

Supplementary Materials: The Role of Natural Deep Eutectic Solvents in a Hydrogel Formulation Containing Lidocaine

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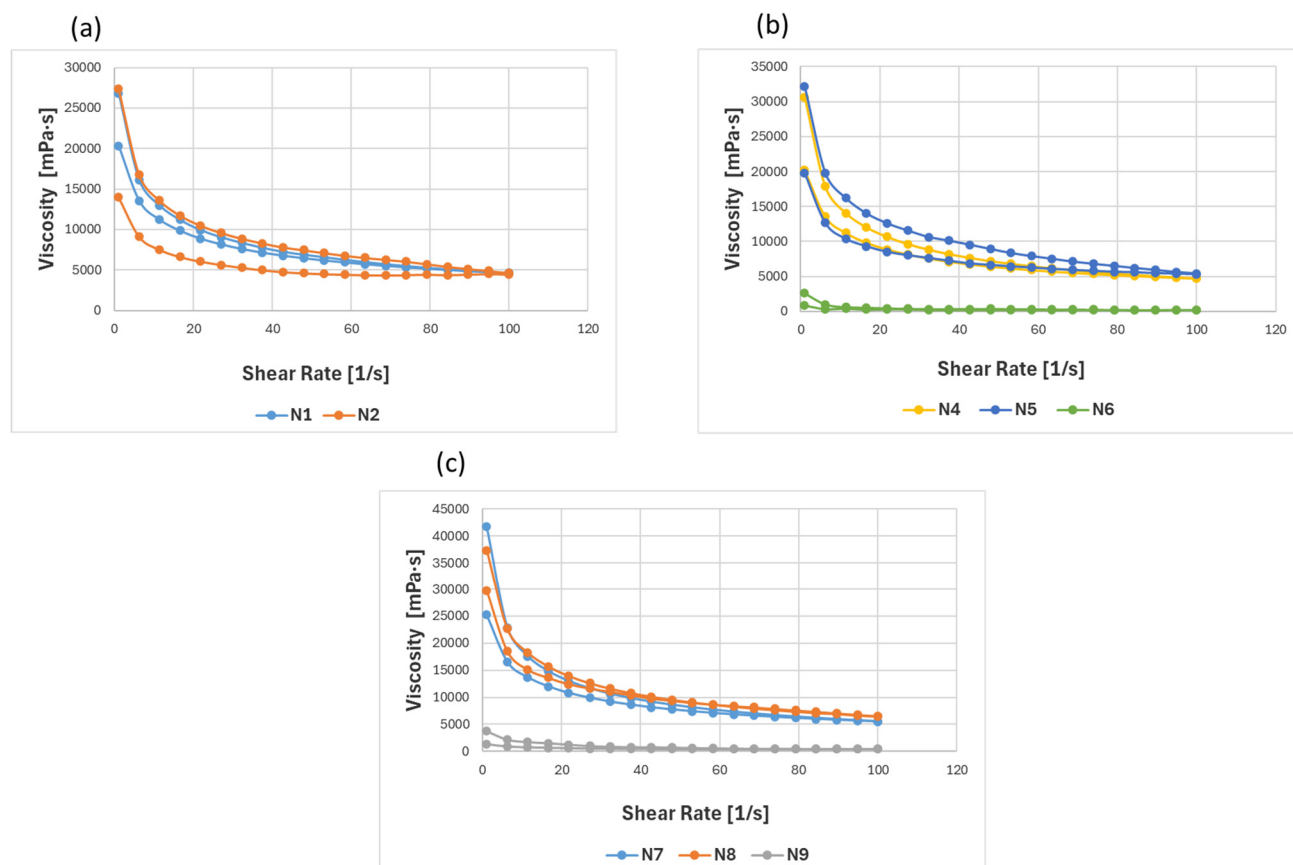
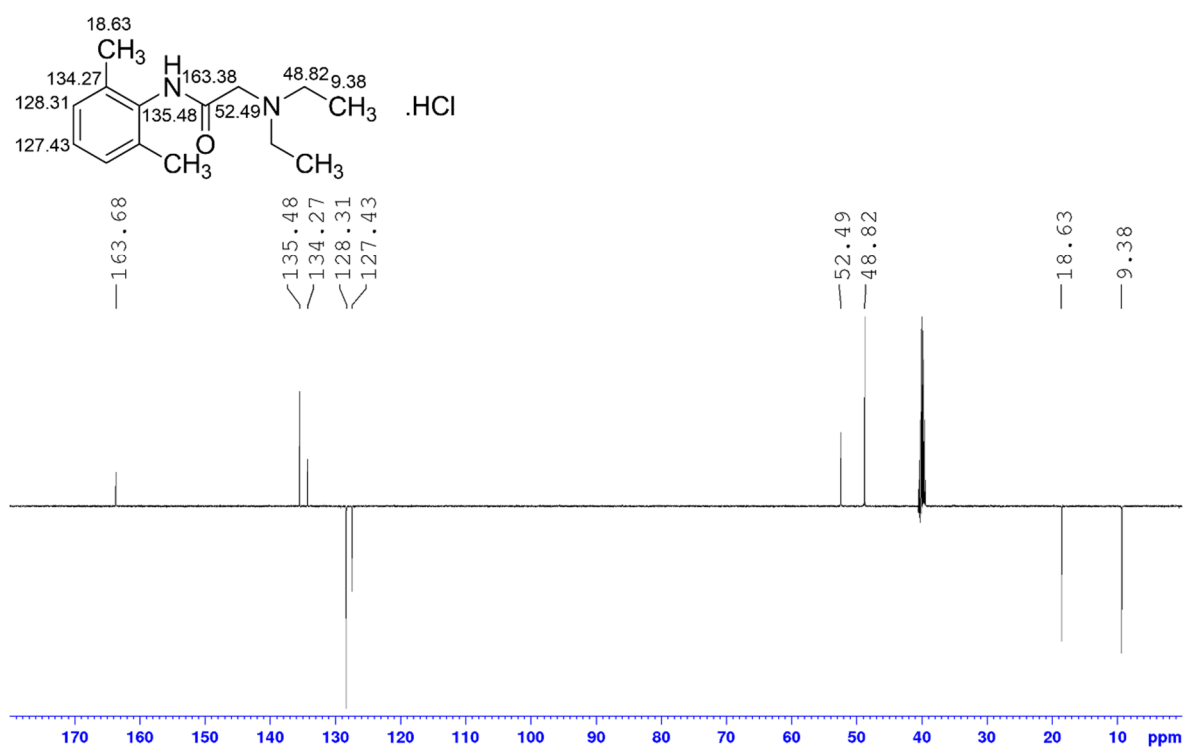
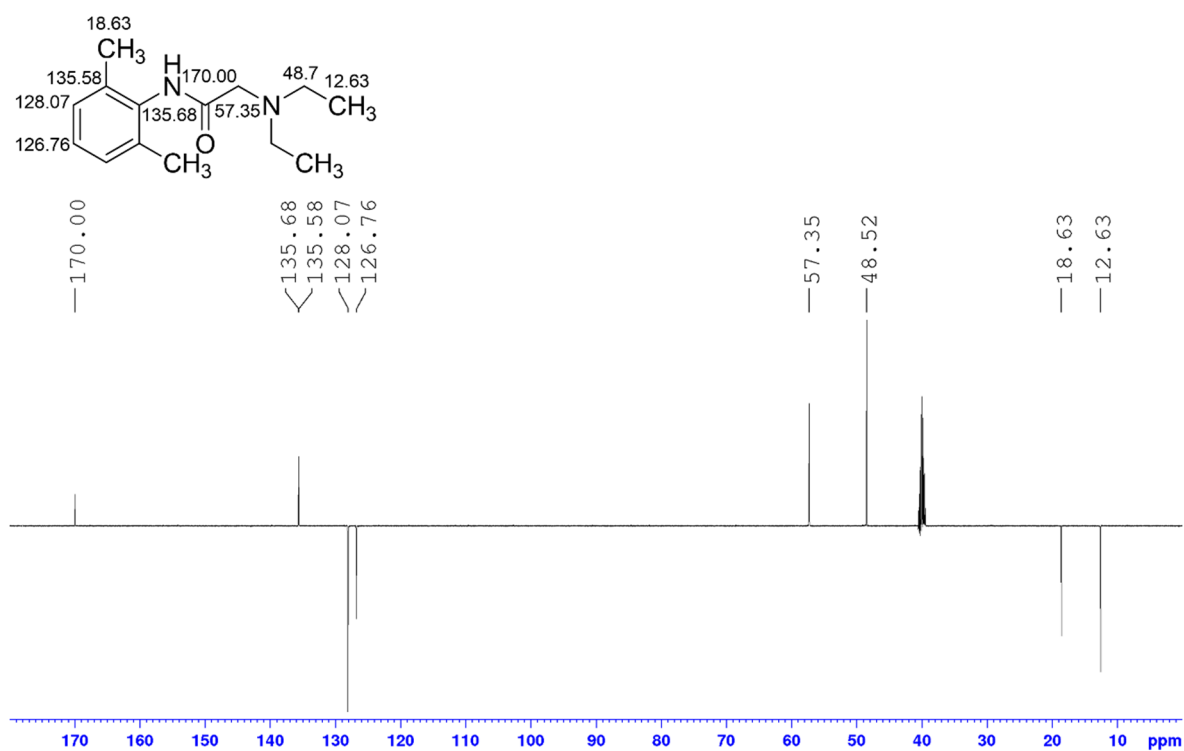
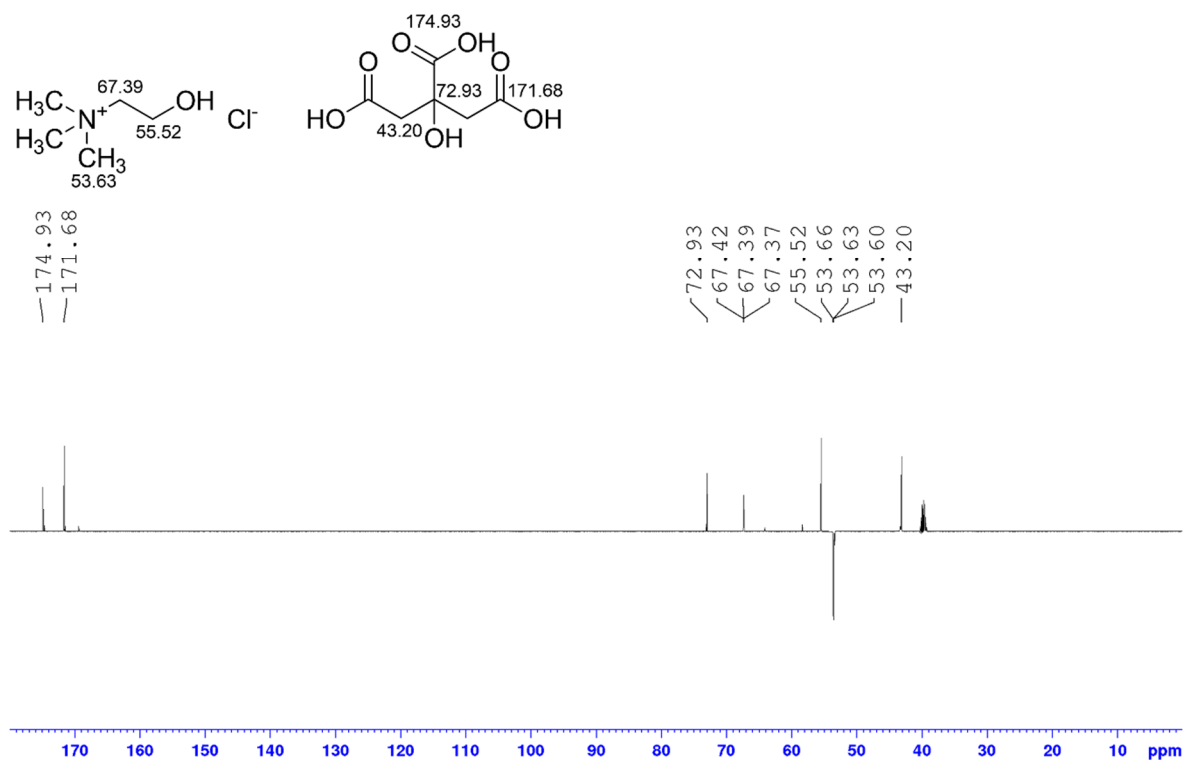
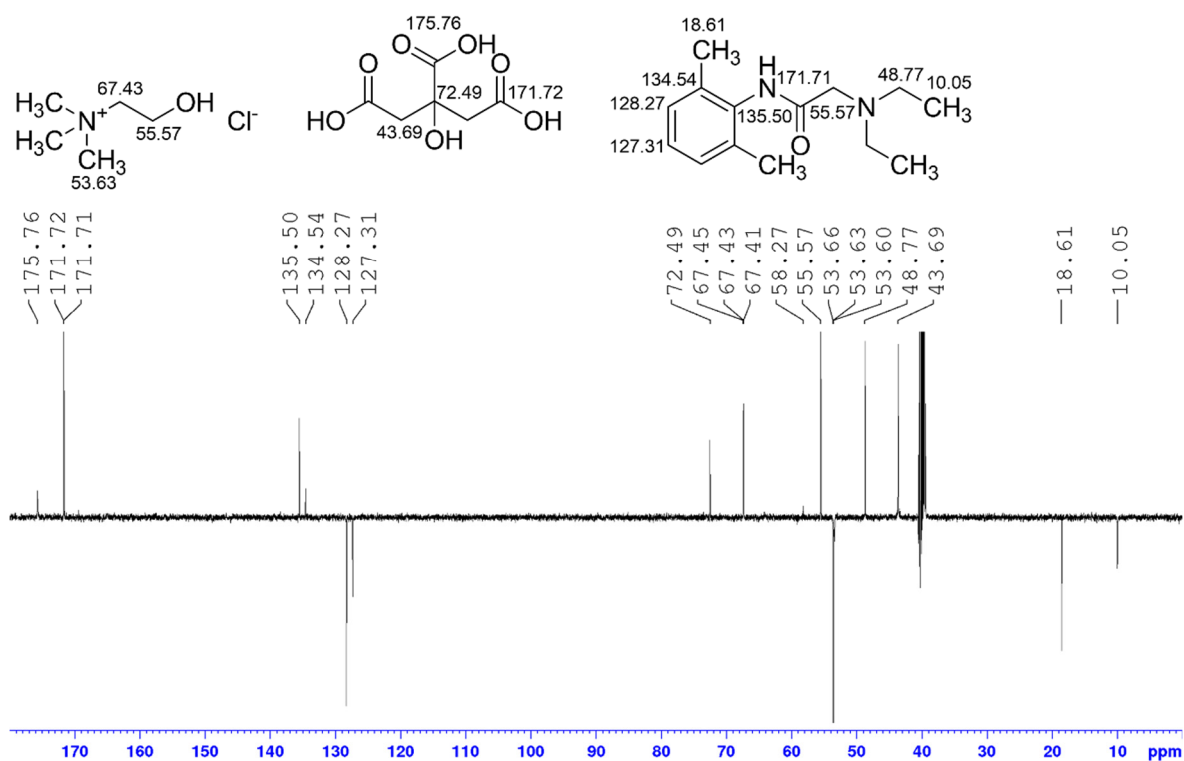


Figure S1. Viscosity curves of hydrogel formulations from the Design of Experiments (DoE) with varying concentrations of NADES and sodium citrate .



Figure S2c. ^{13}C -NMR spectrum of NADES (S7) in $\text{DMSO-}d_6$.Figure S2d. ^{13}C -NMR spectrum of NADES (S7) and lidocain base in $\text{DMSO-}d_6$.

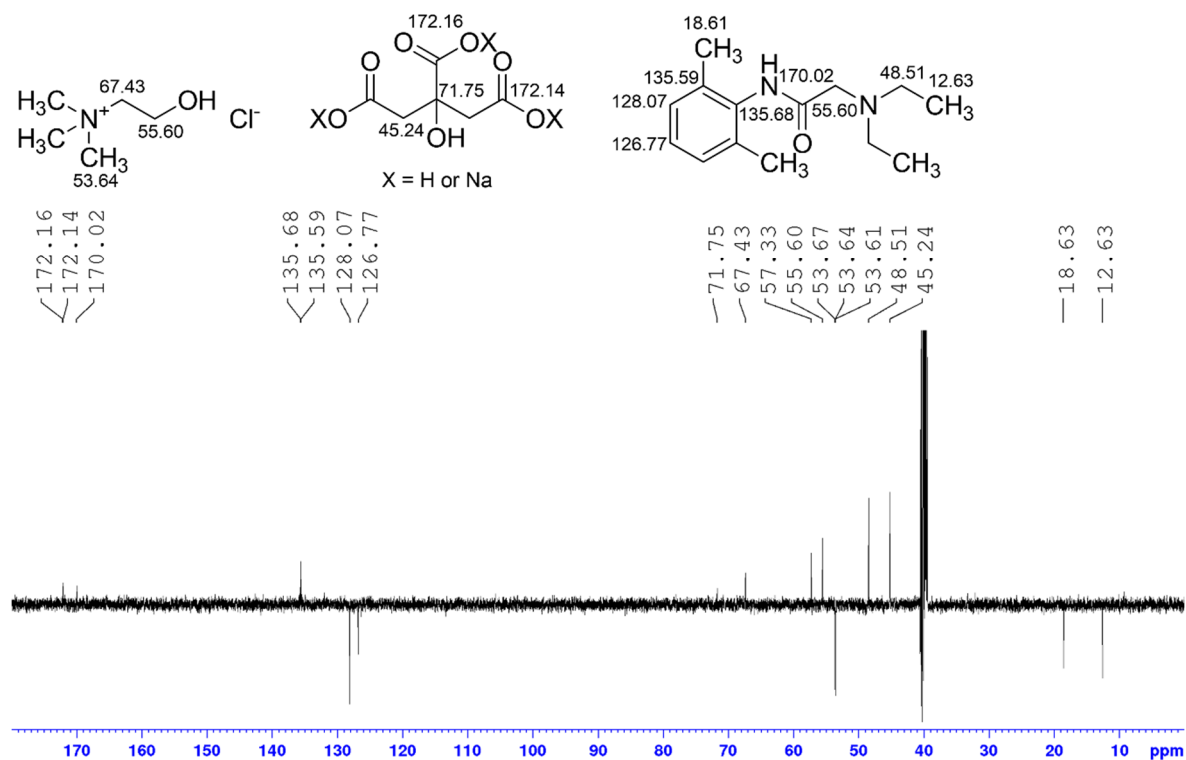


Figure S2e. ^{13}C -NMR spectrum of NADES(S7) and lidocaine buffered with sodium citrate in $\text{DMSO-}d_6$.

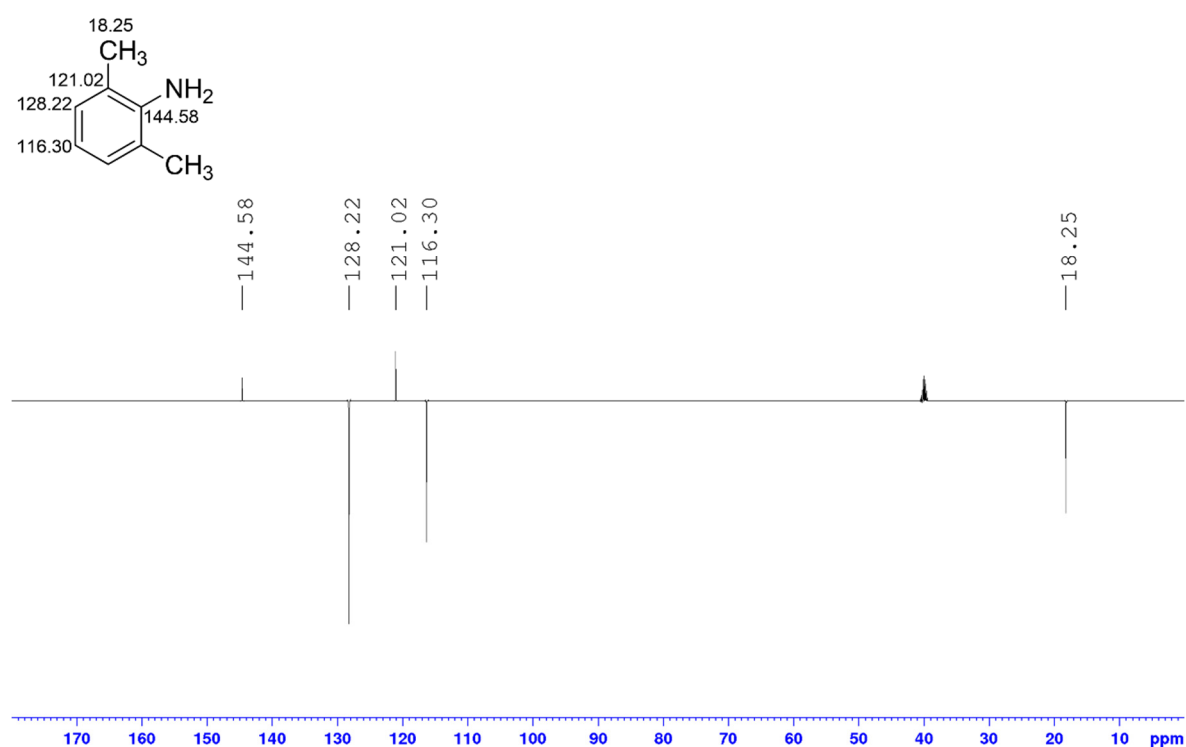
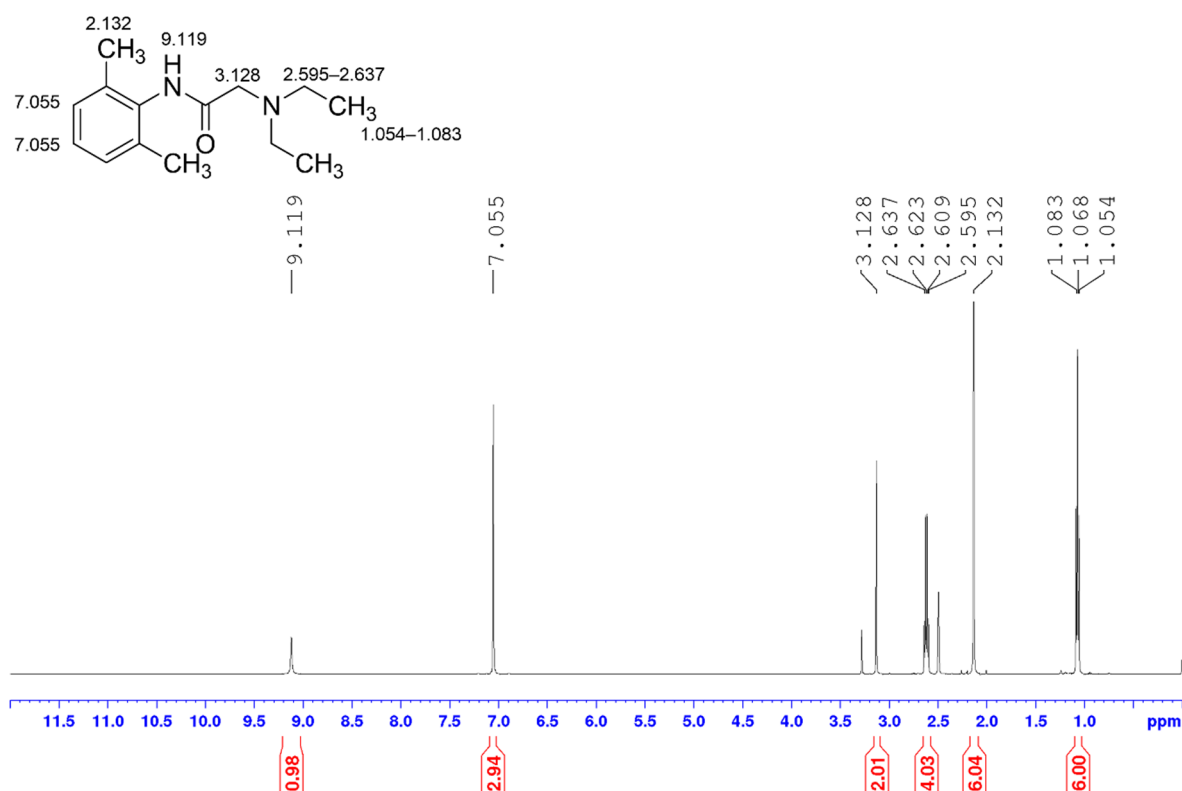
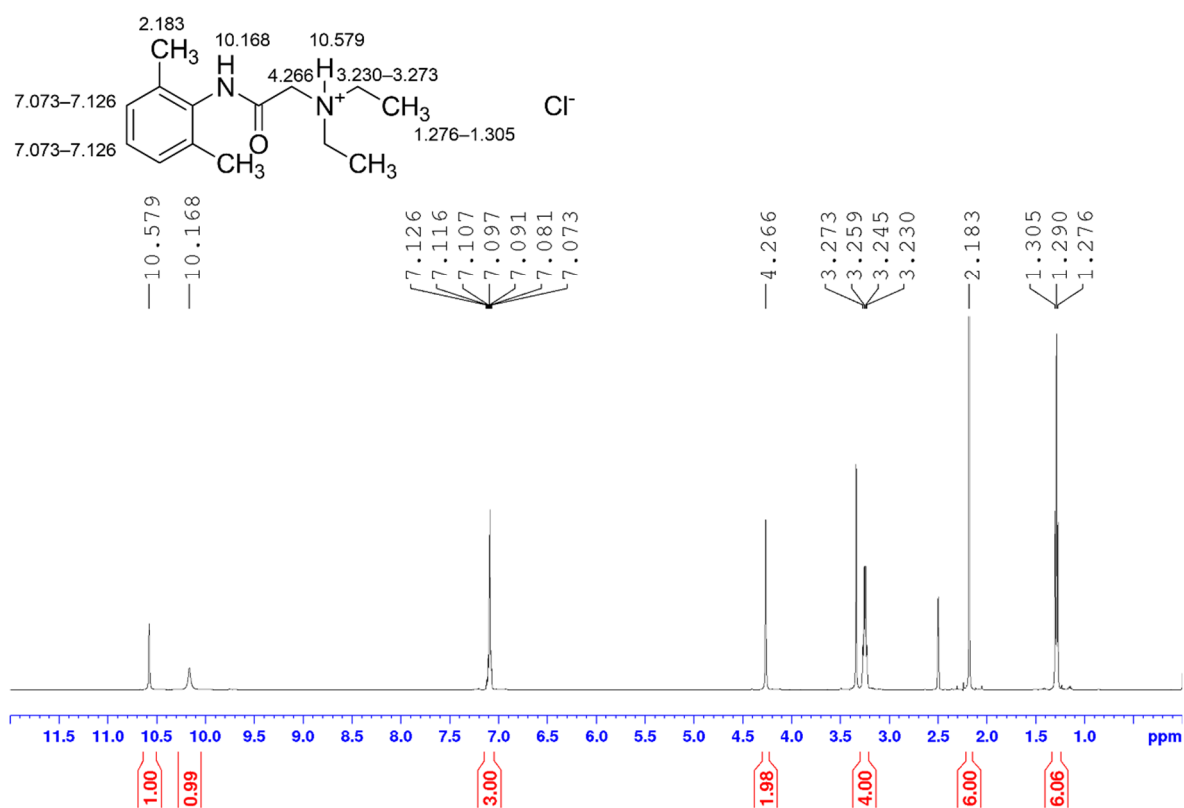


Figure S2f. ^{13}C -NMR spectrum of 2,6-dimethylaniline in $\text{DMSO-}d_6$.

Figure S2g. ¹H-NMR spectrum of lidocaine base in DMSO-*d*₆.Figure S2h. ¹H-NMR spectrum of lidocaine hydrochloride in DMSO-*d*₆.

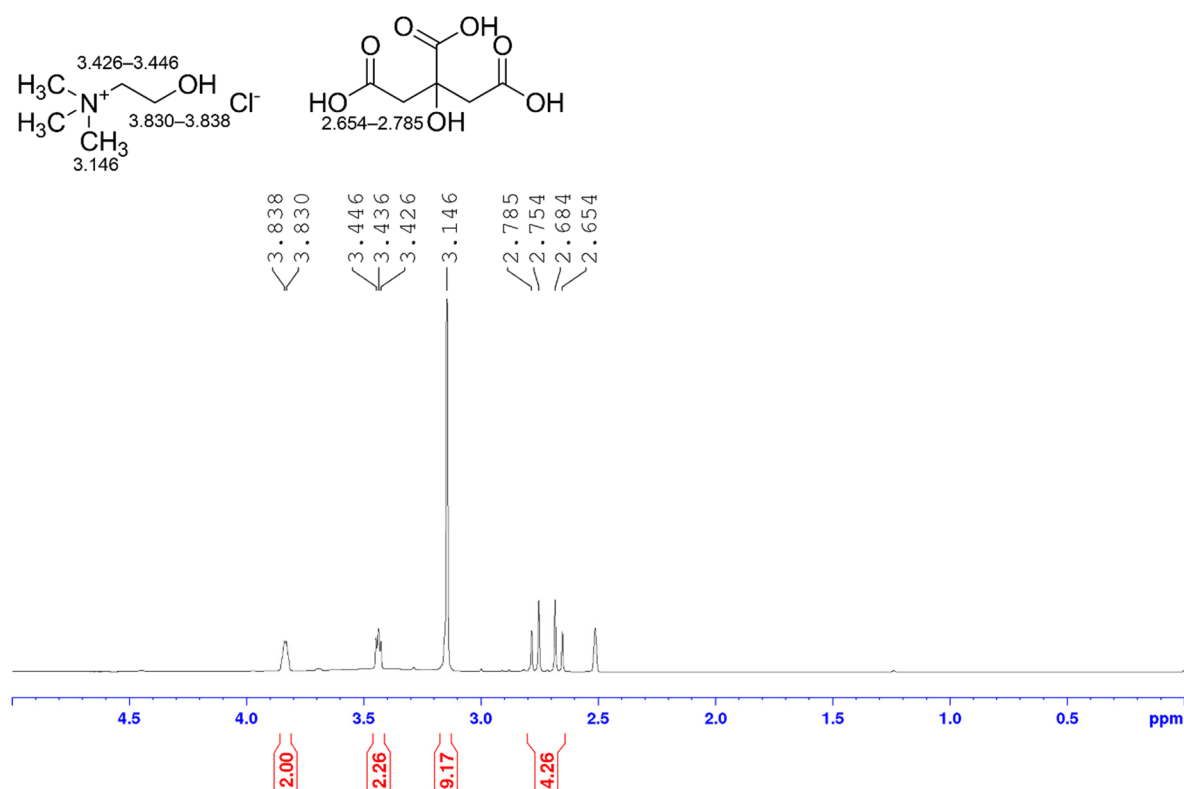


Figure S2i. ^1H -NMR spectrum of NADES (S7) in $\text{DMSO}-d_6$.

Table S1. Results of cumulative amount of lidocaine in each sampling time (IVRT).

Time(min)	square root of time (min)	Hydrogel NADES		Hydrogel Ref		Ointment Ref	
		Average ($\mu\text{g}/\text{cm}^2$)	SD	Average ($\mu\text{g}/\text{cm}^2$)	SD	Average ($\mu\text{g}/\text{cm}^2$)	SD
30	5.48	2137.08	108.91	1564.35	71.96	649.60	36.77
60	7.75	4328.16	196.98	2373.78	109.94	1441.19	66.92
120	10.95	6238.04	465.60	3595.33	192.74	2856.35	65.81
180	13.42	6992.76	801.79	4412.58	321.95	3663.84	230.88
240	15.49	7449.82	969.72	5003.58	436.87	4105.61	357.22
360	18.97	7319.40	1190.20	5946.01	211.32	4668.14	88.41

Table S2. Hydration values in all evaluating times (mean $\pm$ SD).

Time(min)	Hydrogel Ref		Hydrogel NADES		Ointment Ref	
	Mean hydration (%)	SD	Mean hydration (%)	SD	Mean hydration (%)	SD
30	30.43	19.45	23.38	18.32	45.34	15.44
60	20.44	14.47	13.77	9.28	42.01	15.23
90	26.01	22.47	18.35	12.72	31.52	13.36
120	28.94	24.44	22.06	8.28	34.21	21.19
150	17.19	18.43	14.50	17.40	25.89	17.06

Table S3. TEWL values in all evaluating times (mean $\pm$ SD).

Time(min)	Hydrogel Ref		Hydrogel NADES		Ointment Ref	
	Mean TEWL (%)	SD	Mean TEWL (%)	SD	Mean TEWL	SD
30	26.03	20.33	16.28	18.710	8.30	10.73
60	1.69	19.26	3.16	21.02	11.95	22.95
90	3.44	16.51	-2.24	14.25	13.97	10.31
120	2.89	15.98	-0.34	12.72	19.94	12.49
150	0.02	19.95	-1.04	12.89	14.11	18.94