Supplementary Materials:

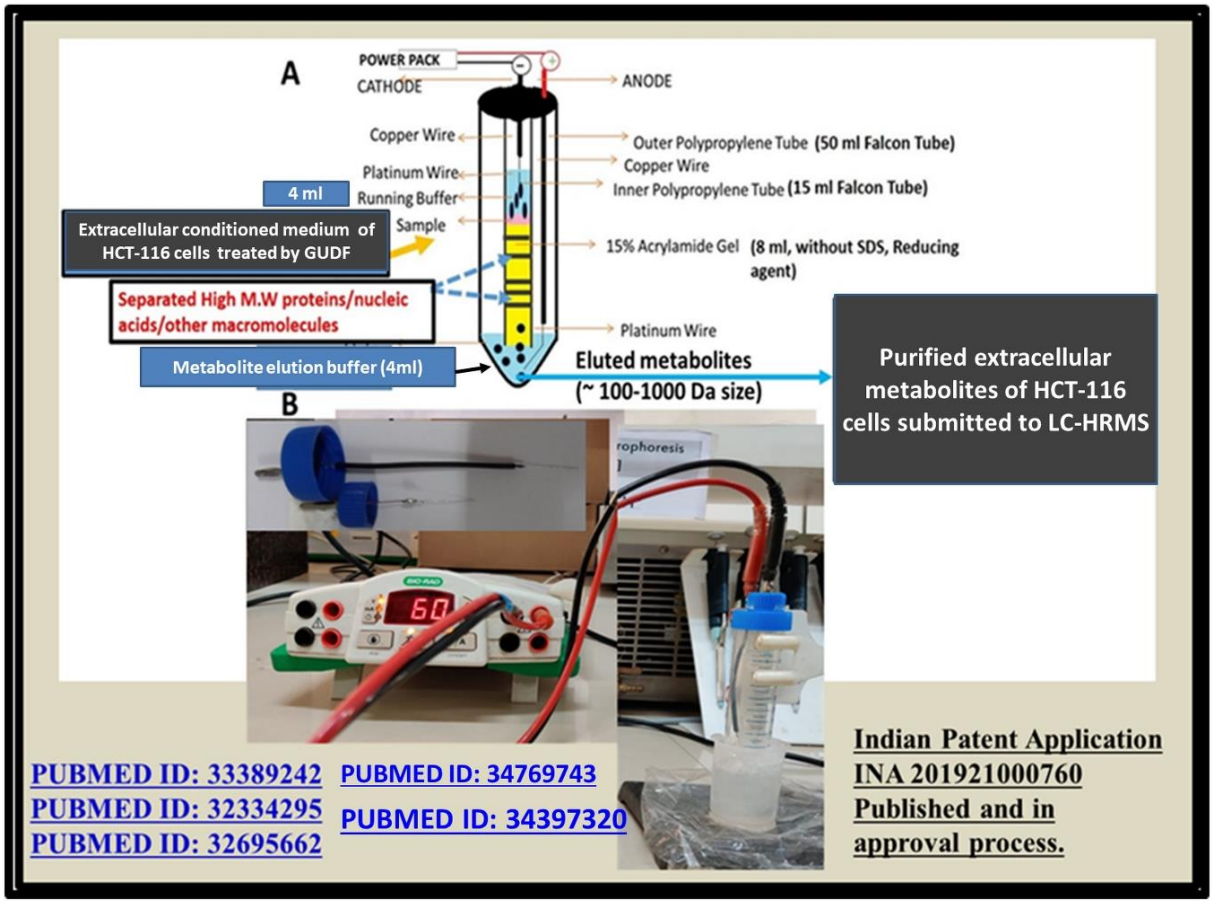
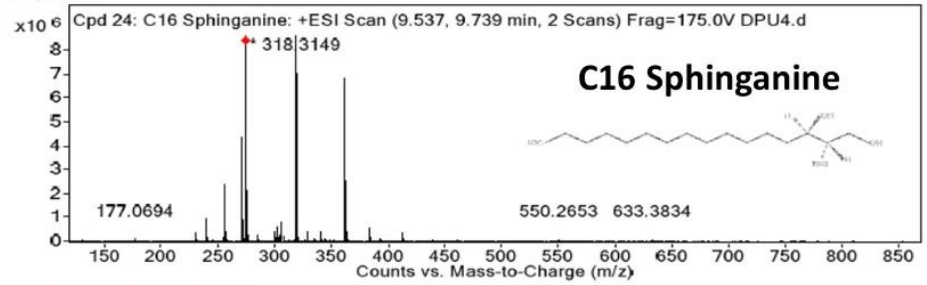


Figure S1. A flow and working model of VTGE.

Compound Label	Name	*m/z*	RT	Algorithm	Mass
Cpd 24: C16 Sphinganine	**C16 Sphinganine**	274.2745	9.65	Auto MS/MS	273.2669

MS Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
256.263			1	2355210.25		
271.2739			1	4331907.5		
274.2745	274.2741	-1.72	1	8575711	C16 H35 N O2	(M+H)+
275.2762	275.2774	4.02	1	2140027.25	C16 H35 N O2	(M+H)+
276.2794	276.2802	2.69	1	208381.69	C16 H35 N O2	(M+H)+
318.3149				9226583		
319.3061			1	7002581		
320.3053			1	1470348.88		
362.3287			1	6824550		
363.3286			1	2502715.5		

MSMS Spectrum

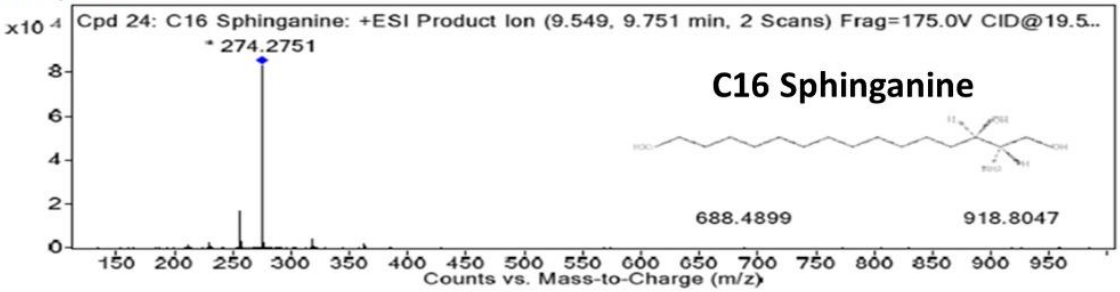
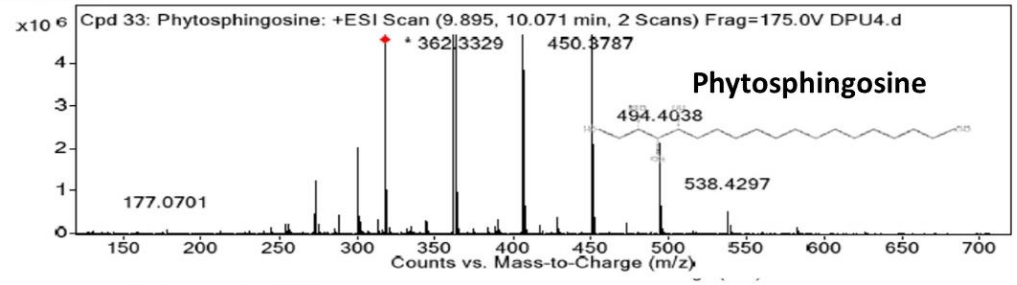


Figure S2. C16 sphinganine, a form of sphingolipid base is secreted in the extracellular conditioned medium of HCT-116 colon cancer cells treated by GUDF.
Positive mode ESI MS and MS/MS fragment ion spectra of C16 sphinganine in GUDF treated HCT-116 cancer cells.

Compound Label	Name	*m/z*	RT	Algorithm	Mass
Cpd 33: Phytosphingosine	**Phytosphingosine**	318.3003	9.995	Auto MS/MS	317.2929

MS Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
318.3003	318.3003	-0.06	1	4660630.5	C18 H39 N O3	(M+H)+
319.3029	319.3036	2.1	1	1001724.81	C18 H39 N O3	(M+H)+
320.3057	320.3063	2.1	1	119220.59	C18 H39 N O3	(M+H)+
362.3329			1	11748284		
363.3305			1	5763947		
406.3557			1	9796752		
407.3553			1	3817120		
450.3787			1	7390197		
451.3808			1	2094961.75		
494.4038			1	2121758.5		

MSMS Spectrum

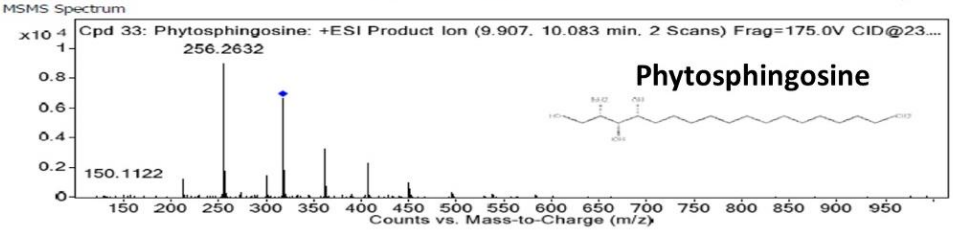
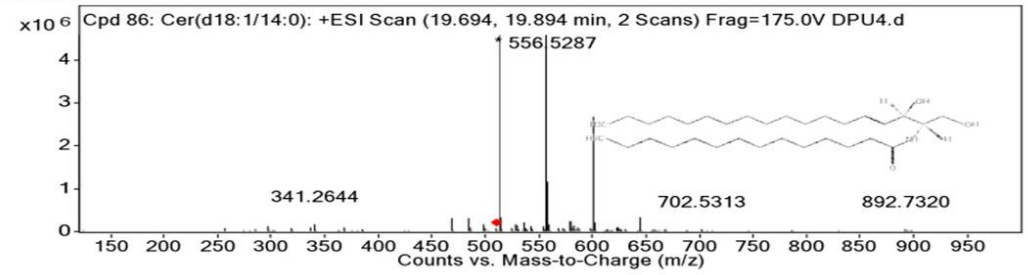


Figure S3. Phyosphingosine, a form of sphingolipid base is detected in the extracellular conditioned medium of HCT-116 colon cancer cells treated by GUDF.
Positive mode ESI MS and MS/MS fragment ion spectra of C16 phytosphingosine in GUDF treated HCT-116 cancer cells.

Compound Label	Name	*m/z*	RT	Algorithm	Mass
Cpd 86: Cer(d18:1/14:0)	**Cer(d18:1/14:0)**	510.4845	19.819	Auto MS/MS	509.4777

MS Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
510.4845	510.4881	7.05	1	75532.67	C32 H63 N O3	(M+H)+
511.4899	511.4914	3.06	1	25725.7	C32 H63 N O3	(M+H)+
512.5014			1	4581715		
513.5038			1	1755403.5		
514.5073			1	327301.81		
556.5287			1	11498224		
557.53			1	5588620		
558.5326			1	1150085.25		
600.5519			1	2676864.5		
601.5553			1	1079436.5		

MSMS Spectrum

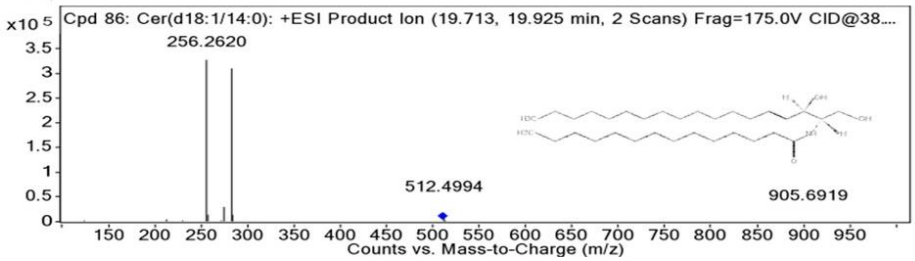
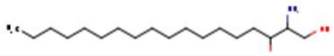


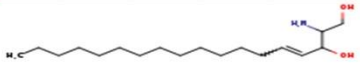
Figure S4. Ceramide (d18:1/14:0), a form of sphingolipid base is detected in the extracellular conditioned medium of HCT-116 colon cancer cells treated by GUDF.
Positive mode ESI MS and MS/MS fragment ion spectra of Ceramide (d18:1/14:0) in GUDF treated HCT-116 cancer cells.

A Sphinganine



Quer	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxic	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhib	P-gp Subs	hERG Block	MMP	AMES	MRTD (mg/c
	No	Yes	Yes	No	No	Yes	No	No	Yes	No	No	No	No	No	37951

B Sphingosine



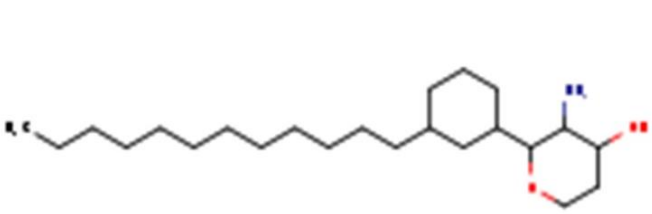
Quer	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxic	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhib	P-gp Subs	hERG Block	MMP	AMES	MRTD (mg/c
	No	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No	82167

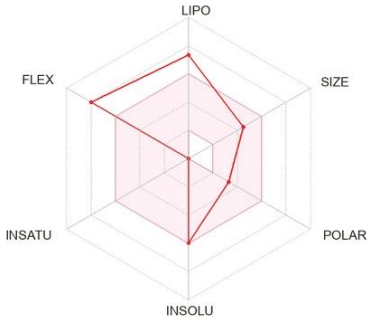
C MMS (Canonical SMILES: CCCCCCCCCCCCC1CCCC(C1)C2C(C(CCO2)O)N)

Quer	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxic	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhib	P-gp Subs	hERG Block	MMP	AMES	MRTD (mg/c
	No	No	Yes	No	No	No	No	No	Yes	No	Yes	No	No	No	5128

Figure S5. Comparison of ADMET profile of Sphinganine, sphingosine and MMS shows distinct cytotoxicity prediction.

ADMET profile is generated using v-NN/ADMET server. (A) Sphinganine and (B) Sphingosine, (C) MMS





Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-3.32 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 1 violation: #atoms>70
Veber	No; 1 violation: Rotors>10
Egan	Yes
Muegge	No; 1 violation: XLOGP3>5
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	5.06

Figure S6. Pharmacokinetics, druglikeness and medicinal chemistry of modified mimetic sphinganine (MMS) shows favourable inhibitor candidate

ADME profile of MMS is generated by using SWISADME server.