**Formulating Abiraterone Acetate-HPMCAS based Amorphous Solid Dispersion: Insight into In-Vitro and Biorelevant Dissolution Assessment and Pharmacokinetic Evaluation**

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**Supplementary Information**

**Composition of in-vitro dissolution media**

*pH 1.2*

To prepare a hydrochloric acid buffer solution with a pH of 1.2, 8.5 mL of concentrated hydrochloric acid (approximately 37% w/w) was measured. The measured acid was then poured into a 1000 mL volumetric flask containing about 900 mL of distilled water. The solution was mixed thoroughly to ensure even distribution. Finally, the solution was diluted to the final volume of 1000 mL with distilled water and mixed again to achieve a uniform solution.

*pH 4.5*

56.5 mM of monobasic sodium phosphate was dissolved in water. The pH was adjusted to 4 using 5 N sodium hydroxide or phosphoric acid. After that 0.25% sodium lauryl sulphate was added to the above solution.

*pH 6.8*

Disodium hydrogen phosphate (28.20 g) and potassium dihydrogen phosphate (11.45 g) were dissolved in sufficient water to produce a final volume of 1000 mL.

**Supplementary Table**

**Table 1S.** Estimation of solubility parameter of ABTA using the Hansen Group Contribution theory

| Structural group | Frequency | $F_d$ (MJ/m³)^0.5. mol | $F_P$ (MJ/m³)^0.5. Mol | $E_h$ (j/mol) | $V_m$ | $F_d$ (MJ/m³)^0.5. mol | $F_P$ (MJ/m³)^0.5. mol | $E_h$ (j/mol) | $V_m$ |
|---|---|---|---|---|---|---|---|---|---|
| --CH₃ | 3 | 420 | 0 | 0 | 33.5 | 1260 | 0 | 0 | 67 |
| CH₂ | 7 | 270 | 0 | 0 | 16.1 | 1890 | 0 | 0 | 112.7 |
| >CH | 5 | 80 | 0 | 0 | -1 | 400 | 0 | 0 | -5 |
| >C< | 1 | -70 | 0 | 0 | 19.2 | -70 | 0 | 0 | -19.2 |
| =CH | 8 | 200 | 0 | 0 | 13.5 | 1600 | 0 | 0 | 108 |
| =C< | 3 | 70 | 0 | 0 | -5.5 | 210 | 0 | 0 | -16.5 |
| -N | 1 | 20 | 0 | 0 | 5 | 0 | 0 | 0 | 5 |
| -COO | 1 | 390 | 490 | 7000 | 18 | 390 | 490 | 7000 | 18 |
| | | | | | Total | 5700 | 490 | 7000 | 303.5 |
| | | | | | | $\delta_d$ = 18.78 | $\delta_p$=0.072 | $\delta_h$=4.80 | |
| | | | | Total solubility parameter | | 19.38 | | | |

**Table 2S.** Estimation of Solubility Parameter of HPMCAS using the Hansen Group Contribution theory

| HPMCAS | Polar forces | Dispersive forces | Hydrogen bonding | Total solubility parameters |
|---|---|---|---|---|
| | $\delta p$ | $\delta d$ | $\delta h$ | |
| **HPMCAS 716** | 11.87 | 17.77 | 10.19 | 23.67 |
| **HPMCAS 912** | 12.37 | 16.73 | 10.33 | 23.22 |

**Table 3S: Dissolution parameters of ABTA and ABTA SD in different dissolution media**

| Formulation | Model | AIC | MSC |
|---|---|---|---|
| Dissolution media | **pH 1.2** | | |
| ABTA | KP | 53.02 | 1.05 |
| F2 | KP | 27.32 | 3.40 |
| F5 | KP | 37.39 | 2.58 |
| Dissolution media | **pH 4.5** | | |
| ABTA | KP | 22.36 | 3.45 |
| F2 | KP | 27.68 | 3.38 |
| F5 | KP | 17.19 | 4.47 |
| Dissolution media | **pH 6.8** | | |
| ABTA | KP | -17.18 | 1.73 |
| F2 | KP | 27.68 | 2.12 |
| F5 | KP | 17.19 | 2.17 |
| Dissolution media | **FaSSIF (pH 6.5)** | | |
| ABTA | KP | 11.10 | 2.16 |
| F2 | KP | 17.33 | 3.13 |
| F5 | KP | 14.25 | 3.04 |
| Dissolution media | **FeSSIF (pH 5.0)** | | |
| ABTA | KP | 38.25 | 1.39 |
| F2 | KP | 37.05 | 2.47 |
| F5 | KP | 35.21 | 2.70 |

**Supplementary Figure**
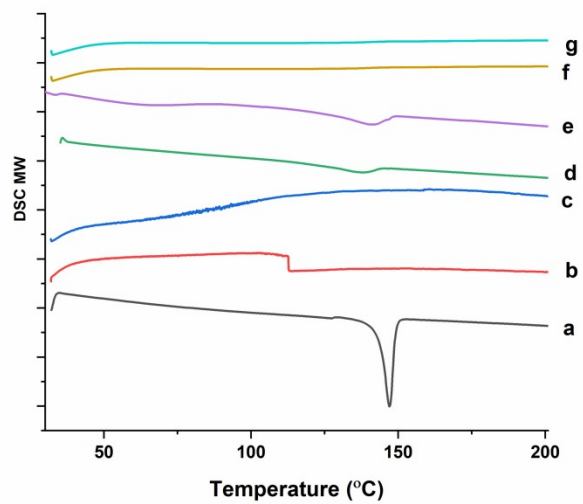


**Fig.1S.** DSC of [a] ABTA; [b] HPMCAS 716; [c] HPMCAS 912; [d] ABTA: HPMCAS 716 PM; [e] ABTA: HPMCAS 912 PM; [f] ABTA: HPMCAS 716 SD; [g] ABTA: HPMCAS 912 SD
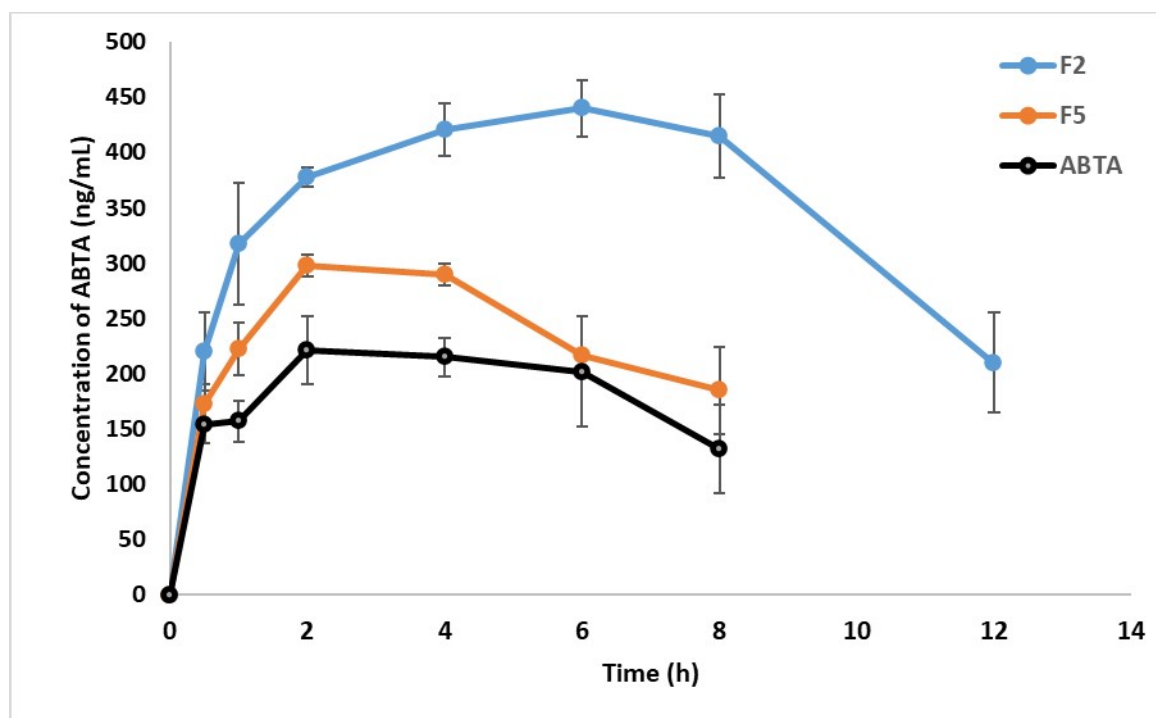
**Fig. 2S** Plasma concentration-time profile of unformulated ABTA and ABTA SD after oral administration (Values represent mean + SEM) (n=3)