Supporting Information

1. General

All chemicals unless otherwise stated were purchased from Aldrich Chemical Company (Dorset, UK) in reagent grade ≥98% and used without further purification.

Thermogravimetrical Analysis (TGA). Thermogravimetric analysis was performed on a Mettler Toledo Stare TGA/DSC unit (Leicester, UK) under nitrogen. Samples between 5 and 10 mg were placed in open alumina pans and were heated from 25 °C to 600 °C with a heating rate of 5 °C/min. Decomposition temperatures ($T_{5\%dec}$) were reported from onset to 5 wt% mass loss.

Differential Scanning Calorimetry (DSC). Differential scanning calorimetry was performed on a Mettler Toledo Star DSC unit (Leicester, UK) under nitrogen. Samples were placed in closed aluminum pan perforated with a pin-hole to equilibrate pressure from potential expansion of evolved gases or residual solvents. An empty closed pan was used as a reference. For standard DSC experiments, samples between 5 and 10 mg were heated from 25 °C to 110 °C at a heating rate of 5 °C/min followed by a 5 min isotherm. A cooling rate of 5 °C/min to -70 °C was followed by a 5 min isotherm at -70 °C, and the cycle was repeated twice. Second and third cycles proved to be identical and only the third heating run was used for data collection. For the collection of eutectic diagrams, the heating and cooling rate was reduced to 1 °C/min.

For Lidocaine:Oleic acid samples, a DSC 2920 Modulated DSC, TA Instruments, Inc. (New Castle, DE) differential scanning calorimeter was also used to determine melting points, glass transitions, and crystallization temperatures. The instrument was temperature calibrated with indium (T_m 156.61 ^oC; ΔH = 28.71 J g^{-1}) and DI water before data was collected. Data was collected at constant atmospheric pressure using samples between 3-10 mg. Samples were placed in closed aluminum pan (KLD-202, KEtecand Lab Devices, Inc., Mount Berry, GA) perforated with a pin-hole to equilibrate pressure from potential expansion of evolved gases or residual solvents. An empty closed pan was used as a reference. The DSC was adjusted so that zero heat flow was between 0 and -0.5 mW and the baseline drift was less than 0.1 mW over the temperature range of 0-180 ^oC.

The experimental protocol was as follows. Heating was conducted at constant a rate 5 ^oC /min. After a 5 min isotherm at maximal temperature, samples were cooled to -110 ^oC. A 5 minute equilibration interval was applied and the entire process was repeated twice (3 cycles total). Liquid samples were first cooled to -110 °C, and then heated to a temperature no greater that 30 °C below $T_{5\%dec,}$ previously established by TGA. After a 5 minute equilibration interval, the process was repeated twice (3 cycles total).

Fourier Transform Infra Red Spectroscopy (FTIR). Infrared spectra were obtained by direct measurement of the neat samples utilizing a Perkin-Elmer Spectrum 100 FT-IR instrument (Waltham, MA) featuring an ATR force gauge (Shelton, CT). Spectra were obtained in the range of 650 – 4000 cm^{-1}. Infrared spectra for all Lidocaine:fatty acid samples in the ratio 1:1 were also recorded as neat samples from 650 - 4000 cm^{-1} on a Perkin-Elmer (Dublin, Ireland) Spectrum 100 FT-IR spectrometer fitted with a Universal ATR Sampling Accessory.

Nuclear Magnetic Resonance Specroscopy (NMR). ^{1}H and ^{13}C NMR spectra were collected utilizing a Bruker spectrometer 500 MHz Bruker Avance Spectrometer Bruker/Magnex UltraShield 500 MHz magnet operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C spectra, respectively. NMR in solvent were conducted in acetone-d_6. Neat NMRs were taken at 363 K in a 5 mm NMR tube with a coaxial capillary for the external lock (DMSO-d_6). All chemical shifts are given in δ (ppm).

^{15}N NMR data and ^{15}N 2D Heteronuclear Multiple-Bond Quantum Coherence (HMBC) data were collected utilizing a Bruker spectrometer 600 MHz Bruker Avance Spectrometer Bruker/Magnex UltraShield 600 MHz magnet. Chemical shifts were measured in δ (ppm). ^{15}N 2D HMBC spectra were taken at a temperature of 23 ^{o}C (296 K) for all mixtures, except for 10 and 20 mol% oleic acid due to high viscosity and 66 mol% oleic acid due to sample solidification.

Viscosity. Viscosity was measured employing a Cannon Fenske viscometer, constant 0.5 mm^2/s^2 (cSt/s). To obtain kinematic viscosity in mm^2/s (cSt) the efflux time in seconds was multiplied by the viscometer constant. To obtain viscosity in mPas (cP), the viscosity in mm^2/s (cSt) was multiplied by the density in grams per milliliter.

Density. The density was determined by mass to volume ratio (for liquid samples only). The density of each sample was determined three times and if found in good correlation, the values were averaged to obtain the final reported density.

Water content. Water content was measured by Karl-Fischer-titration with a Mettler Toledo Titrator (Hiranuma Sangyo, Japan). The water content of all samples was found to be below 1500 ppm.

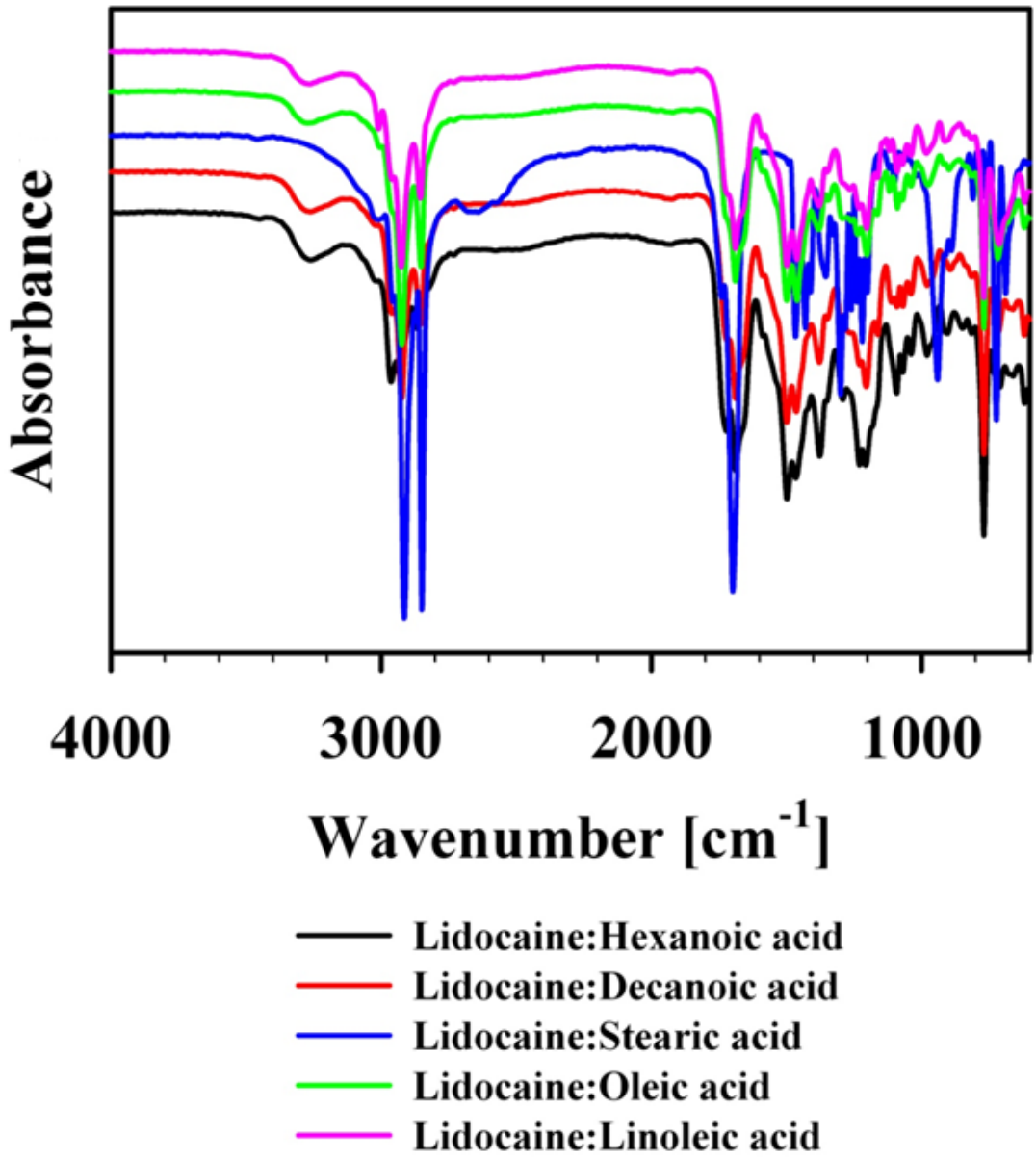
2. Experimental

Representative syntheses

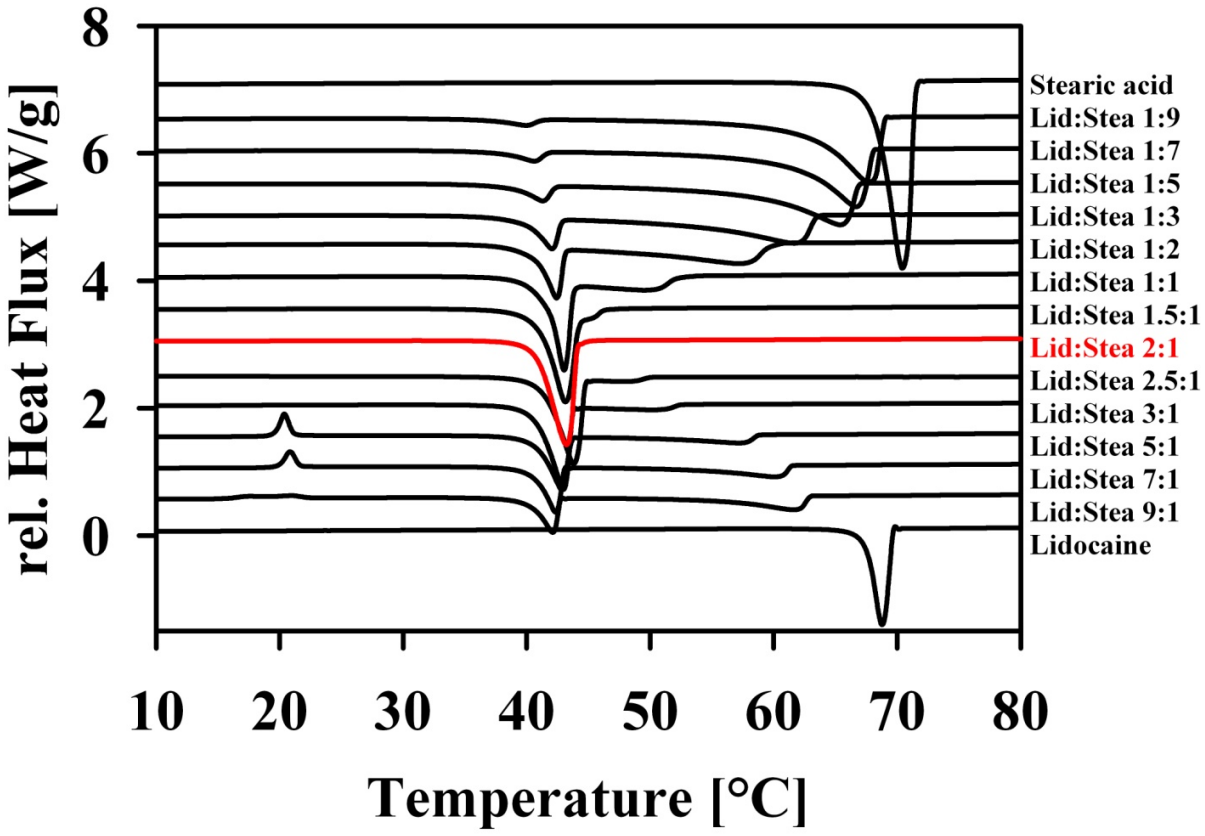
(1:1) A screw-cap vial was charged with lidocaine (1.172 g, 5 mmol) and stearic acid (1.422 g, 5 mmol) under an atmosphere of nitrogen and sealed. The solid mixture was heated with a heat gun with shaking until a clear homogenous liquid was obtained and kept at this temperature for 5 min. The product was cooled to room temperature to yield the lidocaine:stearic acid mixture in quantitative yield as a waxy colourless solid.

(X:X) Oleic acid:lidocaine compositions (χ_{oleic} = 0.1 - 0.9) were prepared as above. Calculated molar ratios of both components (fatty acid and lidocaine) were placed in a screw-cap vial under an atmosphere of nitrogen and sealed. The mixture was then heated with a heat gun with shaking until a clear homogenous liquid was obtained. The product was cooled to room temperature to yield the lidocaine:oleic acid compositions in quantitative yield.

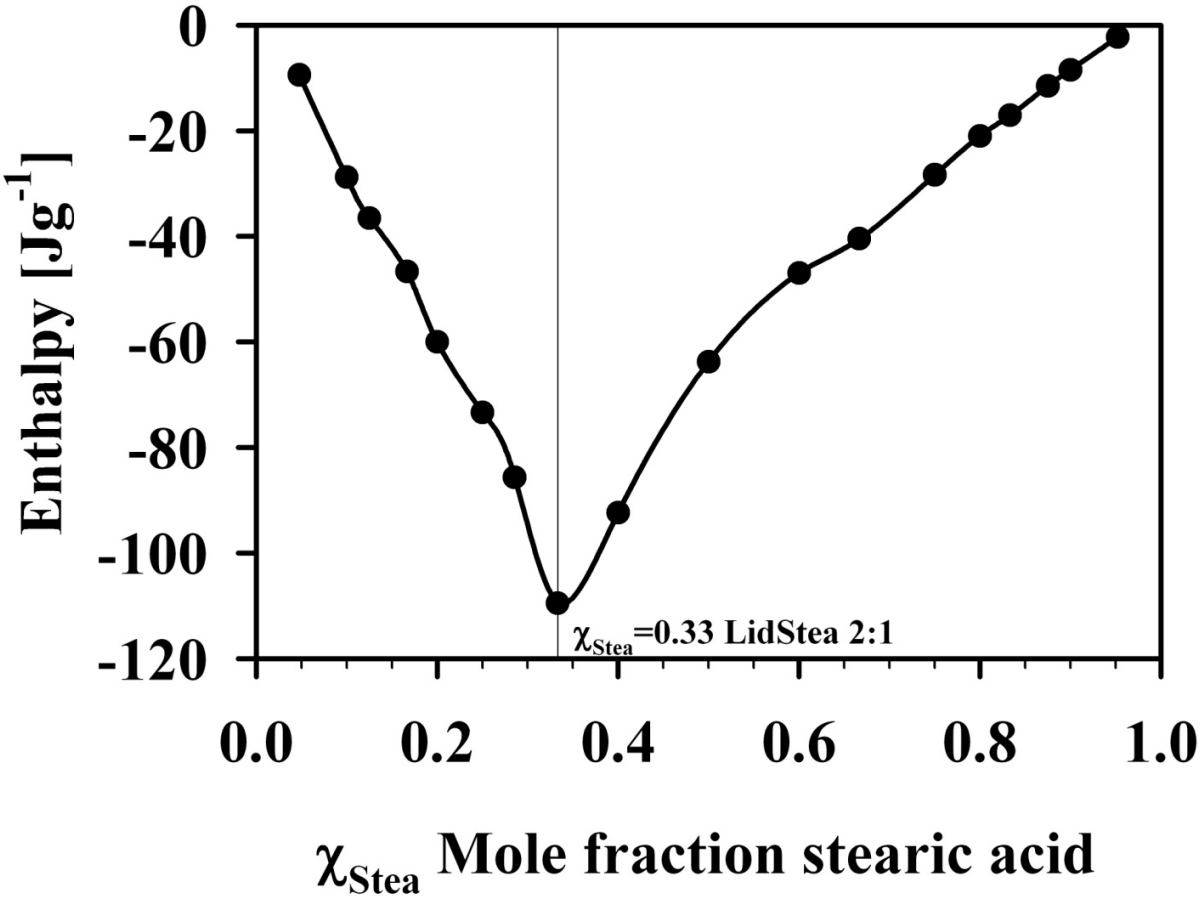
3. Figure S1. IR spectra of all Lidocaine:fatty acid mixtures in the ratio 1:1.



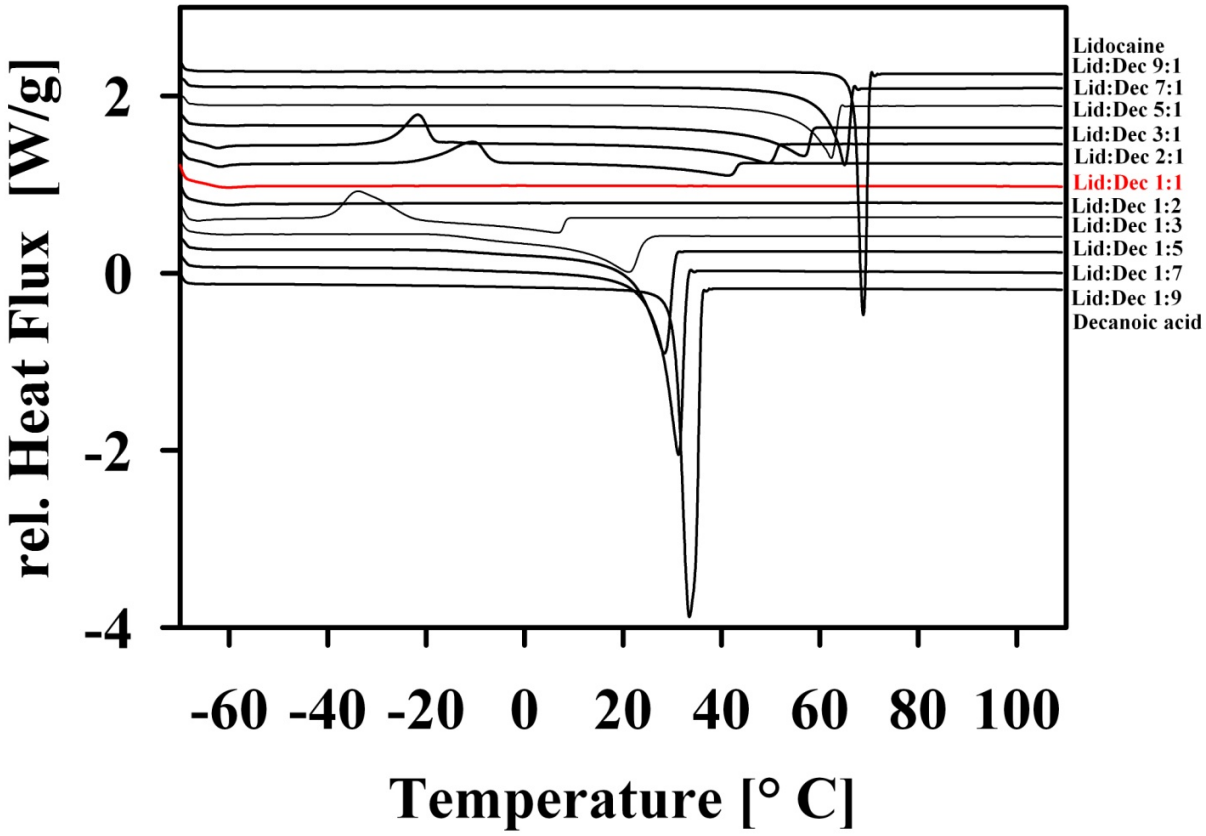
4. **Figure S2.** DSC traces of Lidocaine:Stearic acid mixtures in different composition



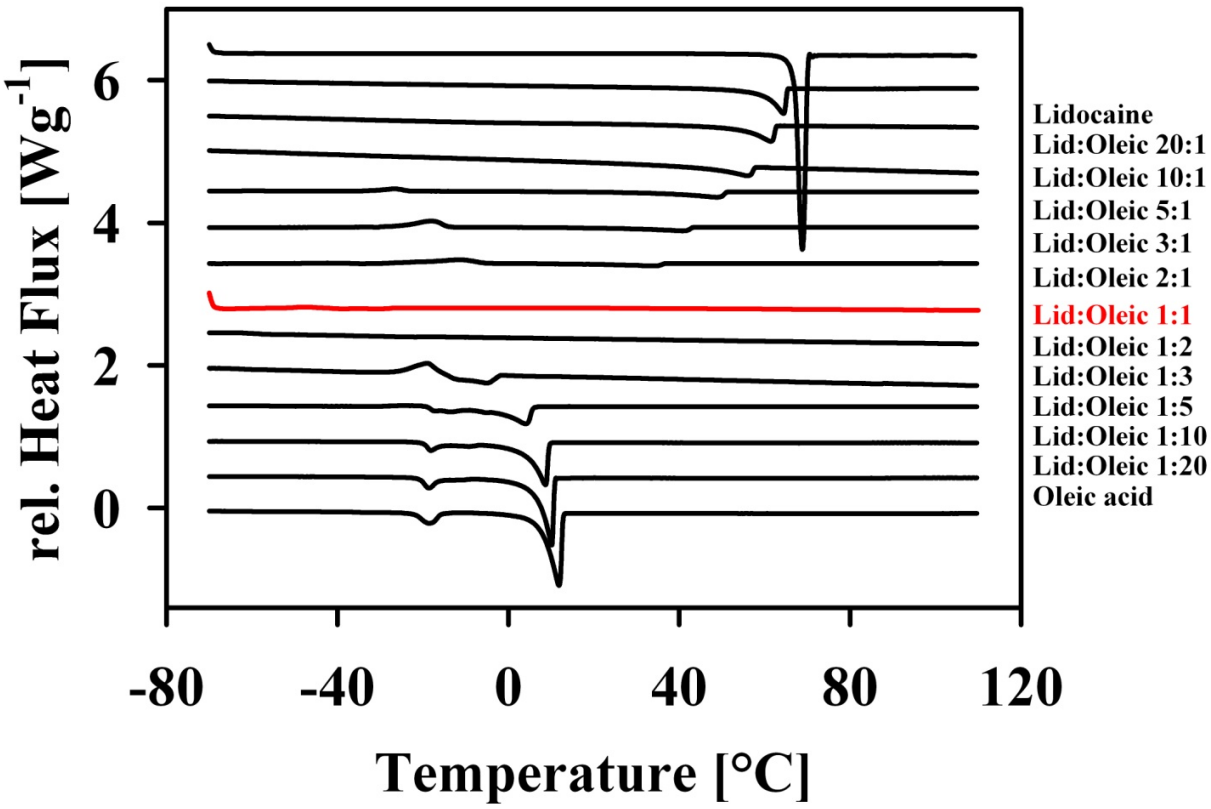
5. Figure S3. Eutectic composition of Lidocaine:Stearic acid.



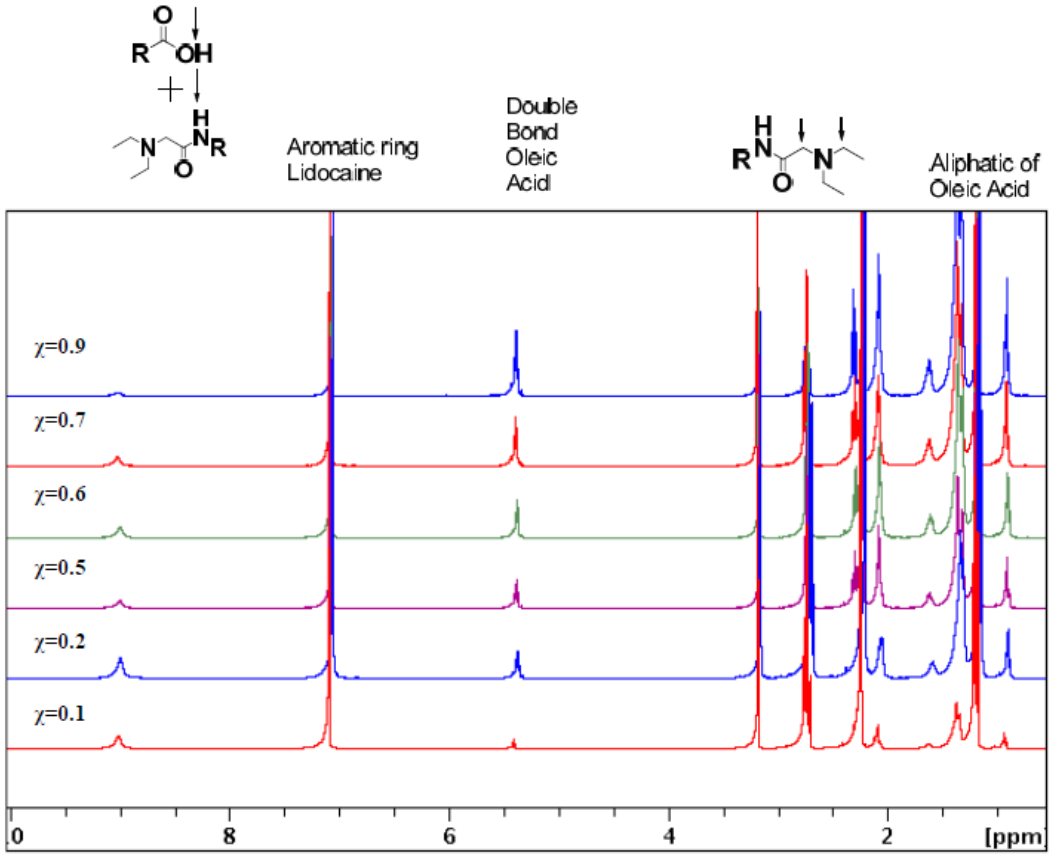
6. **Figure S4**. DSC traces of Lidocaine:Decanoic acid mixtures in different compositions.



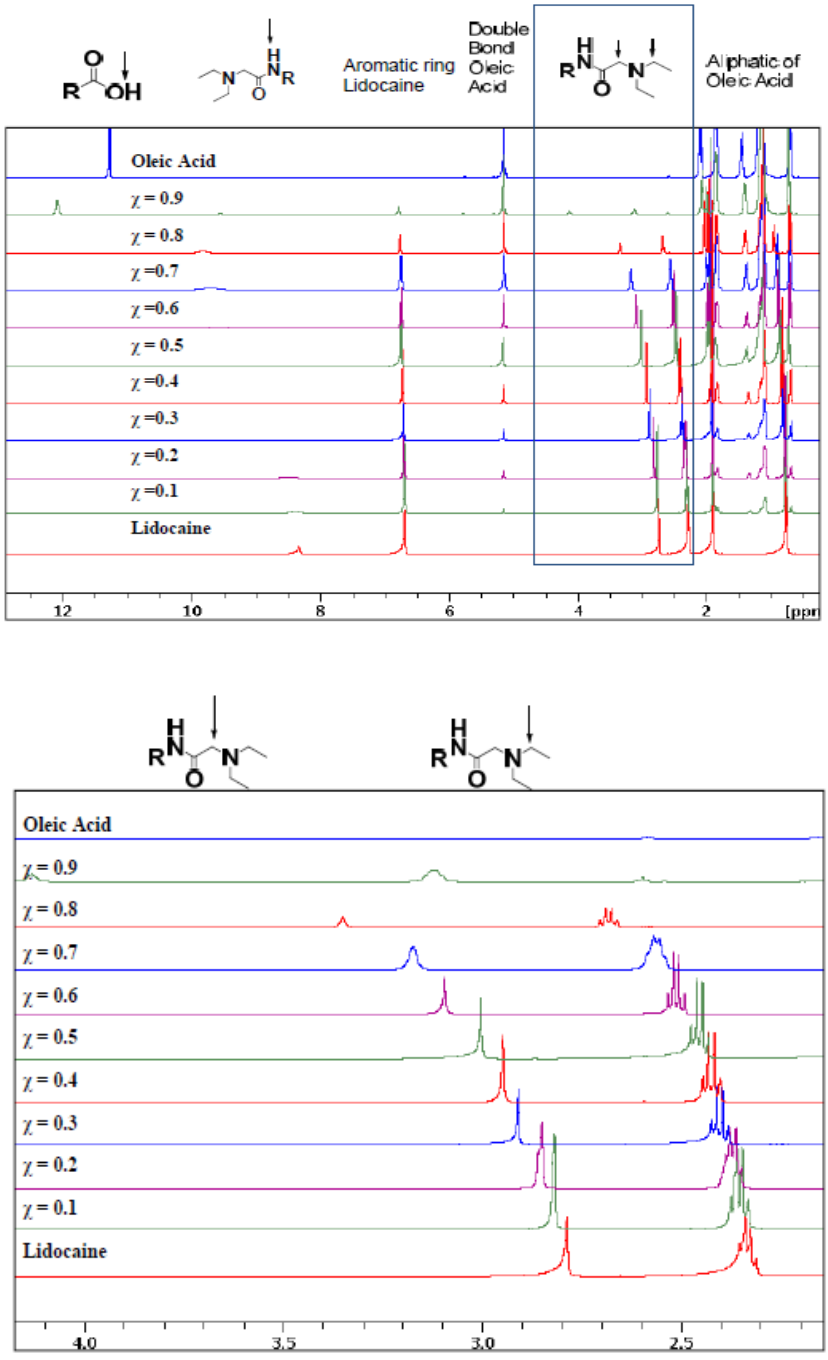
7. **Figure S5.** DSC traces of Lidocaine:Oleic acid mixtures in different compositions.



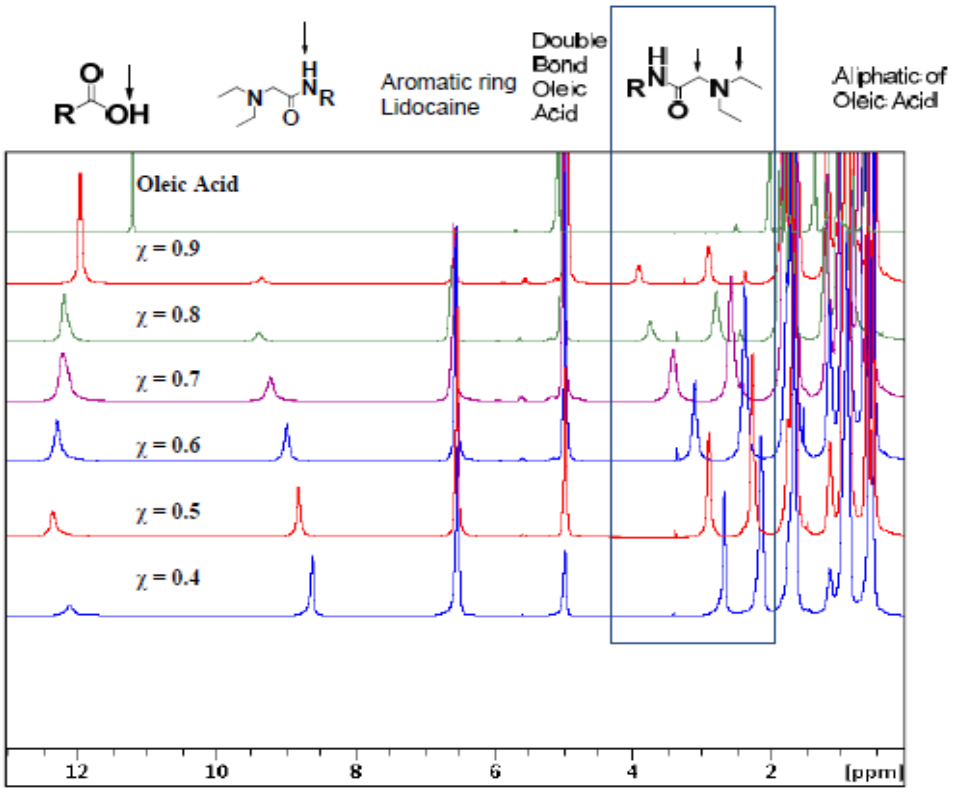
8. Figure S6. The comparison of different lidocaine:oleic acid compositions in acetone-d_6.

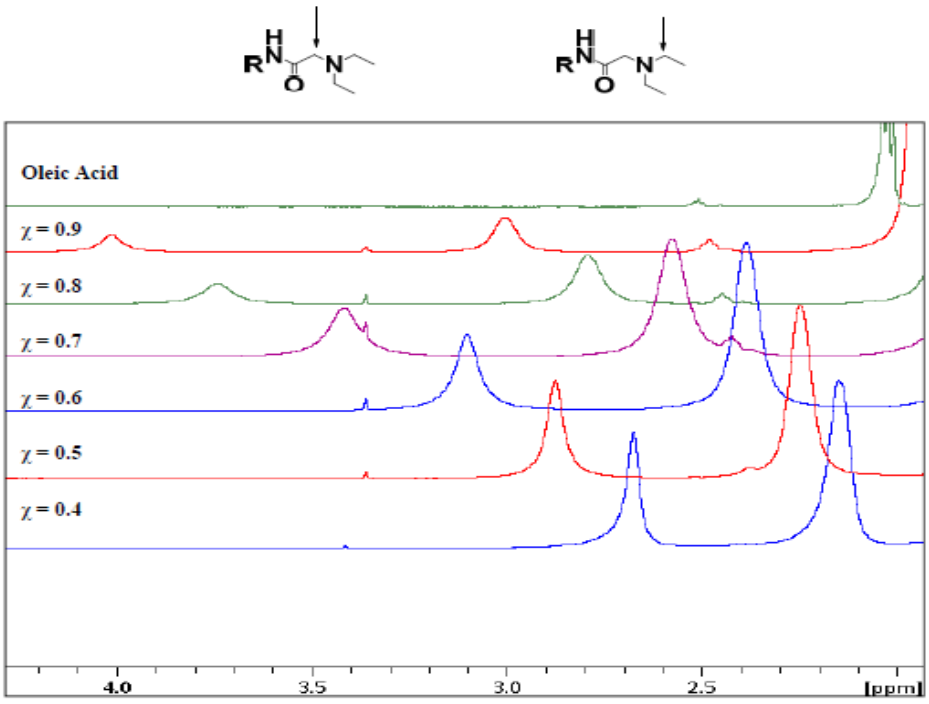


9. **Figure S7.** Neat NMRs of lidocaine:oleic acid compositions at 363 K in a 5 mm NMR tube with a coaxial capillary for the external lock (DMSO - d_6).

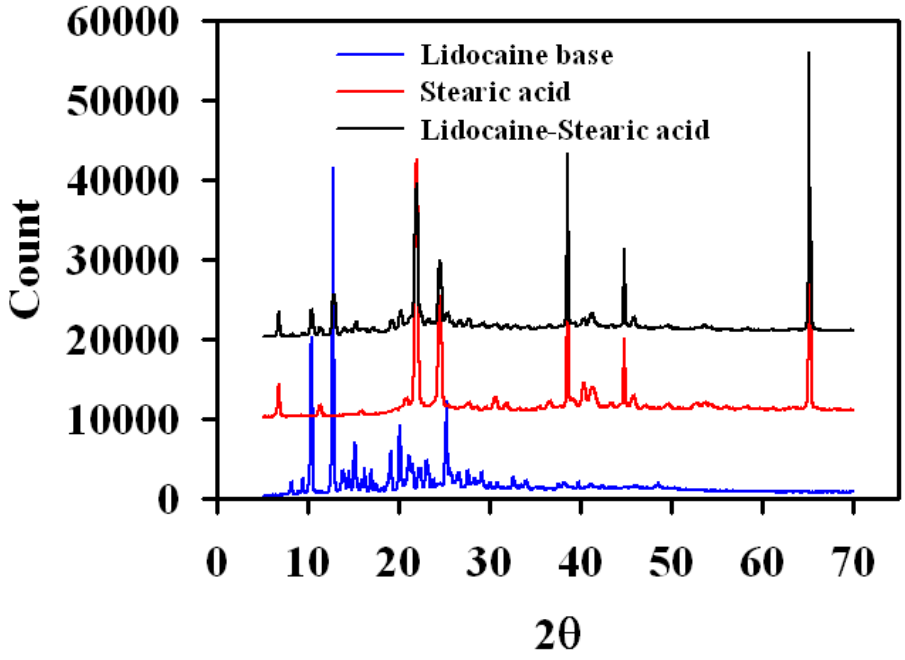


10. Figure S8. Neat NMRs of lidocaine:oleic acid compositions at 298 K in a 5 mm NMR tube with a coaxial capillary for the external lock (DMSO - d_6).




Oleic Acid
χ = 0.9
χ = 0.8
χ = 0.7
χ = 0.6
χ = 0.5
χ = 0.4
4.0
3.5
3.0
2.5
[ppm]

11. Figure S9. PXRD of Lidocaine-Stearic acid composition 1:1



12. Table S1. Physical properties of lidocaine:fatty acid formulations in 1:1 ratio.

Compound	T_g [a] [°C]	$T_{onset5\%}$ [b] [°C]
Lidocaine:Hexanoic acid **2**	-55.9	100.0
Lidocaine:Decanoic acid **3**	-61.0	143.3
Lidocaine:Stearic acid **4**	T_m 42.8	179.2
Lidocaine:Oleic acid **5**	T_t -47.4	175.4
Lidocaine:Linoleic acid **6**	-71.1	163.7
Lidocainium Docusate **7**	-30.1	212.4

[a]Determined on a Mettler Toledo Star[e] DSC by heating to 110 °C at 5 °C/min and cooling at 5 °C/min to -80 °C for 3 cycles. [b]Determined on a Mettler Toledo Star[e] TGA/DSC by heating from 25 °C to 600 °C at 5 °C/min under nitrogen

13. Table S2. ^{15}N Chemical shift value for different compositions and difference of chemical shift value from chemical shift of previous composition.

Composition / Temperature, K	**^{15}N Shift**	**Δ ^{15}N (difference with previous composition)**
χ = 0.9, 313 K	50.0 ppm	-
χ = 0.8, 313 K	48.8 ppm	1.2
χ = 0.7, 296 K	47.6 ppm	1.2
χ = 0.66, 296 K	46.6 ppm	1.0
χ = 0.6, 296 K	46.1 ppm	1.5
χ = 0.5, 296 K	43.9 ppm	3.8
χ = 0.33, 313 K	42.4 ppm	1.5

14. Table S3. Density, viscosity and conductivity values for different compositions (only liquid samples).

Composition LO	**D, g/mL (average)**	**η, cP (average)**	**Molar Conductivity, Scm^2/mol**
χ = 0.9	0.903	0.597	4.73512×10^{-7}
χ = 0.8	0.921	1.120	2.92633×10^{-5}
χ = 0.7	0.936	1.593	0.000147335
χ = 0.6	0.941	1.605	0.000138999
χ = 0.5	0.952	1.457	0.000163109