

Curcumin-Artemisinin Coamorphous Solid: Xenograft Model Preclinical Study

M. K. Chaitanya Mannava ^{1,2}, Kuthuru Suresh ^{1,2}, Manish Kumar Bommaka ¹, Durga Bhavani Konga ⁴ and Ashwini Nangia ^{1,2,3,*}

¹ School of Chemistry, University of Hyderabad, Hyderabad, Hyderabad 500 046, India; mchaitanya@gmail.com (M.K.C.M.); kuturusuresh@gmail.com (K.S.); mani071115@gmail.com (M.K.B.)

² Technology Business Incubator, University of Hyderabad, Hyderabad 500 046, India

³ Council of Scientific and Industrial Research National Chemical Laboratory, Pune 411 008, India

⁴ Virchow Biotech Pvt. Ltd., Animal House Facility, Hyderabad 500 055, India; kongabilwakshi@gmail.com

* Correspondence: ashwini.nangia@gmail.com or ak.nangia@ncl.res.in; Tel.: +91-202-590-2600

Table S1. Acute oral toxicity of CUR-PYR cocrystal in Sprague Dawley Rats (Male and Female).

Body weights (g)—Male					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	210.68 ± 4.15 (6)	213 ± 3.88 (6)	216.16 ± 3.79 (6)	219.25 ± 3.37 (6)	220.66 ± 3.26 (6)
	209.16 ± 4.03 (6)	211.83 ± 1.91 (6)	215.58 ± 4.97 (6)	219.08 ± 5.31 (6)	219.83 ± 5.24 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC—Vehicle Control

TG—Theraupatic Group

Body weights (g)—Female					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	206.91 ± 3.92 (6)	210.5 ± 3.84 (6)	214.58 ± 3.74 (6)	218.0 ± 3.68 (6)	218.73 ± 3.94 (6)
	206.7 ± 3.34 (6)	210.16 ± 3.43 (6)	213.91 ± 3.07 (6)	216.48 ± 2.96 (6)	218.83 ± 2.90 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC—Vehicle Control

TG—Theraupatic Group

Organ Weights (g)—Male							
Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Testis
VC	0.86 ± 0.03 (6)	1.17 ± 0.05 (6)	9.20 ± 0.05 (6)	1.44 ± 0.01 (6)	0.84 ± 0.16 (6)	1.90 ± 0.04 (6)	1.76 ± 0.07 (6)
	0.87 ± 0.06 (6)	1.14 ± 0.01 (6)	9.10 ± 0.12 (6)	1.39 ± 0.03 (6)	0.83 ± 0.18 (6)	1.89 ± 0.03 (6)	1.73 ± 0.11 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC—Vehicle Control

TG—Theraupatic Group

Organ Weights (g)—Female							
Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Ovaries
VC	0.80 ± 0.04 (6)	1.11 ± 0.06 (6)	7.40 ± 0.09 (6)	1.33 ± 0.05 (6)	0.54 ± 0.03 (6)	1.83 ± 0.06 (6)	0.05 ± 0.02 (6)
	0.82 ± 0.02 (6)	1.10 ± 0.03 (6)	7.43 ± 0.7 (6)	1.13 ± 0.07 (6)	0.56 ± 0.08 (6)	1.82 ± 0.05 (6)	0.06 ± 0.02 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC—Vehicle Control

TG—Theraupatic Group

Table S2. Acute oral toxicity of CUR-ART coamorphous in Sprague Dawley Rats (Male and Female).

Body weights (g)—Male					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	215.61 ± 2.8 (6)	207.08 ± 2.85 (6)	209.83 ± 3.98 (6)	213.0 ± 2.75 (6)	214.41 ± 2.51 (6)
	214.7 ± 2.43 (6)	216.16 ± 2.18 (6)	218.5 ± 2.07 (6)	220.75 ± 1.69 (6)	221.83 ± 1.47 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

Body weights (g)—Female					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	185.85 ± 2.28 (6)	187.0 ± 2.54 (6)	190.91 ± 1.88 (6)	193.28 ± 1.36 (6)	196.58 ± 1.02 (6)
	195.65 ± 3.18 (6)	197.83 ± 2.65 (6)	201.5 ± 2.88 (6)	204.51 ± 1.62 (6)	206.35 ± 2.06 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

Organ Weights (g) —Male							
Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Testis
VC	0.82 ± 0.09 (6)	1.15 ± 0.01 (6)	9.12 ± 0.01 (6)	1.42 ± 0.07 (6)	0.83 ± 0.05 (6)	1.95 ± 0.03 (6)	1.75 ± 0.09 (6)
	0.87 ± 0.06 (6)	1.14 ± 0.01 (6)	9.10 ± 0.12 (6)	1.39 ± 0.03 (6)	0.83 ± 0.18 (6)	1.89 ± 0.03 (6)	1.73 ± 0.11 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

Organ Weights (g) —Female							
Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Ovaries
VC	0.82 ± 0.08 (6)	1.12 ± 0.13 (6)	7.50 ± 0.07 (6)	1.30 v 0.01 (6)	0.61 ± 0.07 (6)	1.88 ± 0.017 (6)	0.07 ± 0.01 (6)
	0.81 ± 0.02 (6)	1.05 ± 0.06 (6)	7.56 ± 0.4 (6)	1.28 ± 0.09 (6)	0.59 ± 0.07 (6)	1.87 ± 0.015 (6)	0.05 ± 0.01 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

Table S3. Acute oral toxicity of CUR-ART coamorphous in Swiss Albino Mice (Male and Female).

Body weights (g)—Male					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	18.8 ± 0.4 (6)	19.75 ± 0.52 (6)	21.4 ± 0.37 (6)	24.0 ± 0.63 (6)	25.58 ± 0.58 (6)
	20.81 ± 0.9 (6)	21.7 ± 0.89 (6)	23.41 ± 0.37 (6)	24.66 ± 0.25 (6)	26.43 ± 0.38 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

Body weights (g)—Female					
Groups	Day 0	Day 4	Day 8	Day 12	Day 15

VC	17.83 ± 0.12 (6)	19.0 ± 0.44 (6)	19.9 ± 0.49 (6)	21.91 ± 0.49 (6)	23.5 ± 0.44 (6)
TG	19.03 ± 0.50 (6)	20.41 ± 0.37 (6)	22.16 ± 0.40 (6)	23.83 ± 0.25 (6)	24.91 ± 0.73 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraapeutic Group

Organ Weights (g)—Male

Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Testis
VC	0.14 ± 0.05 (6)	0.41 ± 0.07 (6)	1.3 ± 0.04 (6)	0.4 ± 0.05 (6)	0.06 ± 0.01 (6)	0.4 ± 0.005 (6)	0.22 ± 0.03 (6)
TG	0.14 ± 0.01 (6)	0.34 ± 0.06 (6)	1.30 ± 0.03 (6)	0.49 ± 0.05 (6)	0.061 ± 0.01 (6)	0.47 ± 0.005 (6)	0.22 ± 0.02 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraapeutic Group

Organ Weights (g)—Female

Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Ovaries
VC	0.11 ± 0.013 (6)	0.30 ± 0.07 (6)	1.03 ± 0.08 (6)	0.30 v 0.026 (6)	0.07 ± 0.002 (6)	0.47 ± 0.06 (6)	0.05 ± 0.01 (6)
TG	0.11 ± 0.012 (6)	0.32 ± 0.05 (6)	1.06 ± 0.04 (6)	0.38 ± 0.022 (6)	0.07 ± 0.002 (6)	0.45 ± 0.08 (6)	0.02 ± 0.01 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraapeutic Group

Table S4. Acute oral toxicity of CUR-PYR cocrystal in Swiss Albino Mice (Male and Female).

Body weights (g)—Male

Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	18.93 ± 1.57 (6)	20.5 ± 1.94 (6)	23.08 ± 2.17 (6)	25.41 ± 2.51 (6)	25.38 ± 3.24 (6)
TG	19.23 ± 1.70 (6)	21.11 ± 1.35 (6)	23.73 ± 1.32 (6)	26.25 ± 1.89 (6)	26.4 ± 1.41 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraapeutic Group

Body weights (g)—Female

Groups	Day 0	Day 4	Day 8	Day 12	Day 15
VC	20.0 ± 1.44 (6)	21.41 ± 1.15 (6)	23.65 ± 1.14 (6)	25.75 ± 1.3 (6)	26.11 ± 1.70 (6)
TG	18.75 ± 1.44 (6)	20.58 ± 1.90 (6)	22.83 ± 1.63 (6)	25.0 ± 1.34 (6)	25.25 ± 1.80 (6)

Values are expressed in Mean ± S.D

() No. of Animals

VC-Vehicle Control

TG-Theraapeutic Group

Organ Weights (g)—Male

Groups	Heart	Lung	Liver	Kidney	Spleen	Brain	Testis
VC	0.14 ± 0.06 (6)	0.42 ± 0.06 (6)	1.40 ± 0.07 (6)	0.41 ± 0.07 (6)	0.05 ± 0.02 (6)	0.52 ± 0.06 (6)	0.27 ± 0.02 (6)
TG	0.15 ± 0.03 (6)	0.44 ± 0.03 (6)	1.41 ± 0.05 (6)	0.43 ± 0.03 (6)	0.06 ± 0.02 (6)	0.52 ± 0.004 (6)	0.25 ± 0.03 (6)

Values are expressed in Mean \pm S.D

VC-Vehicle Control

TG-Theraupatic Group

() No. of Animals

Groups	Organ Weights (g)—Female						
	Heart	Lung	Liver	Kidney	Spleen	Brain	Ovaries
VC	0.12 \pm 0.02 (6)	0.37 \pm 0.05 (6)	0.97 \pm 0.06 (6)	0.4 \pm 0.03 (6)	0.07 \pm 0.001 (6)	0.45 \pm 0.03 (6)	0.03 \pm 0.01 (6)
	0.14 \pm 0.012 (6)	0.32 \pm 0.05 (6)	1.06 \pm 0.04 (6)	0.38 \pm 0.022 (6)	0.07 \pm 0.002 (6)	0.45 \pm 0.08 (6)	0.02 \pm 0.01 (6)

Values are expressed in Mean \pm S.D

() No. of Animals

VC-Vehicle Control

TG-Theraupatic Group

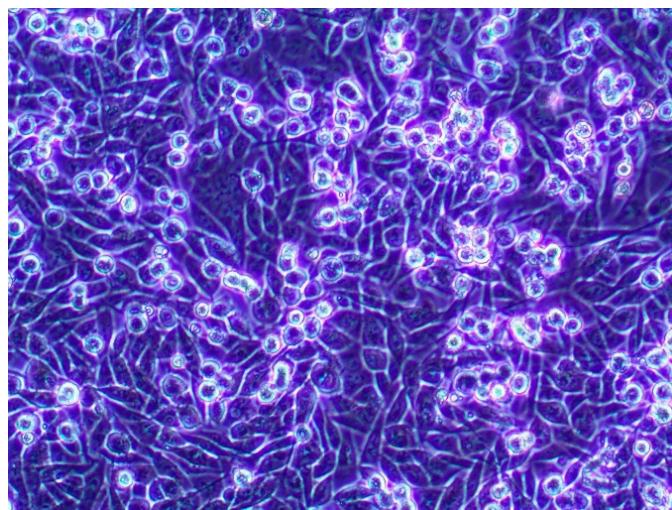


Figure S1. Morphology of PANC-1 cells.

Implantation of cells by S.C. (Subcutaneous) route

PANC-1 xenograft tumors were implanted using matrigel in 6–8-week-old Female nude mice by implanting 1×10^6 PANC-1 cells s.c.



Figure S2. Implantation of cells through subcutaneous route (S.C.) using Matrigel.

PANC-1 cells Implantation for tumour development

We observed tumour development while implanting PANC-1 cell lines after 4 weeks of observation (by implanting 1×10^6 PANC-1 cells).

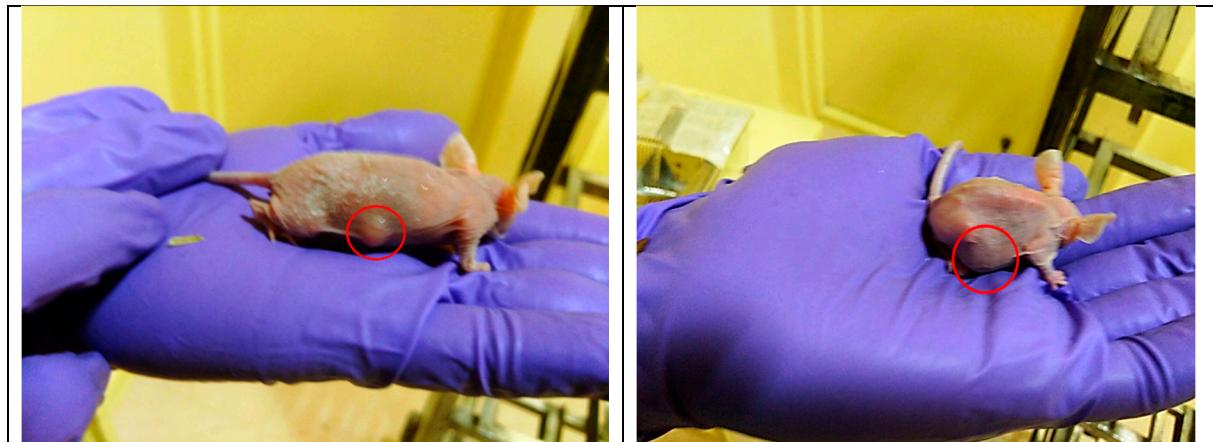


Figure S3. Tumor development of PANC-1 implanted cell lines in mice.

Body weights in (g) for Xenograft study

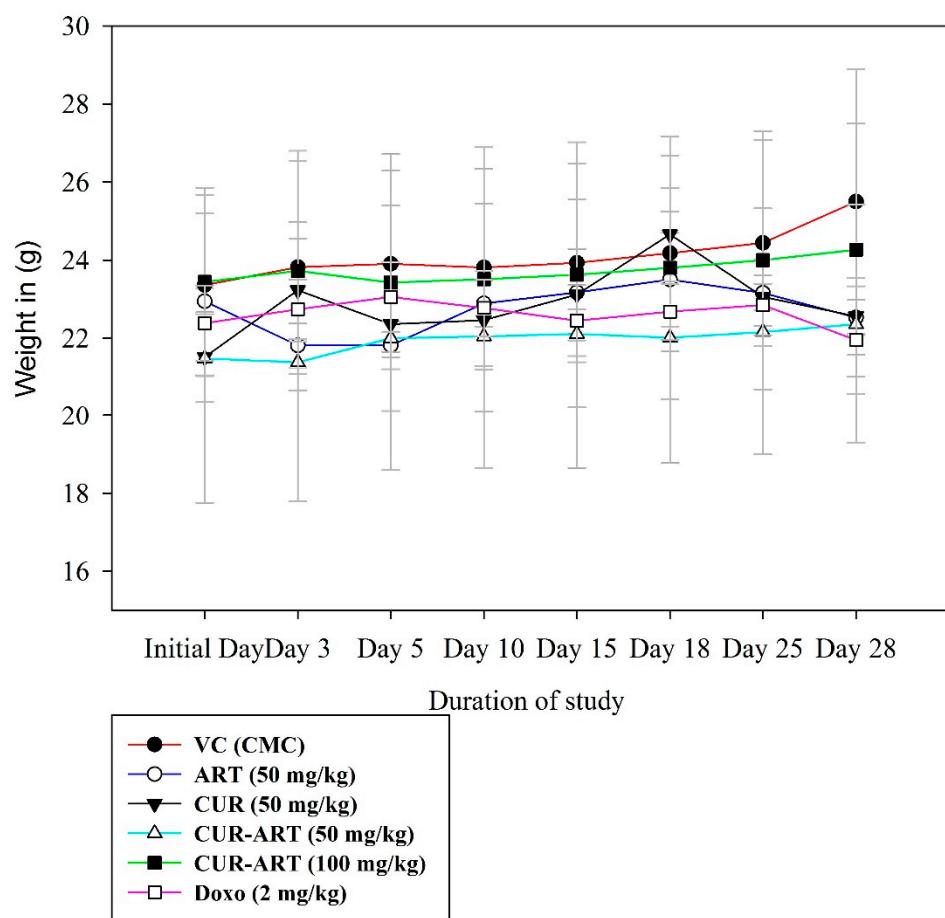


Figure S4. Body weight of selected nude mice for the xenograft studies.