Supplementary information

Engineering novel stent based delivery system for oesophageal cancer using Docetaxel

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S1. HPLC method

HPLC analysis was performed on a Shimadzu unit equipped with a DGU-20AS degasser, LC-20AD liquid chromatograph, SIL-20A HT auto sampler and SPD-M20A DAD detector. Zorbax Eclipse XDB C18 column having 4.6×150 mm dimensions and 3.5 μm particle size was used. The mobile phase contained ammonium acetate buffer (0.02 M, pH 5) and acetonitrile at 43:57 ratio. The mobile phase flow was 1 mL min-1 and detection was performed at 230 nm.

S2. Calculation of solubility parameter using the Small's and Fedors group contribution values [1]

1. Calculation of DTX solubility parameter using Fedors cohesive energy values

Chemical group	Number	Cohesive energy (J mol^{-1})	Molar volume (cm^3 mol^{-1})	Total cohesive energy (J mol^{-1})	Total volume (cm^3 mol^{-1})
$-CH_3$	8	4710.0	33.5	37680.0	268.0
$-CH_2-$	3	4940.0	16.1	14820.0	48.3
phenyl	2	31940.0	71.4	63880.0	142.8
>C<	5	1470.0	-19.2	7350.0	-96.0
>C=	2	4310.0	-5.5	8620.0	-11.0
-OH	4	21850.0	13.0	87400.0	52.0
-CONH-	1	33490.0	9.5	33490.0	9.5
-COO-	3	18000.0	18.0	54000.0	54.0
-CO-	1	17370.0	10.8	17370.0	10.8
>CH-	8	3430.0	-1.0	27440.0	-8.0
Ring closure 3-4 membered	1	1050.0	16.0	1050.0	16.0

Ring more than 5 membered	1	3140.0	18.0	3140.0	18.0
-O-	2	3350.0	3.8	6700.0	7.6
Total cohesive energy				362940.0	512.0

2. Calculation of PUS solubility parameter taking in to consideration the chemical groups present in a polymeric chain

a. Using small's molar attraction constant

Chemical group	Number	Molar attraction constant ($J^{1/2}\ cm^{3/2}\ mol^{-1}$)	Total molar attraction constant (F)
$-CH_3$	0	438.0	0.0
$-CH_2-$	11	272.0	2992.0
-O-	1	143.0	143.0
-OCONH-	4	1200.0	4800.0
Cyclohexyl	6	1620.0	9720.0
-CO-NH-	1	1160.0	1160.0
$(CH_3)_2Si-O$	1	1227.30	1227.30
Ring, 6-membered	6	105.0	630.00
Total molar attraction constant			20672.29

b. Using Fedors cohesive energy values

Chemical group	Number	Cohesive energy (J mol^{-1})	Molar volume ($cm^3\ mol^{-1}$)	Total cohesive energy (J mol^{-1})	Total volume ($cm^3\ mol^{-1}$)
$-CH_3$	2	4710.0	33.5	9420.0	67.0
$-CH_2-$	11	4940.0	16.1	54340.0	177.1
-O-	6	3350.0	3.8	20100.0	22.8
-CONH-	5	33490.0	9.5	167450.0	47.5
Cyclohexyl	6	29180.0	86.0	175080.0	516.0
Si	1	3390.0	0.0	3390.0	0.0
Ring closure	6	1050.0	16.0	6300.0	96.0
Total cohesive energy				436080.0	926.4

3. PTMO solubility parameter calculation

a. Using Small's molar attraction constant

Chemical group	Number	Molar attraction constant ($J^{1/2}\ cm^{3/2}\ mol^{-1}$)	Total Molar attraction constant (F)
$-CH_2-$	4	272.0	1088.0
-O-	1	143.0	143.0
Total molar attraction constant			1231.0

b. Using Fedors cohesive energy values

Chemical group	Number	Cohesive energy (J mol^{-1})	Molar volume (cm^3 mol^{-1})	Total cohesive energy (J mol^{-1})	Total volume (cm^3 mol^{-1})
$-CH_2-$	4	4940.0	16.1	19760.0	64.4
-O-	1	3350.0	3.8	3350.0	3.8
Total cohesive energy				23110.0	68.2

4. HMDI-BD solubility parameter calculation

a. Using Small's molar attraction constant

Chemical group	Number	Molar attraction constant ($J^{1/2}$ $cm^{3/2}$ mol^{-1})	Total Molar attraction constant (F)
$-CH_2-$	5	272.0	1360.0
-O-	2	143.0	286.0
Cyclohexyl	2	1620.0	3240.0
-CO-NH-	2	1160.0	2320.0
Ring, 6-membered	2	105.00	210.00
Total molar attraction constant			7416.00

b. Using Fedors cohesive energy values

Chemical group	Number	Cohesive energy (J mol^{-1})	Molar volume (cm^3 mol^{-1})	Total cohesive energy (J mol^{-1})	Total volume (cm^3 mol^{-1})
$-CH_2-$	5	4940.0	16.1	24700.0	80.5
-O-	2	3350.0	3.8	6700.0	3.8
-CONH-	2	33490.0	9.5	66980.0	9.5
Cyclohexyl	2	29180.0	86.0	58360.0	172.0
Ring closure	2	1050.0	16.0	2100.0	32.0
Total cohesive energy				158840.0	311.1

5. PDMS solubility parameter calculation

a. Using Small's molar attraction constant

Chemical group	Number	Molar attraction constant ($J^{1/2}cm^{3/2}mol^{-1}$)	Total Molar attraction constant (F)
$(CH_3)_2Si-O^2$	1	1227.29	1227.29

Total molar attraction constant	1227.29

b. Using Fedors cohesive energy values

Chemical group	Number	Cohesive energy (J mol^{-1})	Molar volume (cm^3mol^{-1})	Total cohesive energy (J mol^{-1})	Total volume (cm^3mol^{-1})
$-CH_3$	2	4710.0	33.5	9420.0	67.0
-O-	1	3350.0	3.8	3350.0	3.8
Si	1	3390.0	0.0	3390.0	0.0
Total cohesive energy				16160.00	70.80

For the calculation of Small's solubility parameter following formula was used

$$\delta_{small} = \frac{F}{V}$$

F is the total molar attraction constant and V is the volume at 298K. V was taken by group contribution as shown in the Fedors calculation table.

For the calculation of solubility parameter using Fedors approach following formula was used,

$$\delta = \left(\frac{E_{coh}}{V}\right)^{\frac{1}{2}}$$

E_{coh} is the total cohesive energy and V is the volume at 298 K.

For the calculation of DTX-PUS interaction parameter and critical interaction parameter following values were used

Table S 1. Values used for the calculation of interaction parameters

Component	Value
Docetaxel molar volume[a] (cm^3/mol)	585.7
PUS Solubility parameter (cal $cm^{-3})^{1/2}$	10.76
Docetaxel Solubility parameter (cal $cm^{-3})^{1/2}$	13.14
PUS volume (cm^3 mol^{-1})	926.4
Real gas constant (cal $K^{-1}mol^{-1}$)	1.987
Temperature (K)	293.15

a- SciFinder

S3. Chemical analysis of the DTX after sterilization studies.

HPLC method detail

Mobile phase A was a mixture of 95% water and 5% acetonitrile with 0.1% acetic acid and mobile phase B contained 95% acetonitrile and 5% water with 0.1% acetic acid. Gradient elution was performed as T min/B %: 0.01/53, 12/53, 13/95, 18/95, 19/53, 13.99/53 and 24/53. The column and the HPLC system are as specified under S1.[3]

1. HPLC chromatograms of the samples analysed after UV irradiation

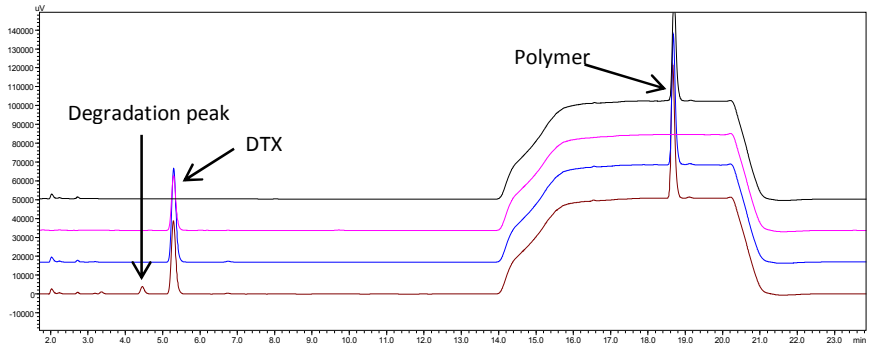

Figure S 1. HPLC chromatograms of the UV stability samples. From top to bottom: blank, DTX stock, control and the UV irradiated sample.

2. HPLC chromatograms of the samples analysed after gamma irradiation

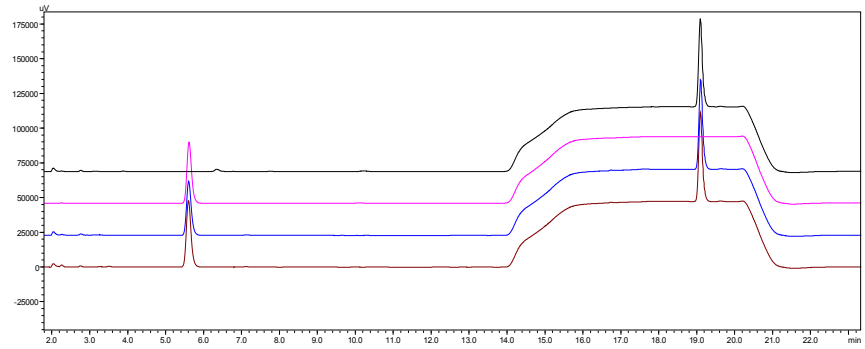

Figure S 2. HPLC chromatograms of the gamma irradiation stability samples. From top to bottom: Blank, DTX stock, control and Gamma radiation irradiated sample

S4. Oesophageal tissue degradation study using impedance measurements.

Silver-silver chloride electrodes were used for electrically connecting the donor and receptor compartment to a signal generator. A current signal of 100 mV RMS at 100 Hz was generated using Tektronix CFG 280 function generator with the help of attenuator. The electrical current and voltage were measured using a true RMS multimeter (Micron Q 1074).

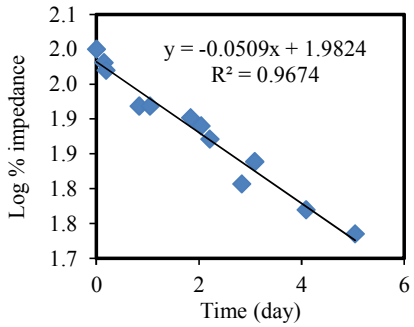

Figure S 3. First order kinetics plot of the log % impedance values against time.

S5. *In-vitro* release from the films after gamma irradiation along with the control sample.

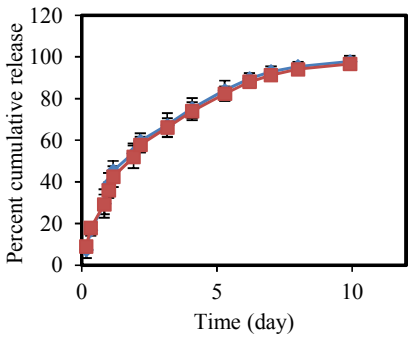

Figure S 4. *In-vitro* release profile of the gamma irradiated (—) and the control (—) sample (n=3).

S6. Fitted film thicknesses and correlation coefficients for the Fick's equation

Group	DTX loading (% w/w)	Film thickness (µm)	Correlation coefficient
Group 1	4.76	95.6±0.00003	0.98±0.0006
	2.44	185.6±0.0002	0.98±0.003
Group 2	4.76	92.1±0.002	0.98±0.008
	2.91	93.1±0.002	0.98±0.007
	0.99	93.2±0.002	0.98±0.002
Group 3	2.44	183.8±0.001	0.98±0.01
	1.48	184.1±0.002	0.98±0.02
	0.50	183.6±0.002	0.97±0.02

S7. Contribution of device and oesophageal tissues towards the flux of DTX delivery.

Table S 2. Amount released in an *in-vitro* release after 48 h- M_{device}.

Group	Cumulative amount release after 48 h (µg cm^{-2})		
DTX loading	**4.76% w/w**	**2.91% w/w**	**0.99% w/w**
Group 2	156.90	97.90	39.60
DTX loading	**2.44% w/w**	**1.48% w/w**	**0.50% w/w**
Group 3	64.10	44.00	11.06

Table S 3. Calculation of fraction contributed by device (F_d) and the oesophageal tissues (F_o) in the *in-vitro* permeation study.

Group	Total amount (permeated+tissue), (µg cm^{-2})			$F_d=M_{total}/M_{device}$			$F_o=1-F_d$		
DTX loading	**4.76% w/w**	**2.91% w/w**	**0.99% w/w**	**4.76% w/w**	**2.91% w/w**	**0.99% w/w**	**4.76% w/w**	**2.91% w/w**	**0.99% w/w**
Group 2	5.03	2.57	1.83	0.032	0.026	0.046	0.968	0.974	0.954
DTX loading	**2.44% w/w**	**1.48% w/w**	**0.5% w/w**	**2.44% w/w**	**1.48% w/w**	**0.5% w/w**	**2.44% w/w**	**1.48% w/w**	**0.5% w/w**
Group 3	2.18	1.57	1.08	0.034	0.036	0.093	0.966	0.964	0.907

Reference

1. Van Krevelen DW, Te Nijenhuis K. 2009. Chapter 7 - Cohesive Properties and Solubility. In Van Krevelen DW, Te Nijenhuis K, editors. Properties of Polymers, 4th ed., Amsterdam: Elsevier. p 189-227.
2. Watanabe H, Miyauchi T 1973. Determination of Solubility Parameter For Siloxane Segment. Journal of Chemical Engineering of Japan 6(2):109-114.
3. Mohsin S, Arellano IH, Choudhury NR, Garg S 2014. Docetaxel epimerization in silicone films: a case of drug excipient incompatibility. Drug Test Anal 6(10):1076-1084.