Supplementary data

Table S1. Input parameters predicted from chemical structure for GastroPlus^{TM} simulation

Parameters	Values
Molecular weight (g/mol)	576.73
Log P	2.8
Human jejunal permeability ($\times 10^{-4}$ cm/s)	1.89
Reference solubility at pH 7 (mg/mL)	0.0282
Biorelevant solubilities (mg/mL)	
SGF (pH 1.2)	0.0356
FaSSIF (pH 6.5)	0.0288
FeSSIF (pH 5.0)	0.15
Diffusion coefficient ($\times 10^{-5}$ cm^2/s)	0.51
Blood/plasma concentration ratio	0.83
Plasma unbound fraction (%)	8.71

SGF, simulated gastric fluid; FaSSIF, fasted state simulated intestinal fluid; FeSSIF, fed state simulated intestinal fluid.

Table S2. Comparison of the 1H NMR data of cerberin (CR) isolated in this study and data reported for cerberin [30] and neriifolin [31]

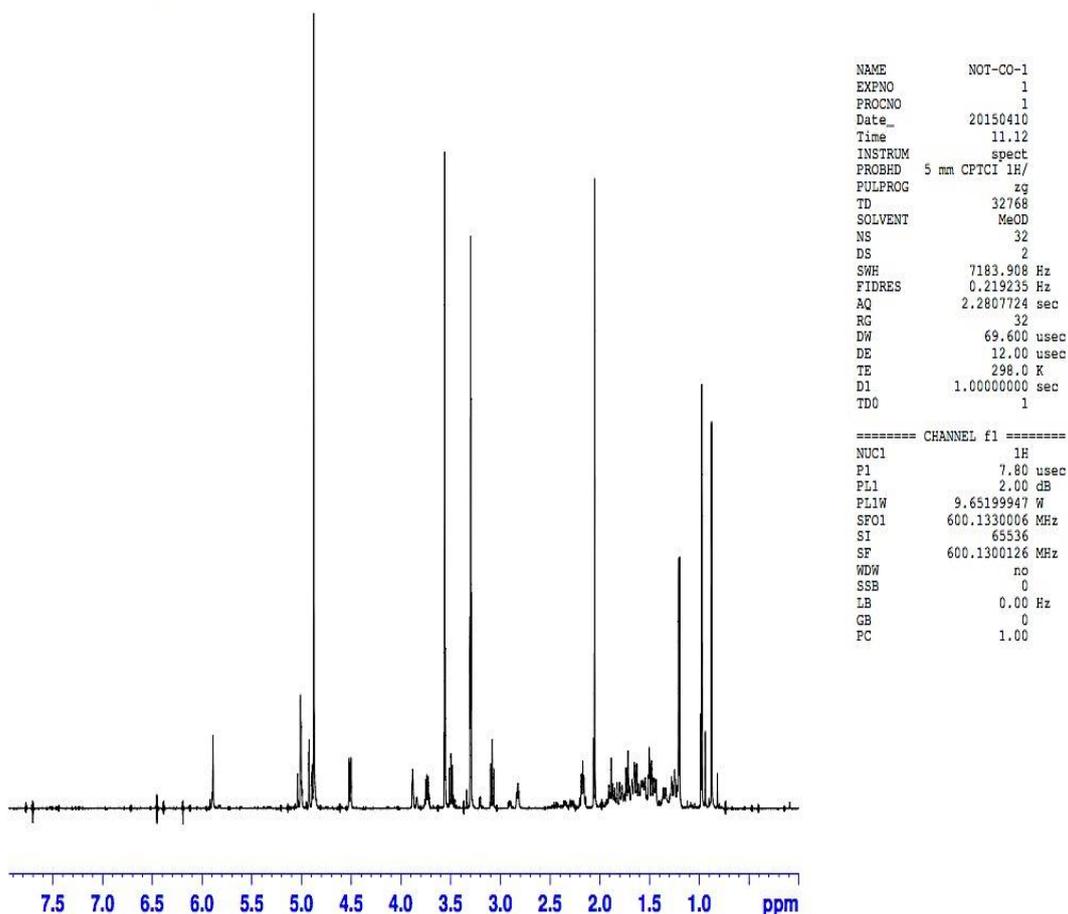|	CR (CD$_3$OD, 600 MHz) δ (ppm), mult (*J* in Hz)	Cerberin (CDCl$_3$, 600 MHz) δ (ppm), mult (*J* in Hz)	Neriifolin (CDCl$_3$, 250 MHz) δ (ppm), mult (*J* in Hz)
18	0.98, 3H, s	0.90, 3H, s	0.88, 3H, s
19	1.20, 3H, d (6.3)	0.98, 3H, s	0.97, 3H, s
6'	0.88, 3H, s	1.30, 3H, d (6)	1.26, 3H, d (6.3)
C2'-O-<u>Ac</u>	2.05, 3H, s	2.08, 3H, s	-
17	2.83, 1H, dd (5.7, 9.1)	2.80, 1H, m	2.78, 1H, dd (5.0, 8.8)
4'	3.08, dd (9.4, 9.4)		3.15, 1H, dd (9.0, 9.0)
3'	3.50, dd (9.2, 9.8)		3.25, 1H, dd (8.9, 8.9)
3	3.88, 1H, m		3.97, m
3'-O-<u>CH$_3$</u>	3.57, 3H, s	3.64, 3H, s	3.69, 3H, s
2'	4.51, 1H, dd (3.8, 10.0)	4.72, dd (4, 10)	3.58, 1H, dd (4.4, 8.9)
5'	3.73, 1H, dq (6.3, 9.4)		3.74, 1H, dq (9.0, 6.3)
21	4.82, 1H, dd (1.5, 18.2)	5.00, 2H, dd (3, 6)	4.82, 1H, dd (1.5, 18.0)
	4.98, 1H, dd (1.5, 18.2)		4.98, 1H, dd (1.5, 18.0)
1'	5.01, 1H, d (3.8)	5.12, 1H, d (4)	4.86, 1H, d (4.4)
22	5.89 1H, t (1.5)	5.97, 1H, bs	5.88, 1H, t (1.5)

NOT-CO-1 CD3OD 1H


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NAME          NOT-CO-1
EXPNO                1
PROCNO               1
Date_         20150410
Time             11.12
INSTRUM          spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zg
TD               32768
SOLVENT           MeOD
NS                  32
DS                   2
SWH         7183.908 Hz
FIDRES      0.219235 Hz
AQ         2.2807724 sec
RG                  32
DW             69.600 usec
DE             12.00 usec
TE             298.0 K
D1        1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1              7.80 usec
PL1             2.00 dB
PL1W      9.65199947 W
SFO1     600.1330006 MHz
SI               65536
SF       600.1300126 MHz
WDW                 no
SSB                  0
LB              0.00 Hz
GB                   0
PC                1.00
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Figure S1. ^{1}H NMR spectra of the isolated compound, cerberin.

Sample identified as Cerberin (IUPAC: [(2*R*,3*S*,4*R*,5*S*,6*S*)-5-Hydroxy-2-[[(3*S*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-14-hydroxy-10,13-dimethyl-17-(5-oxo-2*H*-furan-3-yl)-1,2,3,4,5,6,7,8,9,11,12,15,16,17-tetradecahydrocyclopenta[*a*]phenanthren-3-yl]oxy]-4-methoxy-6-methyloxan-3-yl] acetate).
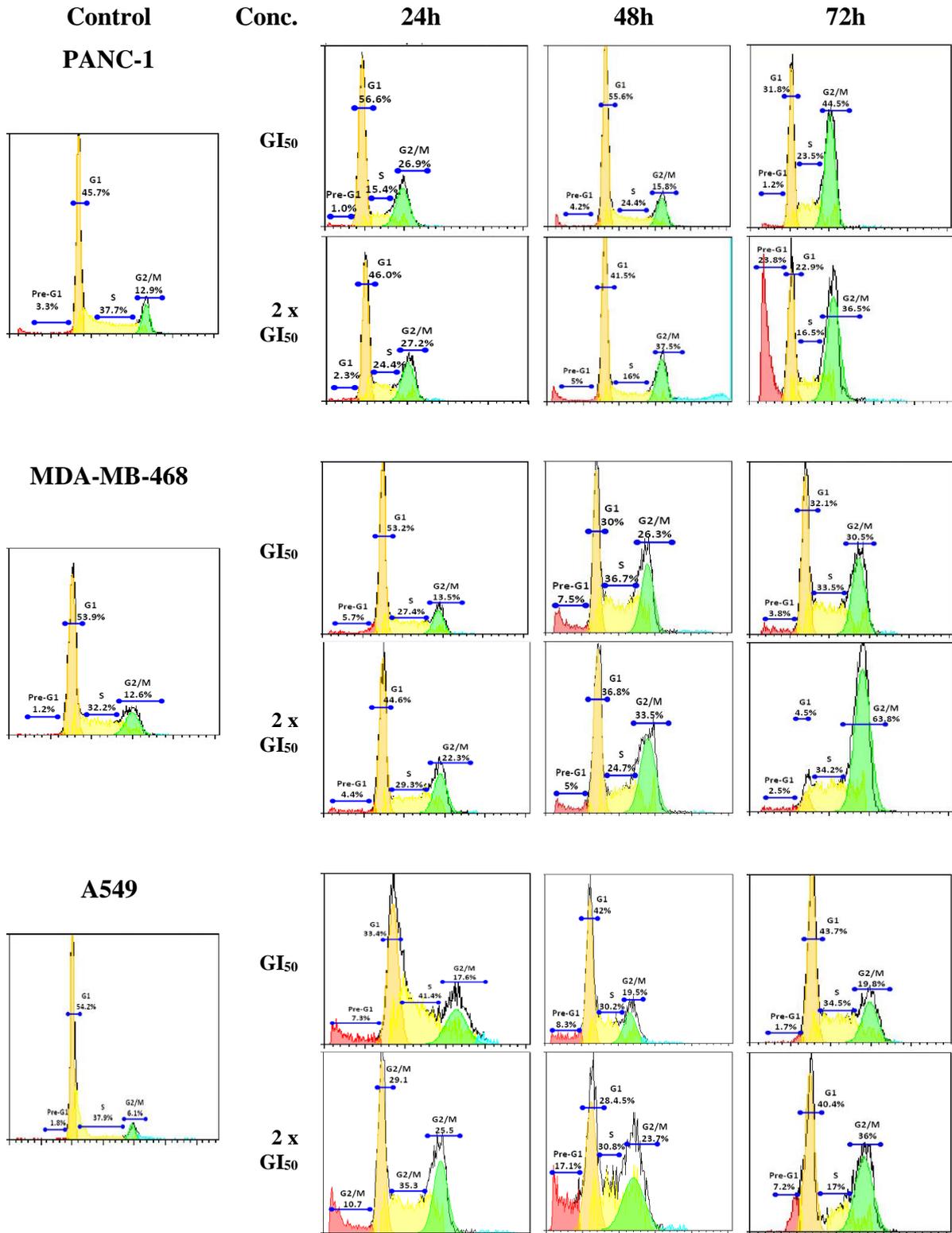
Figure S2. Representative cell cycle histograms from a single trial of PANC-1, MDA-MB-468 and A549 cells treated with CR at respective 1 x GI$_{50}$ and 2 x GI$_{50}$ concentrations for 24 h, 48 h and 72 h.

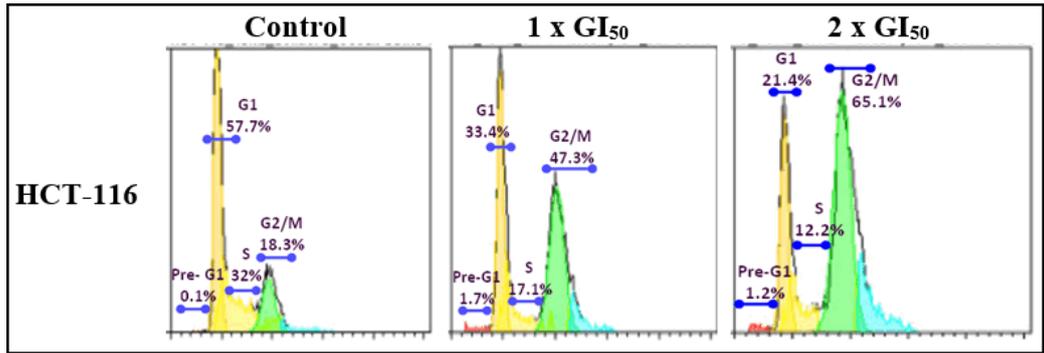**Figure S3. Representative cell cycle histograms from a single trial of HCT-116 cells treated with CR at respective 1 x GI$_{50}$ and 2 x GI$_{50}$ concentrations for 48 h.**
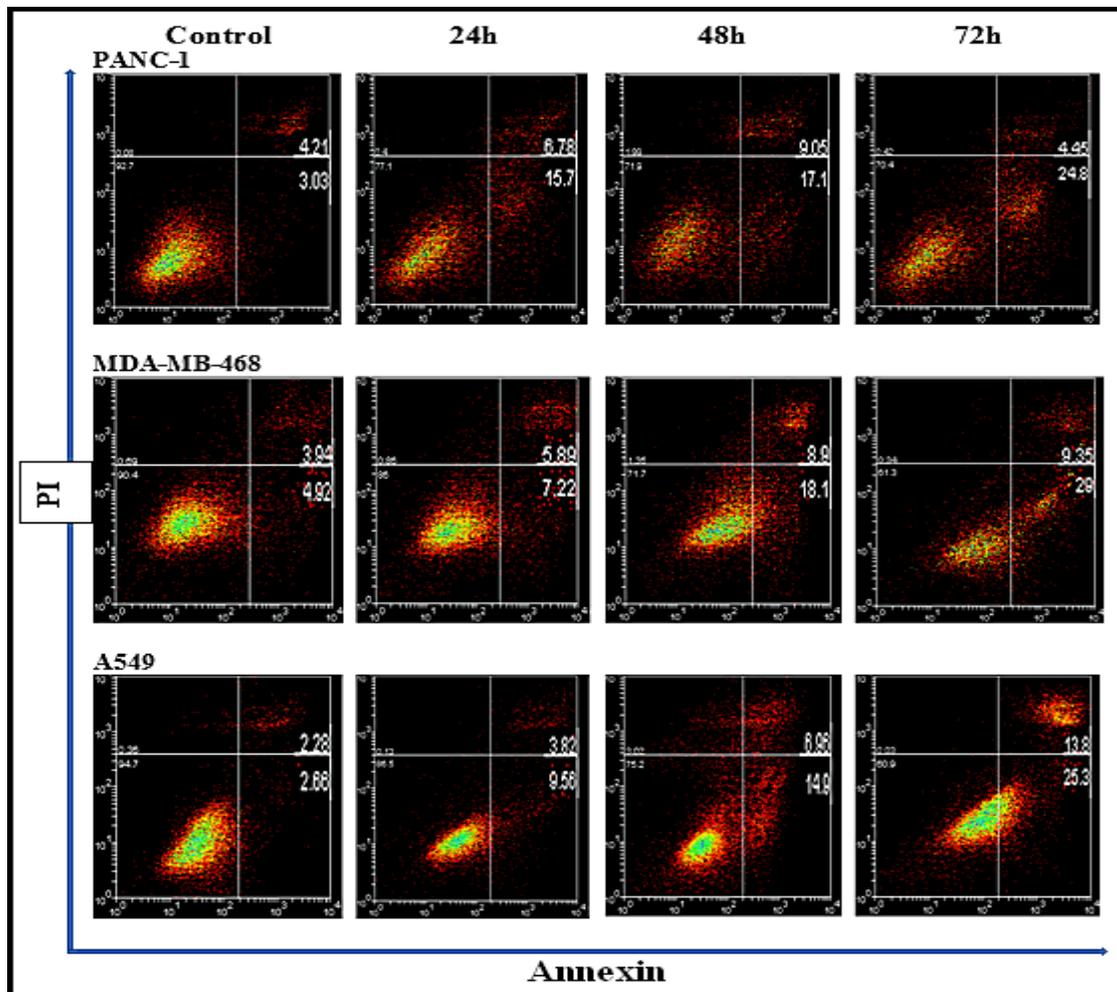

Figure S4. Representative apoptosis quadrant plots illustrating apoptotic effects of CR.

PANC-1, MDA-MB-468, A549 and HK-1 cells were treated with 1x GI$_{50}$ and 2x GI$_{50}$ concentrations of CR for 24 h, 48 h, and 72 h. These are representative quadrant plots analysed

by flow cytometry, 15,000 events were recorded for each experiment. Lower right quadrant contains the early apoptotic (Annexin+/PI-) population and the upper right quadrant contain the late apoptotic or necrotic (Annexin +/PI+) populations.
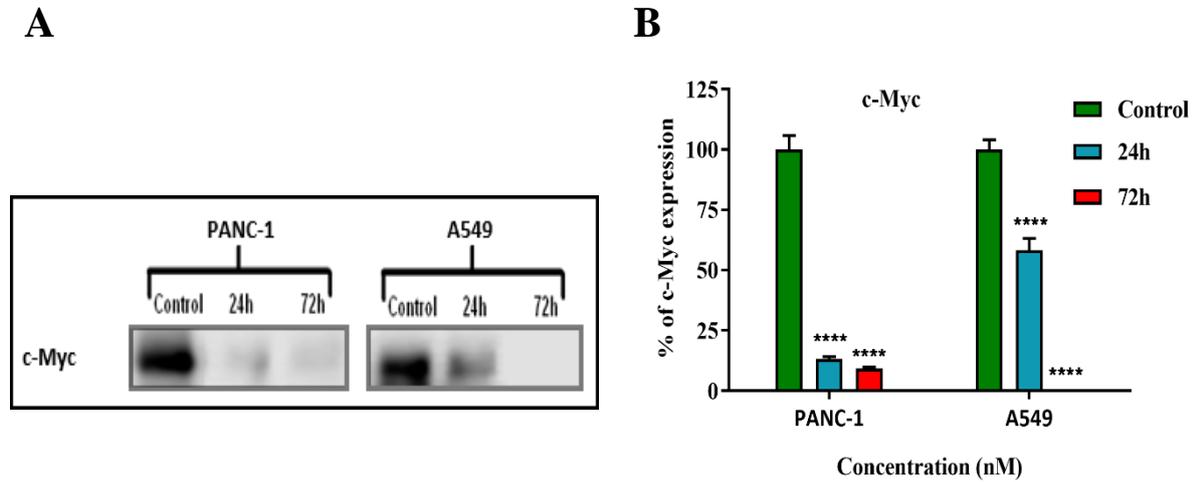
A   **B**

Figure S5. Western blot analysis of c-Myc in PANC-1 and A549 cells (A).

Cells were treated with 2x GI_{50} CR for 24 h and 72 h. GAPDH was used as an internal control (Fig. 10). (B) Collated densitometric measurement of protein expression levels; time-dependent downregulation of c-Myc was observed at 2 x GI_{50} after 24 and 72 h treatment (****$P < 0.0001$ compared to controls, experiment repeated $\geq$ 3 times).
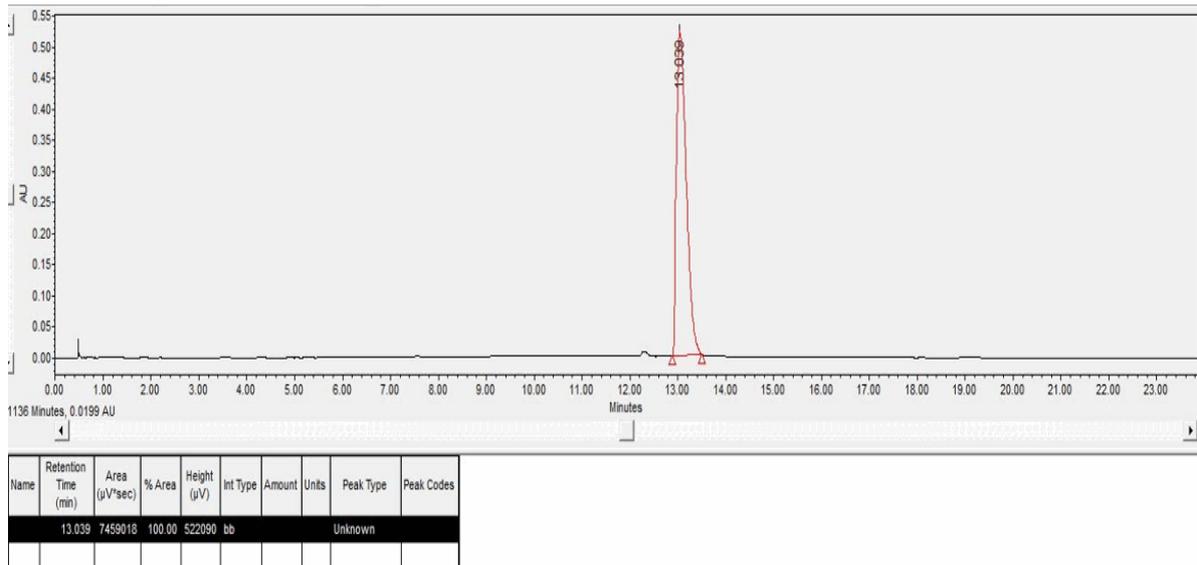

Figure S6. Chromatogram for CR sample, PDA 254 nm.

Total injection volume was 5 µL (5 mg/mL CR stock solution in ACN. Chromatogram with PDA detection at 254 nm was obtained, which showed a single well resolved peak at Rt 13.04 min. No other significant impurity peaks were detected.