Role of valsartan as an anti-plasticizer in development of therapeutically viable drug-drug co amorphous system

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Electronic supplementary information

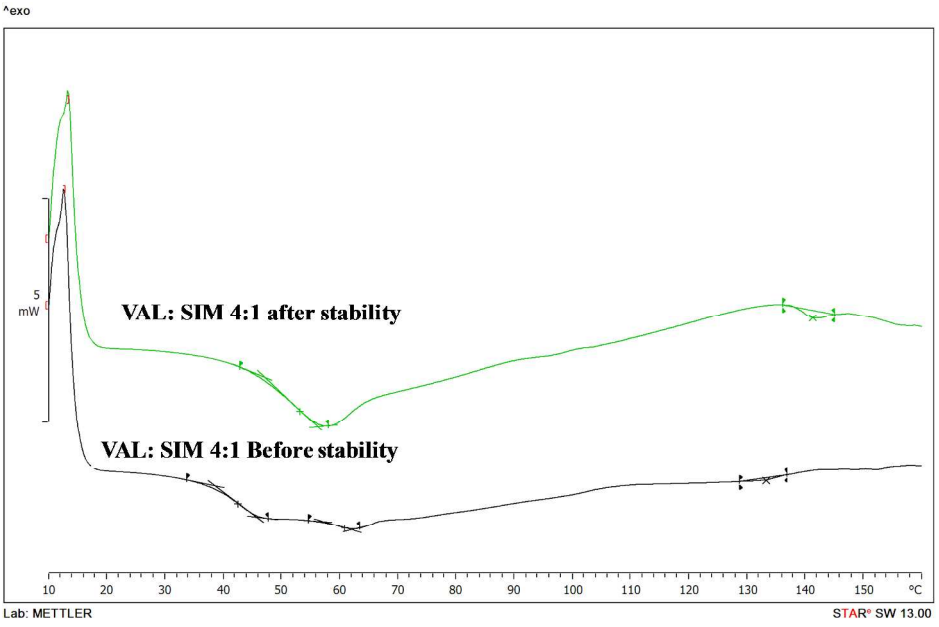

Figure S1 DSC thermogram of co amorphous system valsartan (VAL): simvastatin (SIM) 4:1weight ratio, before and after stability study

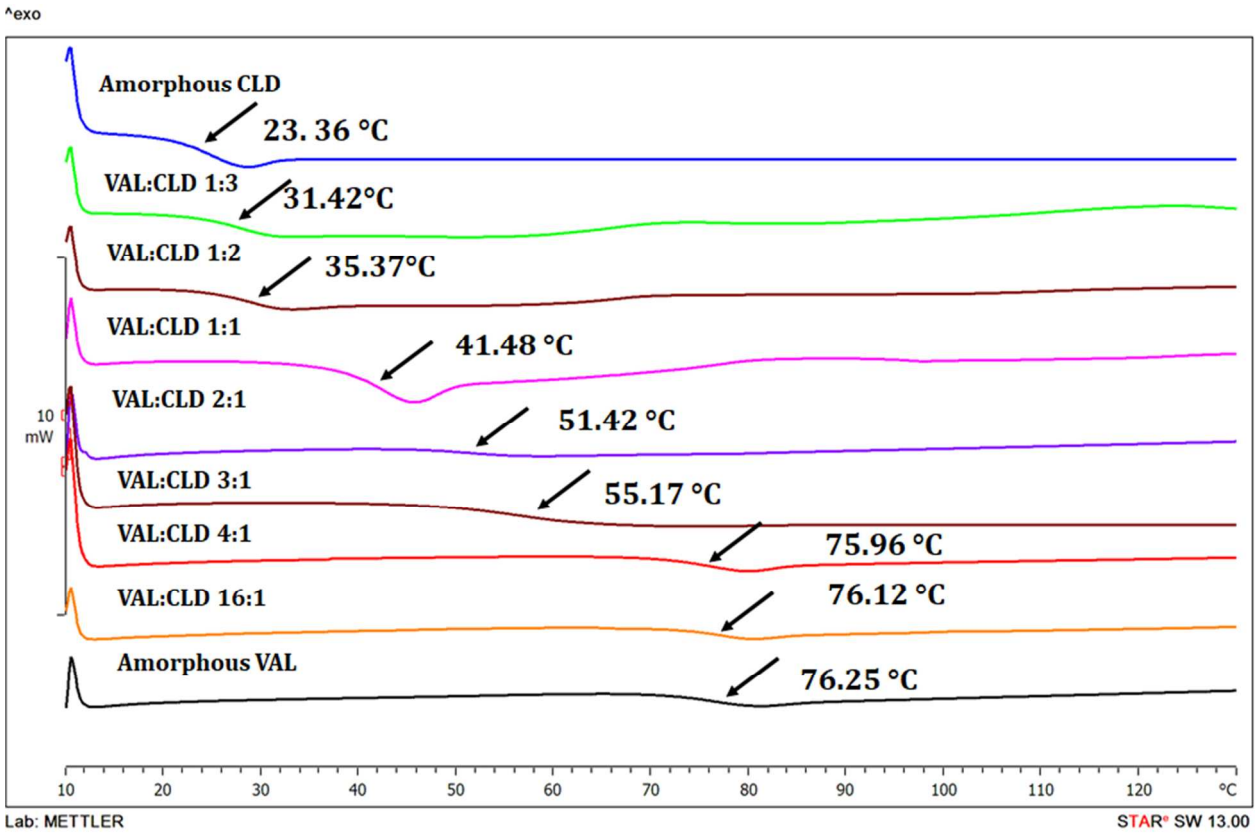

Figure S2 DSC curves of in situ quench cooled cilnidipine (CLD), valsartan (VAL) and VAL-CLD co amorphous systems. Arrow indicates the T_g.

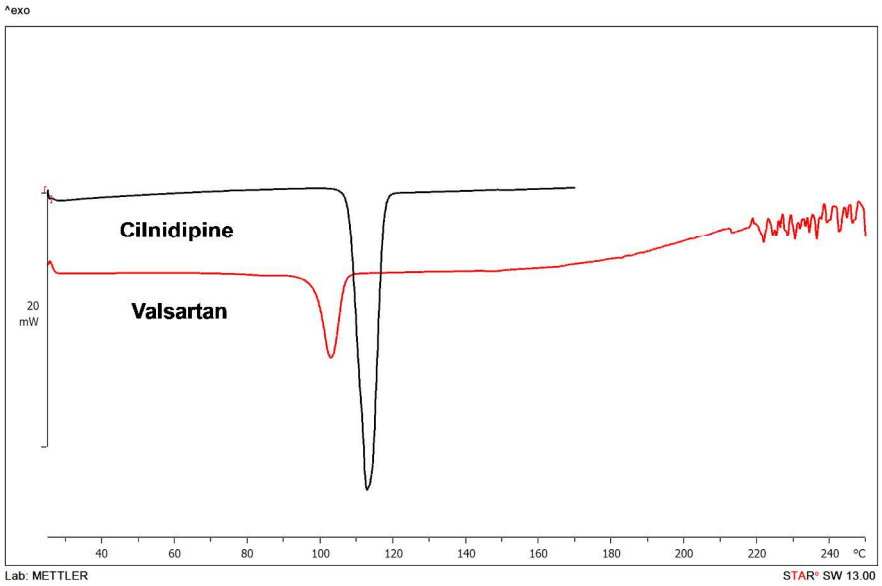

Figure S3 DSC curves of crystalline cilnidipine and valsartan

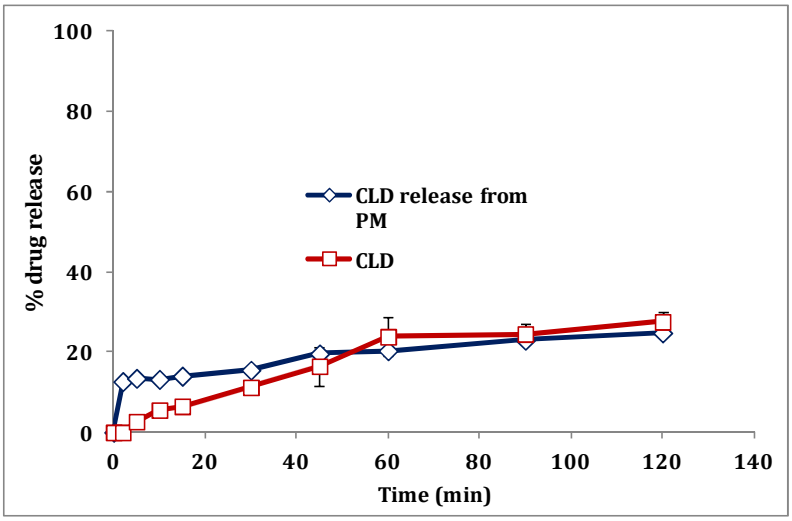

Figure S4 Dissolution profile of plain cilnidipine and its release from physical mixture with valsartan

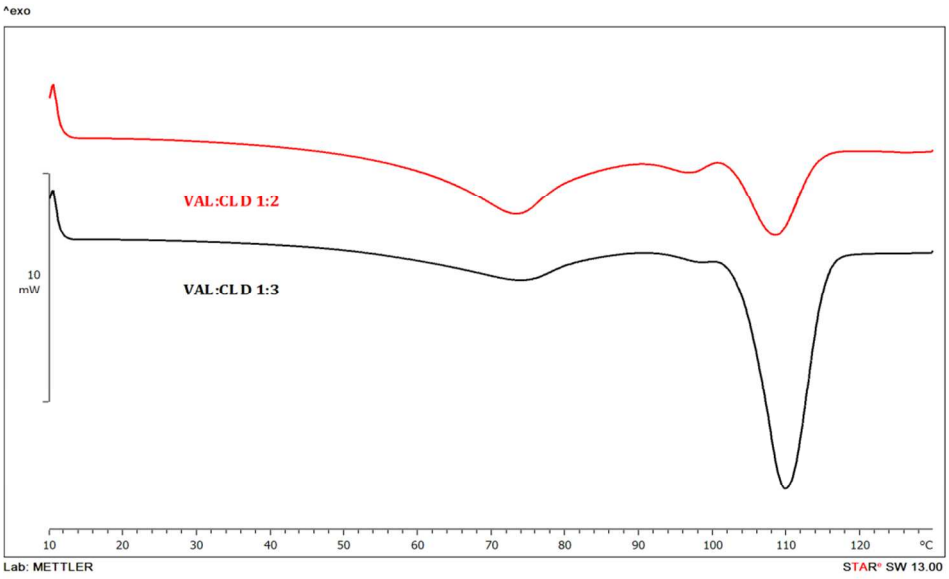

Figure S5 DSC thermograms of stability samples of valsartan (VAL): cilnidipine (CLD) co amorphous system in 1:2 and 1:3 ratio

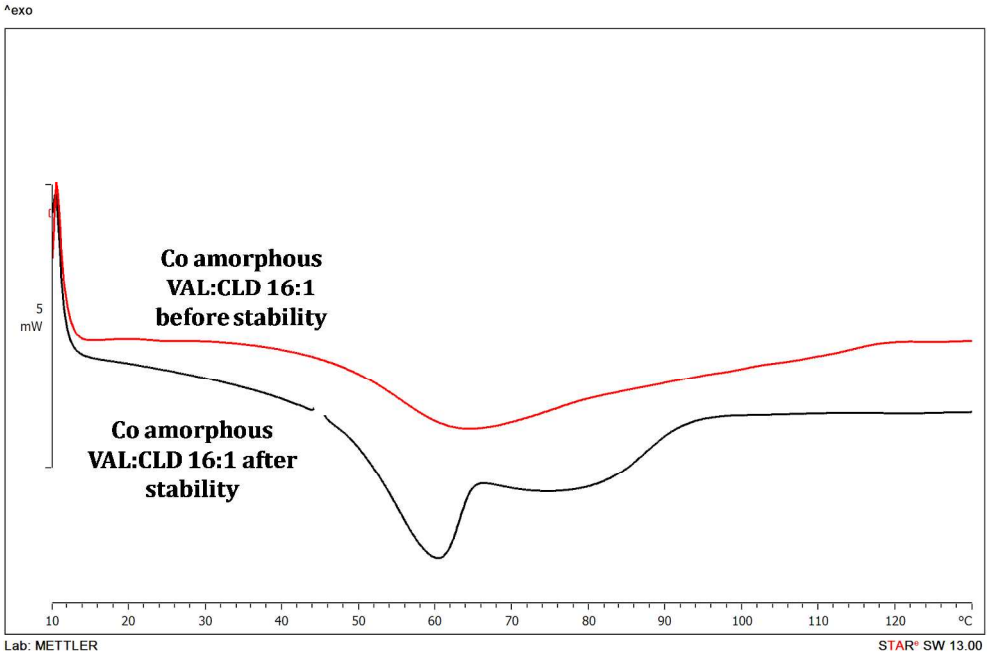

Figure S6 DSC thermograms of stability samples of valsartan (VAL): cilnidipine (CLD) co amorphous system in 16:1 ratio before and after 1 month

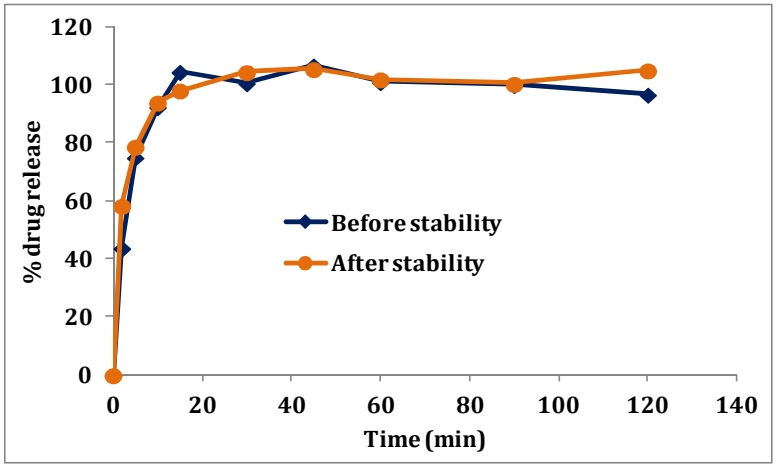

Figure S7 Dissolution profile of valsartan: cilnidipine 16:1 co amorphous system before and after stability studies

Tables

Table S1 Chromatographic parameters for HPLC analysis

HPLC Parameter	Optimized values
Mobile phase	Acidified water (pH 3 with ortho-phosphoric acid): acetonitrile (40:60 v/v)
Elusion	Isocratic
Flow rate	1 ml/min
Wavelength	Cilnidipine (240 nm) and valsartan (247 nm)
Injection volume	20 µl
Column	Inertsustain C18, 5 µ, 4.6 × 100 mm

Table S2 Glass transition temperature (Tg) of cilnidipine (CLD), valsartan (VAL) and their co amorphous systems in different ratios.

Sample	Experimentally prepared quench cooled systems	*In situ* generated quench cooled systems
	T_g (°C) with SD	T_g (°C)
CLD	23.21 ± 0.18	23.36
VAL:CLD 1:3	31.05 ± 0.68	31.42
VAL:CLD 1:2	35.33 ± 0.31	35.37
VAL:CLD 1:1	41.41 ± 0.27	41.48
VAL:CLD 2:1	51.14 ± 0.47	51.42
VAL:CLD 3:1	55.06 ± 0.81	55.17
VAL:CLD 4:1	74.26 ± 0.31	75.96
VAL:CLD 16:1	75.60 ± 0.48	76.12
VAL	76.14 ± 0.10	76.25

Table S3 Comparison of cilnidipine release from valsartan (VAL): cilnidipine (CLD) co amorphous system with crystalline cilnidipine

Sample (with reference to plain crystalline cilnidipine)	F2 value	DE_{15}
CLD	-	3.63
VAL:CLD 1:1 co amorphous	34.14	12.71
VAL:CLD 2:1 co amorphous	25.79	33.21
VAL:CLD 3:1 co amorphous	32.82	19.19
VAL:CLD 4:1 co amorphous	18.17	43.67
VAL:CLD 16:1 co amorphous	8.40	78.41
VAL:CLD 16:1 PM	60.71	12.44

Table S4 Comparison of valsartan release from co amorphous system valsartan (VAL): cilnidipine (CLD) with crystalline cilnidipine

Sample (with reference to plain crystalline valsartan)	F2 value	DE_{15}	DE_{60}
VAL	-	09.50	16.50
AVAL	90.34	09.50	16.66
VAL:CLD 1:1 co amorphous	58.67	04.39	9.18
VAL:CLD 2:1 co amorphous	73.96	09.90	13.96
VAL:CLD 3:1 co amorphous	75.05	10.30	18.06
VAL:CLD 4:1 co amorphous	54.90	11.68	21.33
VAL:CLD 16:1 co amorphous	46.14	15.32	25.35
VAL:CLD 16:1 PM	47.44	14.82	23.67