Electrospun nanofiber membrane of chitosan/polyvinyl alcohol embedded with DOX-loaded V-MOFs for controlled drug release and multifunctional biological activity

Table S1. Chemical name, formula, and company.

Chemical name	Formula	Company
Chitosan	$C_{56}H_{103}N_9O_3$	Sigma-Aldrich, Germany
Polyvinylalchol	$(C_2H_3O)_n$	Sigma-Aldrich, Germany
Vanadium chloride	VCl_3	Sigma-Aldrich, Germany
benzene-1,3,5-tricarboxylic acid	$C_6H_3(CO_2H)_3$	Sigma-Aldrich, Germany
Methanol	CH_3OH	LOBA CHEMIE PVT.LTD, India
Ethanol	C_2H_6O	Sigma-Aldrich, Germany
Sodium hydroxide (99%, AR)	NaOH	Chimmed, Russia
Hydrochloric acid (37%, AR)	HCl	LOBA CHEMIE PVT.LTD, India

Table S2. Instruments and equibments.

Test name	**Abbrevation**	**Instrument name**	**Company**	**Illustration**
Fourier transformer infrared	FT-IR	A Nicolet IS10 Fourier transform infrared (FTIR) spectrometer	Thermo Fisher Scientific, Waltham, MA, USA	equipped with an attenuated total reflectance accessory and which ran in the 4000-400 cm^{-1} range was used to gather FTIR spectra
Powered X-ray diffraction	PXRD	Siemens diffractometer (model D500, Germany)	Germany	patterns were captured from powder samples through the use of a Siemens diffractometer (model D500, Germany) that was fitted with a Cu-K radiation source (wavelength 1.54 Angstroms (Å)) operating at 30 kV and 20 mA.
Scanning Electron Microscope	SEM	(JSM-6510LV, JEOL Ltd., Tokyo, Japan)	JEOL Ltd., Tokyo, Japan	The morphology of the investigated sorbents was analyzed with the use of a scanning electron microscope
X-ray photoelectron spectroscopy	XPS	K-ALPHA (Themo Fisher Scientific, USA)	Themo Fisher Scientific, USA	Used for determination the elemental analysis for the compound
Braunnar Emmet Teller	BET	Quantachrome Instruments, Anton Paar Quanta Tec, Inc., Boynton Beach, FL,	Quanta Tec, Inc., Boynton Beach, FL, USA	was utilised for surface and pore analysis (Brunauer Emmett-Teller (BET) surface area, porous volume, and pore size), and NovaWin Software (v11.0) was used for data interpretation.

		USA		The BET surface area of material adsorbents was obtained by the application of nitrogen adsorption-desorption isotherms at 77K through the use of a specific analyser (Quadrasorb–EVO, Quantachrome, USA).
UV-visible spectrophotometer	UV spectrophotometer	Perkin-Elmer AA800 spectrophotometer Double beam, with 1 cm cell length.		Measuring the concentration of the adsorbate soulution via using bear lambert law
Energy Dispersive X-ray	EDX	Leo1430VP microscope	Carl Zeiss AG, Jena, Germany	Elemntal analysis of the material
Transmission electron microscopy	TEM	TEM, FEI Teanci G2 F20, USA	FEI Teanci G2 F20, USA	Determination the morphology of the material and size
pH meter	pH	HANNA (model 211)	USA	Measuring the acidity or basicity of the solution
Sonication	Ultrasonic	Elmasonic P300H ultrasonic bath, continuous mode, power 380 W	Elma Schmidbauer GmbH, Singen, Germany	Sonication of the material as well as used ton disperse material on the solution as it decrease the particle size of the material
Water bath	Shaking	GFL Orbital Shaker 3017		

Table S3. True variables, codes, and their BBD levels.

Code	Variables	-1	0	+1
A	pH	5	6.2	7.4
B	Temperature (°C)	25	33.5	42
C	Time (h.)	5	52.5	100

Table S4. Investigate the percentage of DOX release and the surface interactions.

Run	Actual variables			DOX release (%)		
	pH	Time (h)	Temperature (°C)	Investigational	Predicted	Residue
1	6.2	62.5	31	36.179	36.18	0.0000
2	6.2	62.5	31	36.179	36.18	0.0000
3	6.2	5	25	2.556	3.03	-0.4786
4	6.2	62.5	31	36.179	36.18	0.0000
5	5	62.5	37	52.46	52.24	0.2219
6	6.2	5	37	3.88	4.29	-0.4128
7	5	62.5	25	32.7875	32.50	0.2877
8	5	5	31	3.73	3.54	0.1909
9	6.2	120	37	77.2	76.72	0.4786
10	6.2	120	25	50.7895	50.38	0.4128
11	6.2	62.5	31	36.179	36.18	0.0000
12	7.4	5	31	2.5129	1.81	0.7005
13	7.4	62.5	37	32.78	33.07	-0.2877
14	6.2	62.5	31	36.179	36.18	0.0000
15	7.4	62.5	25	24.981	25.20	-0.2219
16	7.4	120	31	50	50.19	-0.1909
17	5	120	31	74.2308	74.93	-0.7005

Table S5. Equations used in this work to fit the data of adsorption experiments.

Serial	Equation	Nmae	Description	Ref.
1	$Q_o^{1/3} - Q_t^{1/3} = K_{HC}.t$	Hixson–Crowell model	Q_0 = Initial amount of drug Q_t = Remaining amount of drug at time t K_{HC} = Hixson–Crowell dissolution rate constant t = Time	[1]
2	$Q_t = Q_0 + K_0.t$	Zero-Order	Q_t = Amount of drug released at time ttt Q_0 = Initial amount of drug in the solution (often 0) K_0 = Zero-order release constant (units: concentration/time) t = Time	[2]
3	$\ln Q_t = \ln Q_0 - K_1.t$	First order	Q_0 = Initial amount of drug Q_t = Amount of drug remaining at time ttt K_1 = First-order rate constant (1/time) t = Time	[3]
4	$\frac{M_t}{M_\infty} = K.t^n$	Korsmeyer–Peppas	Mt = Amount of drug released at time ttt M∞ = Total amount of drug released at infinite time (i.e., final amount) $\frac{M_t}{M_\infty}$ = Fraction of drug released at time t K = Kinetic constant incorporating structural and geometric characteristics n = Release exponent that indicates the mechanism of drug release	[4]
5	$Q_t = K_H\sqrt{t}$	Higuchi	Q_t = Cumulative amount of drug released at time t K_H=Higuchi dissolution constant (units: amount/time^{½}) t = Time	[5]

Table S6. The parameter of the kinetic models of DOX release from V-MOF nanofiber membrane

Kinetic model	**Value of parameters**	
Zero-order	K_o (h)	1.12
	Reduced Chi-Sqr	732.2892
	Residual Sum of Squares	0.94625
	R-Square (COD)	0.89538
	R^2	0.89062
First-order	K_F (h^{-1})	0.39
	Reduced Chi-Sqr	227.04921
	Residual Sum of Squares	0.98205
	R-Square (COD)	0.96443
	R^2	0.96273
Hexson-crowell	K_{HC} (h^{-1})	0.77
	Reduced Chi-Sqr	1507.1648
	Residual Sum of Squares	0.78971
	R-Square (COD)	0.62364
	R^2	0.60653
Kosmeyer-peppas	K_F (h^{-1})	0.12
	n	0.007
	Reduced Chi-Sqr	736.96025
	Residual Sum of Squares	0.94588
	R-Square (COD)	0.8947
	R^2	0.88991
Higuchi	K_H	1.82
	Reduced Chi-Sqr	2086.054
	Residual Sum of Squares	0.9378
	R-Square (COD)	0.863
	R^2	0.858

Table S7. The models have been subjected to analysis of variance.

Source	Sum of squares	df	Mean squares	F-value	P-value	
Model	8266.13	9	918.46	3036.48	< 0.0001	significant
A-pH	350.26	1	350.26	1157.97	< 0.0001	
B-time	7172.51	1	7172.51	23712.79	< 0.0001	
C-Temperature	380.96	1	380.96	1259.49	< 0.0001	
AB	132.41	1	132.41	437.75	< 0.0001	
AC	35.25	1	35.25	116.52	< 0.0001	
BC	157.33	1	157.33	520.15	< 0.0001	
A^2	2.11	1	2.11	6.97	0.0335	
B^2	34.28	1	34.28	113.32	< 0.0001	
C^2	0.3314	1	0.3314	1.10	0.3300	
Residual	2.12	7	0.3025			
Lack of Fit	2.12	3	0.7058			
Pure Error	0.0000	4	0.0000			
Cor Total	8268.24	16				
Std. Dev.	0.5500					
Mean	34.64					
C.V. %	1.59					
R^2	0.9997					
Adjusted R^2	0.9994					
Predicted R^2	0.9959					
Adeq Precision	177.5884					
PRESS	33.88					
-2 Log Likelihood	12.83					
BIC	41.16					
AICc	69.50					

Table S8. Comparison of different nanocarriers based on MOFs for DOX delivery.

Materials	Drug release	Cell lines	Cell viability	Concentration	Treatment	Ref.
LDH-Fe_3O_4/Cu MOF-DOX-CS@CAR	pH 5.5 / 72h / 60%	L929	95%	62.5 µg/mL	48h	[6]
CS (chitosan), CAR (carrageenan hydrogel)	pH 7.4 / 72h / 23%	MCF-7	50%			
DOX- CS/Fe_3O_4/Cu-MOF	pH 4.5 / 96h / 60%	MCF-7	65%	16 µg/mL	48h	[7]
CS (chitosan)	pH 7.4 / 96h / 20%					
CS/DOX@Ti-MOF	pH 6.5 / 48h / 76%	MNNG/HOS	30%	6 µg/mL	48h	[8]
Cs (chitosan)	pH 7.4 / 48h / 10%	MDA-MB-231	20%			
SiO2@Fe_3O_4-HA-MIL-100-GQDs-DOX	pH 5 / 70h / 67%	MCF-7	5%	32 µg/mL	72h	[9]
HA (hydroxyapatite), GQDs (graphene quantu0m dots)	pH 7.4 / 70h / 29%					
Alg-DOX-Cu MOF-LDH	pH 5 / 72h / 69 %	L929	90%	60 µg/mL	48h	[10]
Alg (alginate)	pH 6.8 / 72h / 39%	MCF-7	10%			
	pH 7.4 / 72h / 29%					
UiO-66 @P @ DOX	pH 4.5/ 200h /90%	HEK-293	40%	50 µg/mL	48h	[11]
P (porphyrin)	pH 5.5 / 200h /70%	HT-29	60%			
	pH 7.4 / 200h /85%	MCF-7	20%			
		MCF-10A	60%			
UiO-66 @P @ DOX@RO	pH 4.5 / 200h / 40%	HEK-293	80%	50 µg/mL	48h	[11]
P (porphyrin), RO (*Rosmarinus officinalis)*	pH 5.5 / 200h / 60%	HT-29	80%			
	pH 7.4 / 200h / 50%	MCF-7	65%			
		MCF-10A	80%			
A520@L@DOX	pH 4.5/ 200h / 94%	HEK-293	95%	50 µg/mL	48h	[12]
	pH 5.5 / 200h / 97%	HeLa	65%			
	pH 7.4 / 200h / 96%	MCF-7	76%			
		PC12	70%			
A520@L@DOX@L	pH 4.5 / 150h / 36%	HEK-293	96%	50 µg/mL	48h	[12]
	pH 5.5 / 150h / 49%	HeLa	90%			
	pH 7.4 / 150h / 88%	MCF-7	90%			
		PC12	83%			

DOX@V-MOF nanofiber membrane	pH 5 / 140h / 96.14% pH 6.2 / 140h / 58.4% pH 7.4 / 10h / 34.6%	HepG-2 MCF-7	97.2 96.4	107.5 μg/mL	50	This study

Table S9. Using different MOFs with different coating agents on different cell lines.

MOFs	Coating agents	Cell lines	Ref.
Silver-Based MOF	Chitosan	L929	[13]
BioMOF	Chitosan	HUVEC	[14]
UiO-66	Fe3O4 Nanoparticles	HeLa, NIH/3T3	[15]
UiO-66	Aloe vera Biopolymer	HFFF2	[16]
UiO-66	PEG	MCF-7	[17]
UiO-68	Aptamer	MDA-MB-23 , MCF-10A	[18]
Cu MOF	L-lysine	MCF-7 , MCF-10A	[19]
Cu MOF	Aptamer	Aptamer	[20]
MIL-100(Fe)	Silica	MCF-7 , MCF-10A	[21]
MIL-100(Fe)	PEG	MCF-7	[22]
ZIF-8	Chitosan & Folic acid	MCF-7	[23]
MIL-88B	Chitosan & Folic acid	M109	[24]
Ni/Ta MOF	Chitosan & Folic acid	MCF-7 , HepG2	[25]
Zn-NMOF	Chitosan & Folic acid	HCT116	[26]
MOF-5	Chitosan & Alginate	HEK-293 , PC12 , HepG2	[27]
MOF-5	Carboxymethylcellulose, Aptamer	HeLa , 4TA	[28]
UiO-66-NH2	Porphyrin	MCF-7 , HT-29	[11]
beta- CD- MOF	Glutamine	MCF-7 , AGS	[29]
Bio-MOF-11	Pectin Biopolymer	SW489	[30]
Fe-BTC MOF	Liposome		[31]
A520	Tp Extract	MCF-7 , HeLa, HEK-293, PC12	[12]
DOX@V-MOF nanofiber membrane	Chitosan and polyvinylalchol	HepG-2, MCF-7	This study

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