Supporting Information

A Scalable and Eco-Friendly Carbohydrate-Based Oleogelator for Vitamin E Controlled Delivery

Elizângela Hafemann Fragal,[a,b] *Lorenzo Metilli,*[a,b] *Frédéric Pignon,*[b] *and Sami Halila*[a*]

[a] Univ. Grenoble Alpes, CNRS, CERMAV 38000 Grenoble (France)

[b] Univ. Grenoble Alpes, CNRS, Grenoble INP (Institute of Engineering Univ. Grenoble Alpes), LRP, F-38000 Grenoble, France

Synthetic procedure for the preparation of sodium salts of β-*C*-glycosybarbiturate derivatives

The yields are indicated below the corresponding ^{1}H NMR spectra.

Sodium 5-(β-D-mannopyranosyl)-1,3-dimethyl barbiturate

Mannose (5.5 mmol) and 1,3-dimethybarbituric acid (5.5 mmol) were dissolved in 5 mL of distilled water, followed by the addition of $NaHCO_3$ (5.5 mmol) to neutralize around pH 7 under magnetic stirring at 80 °C. The reaction was monitored by TLC (7:2:1 ethyl acetate/methanol/H_2O v/v/v). After 4 h, the carbohydrates had been consumed, and the reaction stopped. The purification was performed by precipitation by adding a methanol/ethyl acetate (20/80 v/v) mixture, and the white solid was removed by filtration and washed two times with the same mixture.

Sodium 5-(β-D-galactopyranosyl)-1,3-dimethyl barbiturate

Galactose (5.5 mmol) and 1,3-dimethybarbituric acid (5.5 mmol) were dissolved in 5 mL of distilled water, followed by the addition of $NaHCO_3$ (5.5 mmol) to neutralize around pH 7 under magnetic stirring at 80 °C. The reaction was monitored by TLC (7:2:1 ethyl acetate/methanol/H_2O v/v/v). After 4 h, the carbohydrates had been consumed, and the reaction stopped. The purification was performed by precipitation by adding a methanol/ethyl acetate (20/80 v/v) mixture, and the white solid was removed by filtration and washed two times with the same mixture.

Sodium 5-(β-D-maltosyl)-1,3-dimethyl barbiturate

Maltose (2.7 mmol) and 1,3-dimethybarbituric acid (2.7 mmol) were dissolved in 5 mL of distilled water, followed by the addition of $NaHCO_3$ (2.7 mmol) to neutralize around pH 7 under magnetic stirring at 80 °C. The reaction was monitored by TLC (7:2:1 ethyl acetate/methanol/H_2O v/v). After 4 h, the carbohydrates had been consumed, and the reaction stopped. The purification was performed by precipitation by adding a methanol/ethyl acetate (20/80 v/v) mixture, and the white solid was removed by filtration and washed two times with the same mixture.

Sodium 5-(β-D-glucopyranosyl)-1,3-dicyclohexyl barbiturate

Glucose (0.5 mmol) and 1,3-dicyclohexylbarbituric acid (0.5 mmol) were dissolved in a 3 mL solution of (50/50) H_2O/isopropyl alcohol, followed by the addition of $NaHCO_3$ (0.5 mmol) to neutralize around pH 7 under magnetic stirring at 80 °C. The reaction was monitored by TLC (7:2:1 ethyl acetate/methanol/H_2O v/v/v). After 5 h, the carbohydrates had been consumed, and the reaction stopped. The purification was performed by flash column chromatography on silica gel by solid deposit with silica using as solvent 7:2:1 ethyl acetate/methanol/H_2O v/v/v.

Sodium 5-(β-D-cellobiosyl)-1,3-dicyclohexyl barbiturate

Cellobiose (0.58 mmol) and 1,3-dicyclohexylbarbituric acid (1.1 mmol) (0.58 mmol) were dissolved in a 3 mL solution of (50/50) H_2O/isopropyl alcohol, followed by the addition of $NaHCO_3$ (0.58 mmol) to neutralize around pH 7 under magnetic stirring at 80 °C. The reaction was monitored by TLC (7:2:1 ethyl acetate/methanol/H_2O v/v/v). After 5 h, the carbohydrates had been consumed, and the reaction stopped. The purification was performed by flash column chromatography on silica gel by solid deposit with silica using as solvent 8:2 ethyl acetonitrile/H_2O v/v.

Production of GlcBMe oleogelator

Figure S1. Picture of the synthesis of 1 Kg of β-*C*-glucosyl barbiturate (**GlcBMe**)

^{1}H NMR of sodium salts of β-*C*-glycosyl barbiturates

Sodium 5-(β-D-glucopyranosyl)-1,3-dimethyl barbiturate (GlcBMe)

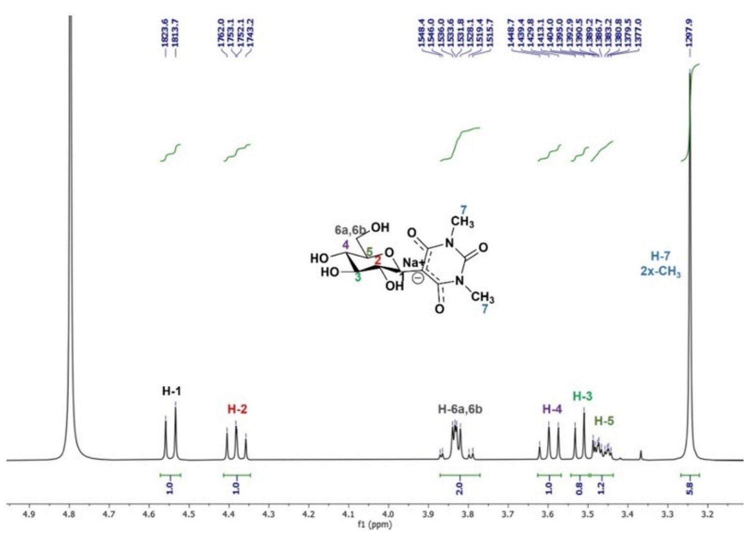

Figure S2. ^{1}H NMR spectrum (400 MHz, D_2O, 298K)

Yield: 98 % (white solid)
^{1}H NMR (400 MHz, D_2O) δ 4.54 (d, 1H, *J* = 9.9, H-1), 4.37 (dd, 1H, *J* = 9.9, 9.0, H-2), 3.86 – 3.76 (m, 2H, H-6a,6b), 3.62 – 3.56 (m, 1H, H-4), 3.51 (d, *J* = 9.0, H-3), 3.49 – 3.43 (m, 1H, H-5), 3.24 (s, 6H, H-7)
HRMS(ESI): calcd for $[C_{12}H_{17}N_2NaO_8 – Na]^–$: 317.09904; found: 317.09795

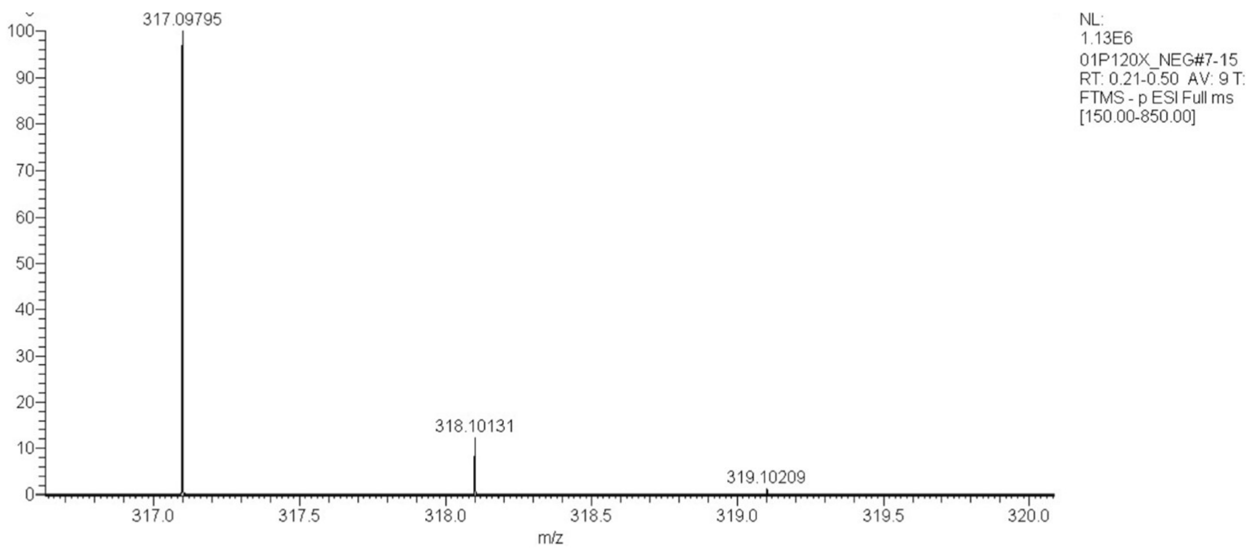

Figure S3. HRMS (ESI) of **GlcBMe**

Sodium 5-(β-D-mannopyranosyl)-1,3-dimethyl barbiturate (ManBMe)

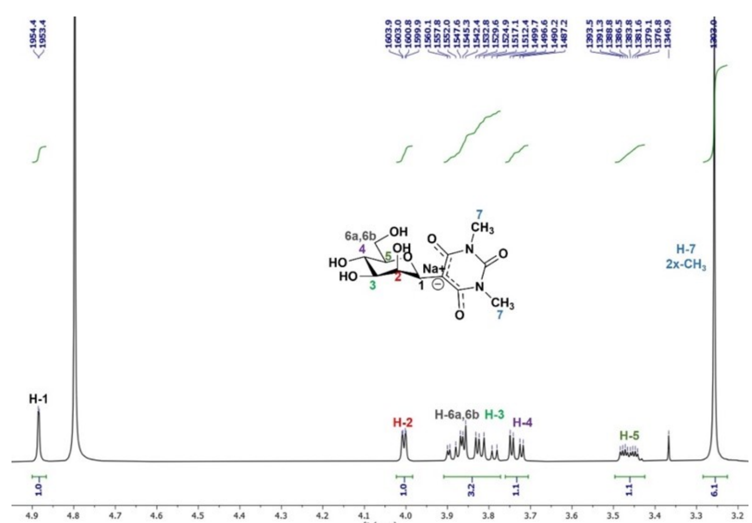

Figure S4. ^{1}H NMR spectrum (400 MHz, D_2O, 298K)

Yield: 92 % (white solid)
^{1}H NMR (400 MHz, D_2O) δ 4.88 (d, 1H, J = 1.0, H-1), 4.00 (dd, 1H, J = 3.1, 0.9, H-2), 3.91 – 3.84 (m, 2H, H-6a,6b), 3.84 – 3.77 (m, 1H, H-3), 3.73 (dd, 1H, J = 9.5, 3.1, H-4), 3.46 (ddd, 1H, J = 9.7, 4.8, 2.3, H-5), 3.26 (s, 6H, H-7).
HRMS (ESI) m/z: calcd for $[C_{12}H_{17}N_2NaO_8 - Na]^-$: 317.09904; found: 317.09821.

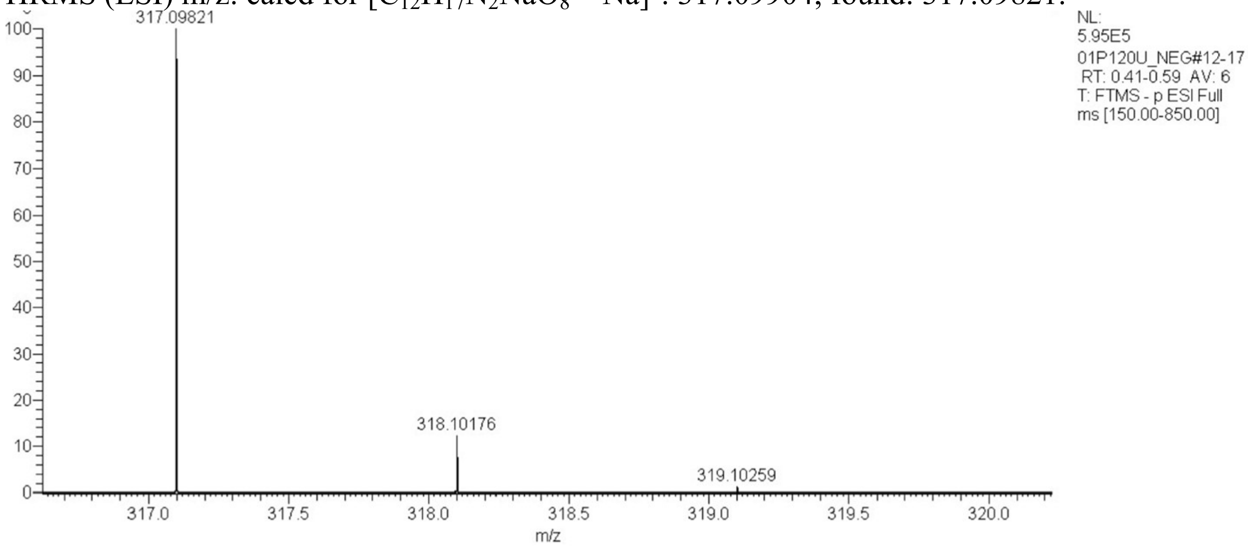

Figure S5. HRMS (ESI) of **ManBMe**

Sodium 5-(β-D-galactopyranosyl)-1,3-dimethyl barbiturate (GalBMe)

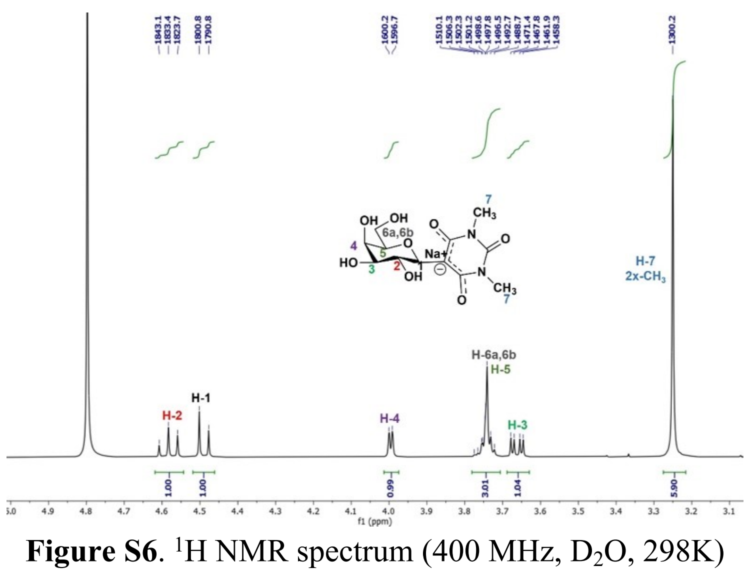

Figure S6. ^{1}H NMR spectrum (400 MHz, D_2O, 298K)
Yield: 88 % (white solid)
^{1}H NMR (400 MHz, D_2O) δ 4.58 (t, 1H, J = 9.7, H-2), 4.49 (d, 1H, J = 9.9, H-1), 4.00 (d, 1H, J = 3.4, H-4), 3.78 – 3.71 (m, 3H, H-5 and H-6a,6b), 3.66 (dd, J = 9.5, 3.5, H-3), 3.25 (s, 6H, H-7)
HRMS(ESI): calcd for $[C_{12}H_{17}N_2NaO_8 - Na]^-$: 317.09904; found: 317.09803

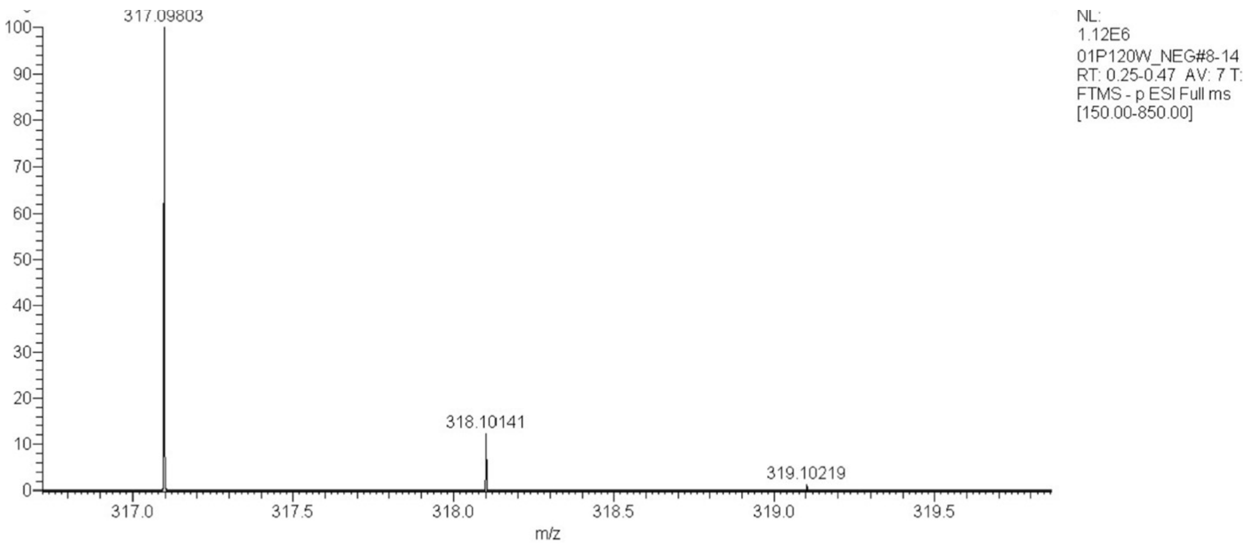

Figure S7. HRMS (ESI) of **GalBMe**

Sodium 5-(β-D-maltosyl)-1,3-dimethyl barbiturate (MalBMe)

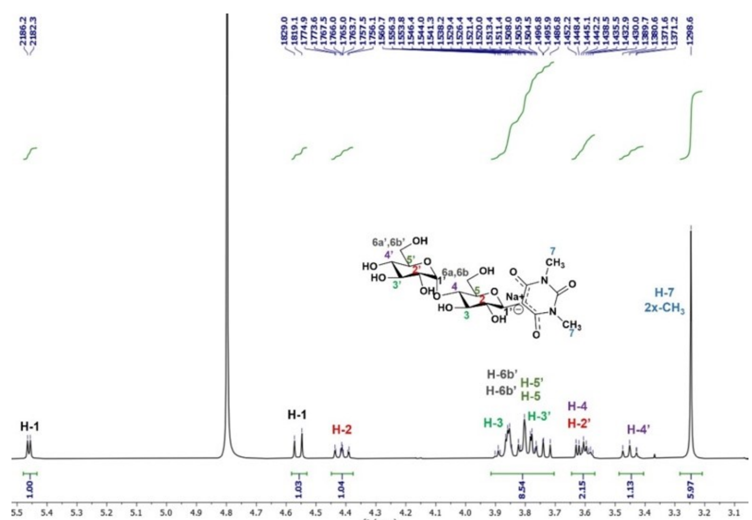

Figure S8. ^{1}H NMR spectrum (400 MHz, D_2O, 298K)

Yield: 96 % (white solid)

^{1}H NMR (400 MHz, D_2O) δ 5.46 (d, 1H, *J* = 3.9, H-1'), 4.56 (d, 1H, *J* = 9.9, H-1), 4.45 – 4.38 (m, 1H, H-2), 3.92 – 3.70 (m, 8H, H-3, H-3', H-5, H-5',H-6a,6b, H-6'a,6'b), 3.65 – 3.57 (m, 2H, H-2', H-4), 3.45 (t, 1H, *J* = 9.1, H-4'), 3.25 (s, 6H, H-7).

HRMS(ESI): calcd for $[C_{18}H_{27}N_2NaO_{13} – Na]^–$: 479.15186; found: 479.15161

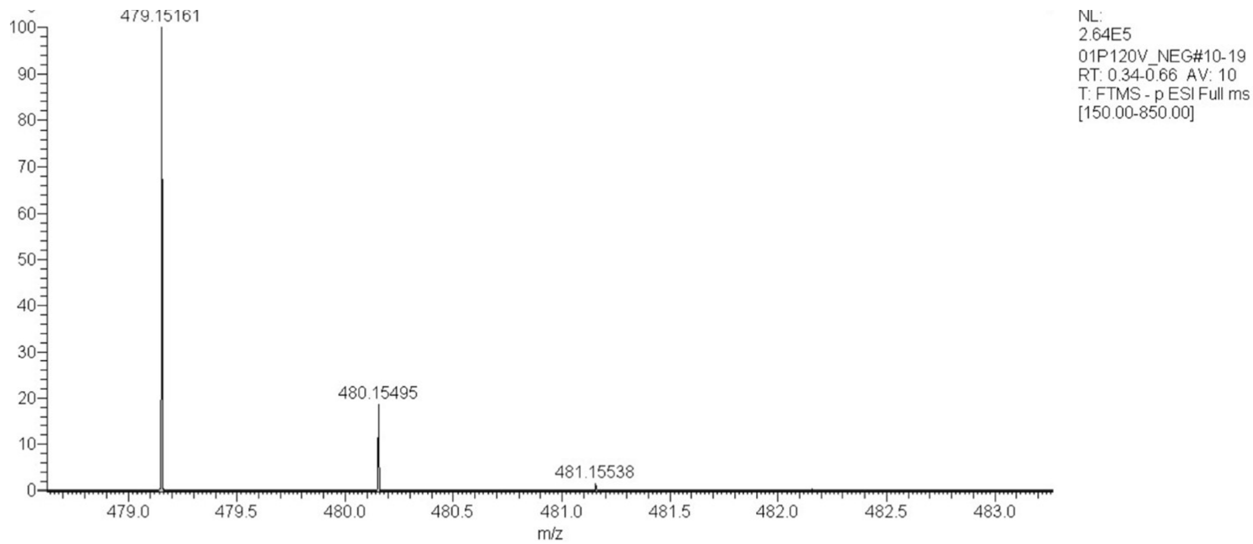

Figure S9. HRMS (ESI) of **MalBMe**

Sodium 5-(β-D-glucopyranosyl)-1,3-dicyclohexyl barbiturate (GlcBCyclo)

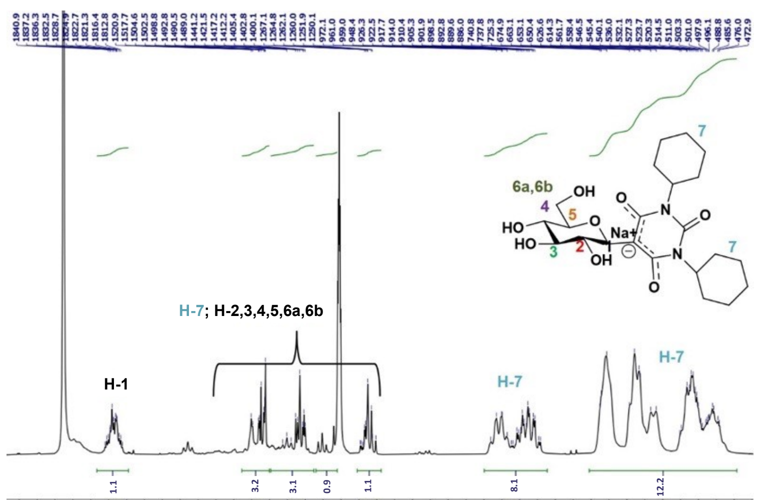

Figure S10. ^{1}H NMR spectrum (400 MHz, MeOH-d$_4$, 298K)

Yield: 60 % (yellow solid)
^{1}H NMR (400 MHz, MeOH-d$_4$) δ 4.57 (m, 1H, H-1), 3.85 –3.06 (m, 8H, H-2, H-3, H-4, H-5, H-6a,6b, 2xH-7), 2.49 – 2.14 (m, 8H, H-7), 1.90 – 1.12 (m, 12H, H-7)
HRMS(ESI): calcd for [$C_{22}H_{33}N_2NaO_8$ – Na]$^-$: 453.22424; found: 453.22408

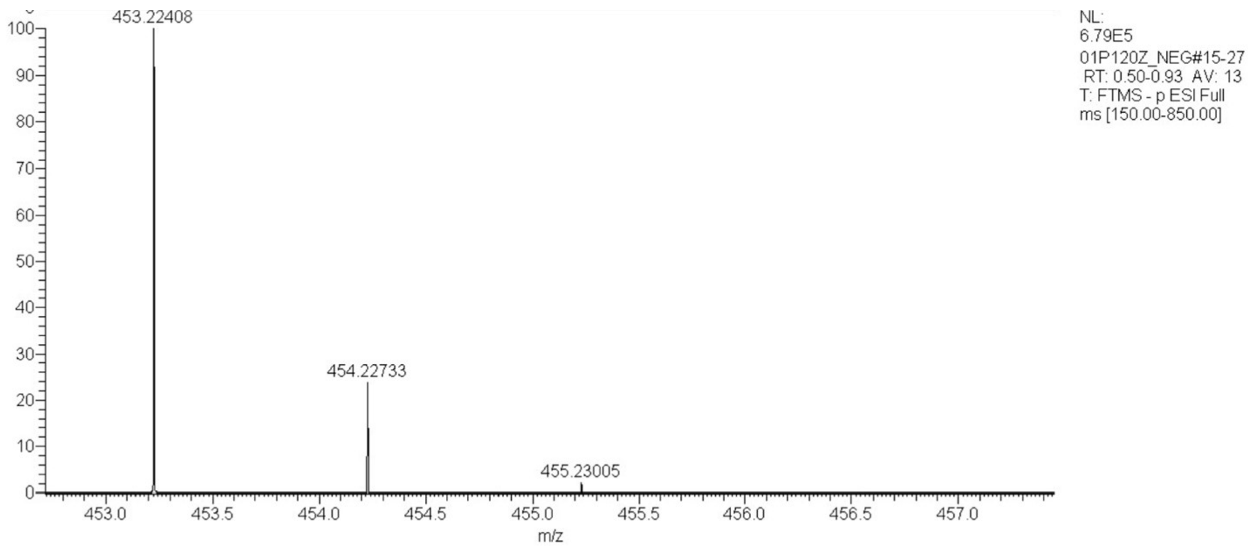

Figure S11. HRMS (ESI) of **GlcBCyclo**

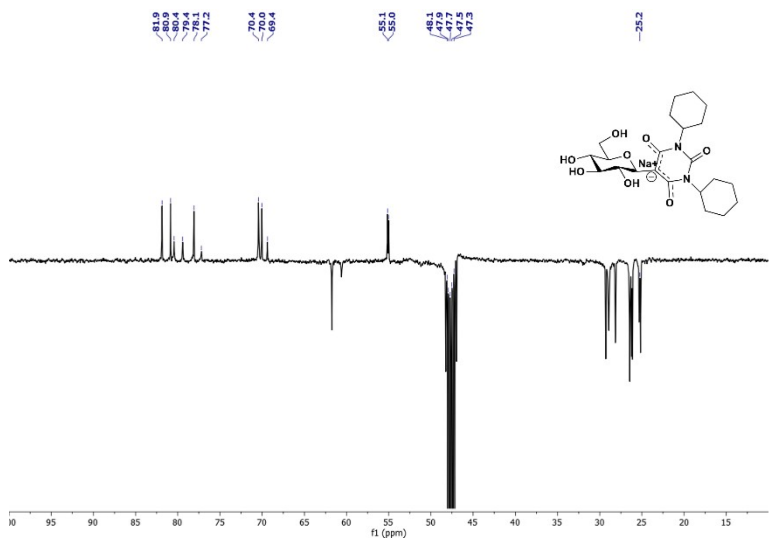

Figure S12. DEPT-135 ^{13}C NMR spectrum (400 MHz, MeOD, 298K)

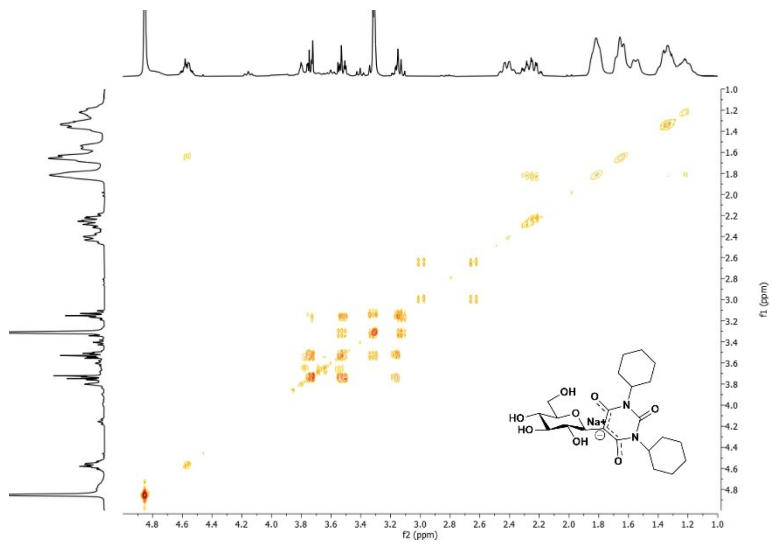

Figure S13. COSY spectrum (400 MHz, MeOD, 298K)

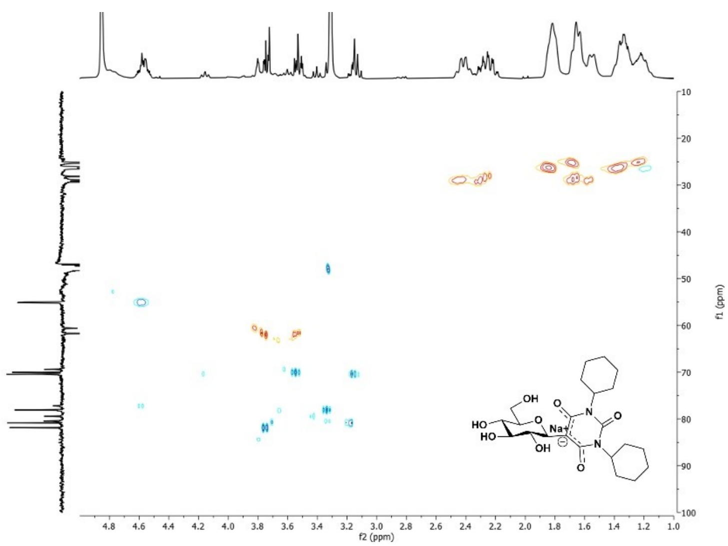

Figure S14. HSQC spectrum (400 MHz, MeOD, 298K)

Sodium 5-(β-D-cellobiosyl)-1,3-dicyclohexyl barbiturate (CelBCyclo)

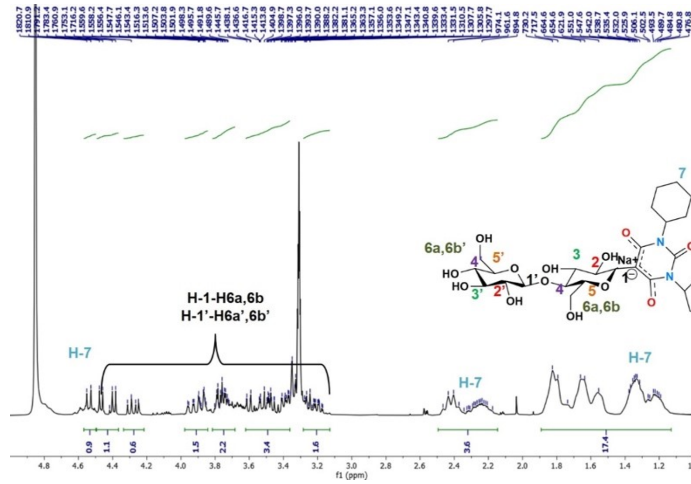

Figure S15. ^1H NMR spectrum (400 MHz, MeOH-d_4, 298K)

Yield: 20 % (pink solid)
^1H NMR (400 MHz, MeOH-d_4) δ 4.54 (d, *J* = 9.8, 1H, H-1), 4.43 (d, *J* = 7.8, H-1'), 4.39 (d, *J* = 7.8, H-4), 4.34 – 4.22 (m, 1H, H-2), 3.98 – 3.13 (m, 12H, H-2', H-3, H-3', H4', H-5, H5', H-6a,6b, H-6'a,6'b, 2xH-7), 2.49 – 2.15 (m, 4H, H-7), 1.89 – 1.13 (m, 16H, H-7).
HRMS(ESI): calcd for $[C_{28}H_{43}N_2NaO_{13} – Na]^–$: 615.27706; found: 615.27594

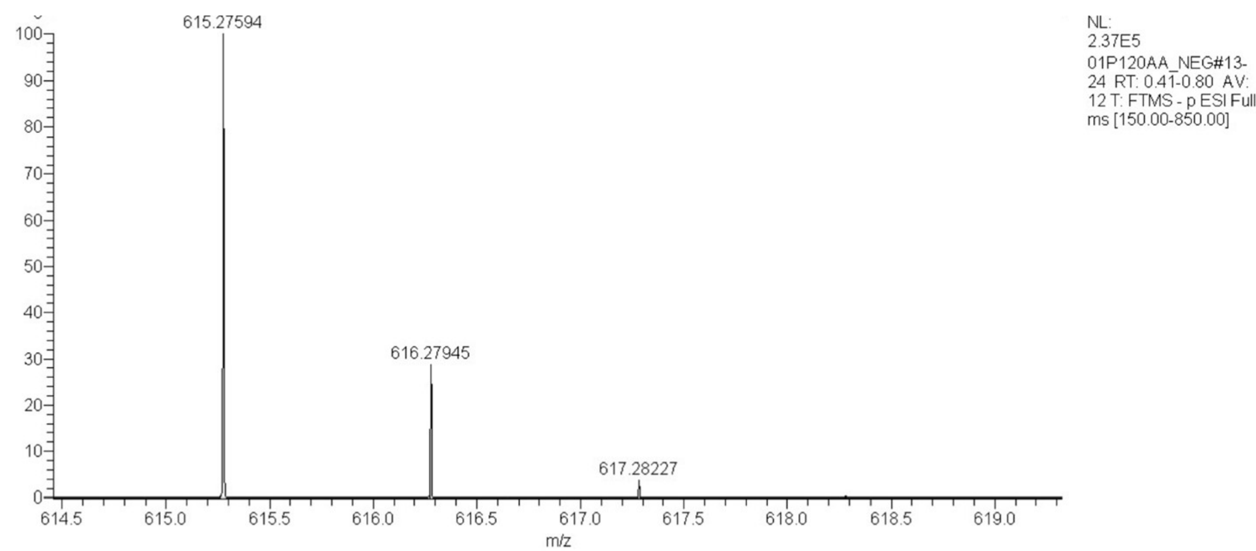

Figure S16. HRMS (ESI) of **CelBCyclo**

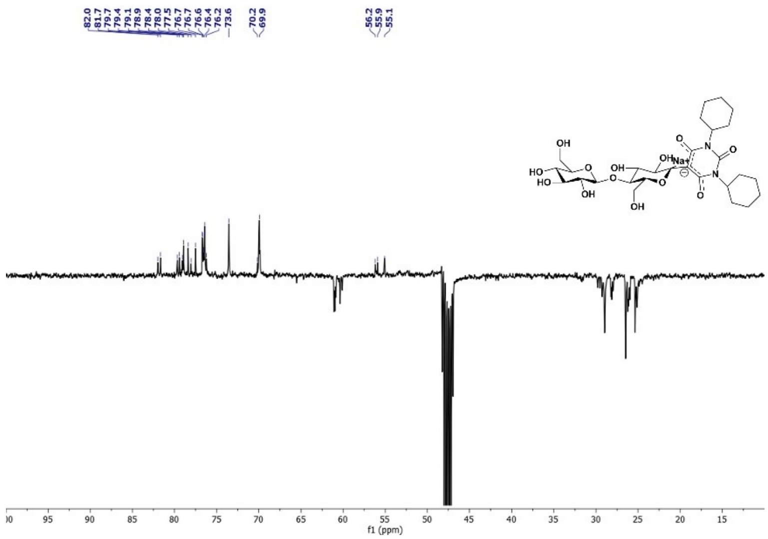

Figure S17. DEPT-135 ^{13}C NMR spectrum (400 MHz, MeOD, 298K)

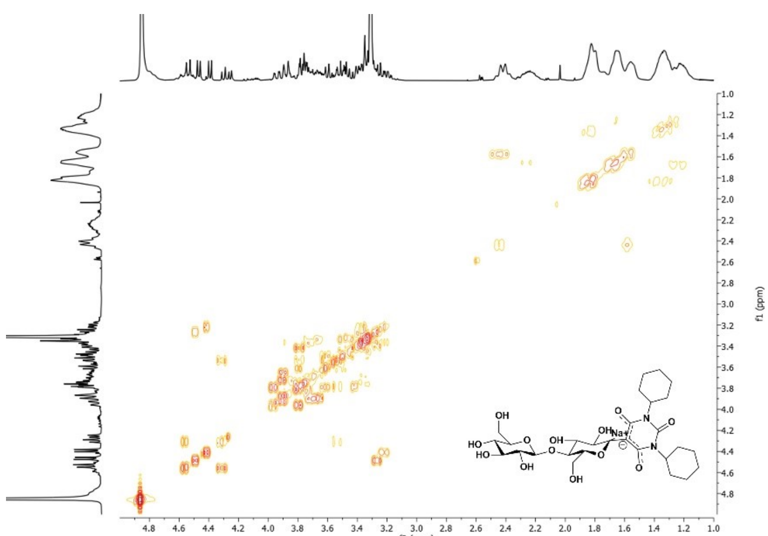

Figure S18. COSY spectrum (400 MHz, MeOD, 298K)

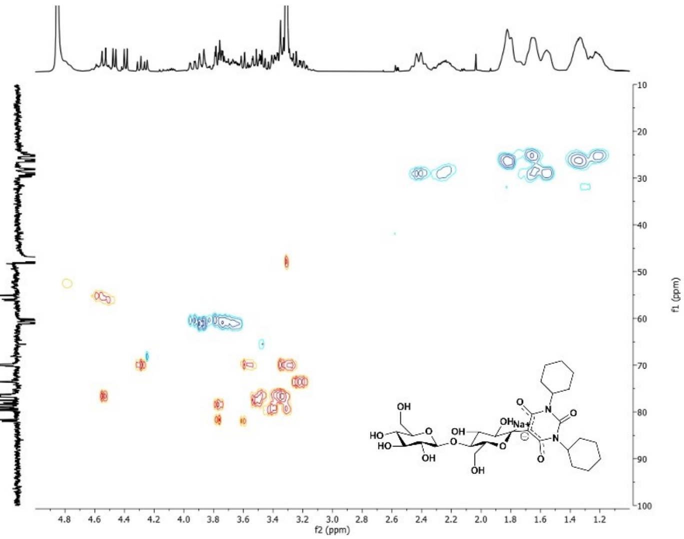

Figure S19. HSQC spectrum (400 MHz, MeOD, 298K)

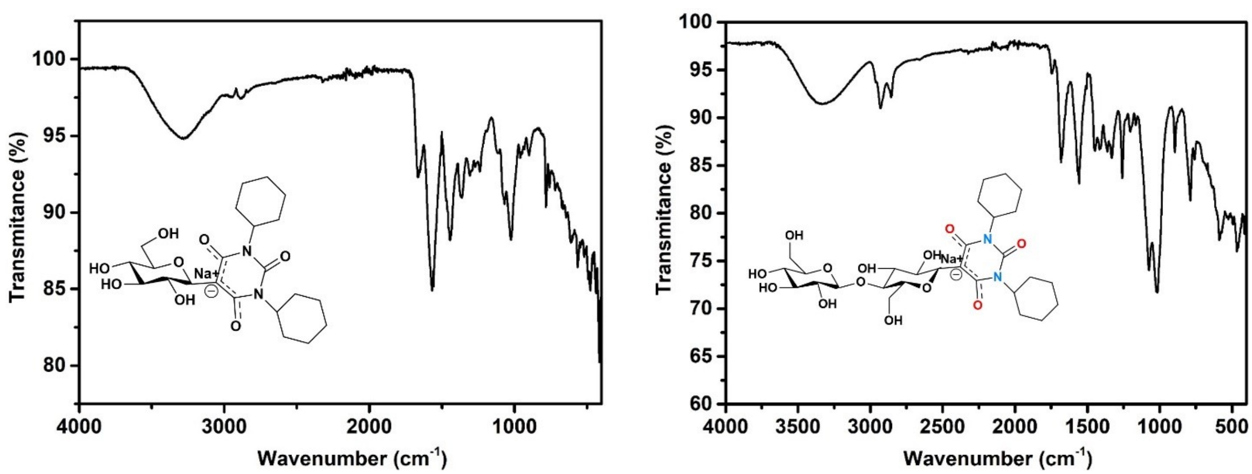

Figure S20. FTIR spectra of sodium 5-(β-D-glucopyranosyl)-1,3-dicyclohexyl barbiturate (GlcBCyclo) and Sodium 5-(β-D-cellobiosyl)-1,3-dicyclohexyl barbiturate (CelBCyclo)

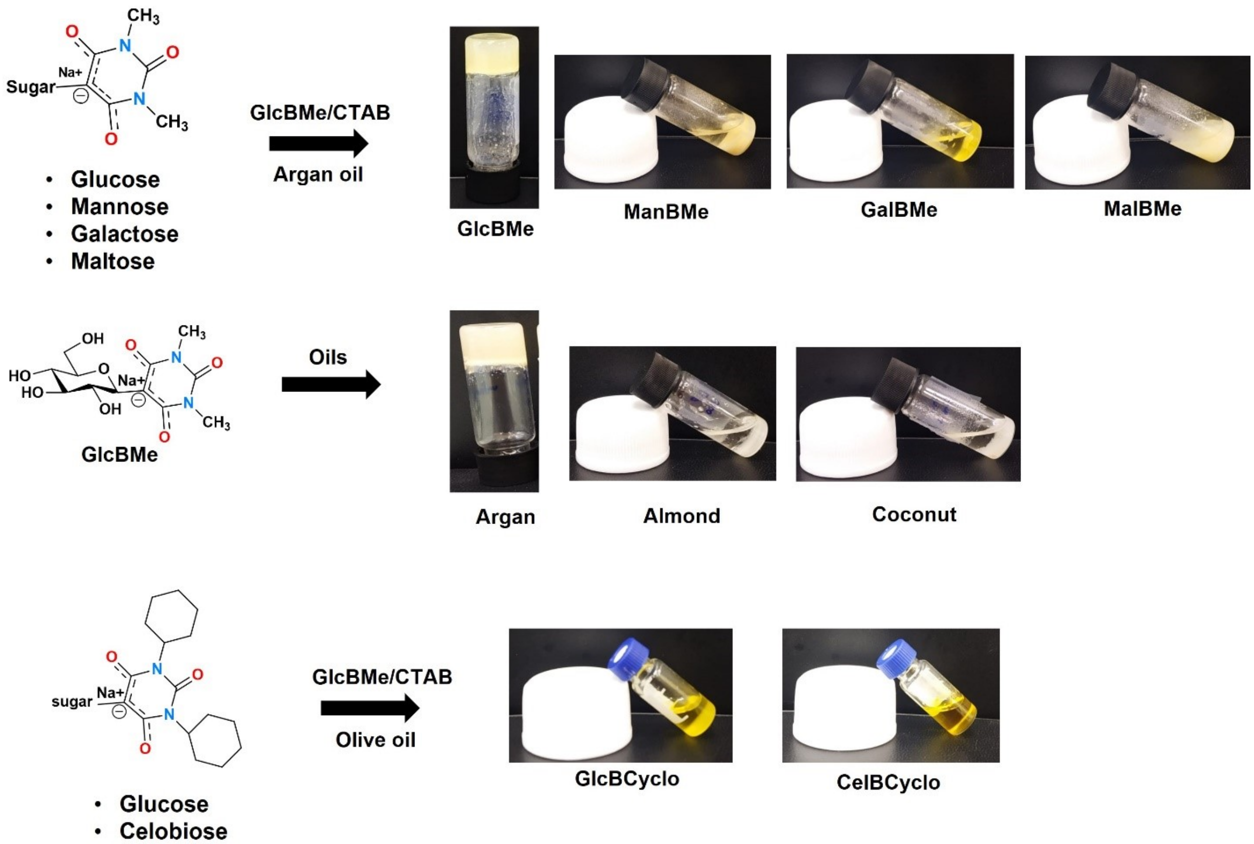

Figure S21. Oleogels prepared based on sodium salt of β-*C*-glycosyl barbiturates

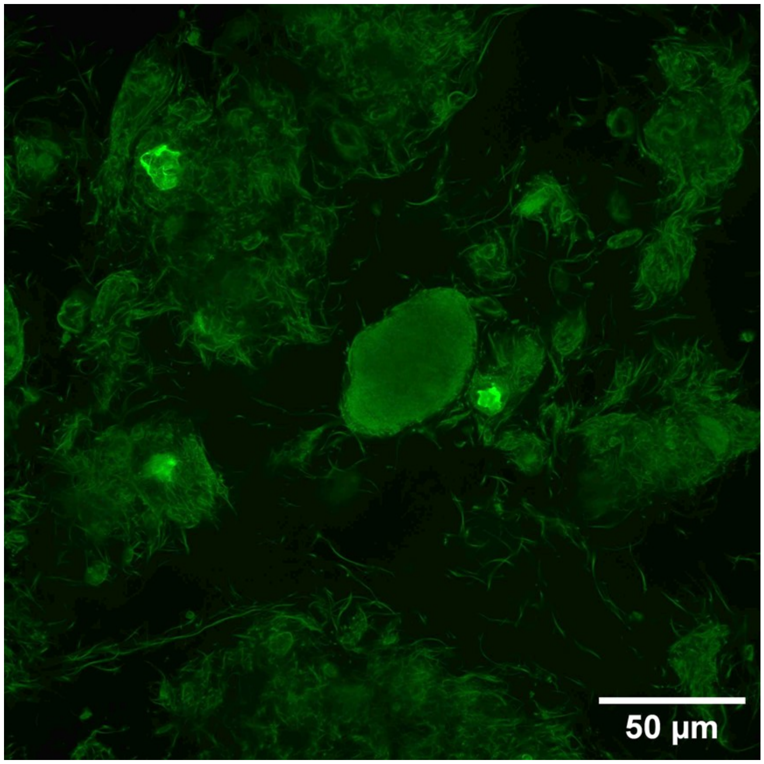

Figure S22. Confocal image for **GlcBMe**-C-Ar

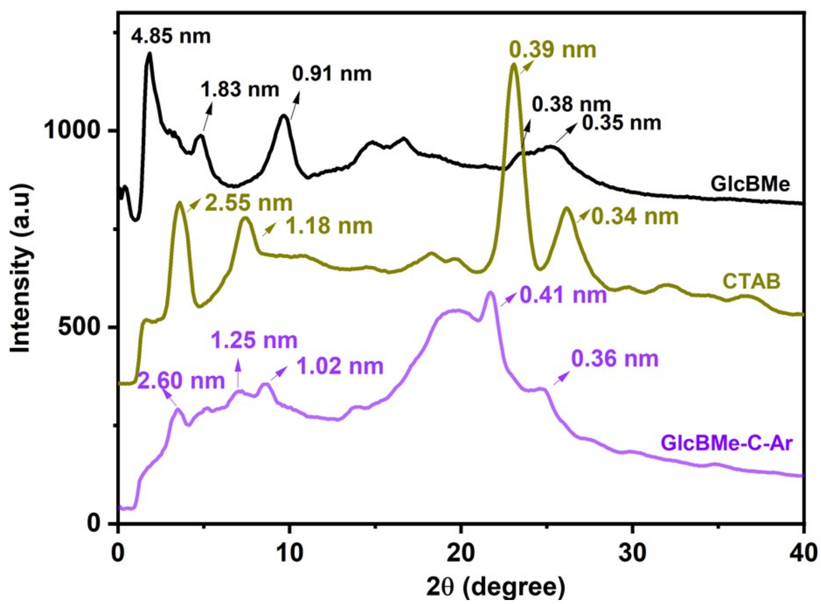

Figure S23. XRD patterns of the **GlcBMe**, CTAB and **GlcBMe**-C-Ar oleogel.

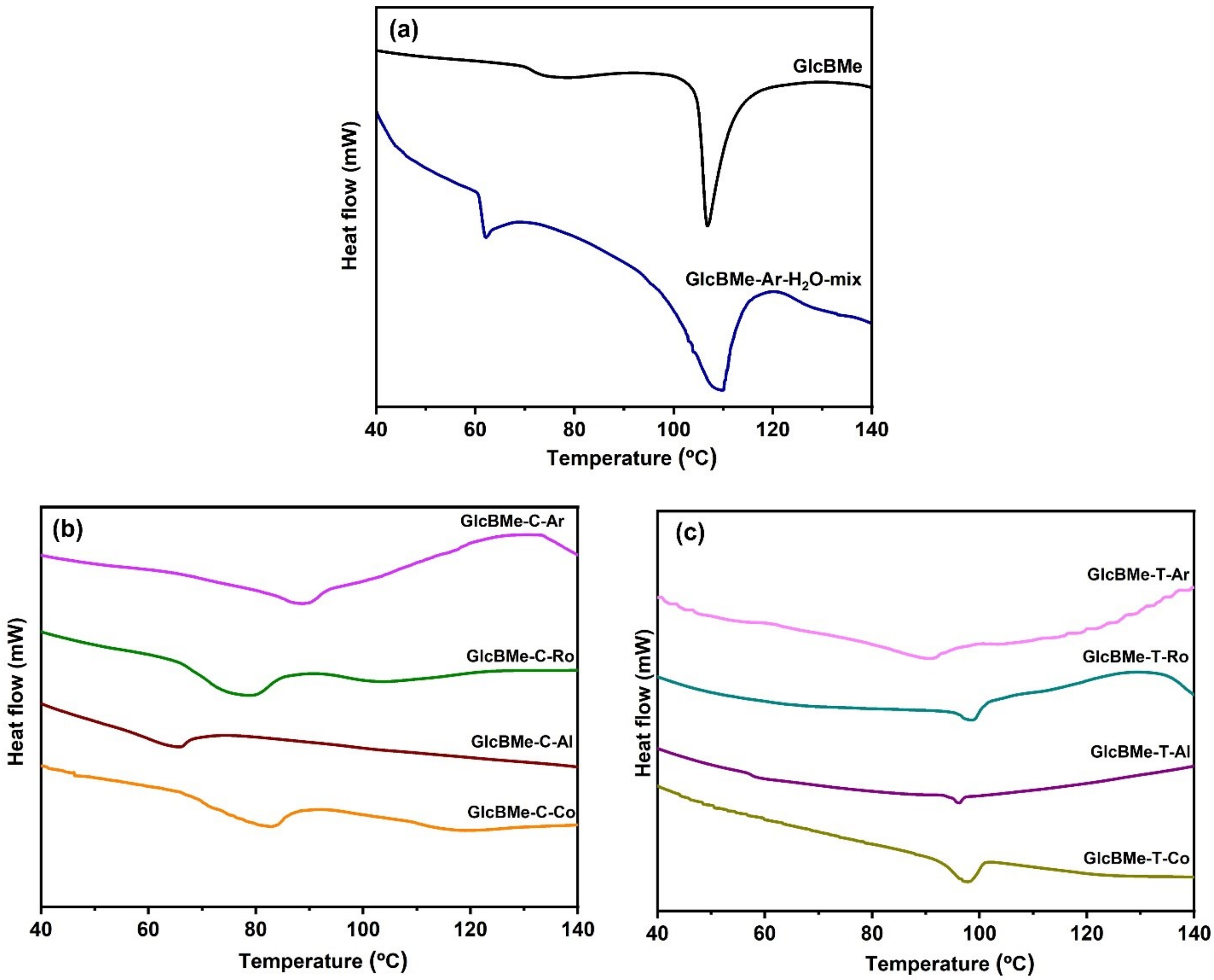

Figure S24. DSC graph of (a) **GlcBMe** and **GlcBMe**-Ar-H_2O-mix (b) **GlcBMe**-C-Ar, **GlcBMe**-C-Ro, **GlcBMe**-C-Al, **GlcBMe**-C-Co (b) **GlcBMe**-T-Ar, **GlcBMe**-T-Ro, **GlcBMe**-T-Al, **GlcBMe**-T-Co

Table S1. Melting temperature and enthalpy of all the samples

Oleogels samples	**T_{on}**	**T_{peak} (°C)**	**ΔH (J g^{-1})**
GlcBMe-C-Ar	72.6	88.6	4.5
GlcBMe-C-Ro	62.8	74.8	3.7
GlcBMe-C-Al	59.6	78.3	2.3
GlcBMe-C-Co	64.9	78.3	2.4
GlcBMe-T-Ar	66.6	89.6	3.31
GlcBMe-T-Ro	95.6	99.1	0.27
GlcBMe-T-Al	94.7	96.1	0.08
GlcBMe-T-Co	92.2	96.9	0.53

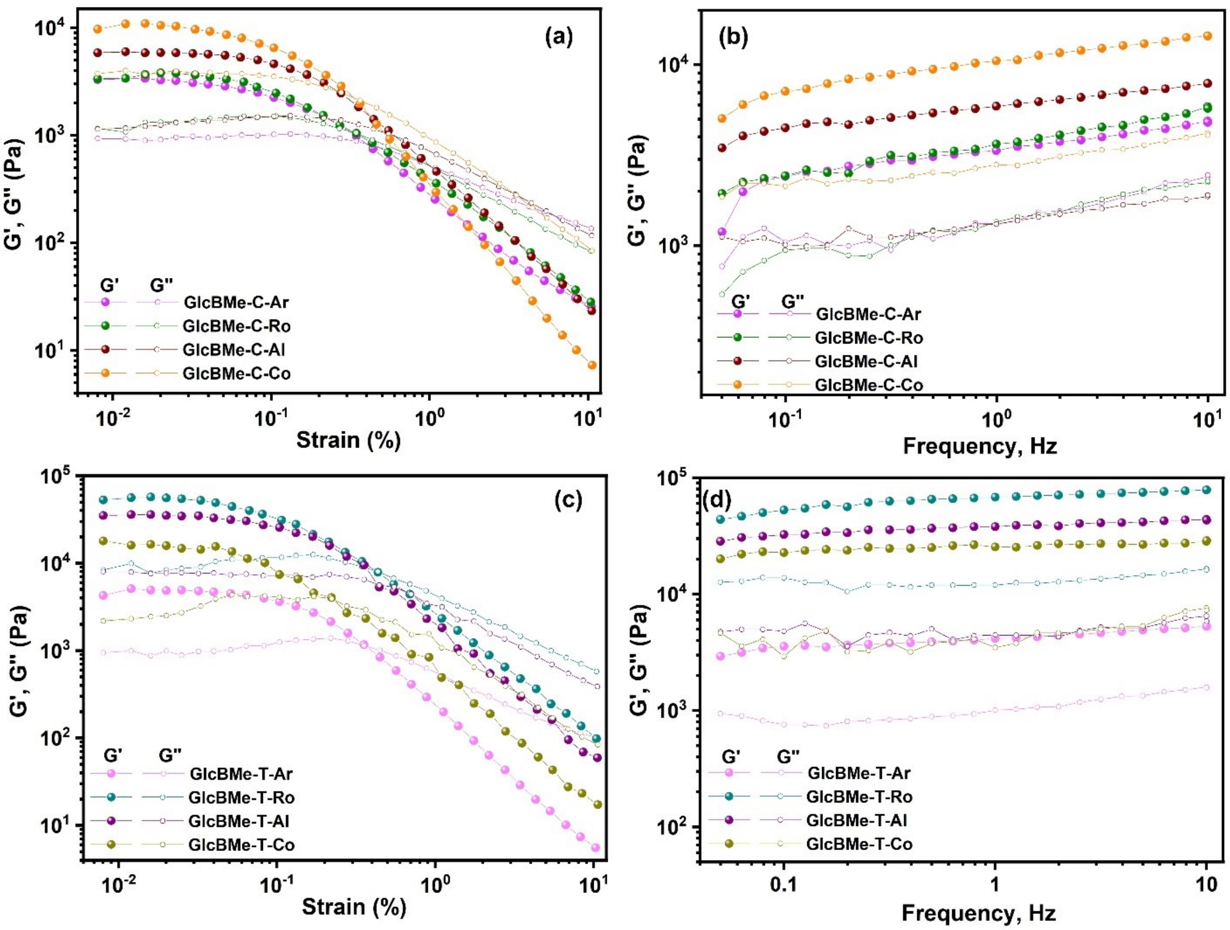

Figure S25. (a) Strain sweeps (b) Frequency sweep for oleogels based different oils in CTAB (c) Strain sweeps (d) Frequency sweep for oleogels based different oils in TBAB

Table S2. Comparison of rheology data

Oleogels samples (2wt%)	Maximum G′ value (Pa)	δ = G″/G′
GlcBMe-C-Ro	3091	0.37
GlcBMe-C-Al	4477	0.22
GlcBMe-C-Co	7128	0.27
GlcBMe-T-Ro	68050	0.18
GlcBMe-T-Al	37880	0.12
GlcBMe-T-Co	25250	0.14
12-hydroxystearic acid[1]	1784	> 0.5
Sorbitan monostearate*[2]	10-100	
Mannitol dioctanoates**[3]	4300	//
Sorbitol dioctanoates**[3]	2052	//
Monoglyceride[4]	3427	0.17
CARBOPOL974[5]	35	1.95
Ethylcellulose[6]	1468	0.10

*10wt.%, ** 5wt.%

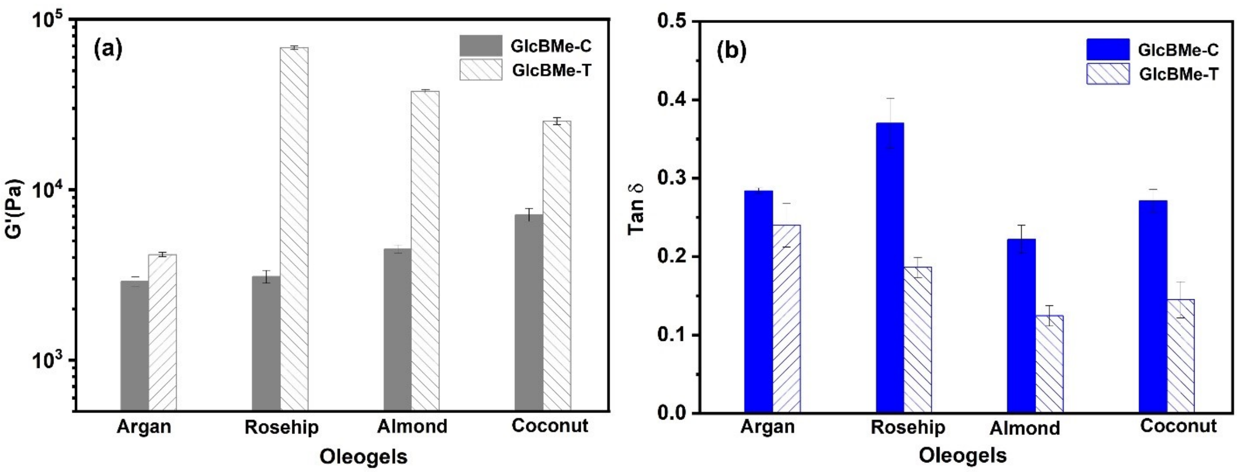

Figure S26. (a) G' *vs.* oleogels samples in CTAB and TBAB (b) Tan δ *vs.* oleogels samples in CTAB and TBAB

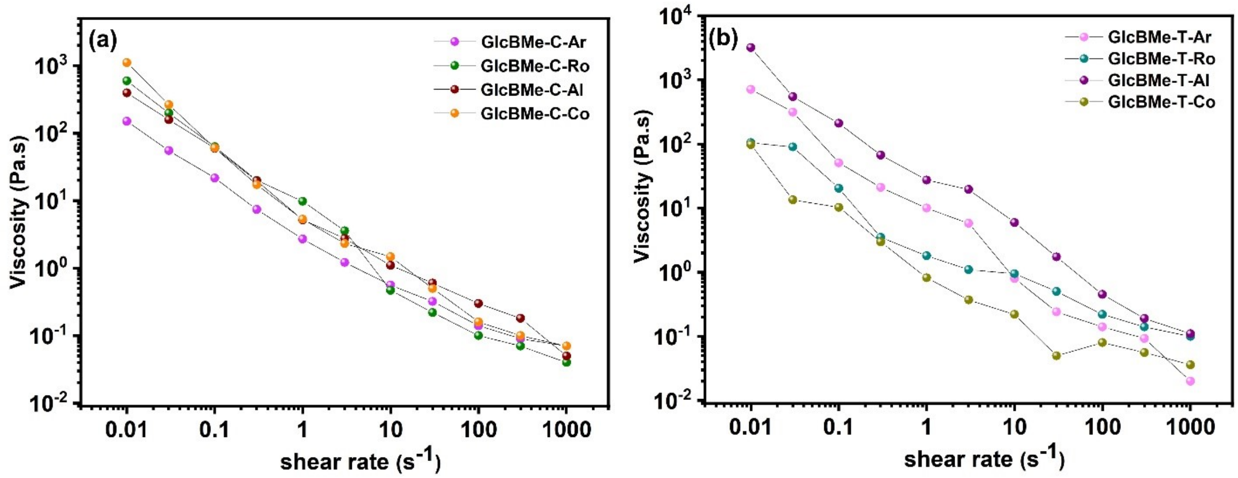

Figure S27. (a) Viscosity versus shear rate for samples based CTAB (b) Viscosity versus shear rate for samples based TBAB

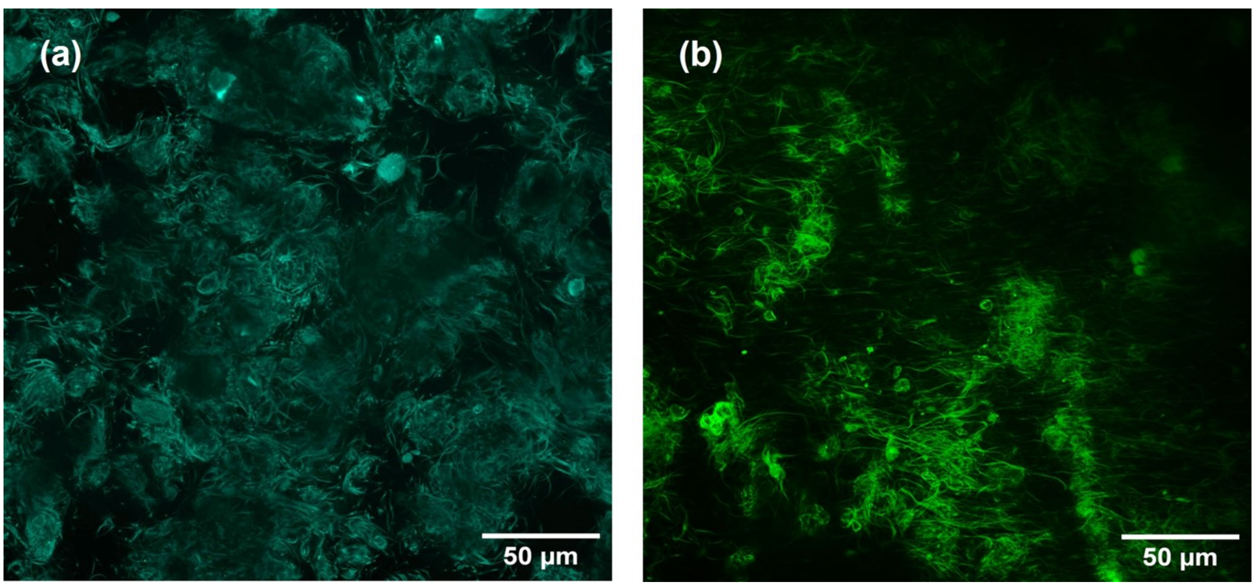

Figure S28. (a) Confocal image before shear (b) Confocal image after shear for **GlcBMe**-C-Ar oleogel

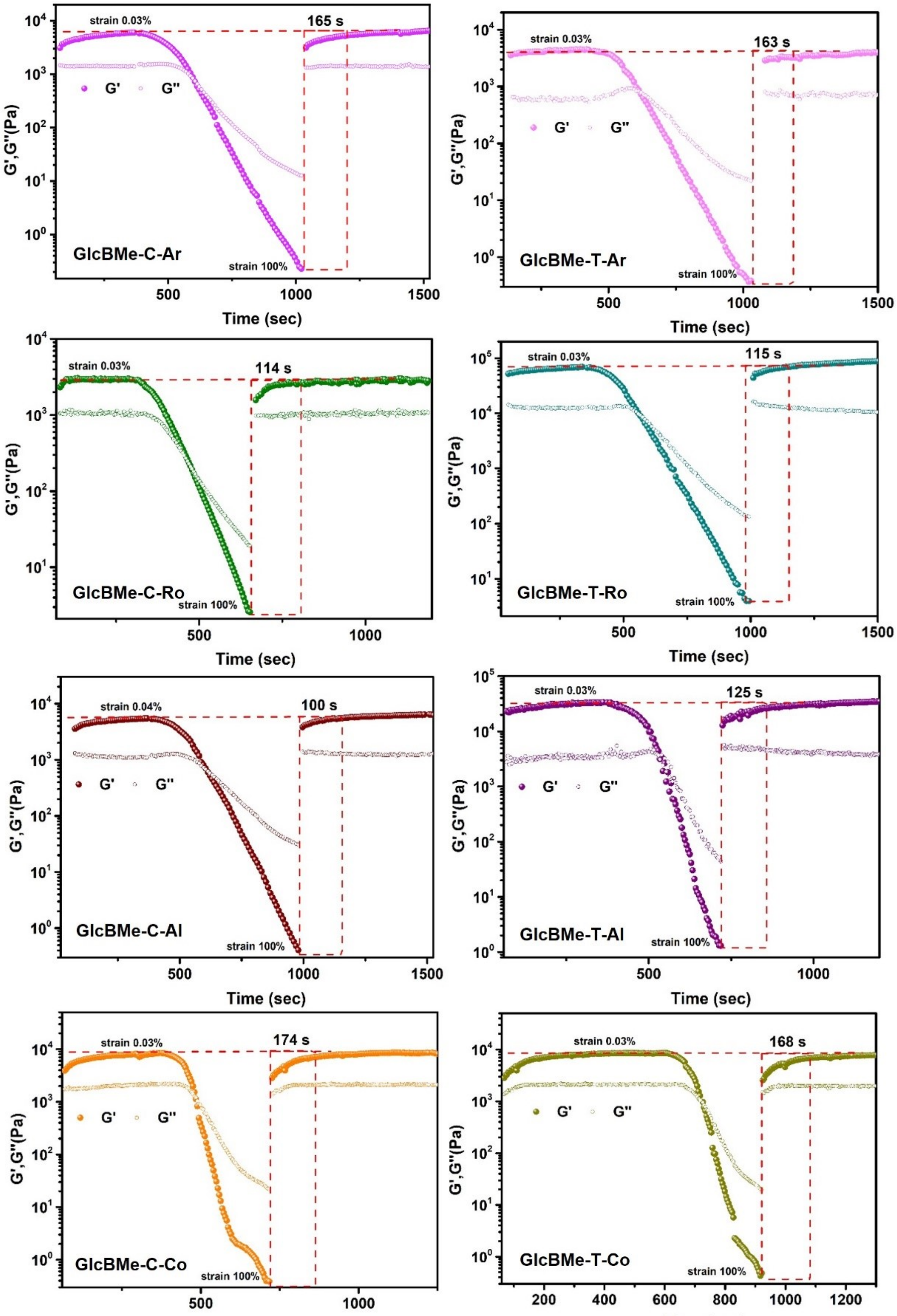

Figure S29. Thixotropic behavior of oleogels based, rosehip, almond, and coconut with CTAB or TBAB

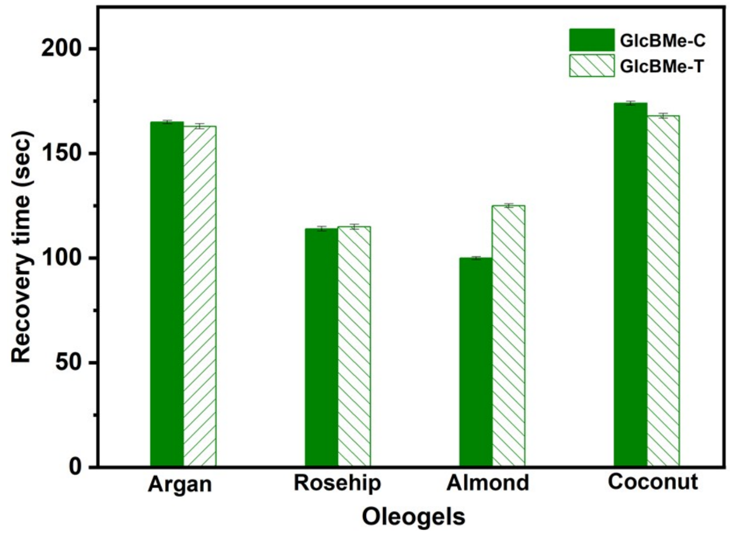

Figure S30. Recovery time (sec) for all samples in CTAB and TBAB

Table S3. Main fatty acid composition (%) of argan, rosehip, almond, and coconut oil

Fatty acid (%)	Argan[7]	Rosehip[8]	Almond[9]	Coconut[10]
Palmitic acid (C16:0)	15.5	3.6	5.5	16.5
Linoleic acid (C18:2)	35	52.5	28	1.6
Stearic acid (C18:0)	8.5	2.3	1.2	3.1
Oleic acid (C18:1)	41.2	19.8	62	9.1
Linolenic acid (C18:3)	//	20.5	//	1.6
Palmitoleic acid (C16:1)	//	//	//	//
Lauric acid (C12:0)	//	//	//	41.2
Miristic acid (C14:0)	//	//	//	23.9
Capric acid (C10:0)	//	//	//	3.9

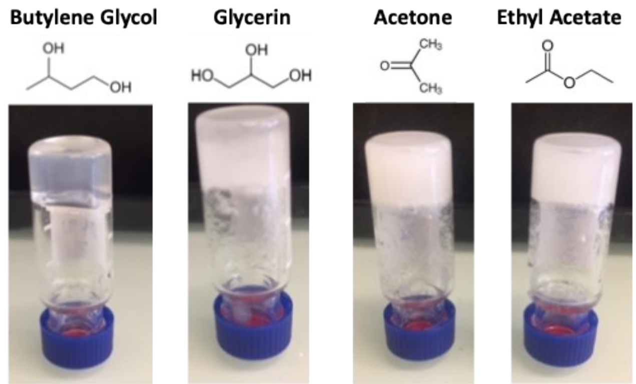

Figure S31. Digital pictures of inverted tubes including gelated butylene glycol, glycerin, acetone, and ethyl acetate

REFERENCES

[1] C.L. Esposito, V. Tardif, M. Sarrazin, P. Kirilov, V.G. Roullin, *Mater. Sci. Eng. C, Mater. Biol. Appl.* **2020**, *114*, 110999.

[2] M.T.H. Swe, P. Asavapichayont, *Asian J. Pharm. Sci.* **2018**, *13* (5), 485–497.

[3] M. Samateh, S.S. Sagiri, R. Sanni, C.A. Chee, S. Satapathy, G. John, *J. Agric. Food Chem.* **2020**, *68* (46), 13282–13290.

[4] S. Pieve, S. Calligaris, E. Co, M. Nicoli, A. Marangoni, A. *Food Biophys.* **2010**, *5*, 211–217.

[5] G. Bonacucina, S. Martelli, G.F. Palmieri, *Int. J. Pharm.* **2004**, *282* (1-2), 115–130.

[6] R. Zhang, Y. Zhang, J. Yu, Y. Gao, L. Mao, *Foods* **2022**, *11* (15), 2364.

[7] S. Gharby, Z. Charrouf, *Front. Nutr. Sci.* **2021**, *8*, 804587.

[8] I. Mármol, C. Sánchez-de-Diego, N. Jiménez-Moreno, C. Ancín-Azpilicueta, M.J. Rodríguez-Yoldi, *Int. J. Mol. Sci.* **2017**, *18* (6), 1137.

[9] Z. Shi, Q. Fu, B. Chen, S. Xu, S. *Chin. J. Chromatogr.* **1999**, *17* (5), 506–507.

[10] A. Suryanto, S. Suprapto, M. Mahfud, *Bull. Chem. React. Eng.* **2015**, *10*(2), 162–168.