Supporting Information

Enhanced solubility of telmisartan phthalic acid cocrystals within the pH range of systemic absorption site

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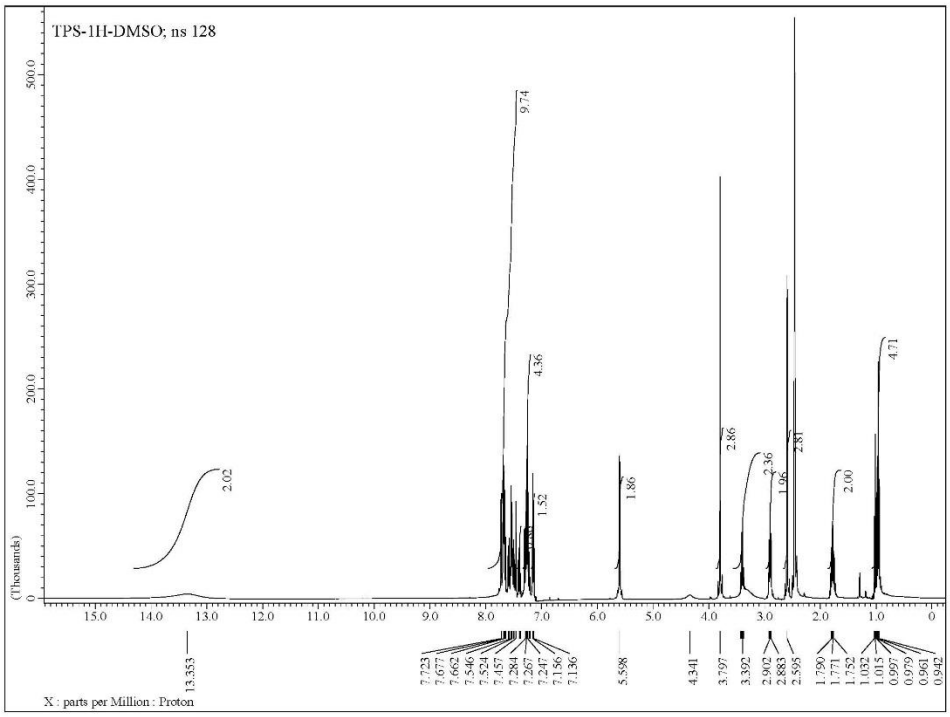
Table S1 Preliminary screening of coformers by solution crystallization method

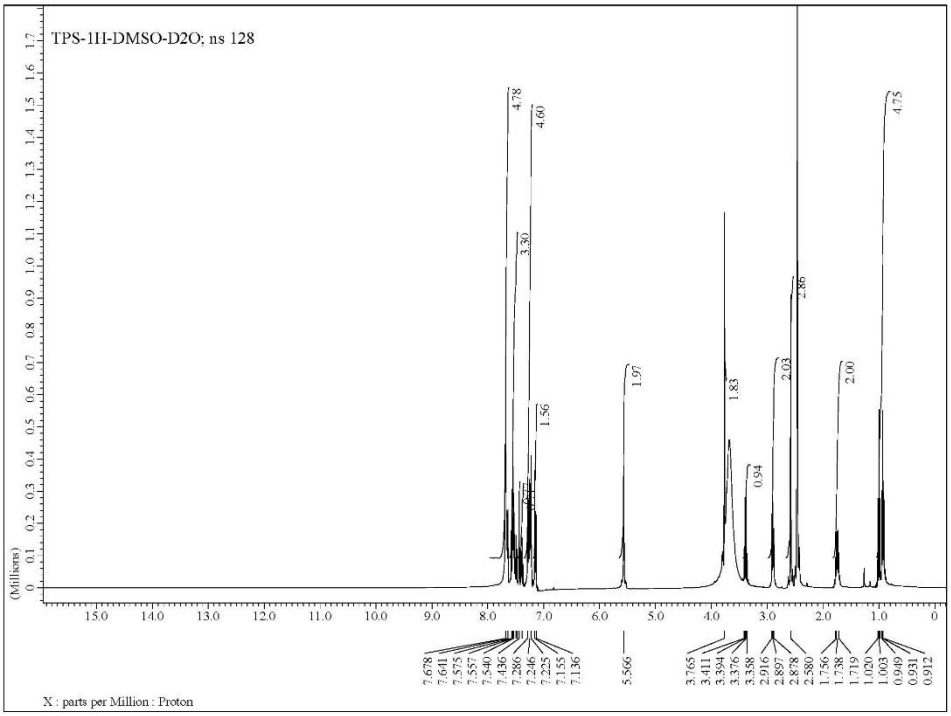
Sl. No.	Coformers [(a)]	pK_a values of coformer	Solvent used for crystallization	Inference
1.	D-Tryptophan[1]	pK_{a1}=2.38 pK_{a2}=9.39	Chloroform: ethanol (1:1)	Sticky mass
2.	Nicotinamide[2]	3.35	Ethanol	Sticky mass
3.	Maleic acid[3]	pK_{a1}=1.94 pK_{a2}=6.22	Chloroform: ethanol (2:1)	**Hit (new solid form)** Crystal size was not suitable for SCXRD analysis.
			Acetone	
4.	Nicotinic acid[4]	pK_{a1}=4.75	Ethanol	Sticky mass
5.	Para amino benzoic acid[5]	pK_{a1} = 2.38 pK_{a2} = 4.85	Chloroform: methanol (1:1)	No crystals obtained
6.	Urea[6]	0.10	Chloroform: ethanol (2:1)	No crystals obtained
7.	Sorbic acid[7]	4.76	Methanol	No crystals obtained
8.	L-proline[8]	pK_{a1}=1.99 pKa_2=10.60	Chloroform: methanol (2:1)	Sticky mass
9.	Phthalic acid[9]	pK_{a1} = 2.76, pK_{a2} = 4.92	Chloroform: ethanol (2:1)	**Hit (Ethanol solvate of Telmisartan phthalic acid cocrystal)**
10.	Malic acid[10]	pK_{a1}= 3.51, pK_{a2}= 5.03	Chloroform: methanol (1:1)	No crystals obtained

11.	Glutamic acid[11]	pK_{a1} = 2.19, pK_{a2}=4.25, pK_{a3} =9.67	Chloroform: 1-propanol (2:1)	Sticky mass
12.	Adipic acid[12]	pK_{a1}= 4.43, pK_{a2}= 5.41	Chloroform: methanol (1:1)	No crystals obtained
13.	Citric acid[13]	2.79	Chloroform: isopropyl alcohol (2:1)	No crystals obtained
14.	Benzoic acid[14]	4.20	Chloroform: methanol (1:1)	No crystals obtained
15.	Oxalic acid[15]	pK_{a1}=1.46, pK_{a2}=4.40	Chloroform: methanol (1:1)	No crystals obtained
16.	Succinic acid[16]	pK_{a1}= 4.20, pK_{a2}= 5.63	Chloroform: methanol (1:1)	No crystals obtained

[a]*One molar equivalent of drug and coformer were used*



(a)



(b)

Figure S1 a) ^{1}H NMR spectrum of TPS cocrystal system showing acidic protons at δ 13.35. **b)** D_2O exchange spectrum of TPS cocrystal system showing disappearance of acidic protons.

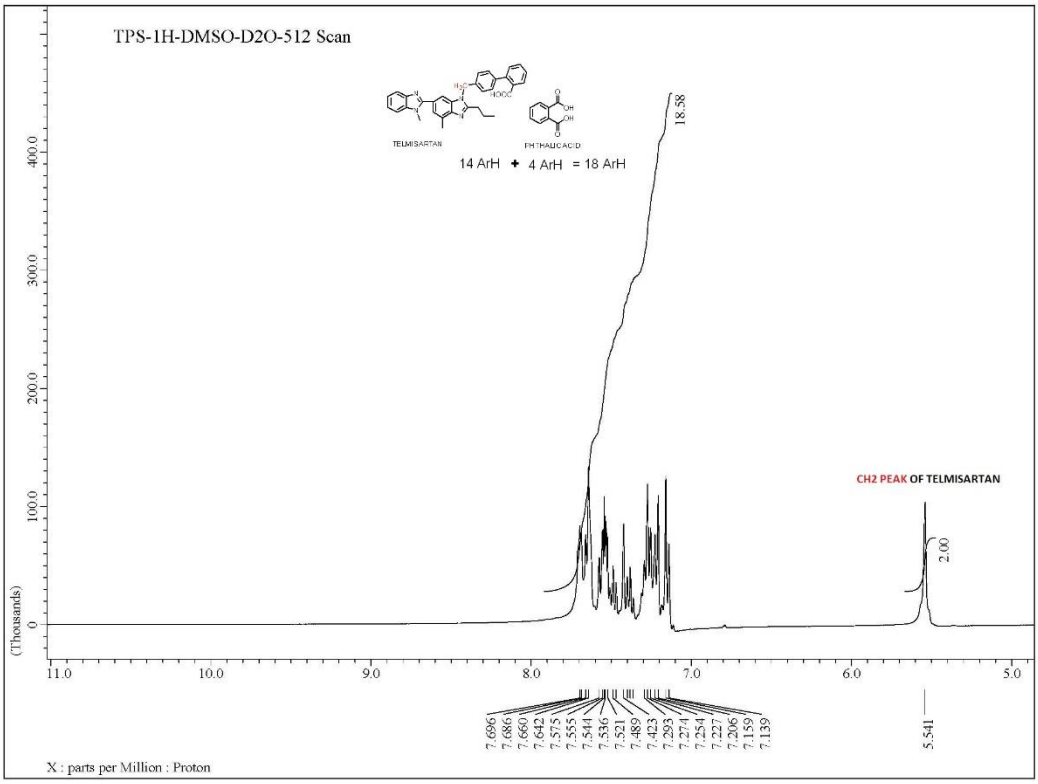


Figure S2 ^{1}H NMR spectrum of TPS cocrystal system showing distinguished CH_2 peak of TLM (δ: 5.54, s, 2H) with 2H integration in comparison to 18 H integration (δ: 7.14-7.69) for aromatic protons. Thus, the presence of 18 aromatic protons in comparison to 2H of TLM confirms the presence of TLM:PH in 1:1 ratio in TPS cocrystal.

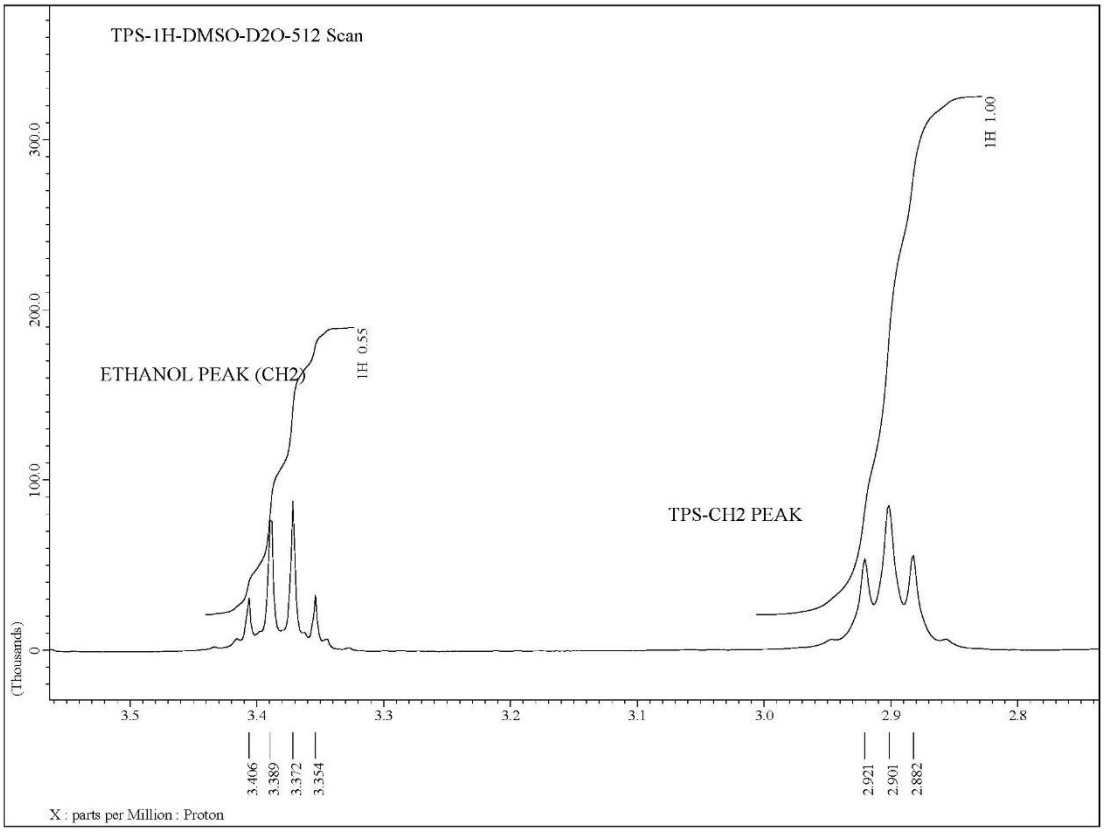
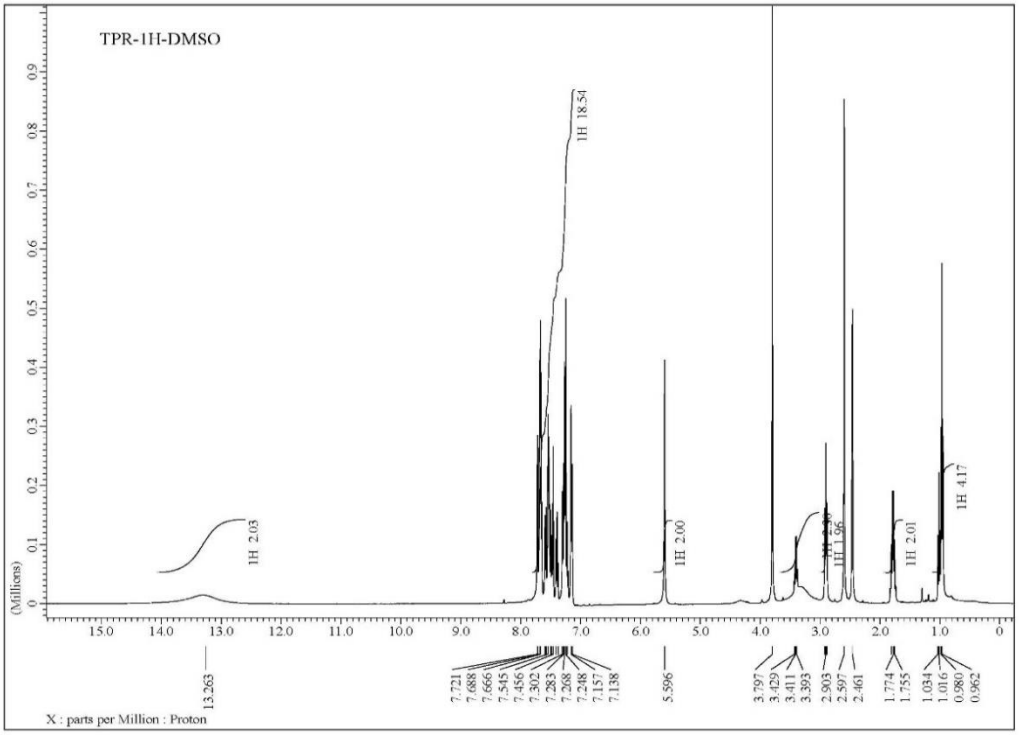
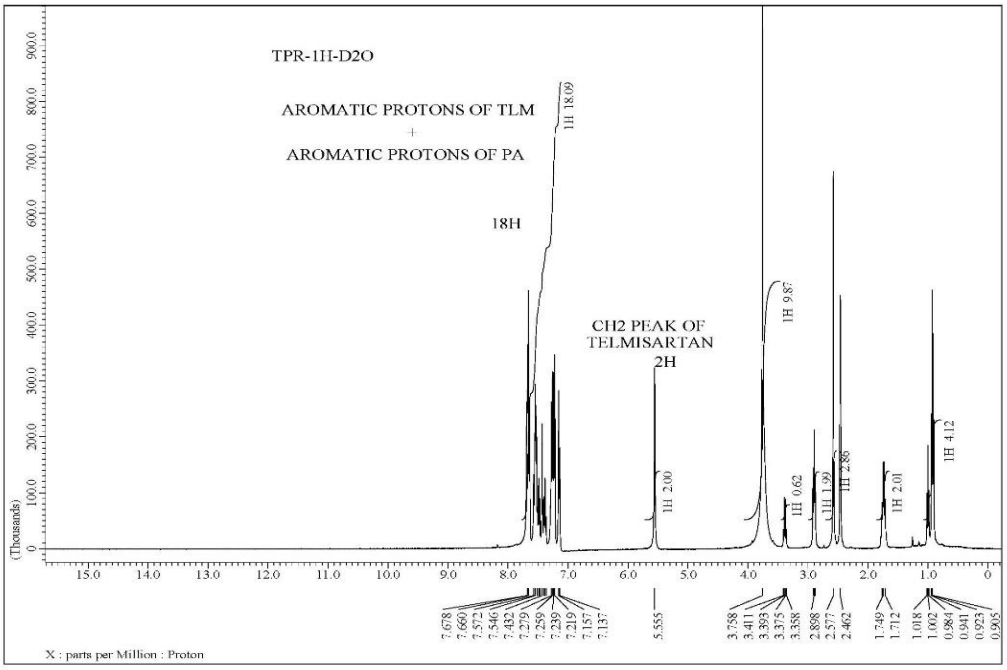


Figure S3 ^{1}H NMR spectrum of TPS cocrystal system showing distinguished CH_2 peak of TLM (blue δ: 2.90, t, 2H) with 1 integration in comparison to 0.5 integration for CH_2 proton of ethanol (δ: 3.35-3.40). Thus, the presence of half ratio of ethanol in comparison to unit ration of TLM confirms the presence of TLM: Ethanol in 1:0.5 ratio in TPS cocrystal.



(a)



(b)

Figure S4 a) ^{1}H NMR spectrum of TPR cocrystal system showing acidic protons at δ 13.26. **b)** D_2O exchange spectrum of TPS cocrystal system showing disappearance of acidic protons. The presence of 18 aromatic protons in comparison to 2H of TLM confirms the presence of TLM (14 ArH):PH (4 ArH) in 1:1 ratio in TPS cocrystal.

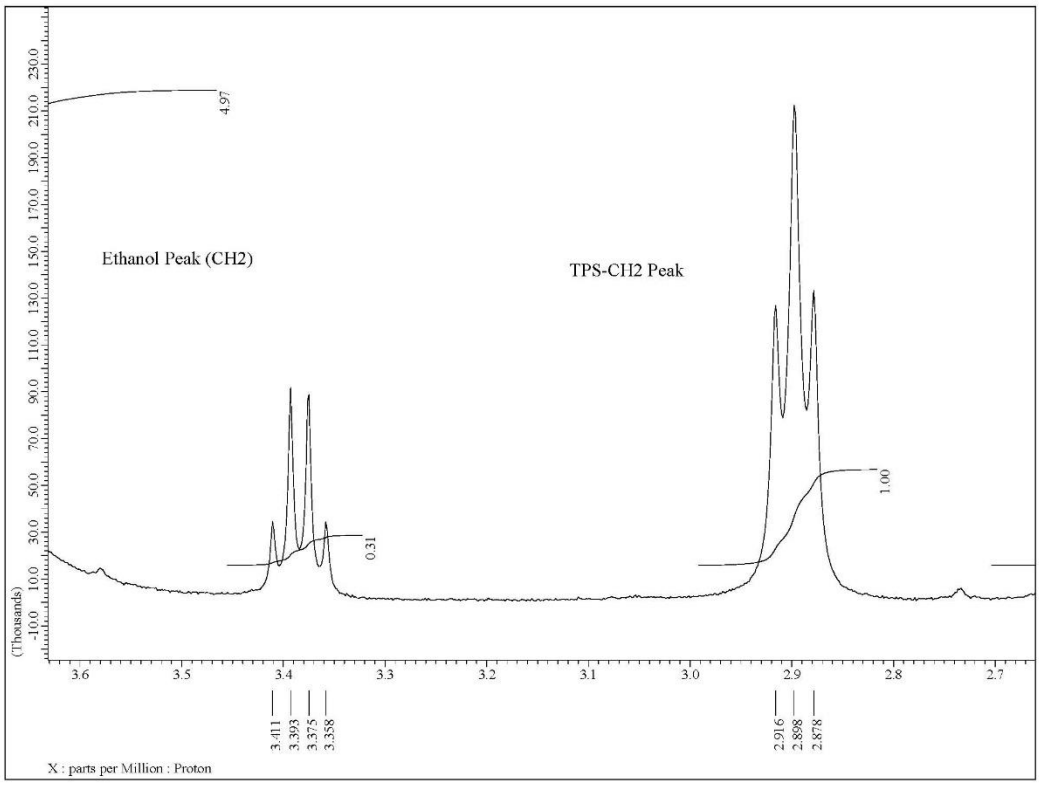


Figure S5 ^{1}H NMR spectrum of TPR cocrystal system showing distinguished CH_2 peak of TLM (blue δ: 2.91, t, 2H) with 1 integration in comparison to 0.3 integration for CH_2 proton of ethanol (δ: 3.35-3.41). Thus, the presence of ethanol in comparison to unit ratio of TLM confirms the presence of TLM: Ethanol in 1:0.3 ratio in TPR cocrystal.

Table S2 Initial and equilibrium solution pH, final solid phases of TLM, TPS and TPR obtained after 72 hr. of solubility experiment

Initial solid phase	Initial solution pH	Equilibrium solution pH
TLM	**3**	**3.09**
	4	**4.23**
	5	**5.32**
	6	**6.12**
	7	**7.03**
	8	**7.98**
	9	**8.8**
	10	**9.29**

Initial solid phase	Initial solution pH	Equilibrium solution pH	Final solid phase as determined by PXRD
TPS	**3**	**3.06**	**TPS**
	4	**3.50**	**TPS**
	5	**3.81**	**TPS**
	6	**5**	**TPS + TLM**
	7	**6.77**	**TPS +TLM**
	8	**6.09**	**TLM**
	9	**7.22**	**TLM**
	10	**7.22**	**TLM**

Initial solid phase	Initial solution pH	Equilibrium solution pH	Final solid phase as determined by PXRD
TPR	**3**	**3.06**	**TPR**
	4	**3.49**	**TPR**
	5	**3.52**	**TPR**
	6	**4.37**	**TPR**
	7	**6.69**	**TPR+TLM**
	8	**7.1**	**TLM**
	9	**7.14**	**TLM**
	10	**6.77**	**TLM**

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