SUPPORTING INFORMATION

Novel salts of the antiemetic drug- Domperidone: Synthesis, characterization and physicochemical property investigation

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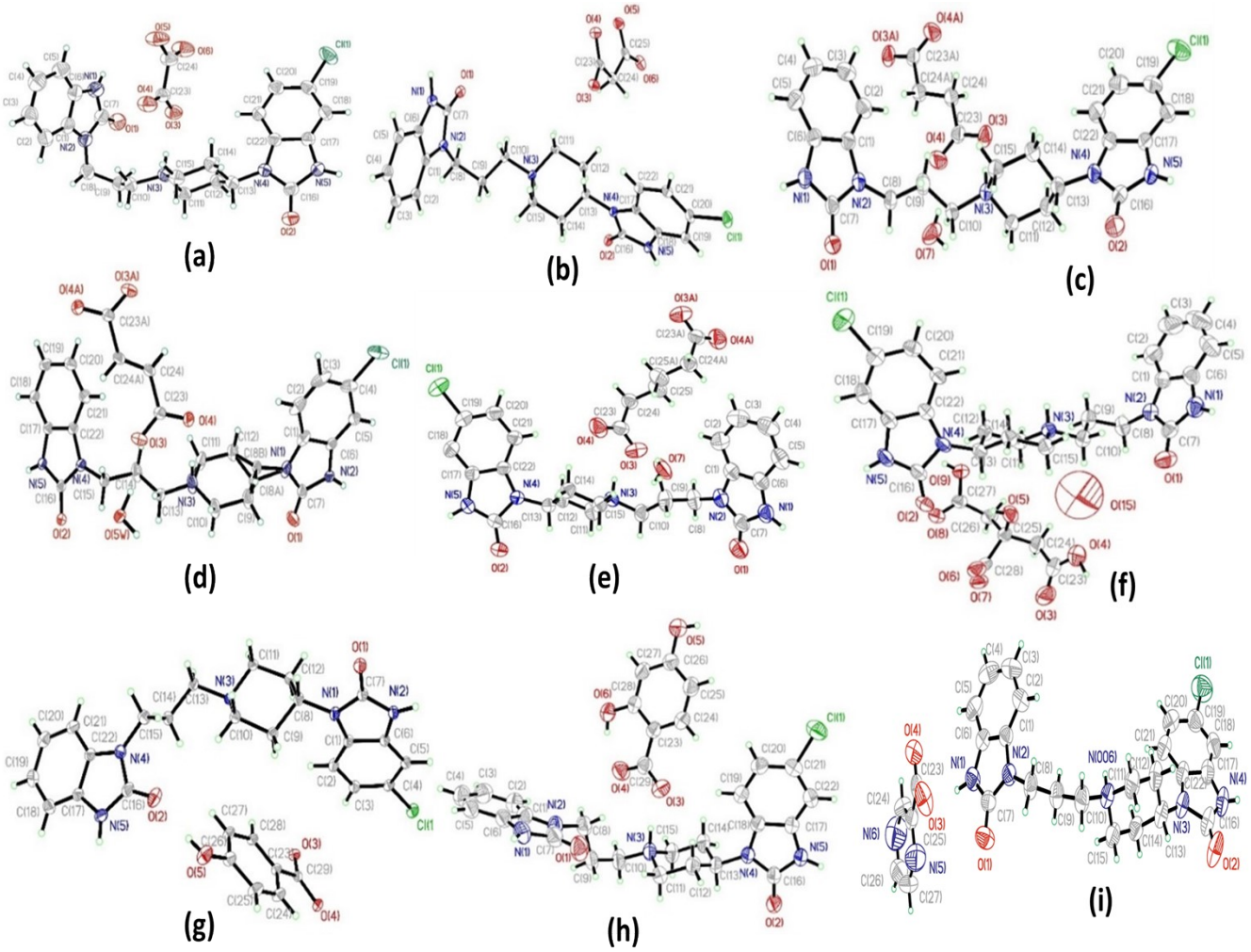


Figure S1: ORTEP view of (a) DOM.OXA, (b) DOM.MAL, (c) DOM.SUA, (d) DOM.FA, (e) DOM.AA, (f) DOM.CA, (g) DOM.4-HBA, (h) DOM.2,4-DHBA and (i) DOM.PCA. Herein, the ellipsoids are drawn with a 50% probability.

Table S1. Hydrogen bond distances (Å) and angles (°) of molecular salts of DOM.

Solid forms	*D*–H···*A*	*D*–H(Å)	H···*A*(Å)	*D*–*A*(Å)	*D*–H···*A*(°)
DOM.OXA	$N3^{+}$–H112···$O3^{-}$	0.921	1.86	2.771(1)	170
	N3–H112···O4	0.921	2.64	3.232(1)	122
	N5–H113···O6	0.901	2.12	2.922(2)	146
	N1–H111···O1	0.780	2.01	2.790(1)	173
	N5–H113···$O3^{-}$	0.901	2.32	3.029(1)	135
	C15–H15A···O2	0.970	2.40	3.237(1)	143
DOM.MAL	$N3^{+}$–H111···$O3^{-}$	1.022	1.69	2.710(1)	174
	N5–H112···O2	0.862	1.88	2.741(1)	172
	N1–H113···O3	0.990	1.83	2.792(1)	163
	N3–H111···O4	1.021	2.43	3.101(1)	123

	C15−H15B···O6	0.991	2.53	3.392(1)	145
	C15−H15B···O5	0.991	2.60	3.353(1)	148
DOM.SUA	C15−H15A···O2	0.971	2.25	3.161(1)	156
	$N3^{+}$−H100···$O3^{-}$	1.019	1.69	2.712(1)	179
	O1−H104···O7	0.730	1.93	2.772(2)	168
	O7−H103···O4	0.810	1.97	2.710(1)	150
	N5−H102···O7	0.801	2.05	2.710(1)	165
	N1−H101···O3	0.870	1.95	2.819(1)	166
DOM.FA	C11−H11B···O1	0.970	2.44	3.174(3)	131
	$N3^{+}$−H3A···$O4^{-}$	0.981	1.98	2.964(1)	174
	N2−H2A···O5W	0.860	1.89	2.724(1)	161
	N5−H5A···O4	0.861	1.97	2.773(1)	153
	O5W−H5WA···O3	0.902	1.81	2.696(2)	163
	O5W−H5WB···O2	0.898	1.87	2.761(1)	168
DOM.4-HBA	N5−H5A···O4	0.860	1.85	2.701(1)	169
	N2−H2A···O4	0.860	1.90	2.731(2)	163
	O2−H5B···O5	0.820	1.86	2.672(1)	172
	$N3^{+}$−H3A···$O3^{-}$	0.980	1.69	2.670(1)	170
DOM.2,4-DHBA	N5−H5A···O6	0.881	1.90	2.781(1)	176
	$N3^{+}$−H100···$O3^{-}$	0.987	1.68	2.642(1)	164
	O5−H5···O1	0.820	1.88	2.673(3)	162
	C14−H14A···O3	0.970	2.51	3.191(2)	127
	C8−H8B···O4	0.969	2.47	3.091(1)	121
DOM.CA	C10−H10A···O15	0.970	2.30	3.071(1)	136
	C15−H15B···O1	0.970	2.41	3.311(1)	145
	C11−H11A···O1	0.970	2.48	3.323(1)	145
	O4−H4···O1	0.830	1.57	2.601(1)	173
	O9−H9···O6	0.820	1.78	2.582(1)	167
	O5−H5···O8	0.820	1.96	2.761(1)	167
	$N3^{+}$−H100···$O3^{-}$	0.910	1.80	2.692(1)	168
DOM.PCA	N4−H102···O3	0.948	1.83	2.761(1)	165
	N4−H103···O4	0.765	2.44	3.072(1)	140
	N4−H103···O3	0.765	2.47	3.101(1)	140
	$N006^{+}$−H101···$O4^{-}$	0.959	1.88	2.772(1)	153

Table S2. Torsion angles corresponding to DOM molecular salt.

crystal forms	torsion angles (°)						
	C1-N1-C2-C3	C1-N1-C2-C9	C3-C4-N2-C5	C9-C10-N2-C5	C4-N2-C5-C6	C10-N2-C5-C6	C8-N3-C7-C6
DOM.OA	**62.47**	**-63.10**	**-155.21**	**175.26**	**-53.42**	**-177.60**	**-113.91**
DOM.MA	**-123.37**	**112.71**	**177.81**	**-176.48**	**-64.00**	**171.48**	**-80.52**
DOM.SA	**-53.38**	**73.44**	**174.83**	**-177.31**	**50.50**	**176.06**	**67.47**
DOM.FA	**100.05** **45.81**	**-127.66** **-84.63**	**-176.70**	**178.44**	**-20.73**	**-178.21**	**-93.57**
DOM.AA	**53.25**	**-72.09**	**-177.97**	**179.42**	**-29.99**	**-154.57**	**-88.79**
DOM.CA	**-61.65**	**62.58**	**179.64**	**155.89**	**86.25**	**-171.34**	**-64.93**
DOM.4HBA	**-61.14**	**63.50**	**-176.03**	**175.76**	**173.51**	**-63.18**	**-82.86**
DOM.2,4-DHBA	**-58.55**	**66.02**	**179.84**	**176.38**	**56.59**	**178.91**	**-101.93**
DOM.PCA	**-56.91**	**67.52**	**-173.58**	**175.96**	**159.43**	**-76.76**	**-77.83**

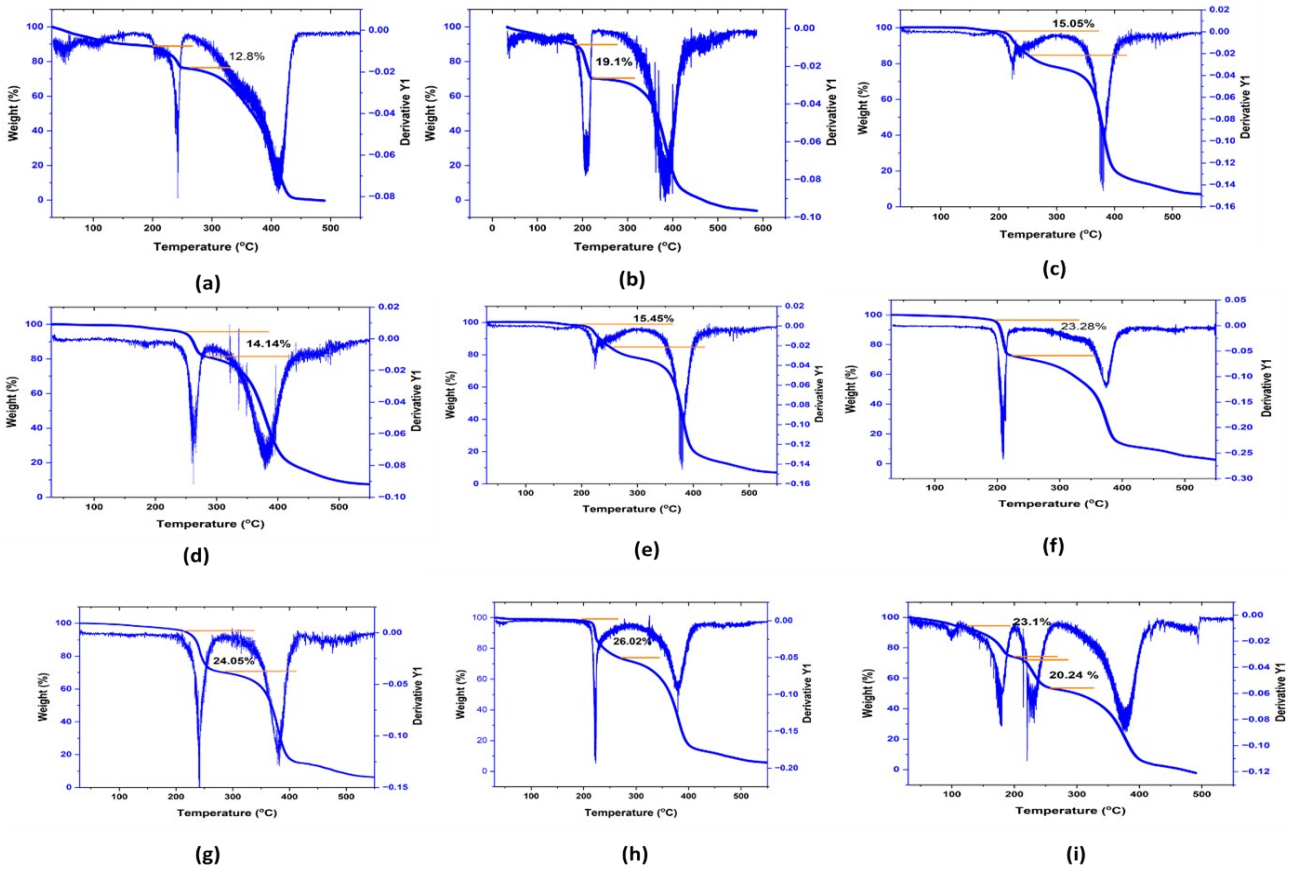
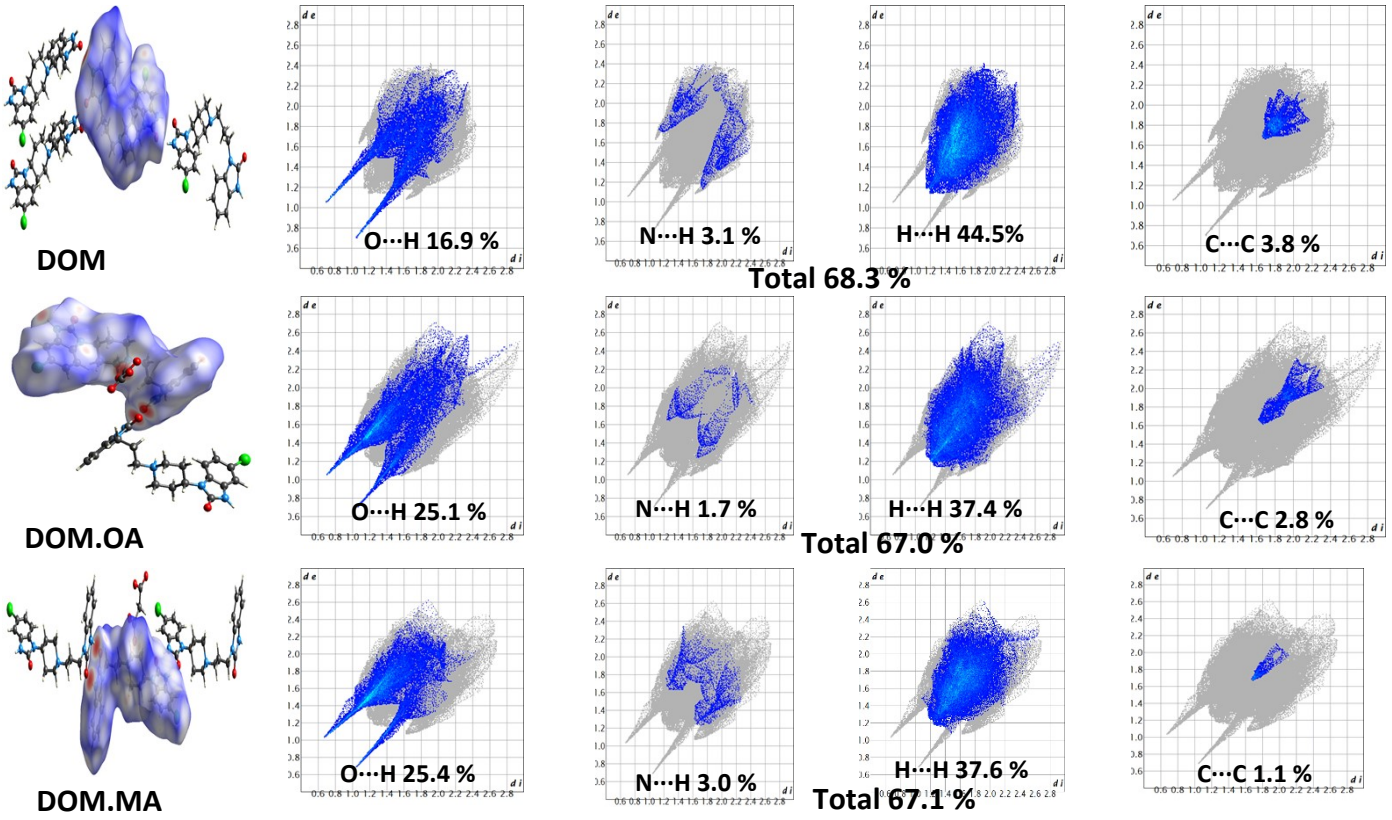


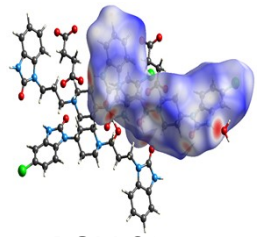
Figure S2: Thermogravimetric (TG) derivative profile of (a) DOM.OA, (b) DOM.MA, (c) DOM.SA, (d) DOM.FA, (e) DOM.AA, (f) DOM.CA, (g) DOM.4-HBA, (h) DOM.2,4-DHBA and (i) DOM.PCA.

Table S3. Details of temperature range and corresponding TGA weight loss of DOM salts.

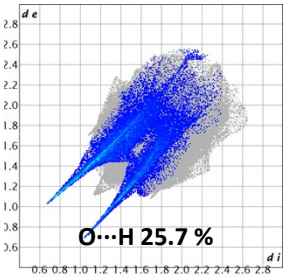
Compounds Name	Temperature Range (°C)	Percentage of weight loss (%)	Inference
DOM.OA	200-264	12.8	Possible weight loss from decomposition of OA (Theoretical weight loss = 17.48 %)
DOM.MA	185-226	19.01	Possible weight loss from decomposition of MA (Theoretical weight loss = 19.78 %)
DOM.SA	197-255	15.05	Possible combine weight loss from lattice water and decomposition of SA (Theoretical weight loss = 15.31 %)
DOM.FA	246-283	14.14	Possible combine weight loss from lattice water and decomposition of FA (Theoretical weight loss = 15.14 %)
DOM.AA	196-253	15.45	Possible weight loss from decomposition of AA (Theoretical weight loss = 14.16 %)
DOM.CA	195-221	23.28	No significant weight loss (Possible decomposition of solid forms)
DOM.4-HBA	212-298	24.05	Possible weight loss from

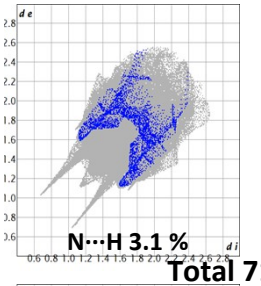
			decomposition of 4-HBA (Theoretical weight loss = 24.48 %)
DOM.2,4-DHBA	198-273	26.02	Possible weight loss from decomposition of 2,4-DHBA (Theoretical weight loss = 28.98 %)
DOM.PCA	120-198	23.01	Possible weight loss from decomposition of PCA (Theoretical weight loss = 22.56 %)

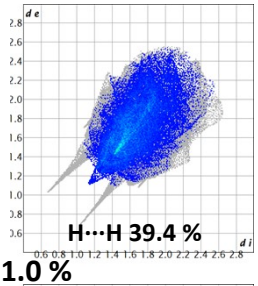


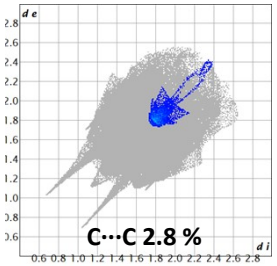


DOM.SA

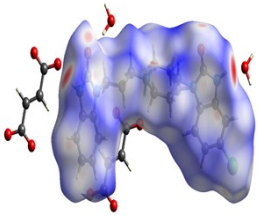




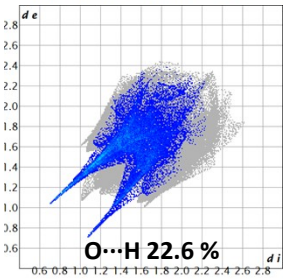


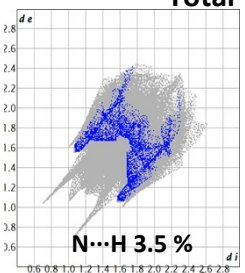


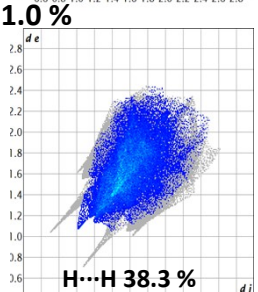
Total 71.0 %

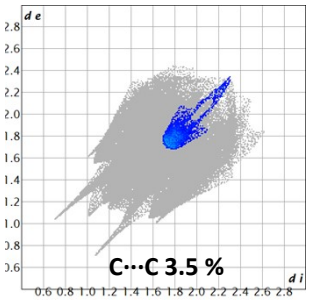


DOM.FA









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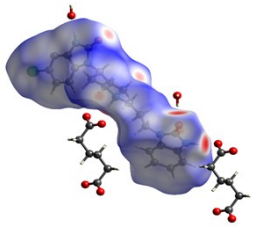
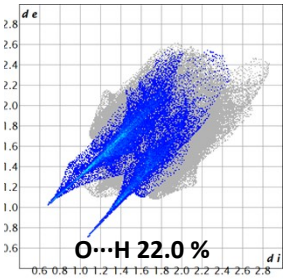
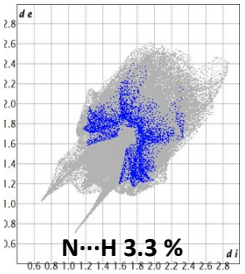
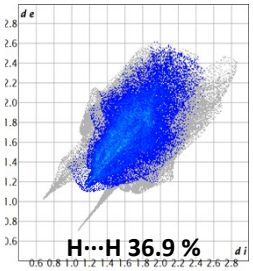
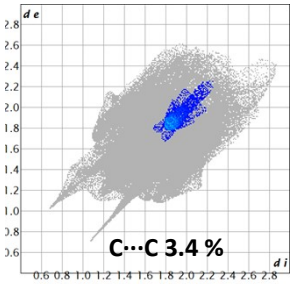


DOM.AA

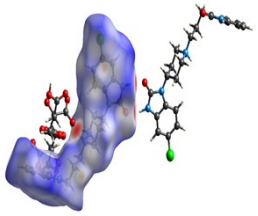




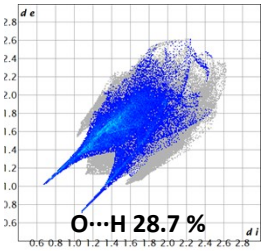


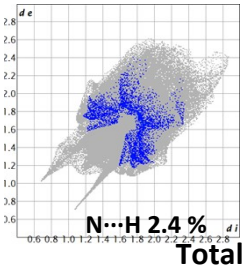


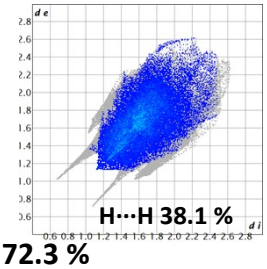
Total 66.9 %

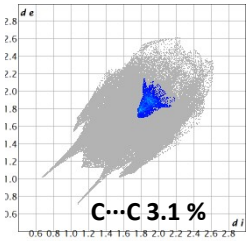


DOM.CA









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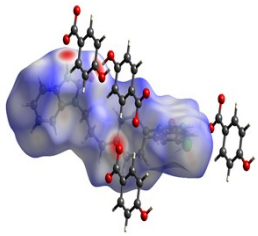
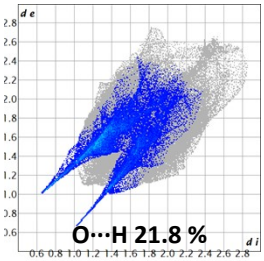
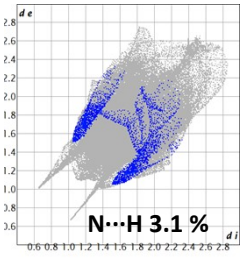
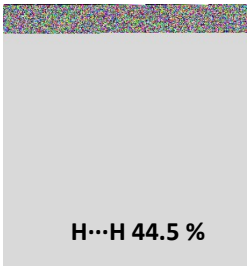
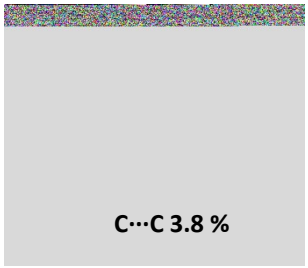


DOM.4-HBA

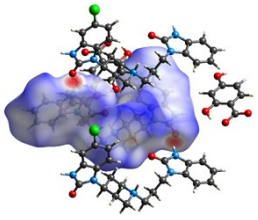




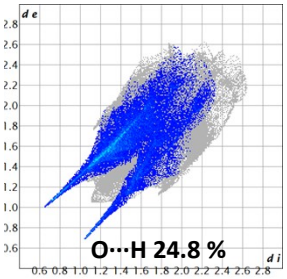


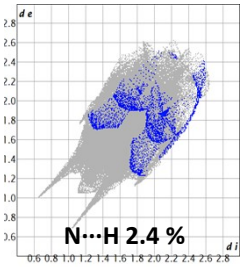


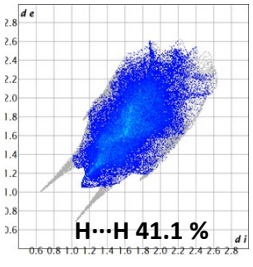
Total 65.4 %

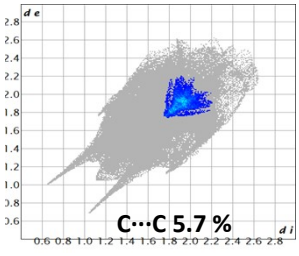


DOM.2,4-DHBA









Total 74.3 %

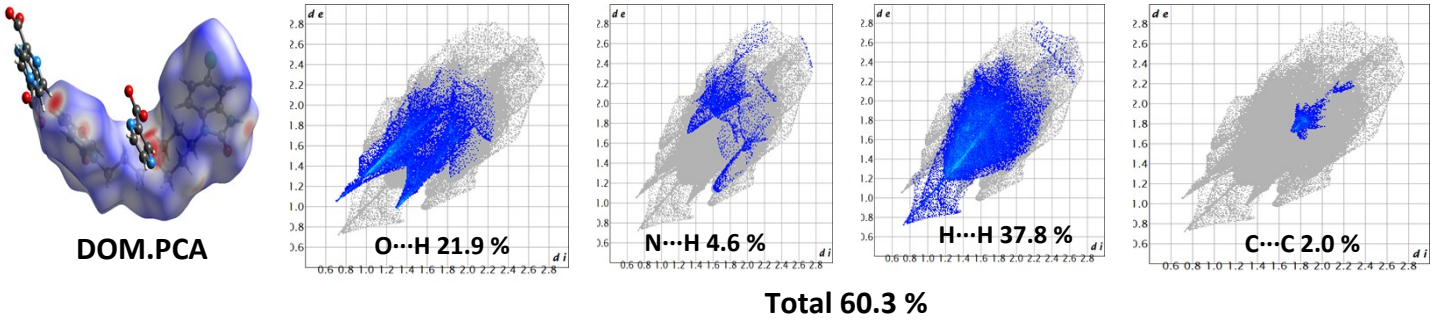
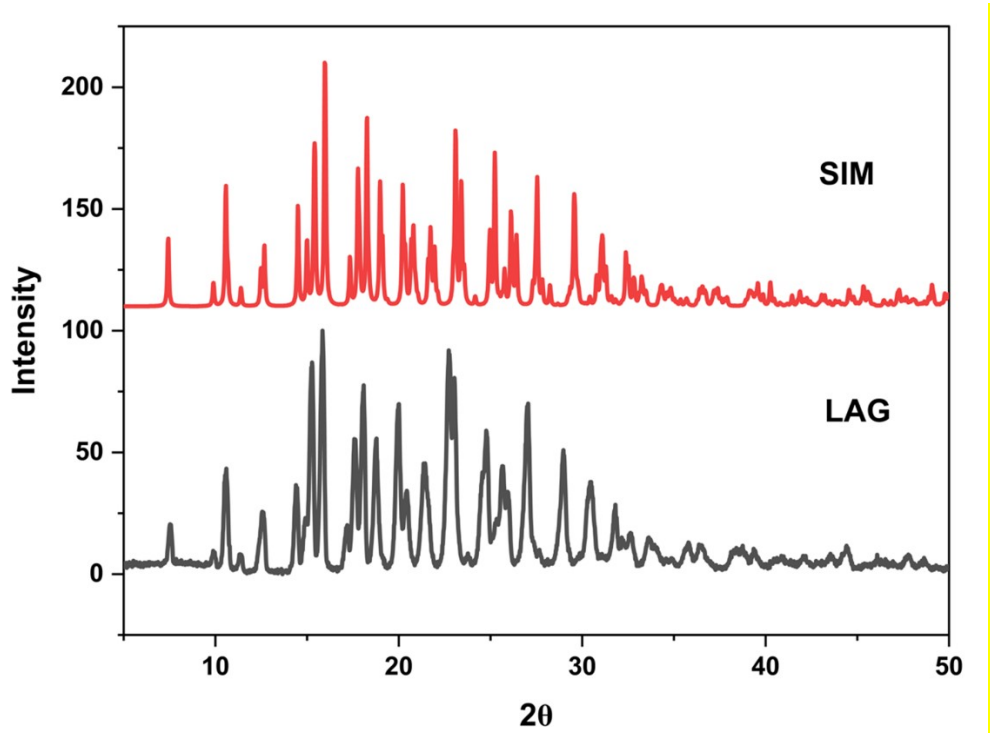


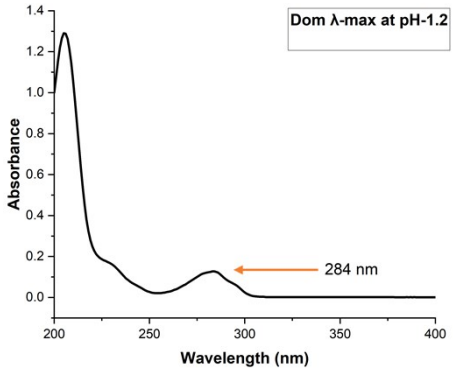
Figure S3. HS 3D maps and 2D fingerprints, the total % of the contacts population involve of DOM and its molecular salts.

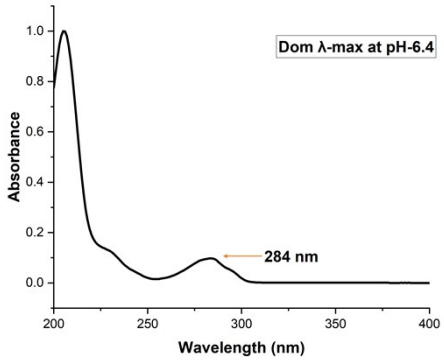
Details procedure for DOM.MAL salt preparation.

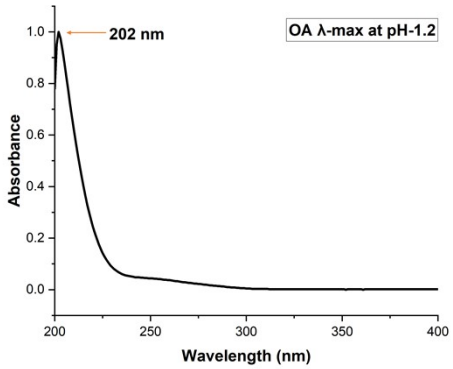
DOM (42.59 mg, 0.1 mmol) and an equivalent amount of MAL were crushed in a mortar pestle for around 30 minutes in the presence of 2-3 drops of methanol as liquid, yielding the relevant micro solid forms. Which is further validated by matching the experimental PXRD pattern with the earlier reported simulated data.[1]

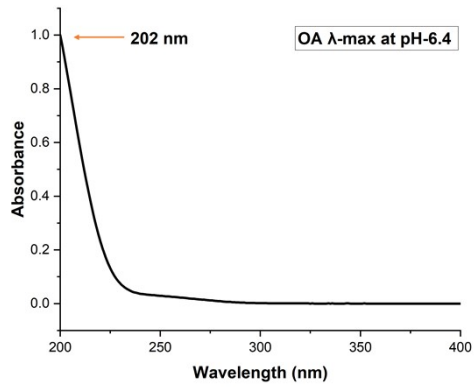


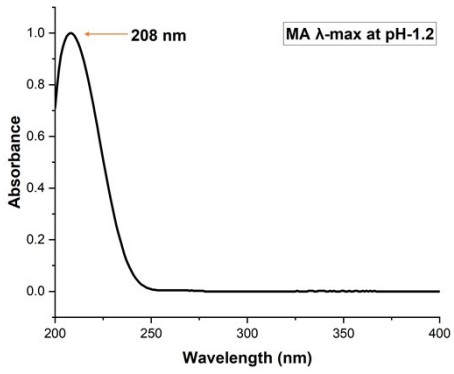
PXRD of 1:1 DOM.MAL ground mixture compared with the simulated pattern

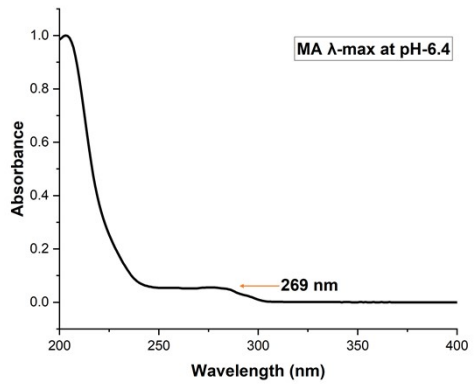

Dom λ-max at pH-1.2
284 nm
Absorbance
Wavelength (nm)

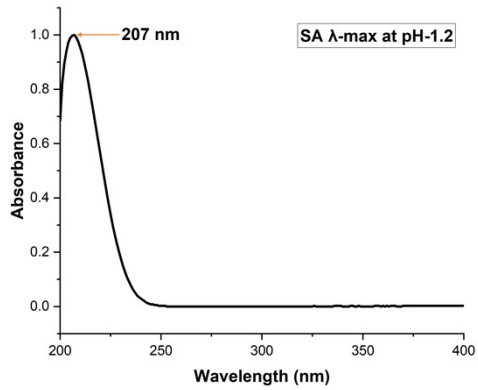

Dom λ-max at pH-6.4
284 nm
Absorbance
Wavelength (nm)

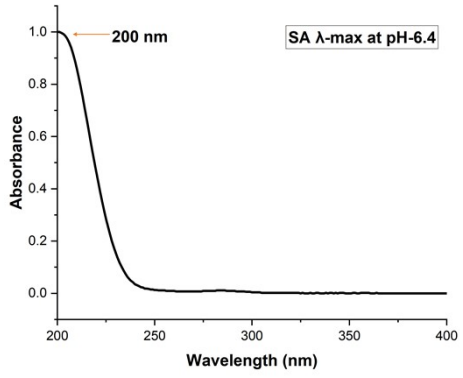

202 nm
OA λ-max at pH-1.2
Absorbance
Wavelength (nm)

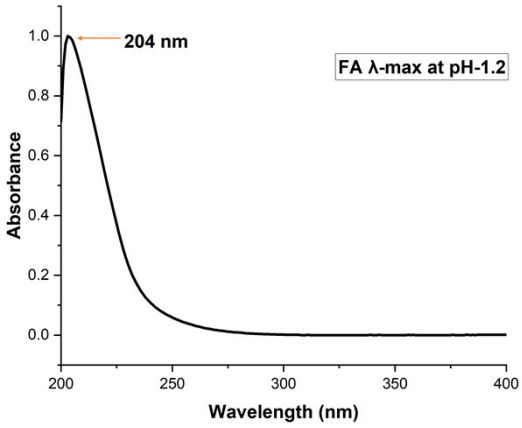

202 nm
OA λ-max at pH-6.4
Absorbance
Wavelength (nm)

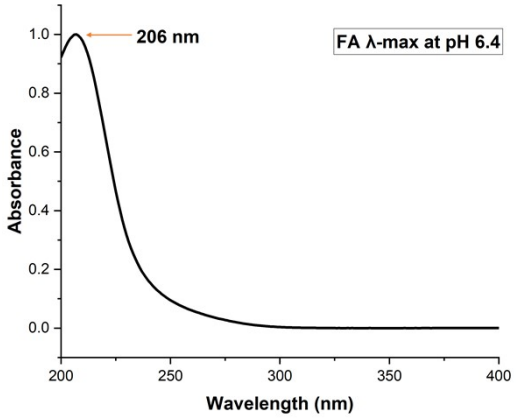

208 nm
MA λ-max at pH-1.2
Absorbance
Wavelength (nm)

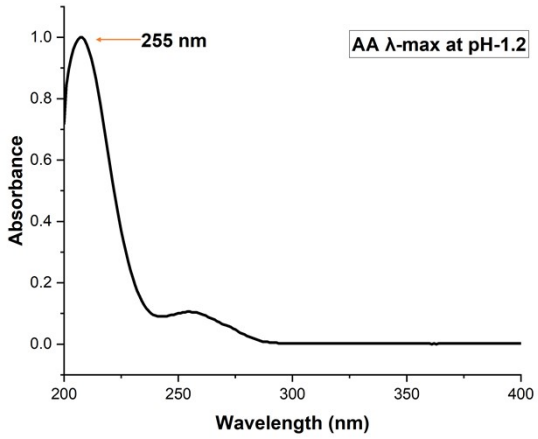

MA λ-max at pH-6.4
269 nm
Absorbance
Wavelength (nm)

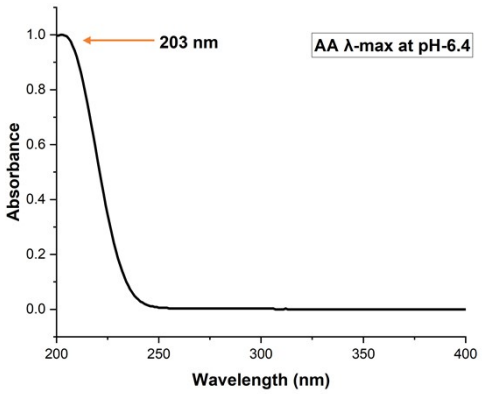

207 nm
SA λ-max at pH-1.2
Absorbance
Wavelength (nm)

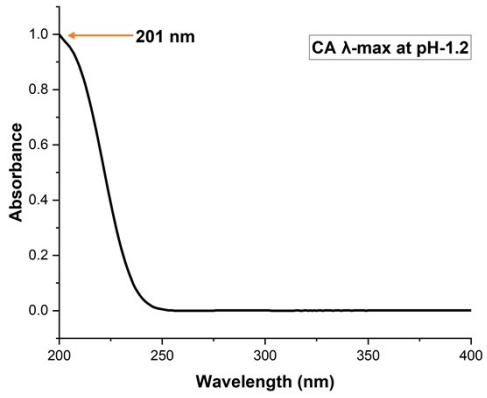

200 nm
SA λ-max at pH-6.4
Absorbance
Wavelength (nm)

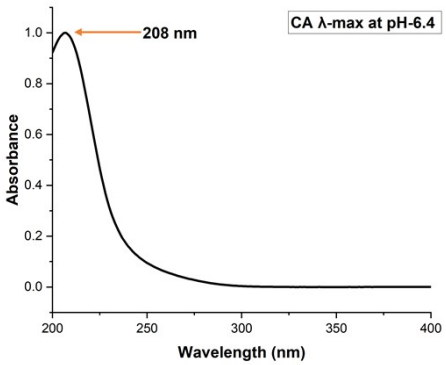

204 nm
FA λ-max at pH-1.2
Absorbance
Wavelength (nm)


206 nm
FA λ-max at pH 6.4
Absorbance
Wavelength (nm)


255 nm
AA λ-max at pH-1.2
Absorbance
Wavelength (nm)


203 nm
AA λ-max at pH-6.4
Absorbance
Wavelength (nm)


201 nm
CA λ-max at pH-1.2
Absorbance
Wavelength (nm)


208 nm
CA λ-max at pH-6.4
Absorbance
Wavelength (nm)

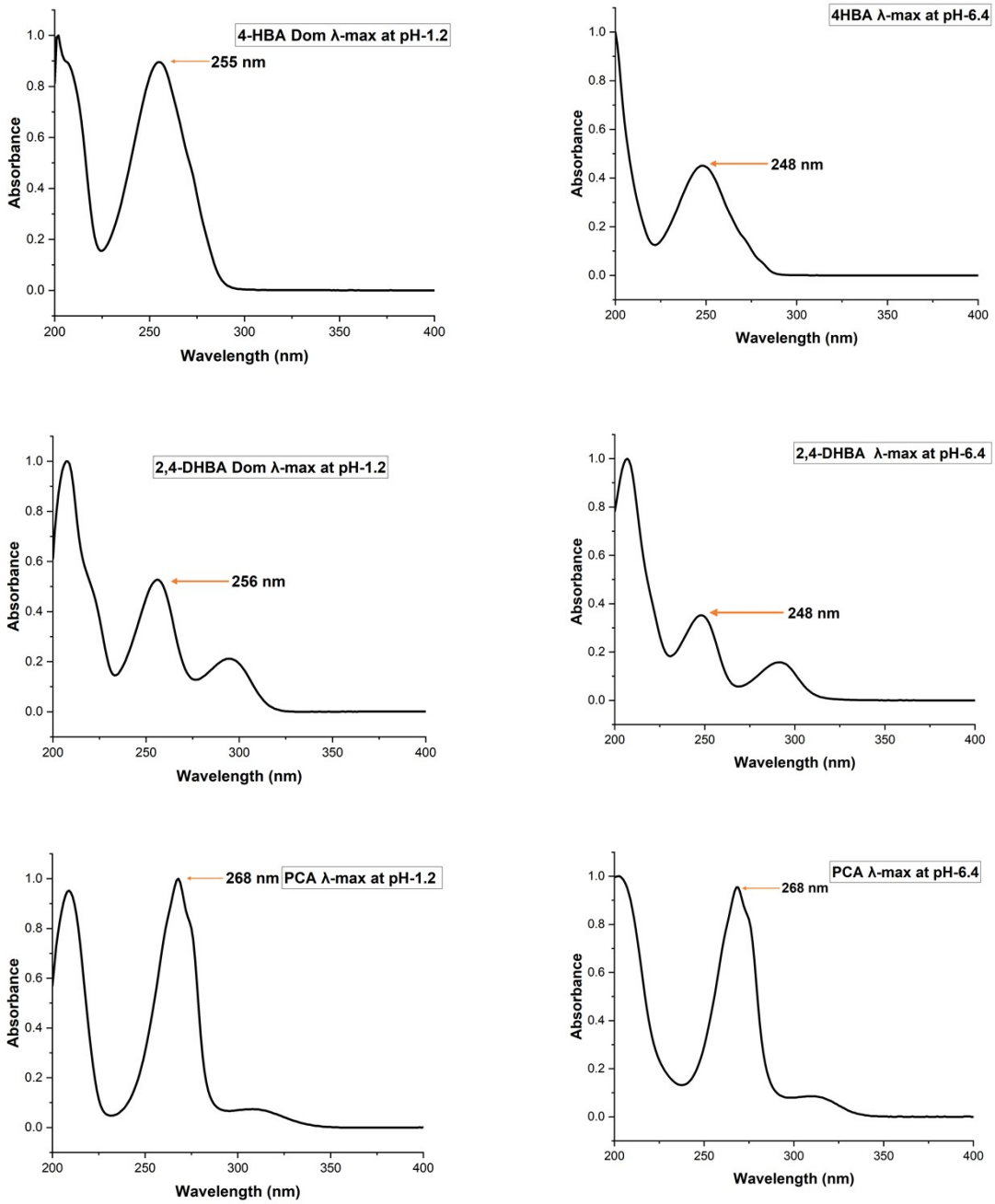
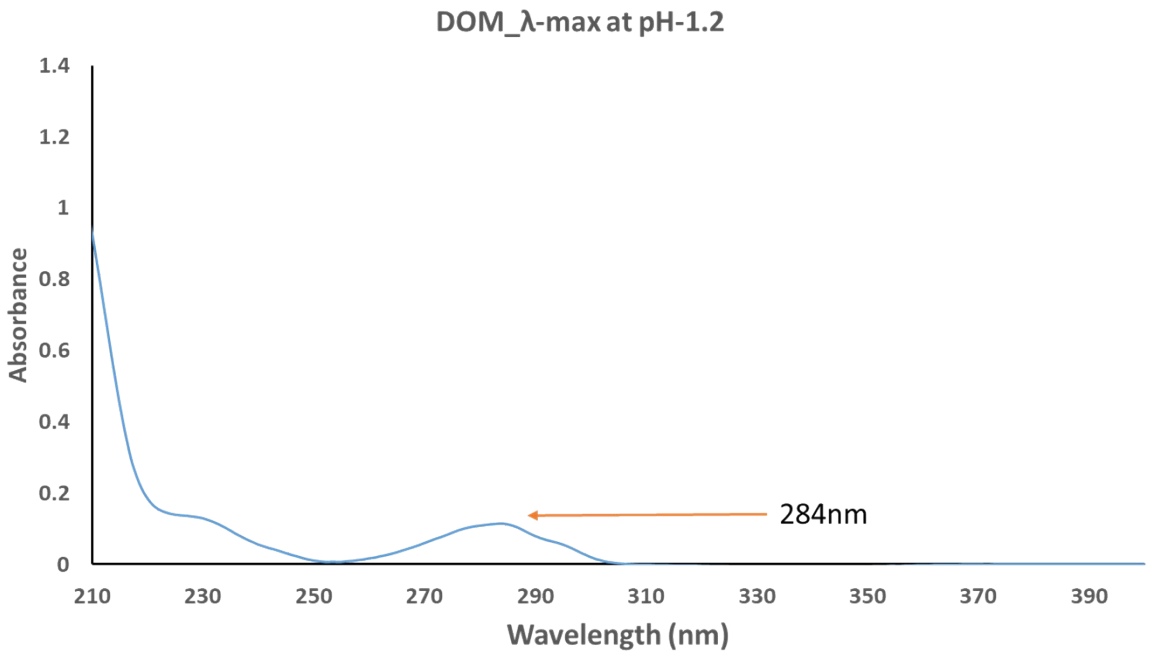
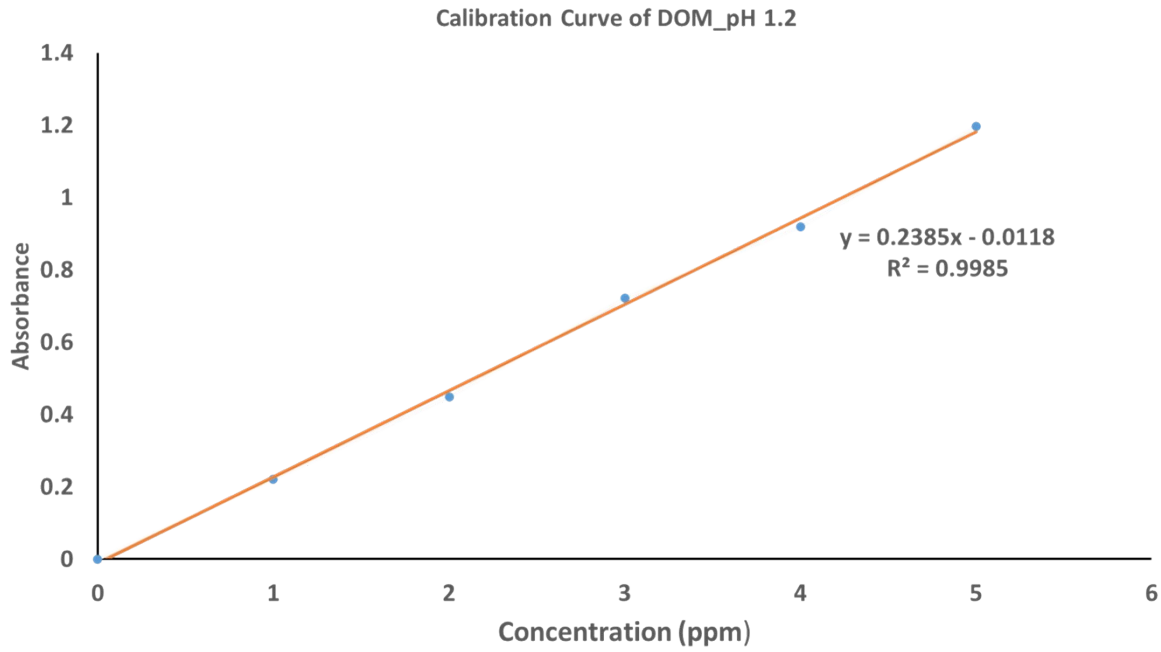


Figure S4: UV absorbance spectra of DOM and its molecular salts at various pH showed the negligible interference in the UV region of 284 nm, where the drug is absorbed.

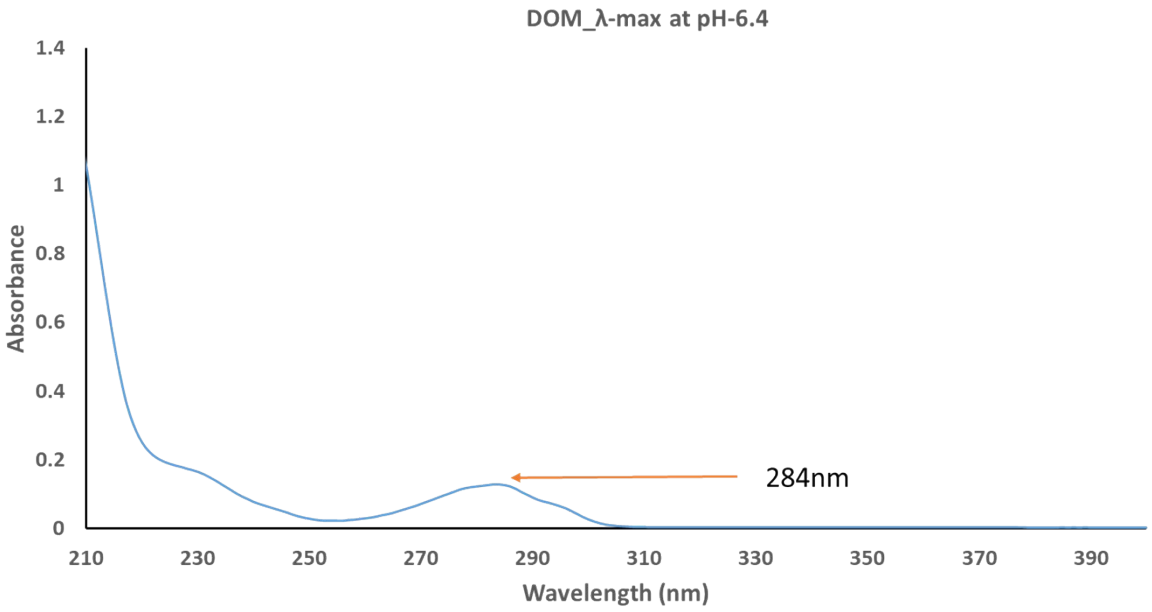
Details of the solubility parameters of DOM molecular salts

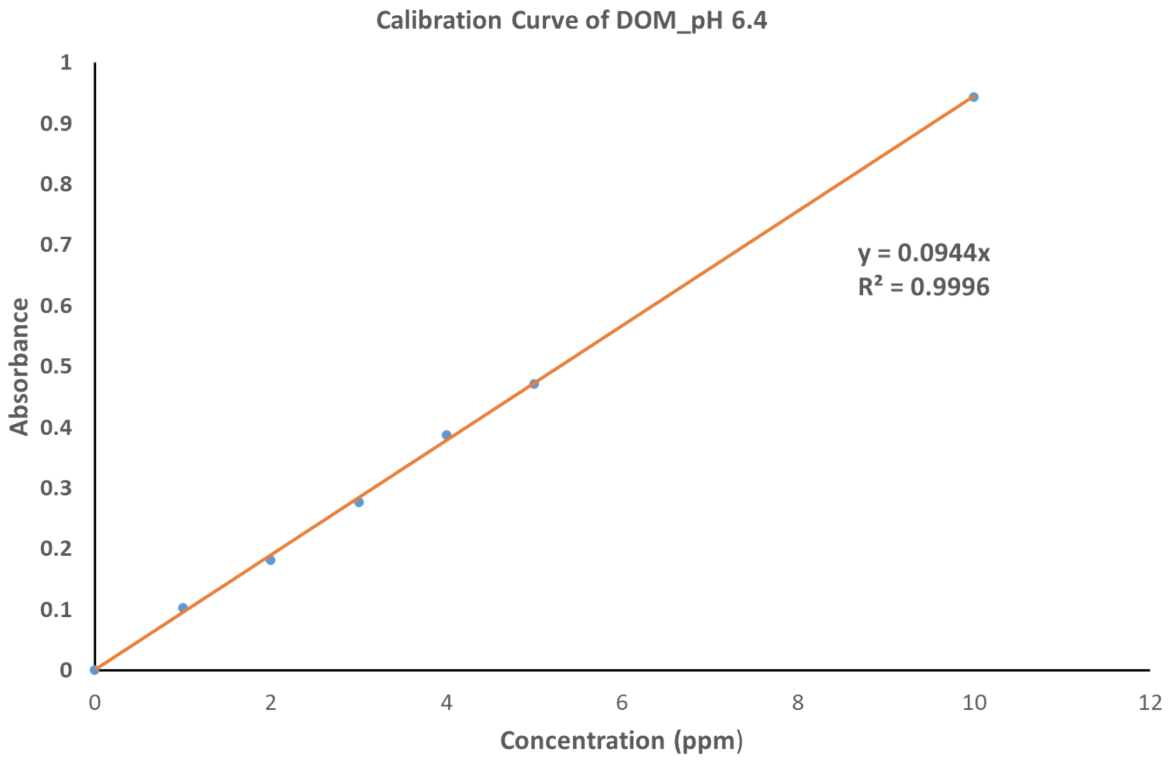




Solubility of DOM in pH 1.2 after applying dilution factor

S.No	Sample Name	Absorbance			Estimated Standard Deviation	After adding the dilution factor (mg/mL)
1	DOM	0.281	0.284	0.285	0.002082	1.100
2	DOM.OA	0.428	0.433	0.427	0.003215	1.6953
3	DOM.AA	0.696	0.697	0.698	0.001	2.7805
4	DOM.SA	0.769	0.768	0.768	0.000577	3.0761
5	DOM.MA	0.565	0.566	0.568	0.001528	2.2512
6	DOM.FA	1.844	1.845	1.850	0.003215	7.4291
7	DOM.CA	0.394	0.396	0.392	0.002	1.5576
8	DOM.PCA	0.638	0.645	0.642	0.003512	2.5456
9	DOM.4-HBA	0.414	0.414	0.416	0.001155	1.6386
10	DOM.2,4-DHBA	0.995	0.997	0.999	0.002	3.9912
11	DOM.MAL	0.354	0.357	0.360	0.003	1.416





Solubility of DOM in pH 6.4 after applying dilution factor

S.No	Sample Name	Absorbance			Estimated Standard Deviation	After adding the dilution factor (mg/mL)
1	DOM	0.243	0.244	0.246	0.001528	1.3443
2	DOM.OA	2.336	2.338	2.331	0.003606	11.8008
3	DOM.AA	3.4766	3.4760	3.4770	0.000503	17.4992
4	DOM.SA	3.25	3.23	3.24	0.01	16.3671
5	DOM.MA	2.75	2.76	2.78	0.015275	13.8691
6	DOM.FA	2.99	3	3.1	0.060828	15.0681
7	DOM.CA	0.451	0.451	0.452	0.000577	2.3835
8	DOM.PCA	0.647	0.648	0.650	0.001528	3.3627
9	DOM.4-HBA	0.171	0.173	0.170	0.001528	0.9846
10	DOM.2,4-DHBA	0.104	0.107	0.103	0.002082	0.6499
11	DOM.MAL	0.292	0.296	0.294	0.002	1.286

Table S4: A comparison of the solubility rate of synthesized molecular solids with respective salt former.

Molecular Solid	Salt former solubility in water	Solubility media	Solubility rate (mg/mL)
DOM	-	pH 1.2/pH 6.4	1.34/1.10
DOM.OA	65.7		1.7/11.81
DOM.MA	197		2.25/13.87
DOM.SA	211		3.07/16.36
DOM.FA	24.1		7.43/15.06
DOM.AA	32.2		2.78/17.50
DOM.CA	106		1.56/2.38
DOM.4-HBA	11.9		1.64/0.98
DOM.2,4-DHBA	5.78		3.99/0.64
DOM.PCA	30.5		2.54/3.36

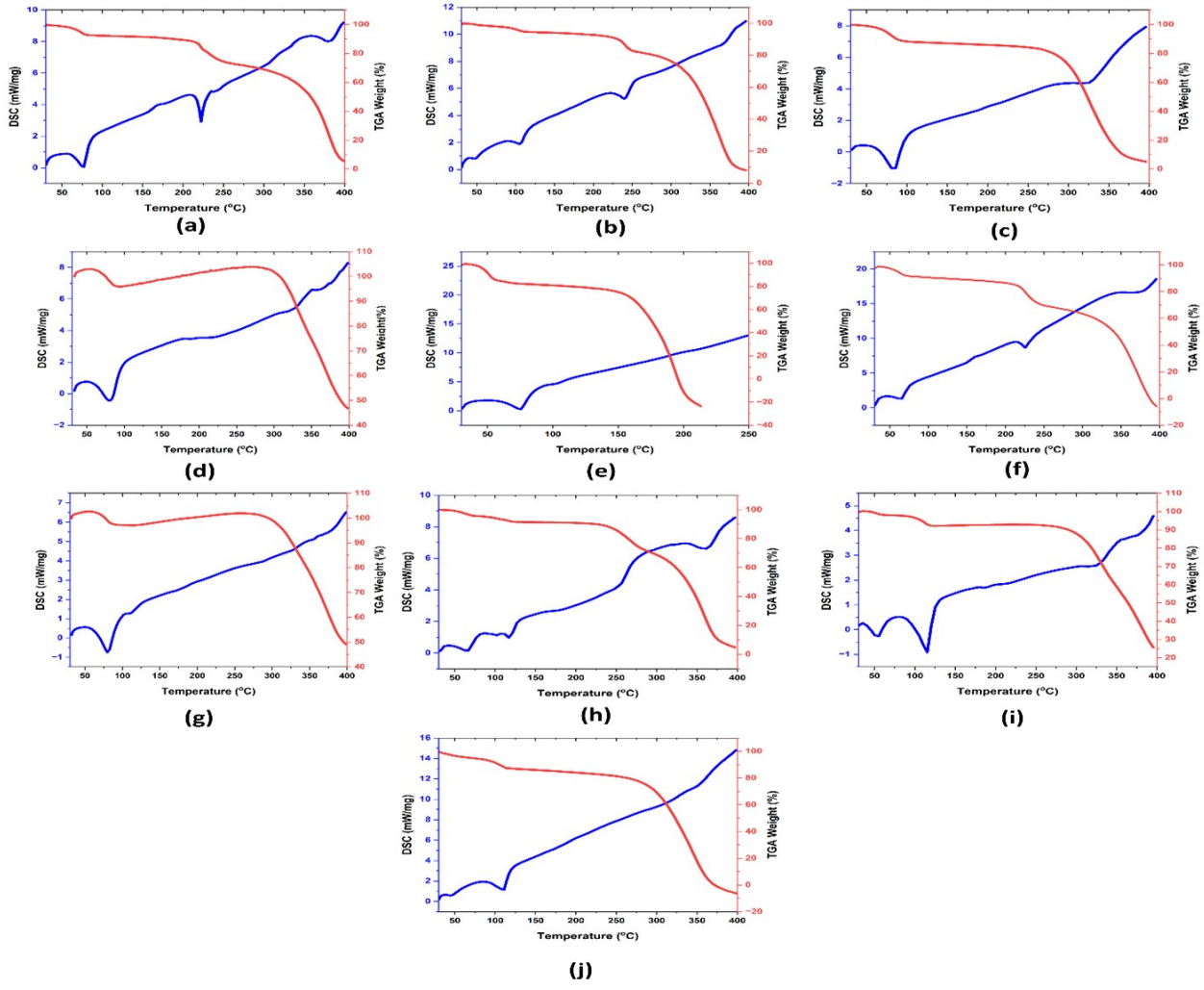


Figure S5: After solubility the thermogravimetric (TG) profile of (a) DOM.CA at pH 6.4 and (b) DOM.OA, (c) DOM.MA, (d) DOM.SA, (e) DOM.FA, (f) DOM.AA, (g) DOM.CA, (h) DOM.4-HBA, (i) DOM.2,4-DHBA and (j) DOM.PCA at pH 1.2.

References:

1 K. Vyas, J. Moses Babu and G. Om Reddy, *Acta Crystallogr. Sect. C*, 1999, **55**, IUC9900104–IUC9900104.