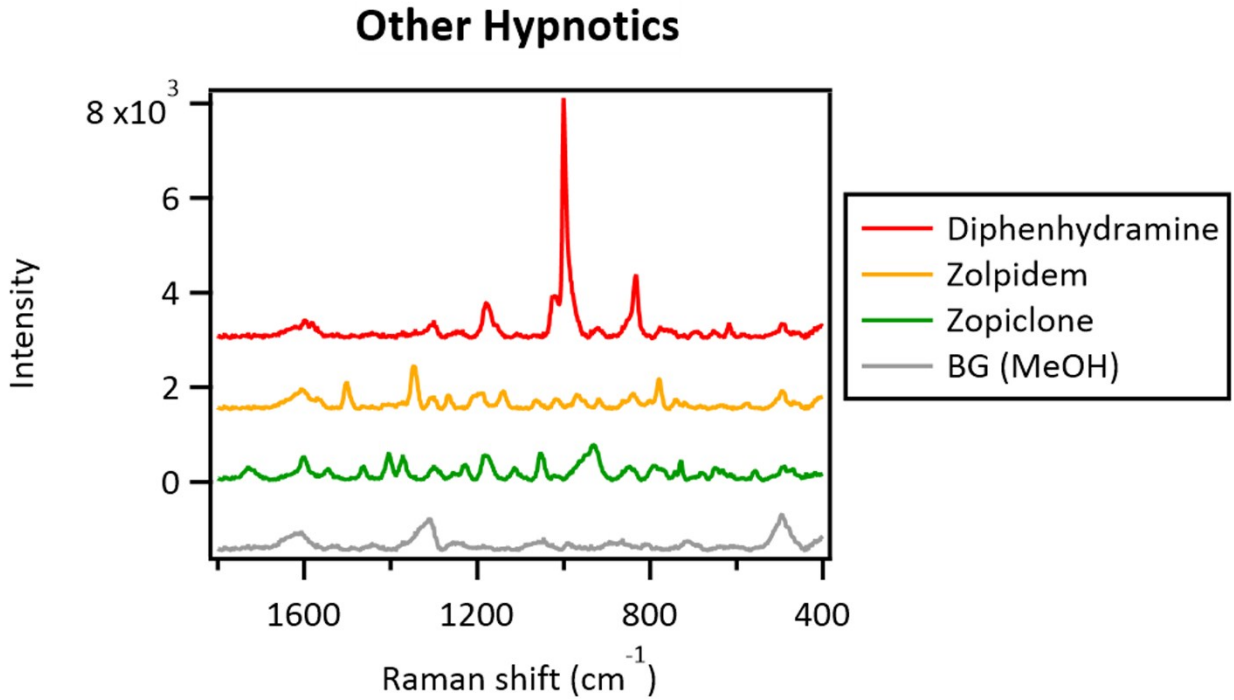
28 time was 1 sec and 100 frames spectra were averaged. All spectra were obtained by gold nanoparticles.

29 BG (MeOH) indicates the background spectra of AuNP aggregates.

(c)



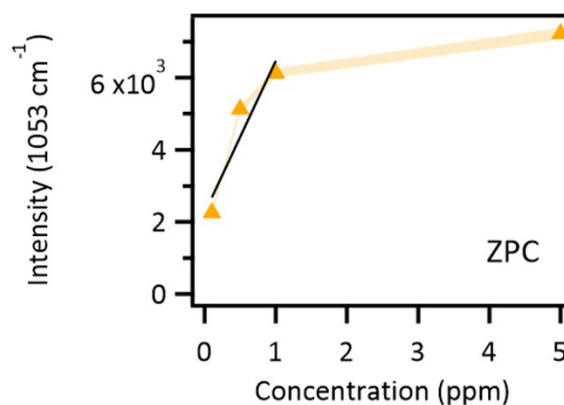
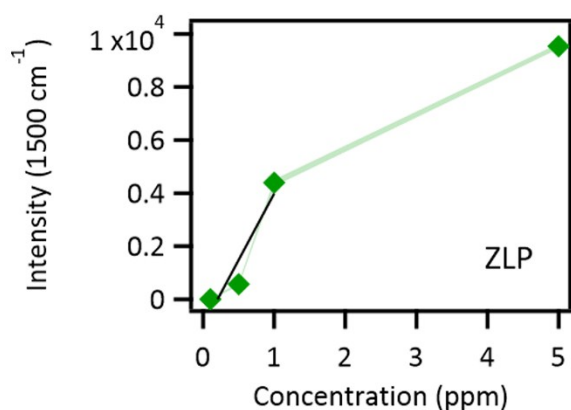
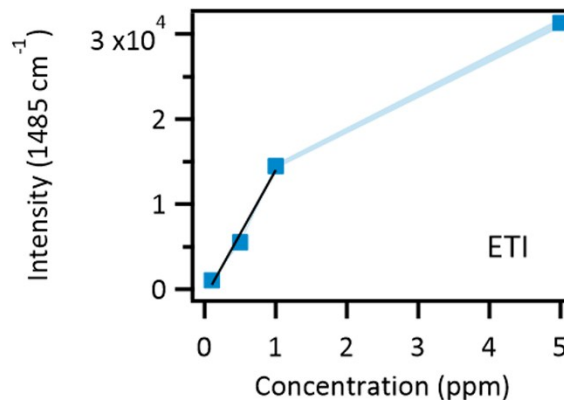
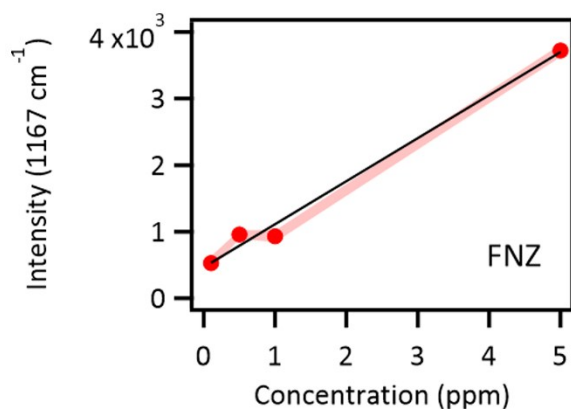
(d)



30

31 Figure S-1 (continued)

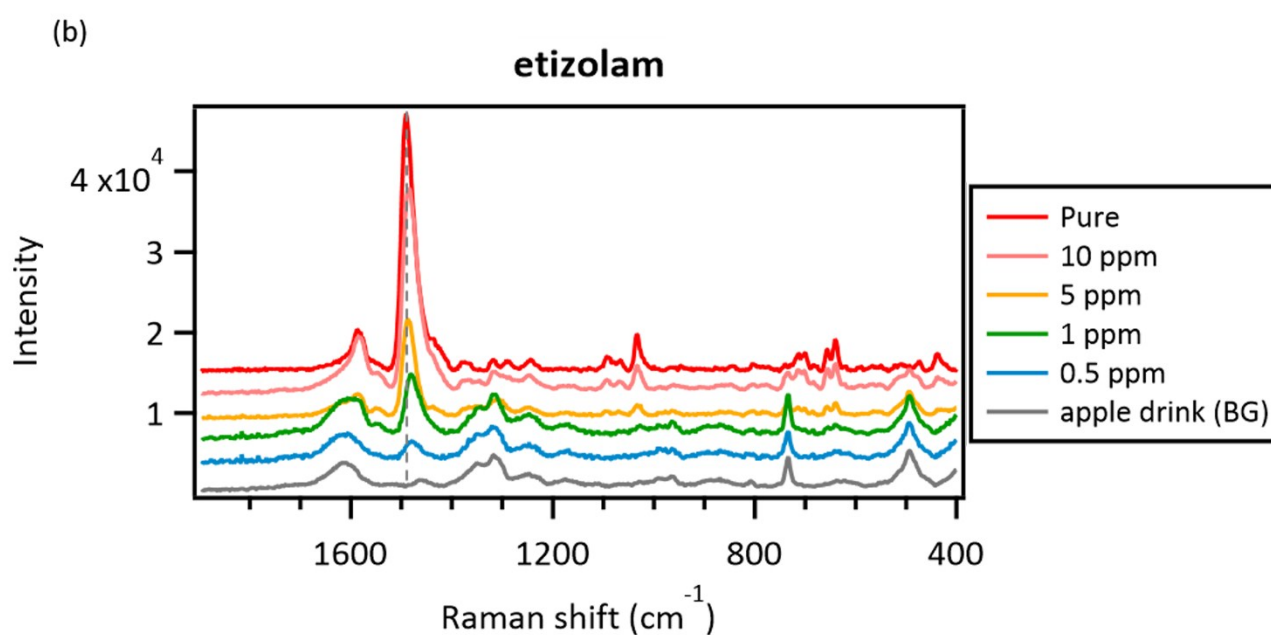
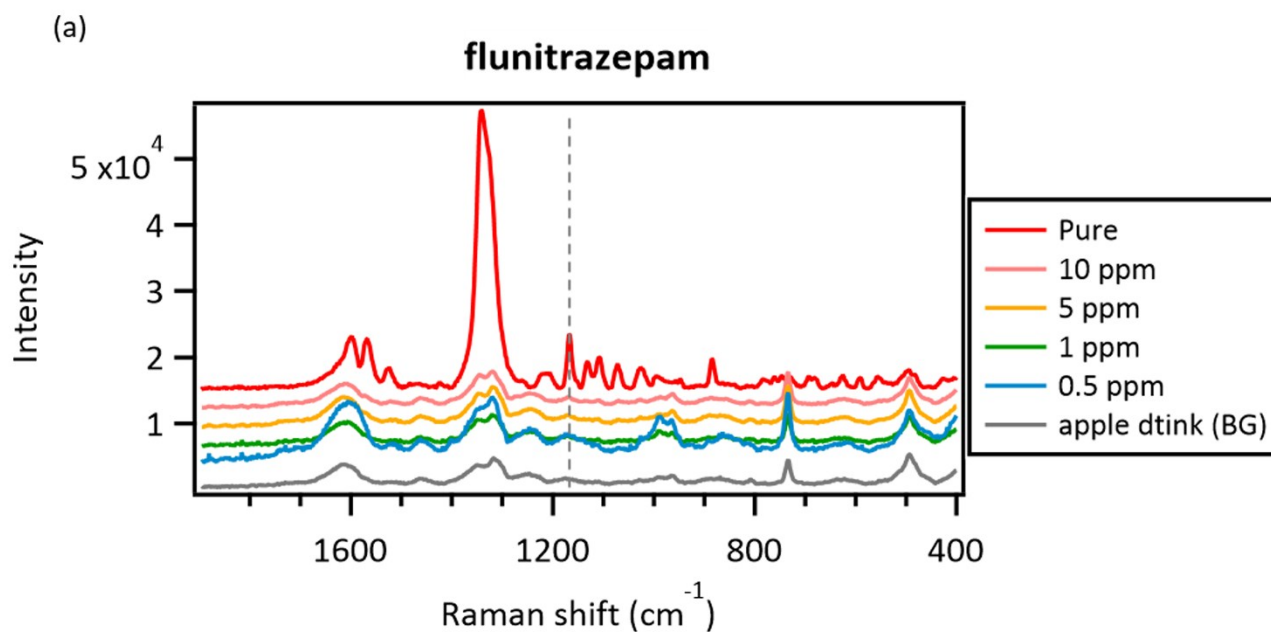
32



33

34 Figure S-2 Enlargement of calibration plots in the low concentration region for four hypnotics,  
 35 flunitrazepam (FNZ), etizolam (ETI), zolpidem (ZLP) and zopiclone (ZPC). Full scale plots are shown  
 36 in Fig. 6a. Shaded area indicate standard deviation of each sample points. Black lines indicates the  
 37 result of linear regression calibrated in 0.1-5 ppm (FNZ) or 0.1-1 ppm (ETI, ZLP and ZPC).

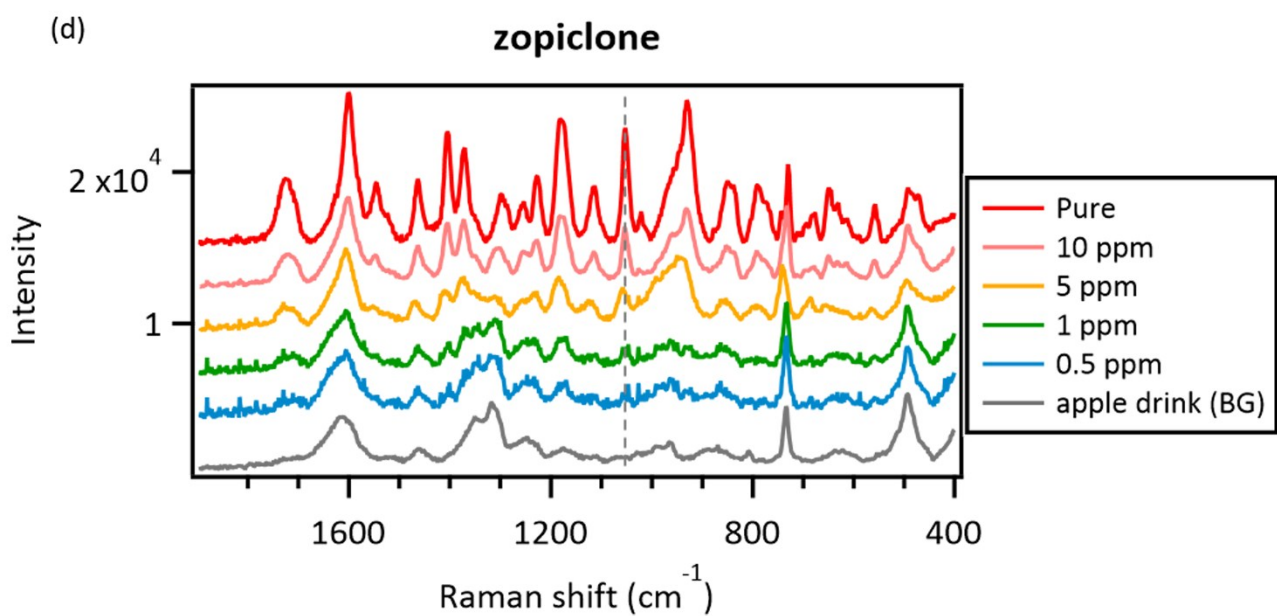
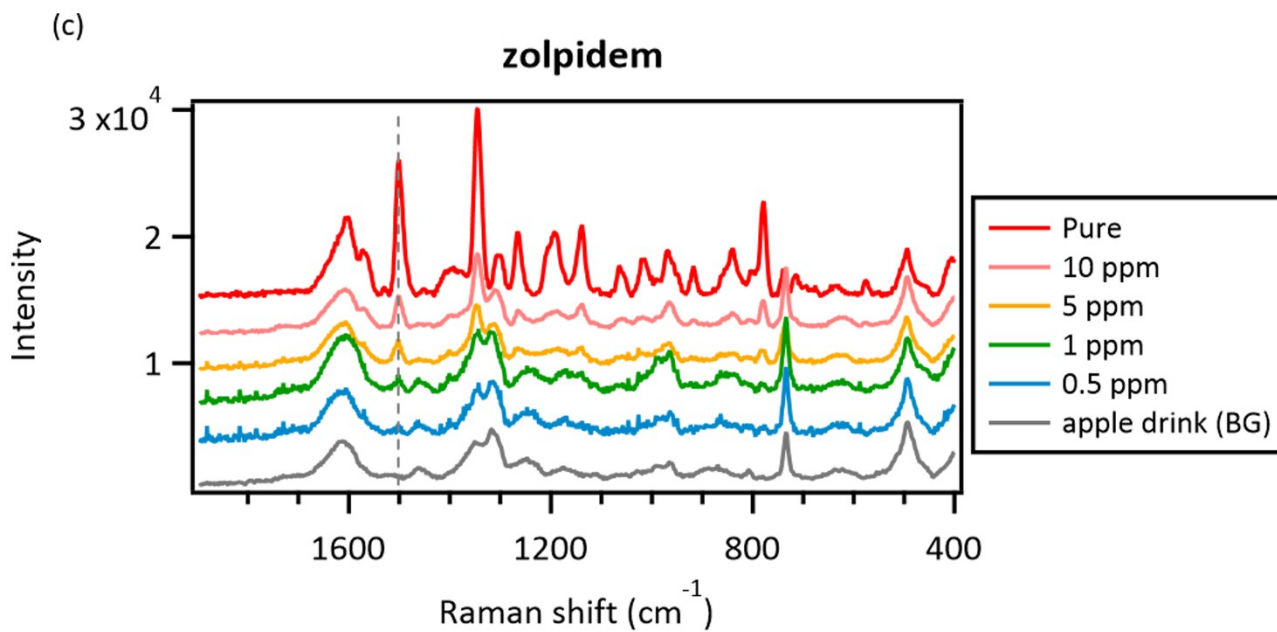
38



39

40 Figure S-3 Surface enhanced Raman scattering spectra obtained from apple drink containing  
 41 hypnotics. Concentrations indicated in the right panels indicate the final concentration of the sample  
 42 after dilution by water. Broken lines in each figure indicate the peak used for calculation of intensity  
 43 and matrix effect. Apple drink (BG) indicates the background spectra obtained by measuring SERS  
 44 from the apple drink without drug molecules.

45



46

47 Figure S-3 (continued).