

Electronic Supplementary Information

Title: In vitro investigation of the interaction between the hepatitis C virus drug sofosbuvir and human serum albumin through ^1H NMR, molecular docking, and spectroscopic analysis

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Journal: New Journal of Chemistry

As a complementary technique, WaterLOGSY NMR experiments were also performed on a Varian 700 MHz Inova spectrometer operating at 298K. All the spectra were acquired by using the following parameters: 256 transients, 32768 complex data points, 9842.52 Hz sweep width and 0.999947 s acquisition time. Introduced by Dalvit in 2000,¹ WaterLOGSY has proven to be an extremely useful ligand-observation technique to characterize interactions between ligands and proteins. For the binder to target protein, the inversion of water signals is selectively transferred to protein via the protein-water intermolecular NOE, then transferred to the small molecule ligand on the binding site.^{2,3} It should be noted that the WaterLOGSY signals are positive for binders but negative for non-binders. As seen in Fig. S1, the positive signals of spectrum (a) corresponding to the methyl groups and the aromatic protons, indicating SOF bound to HSA rather than the negative solvent (DMSO) signal. The WaterLOGSY response to addition of site-marker shows the clear negative signals when titrated with warfarin but not with ibuprofen, thus confirming the STD finding that the binding site of SOF was located preferentially within site I of HSA.

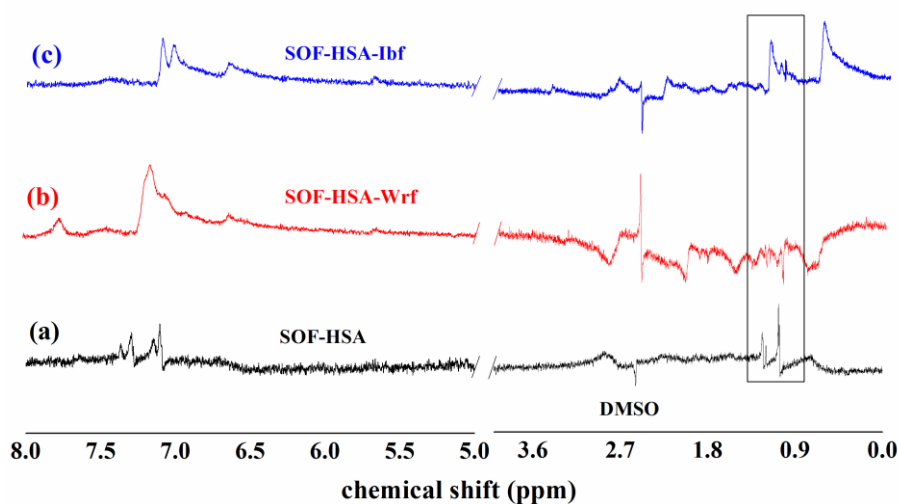


Fig. S1 Competitive WaterLOGSY between SOF and warfarin (Wrf) or ibuprofen (Ibf). The WaterLOGSY effect of SOF (400 μM) in the presence of HSA (10 μM) is shown in (a), while adding Wrf (800 μM) and Ibf (800 μM) is displayed in (b) and (c).

- 1 Dalvit, C. *et al.* Identification of compounds with binding affinity to proteins via magnetization transfer from bulk water*. *J. Biomol. NMR* 2000, **18**, 65-68.
- 2 Dalvit, C., Fogliatto, G., Stewart, A., Veronesi, M. & Stockman, B. WaterLOGSY as a method for primary NMR screening: practical aspects and range of applicability. *J. Biomol. NMR*, 2001, **21**, 349-359.
- 3 D. Gossert, C. Henry, M. J. Blommers, W. Jahnke and C. Fernández, *J. Biomol. NMR*, 2009, **43**, 211-217.