



Rutin-loaded poloxamer 407-based hydrogels for *in situ* administration: stability profiles and rheological properties

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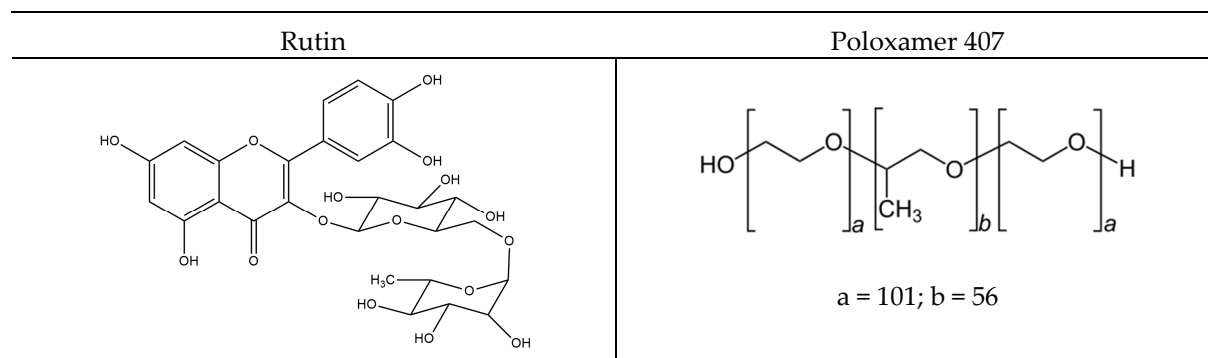


Figure S1. Chemical structure of rutin and poloxamer 407.

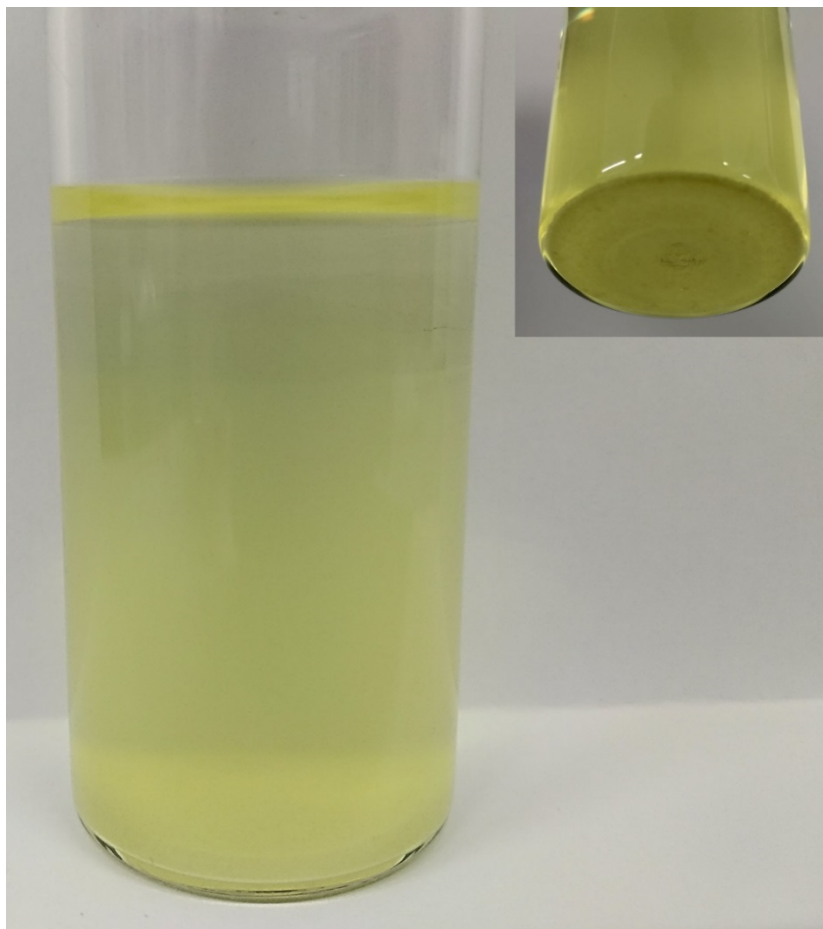


Figure S2. P407-based hydrogel prepared with 0.2% (w/w) of rutin

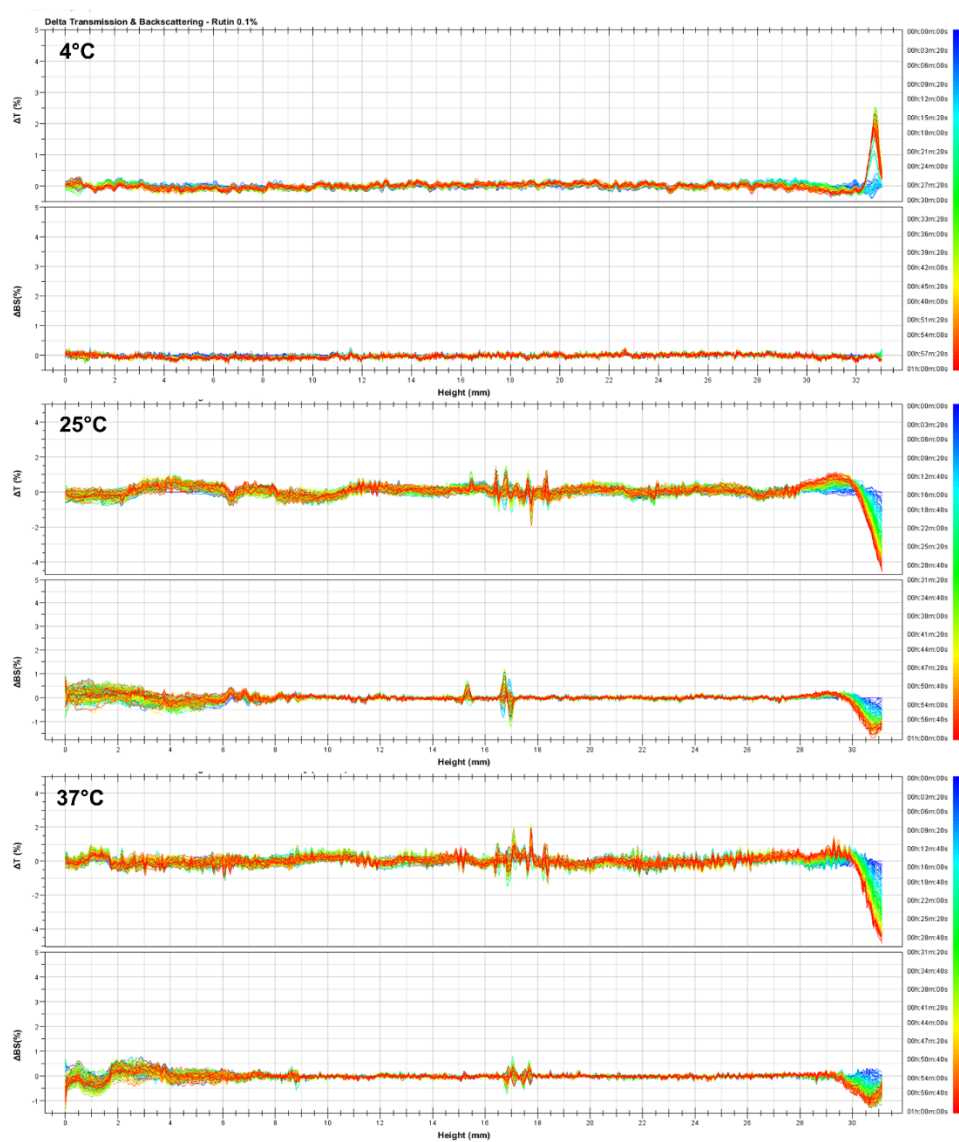


Figure S3. Δ BS and Δ T profiles of P407 hydrogels prepared with 0.1% (w/w) of rutin added in powder form as a function of the temperature and incubation time.

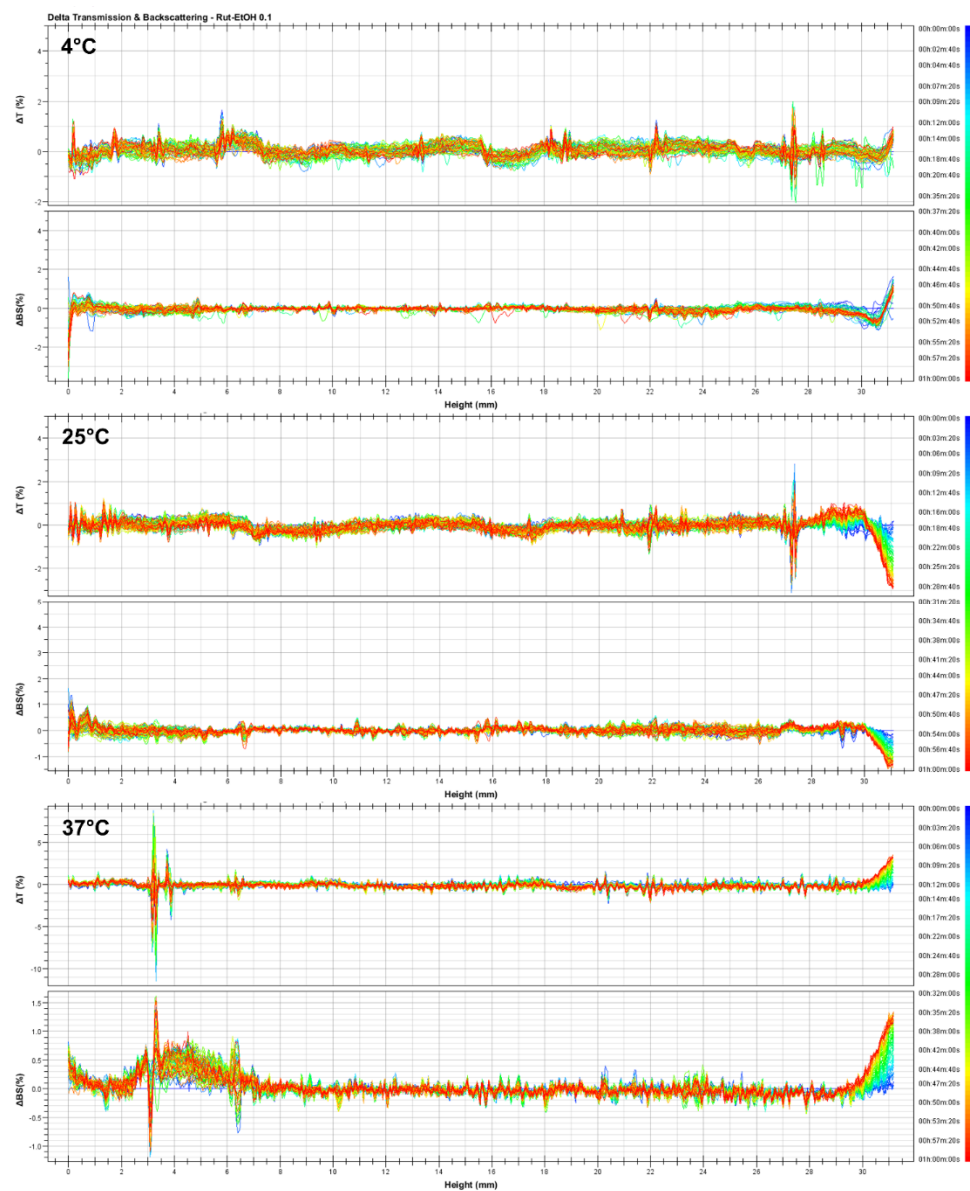


Figure S4. Δ BS and Δ T profiles of P407 hydrogels prepared with 0.1% (w/w) of rutin added as an ethanol solution as a function of the temperature and incubation time.

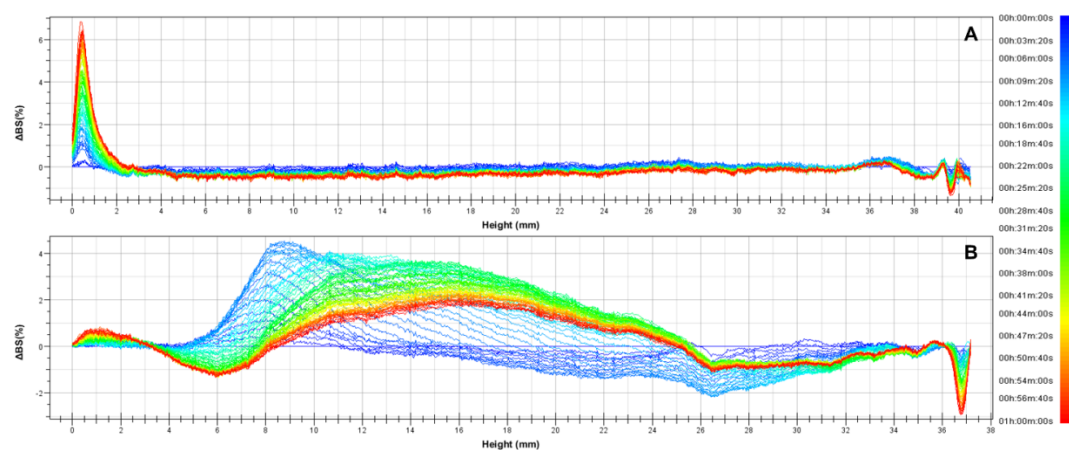
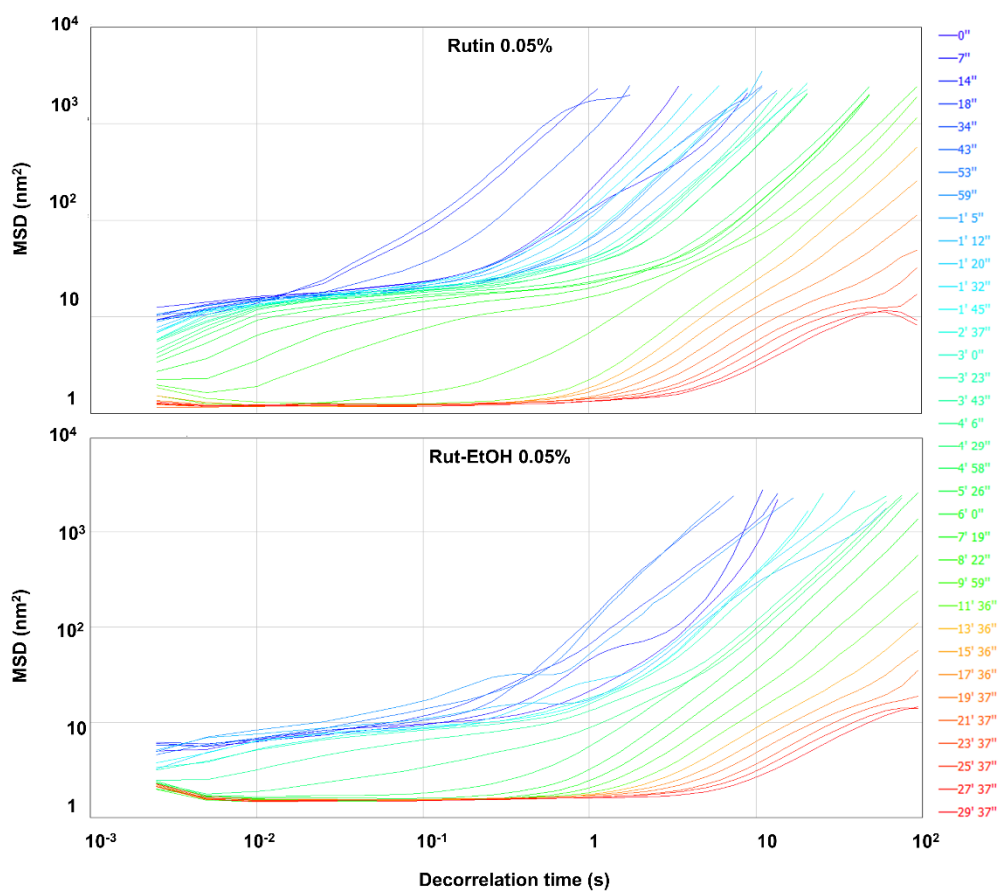
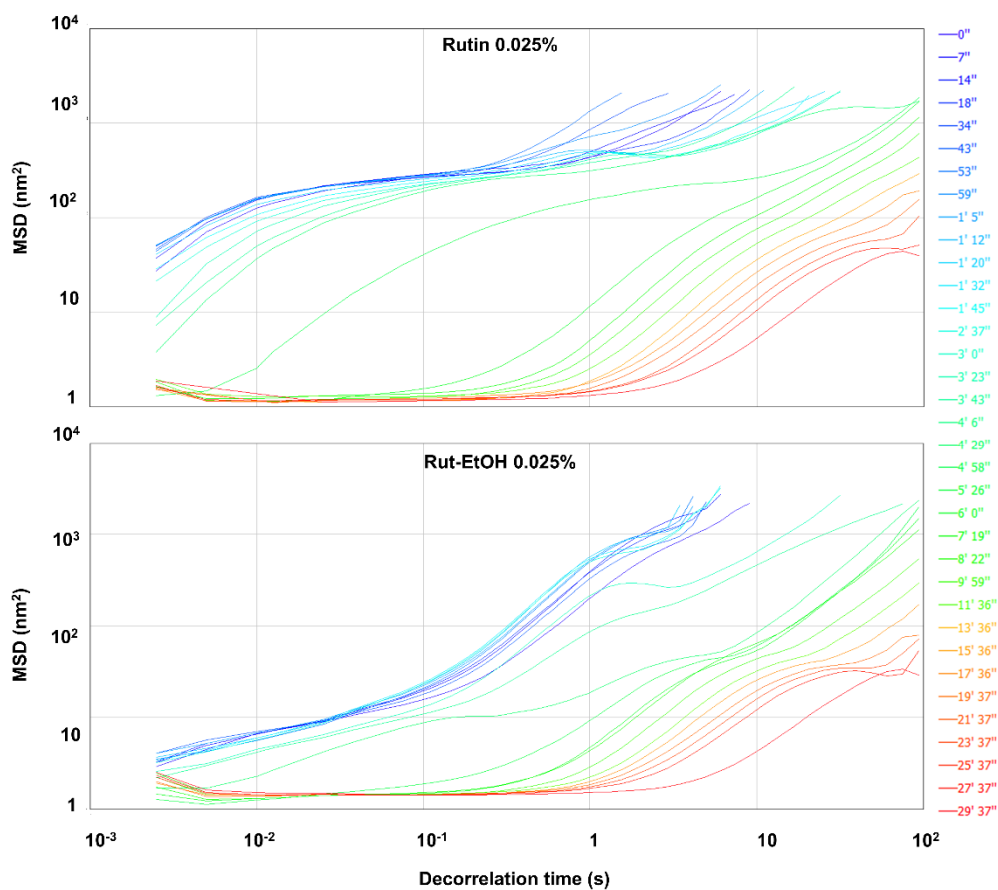


Figure S5. Δ BS profiles of rutin-loaded P407 hydrogels at 4 °C prepared using (A) 0.2% (w/w) and (B) 0.5% (w/w) of the drug. During the analysis a progressive increase of the Δ BS profiles occurred. This was due to the precipitation of the drug in the case of the formulation prepared with 0.2% of rutin and to the formation of macroaggregates in the system with 0.5% of the bioactive.



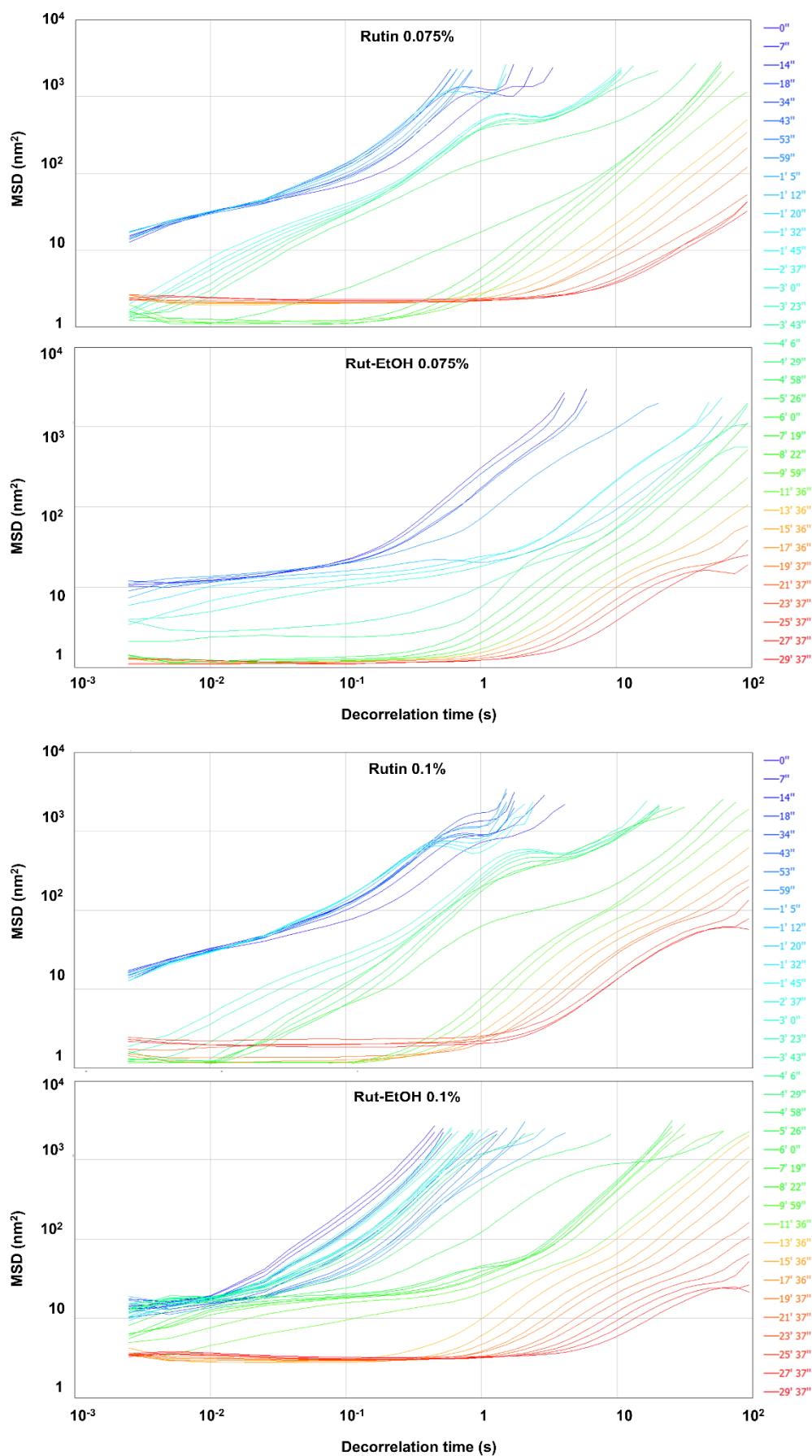


Figure S6. MSD curves of various P407 (20%, w/w)-based hydrogels containing different amounts of rutin as a powder or solubilized in ethanol as a function of the decorrelation time and temperature (from 4 °C to 37 °C).

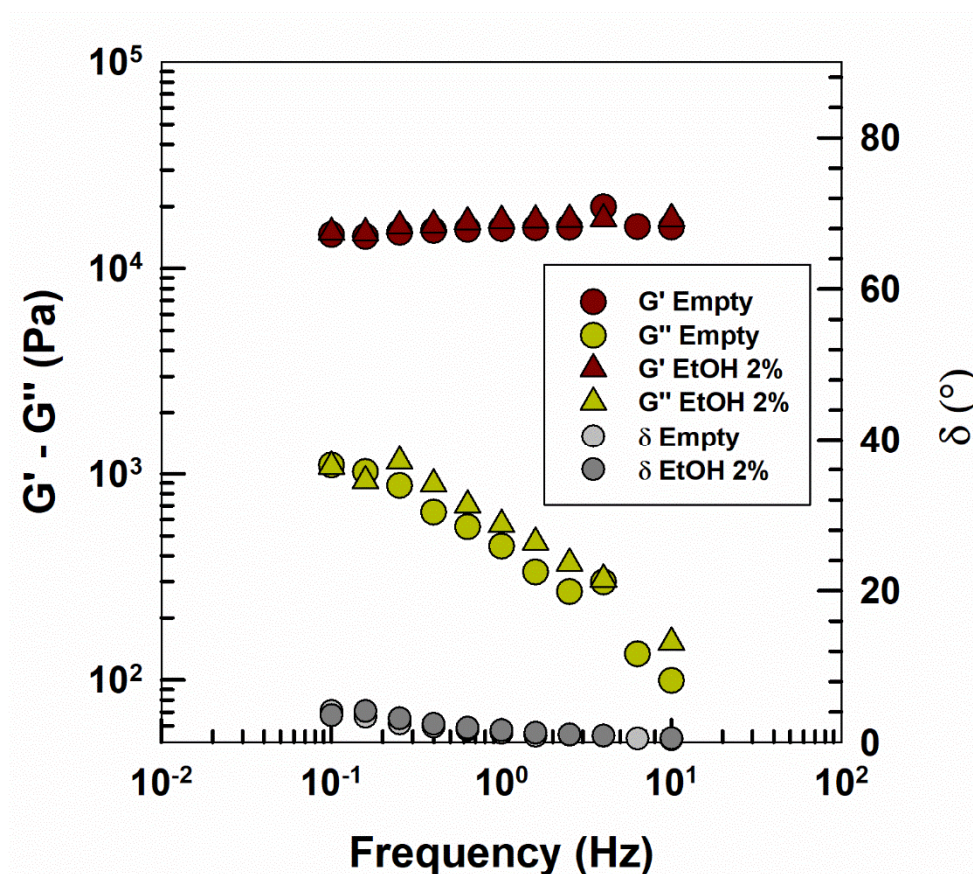


Figure S7. Elastic modulus (G'), viscous modulus (G'') and phase angle (δ) of P407 (20%, w/w) hydrogels as an ethanol-free system or containing the organic solvent (2%, w/w) as a function of frequency. This analysis was performed at 37 °C.

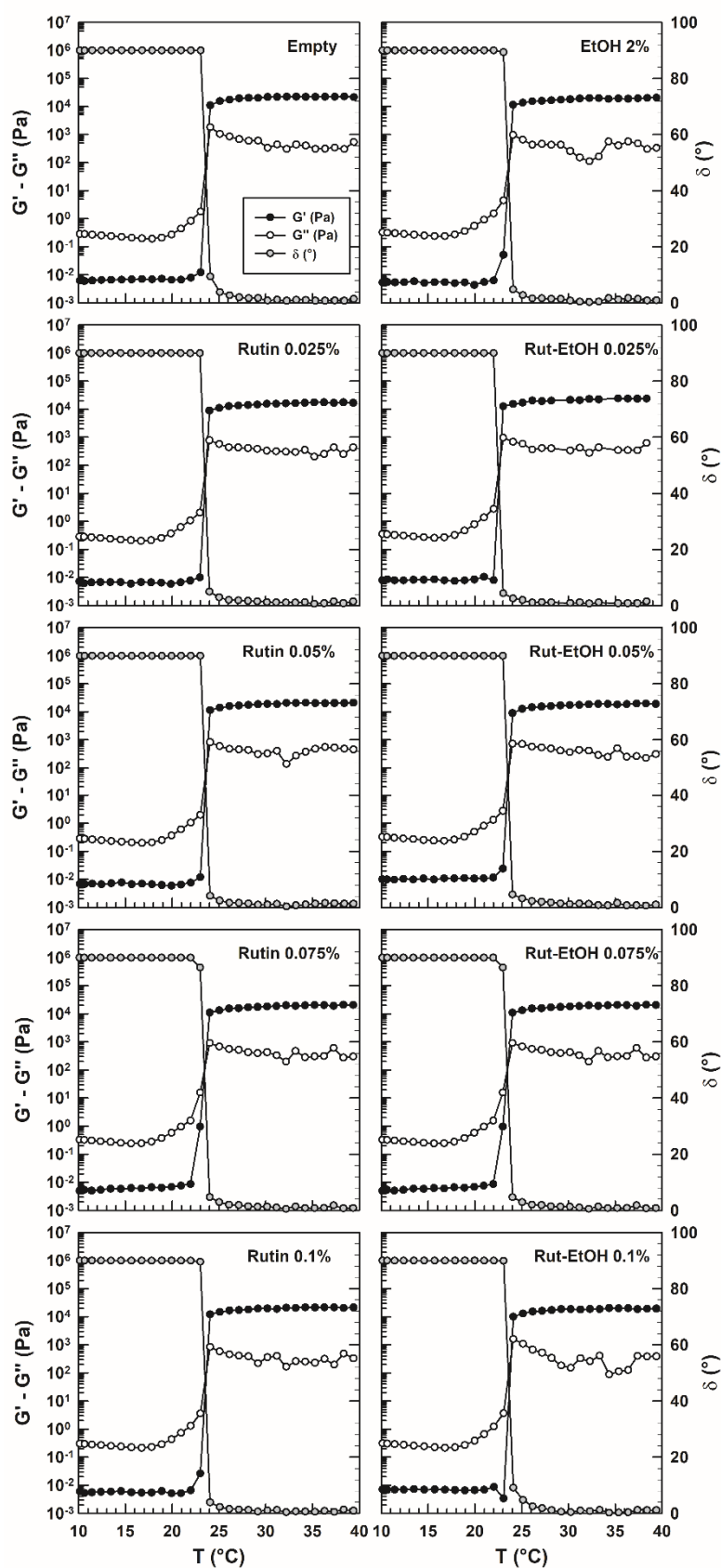


Figure S8. Elastic modulus (G'), viscous modulus (G'') and phase angle (δ) of the various P407-hydrogels as a function of temperature.

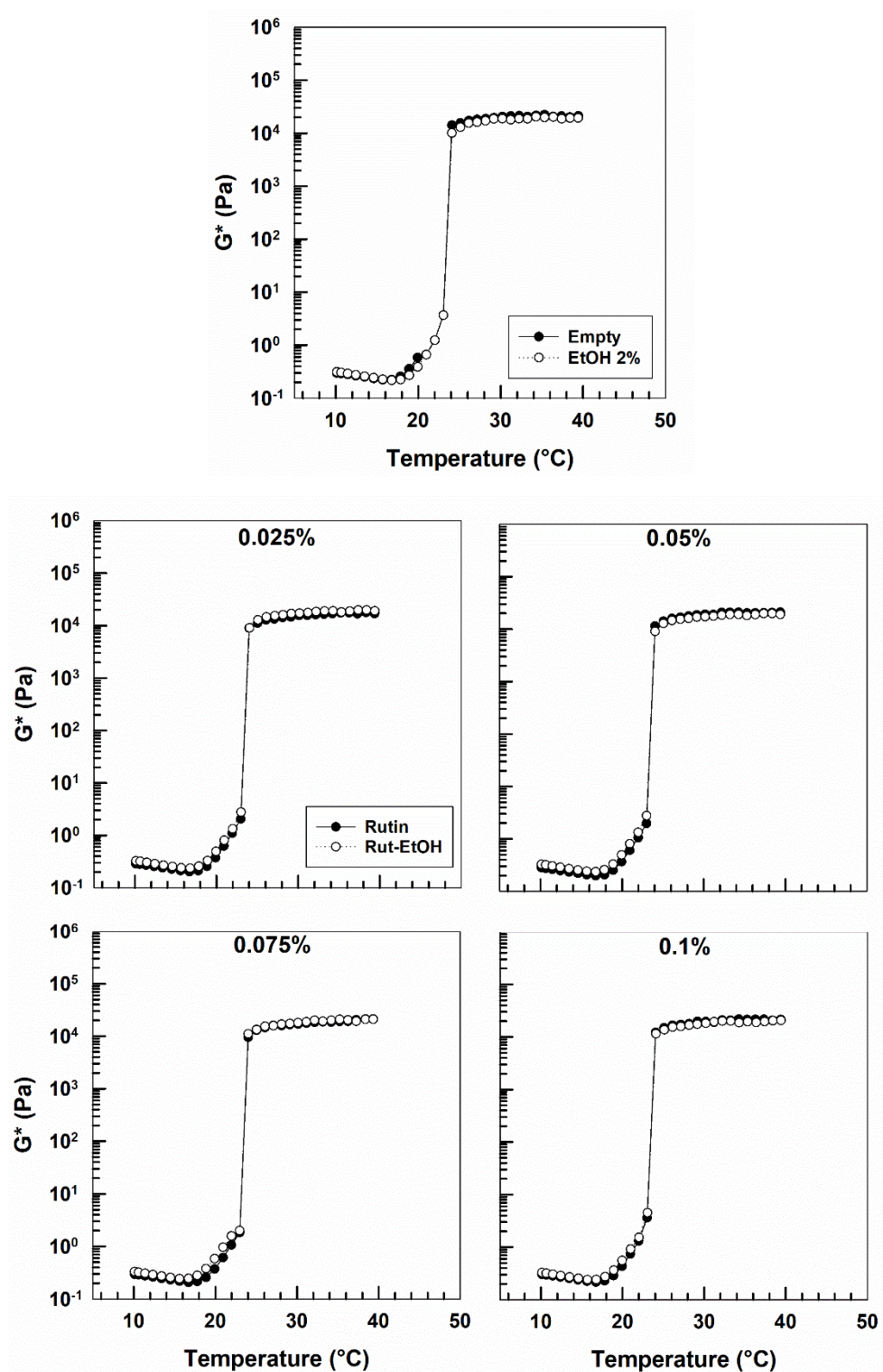


Figure S9. Complex modulus profiles of the various P407-hydrogels as a function of temperature.

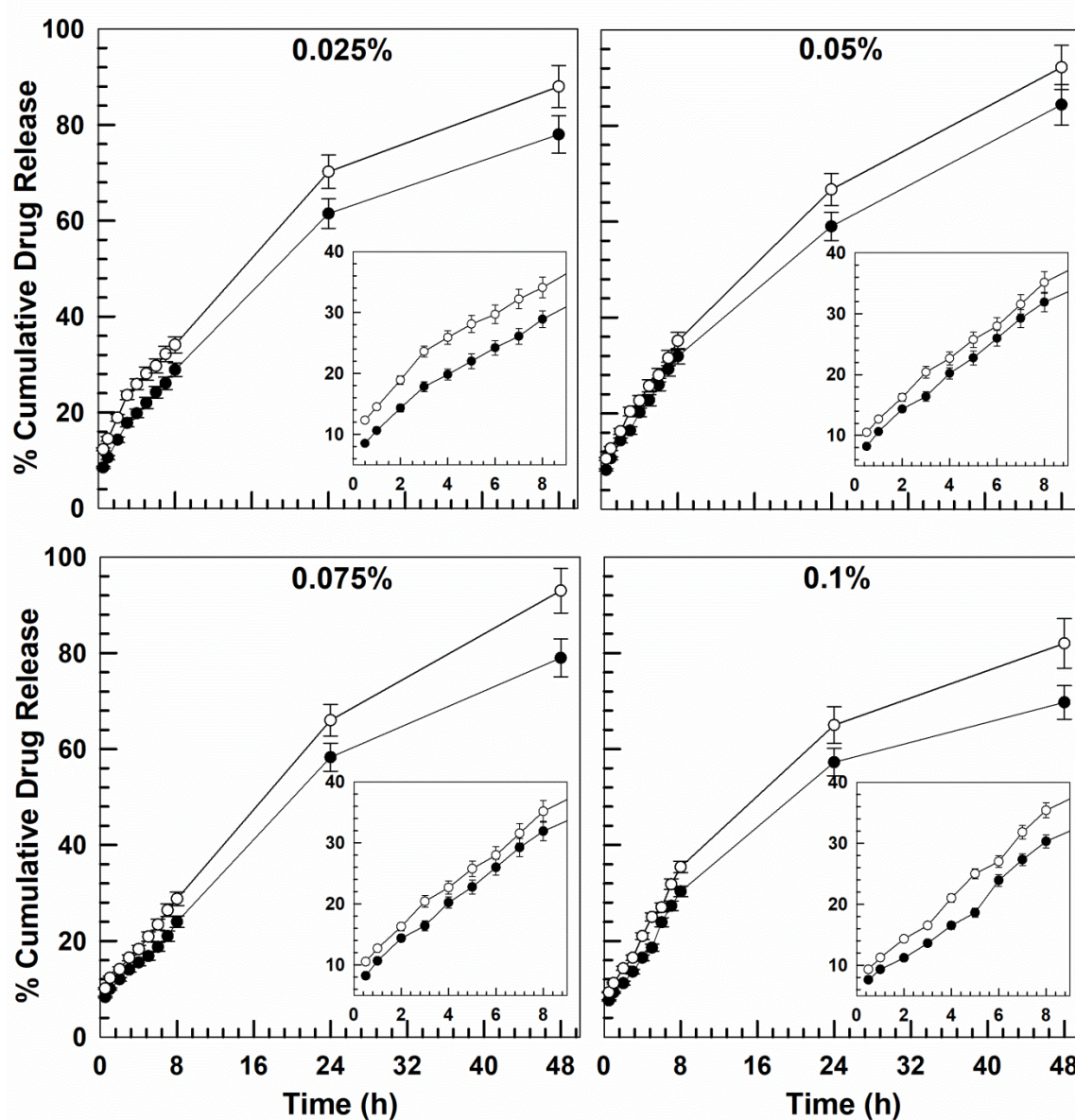


Figure S10. Release profiles of rutin in PBS from P407-based hydrogels. Experiments were carried out below the transition temperature. Values are the average of three different experiments \pm standard deviation.

Table S1. Values of SLB (solid-liquid balance) of the of the various P407-based hydrogels.

Formulations	SLB t_i ¹	SLB t_f ¹
Empty	0.67	0.04
EtOH 2%	0.89	0.03
Rutin 0.025%	0.89	0.02
Rutin 0.05%	0.89	0.02
Rutin 0.075%	0.89	0.02
Rutin 0.1%	0.69	0.02
Rut-EtOH 0.025%	0.86	0.01
Rut-EtOH 0.05%	0.81	0.01
Rut-EtOH 0.075%	0.78	0.01
Rut-EtOH 0.1%	0.80	0.01

¹ t_i : initial time of the analysis; t_f : final time of the analysis**Table S2.** Values of the phase angle (δ) of rutin-loaded P407 hydrogels as a function of frequency at 37 °C.

Frequency (Hz)	Empty	EtOH 2%	Rutin 0.025%	Rutin 0.05%	Rutin 0.075%	Rut-EtOH 0.025%	Rut-EtOH 0.05%	Rut-EtOH 0.05%	Rut-EtOH 0.075%	Rut-EtOH 0.1%
10.0	0.4	0.5	0.6	0.7	0.3	0.8	0.3	0.5	0.7	0.5
6.3	0.5	0.6	0.6	0.6	0.7	0.7	0.4	0.7	0.7	0.6
4.0	0.8	0.8	0.8	0.7	0.7	0.8	0.5	0.8	0.7	0.8
2.5	1.0	1.0	0.8	0.9	1.1	0.9	0.6	0.9	0.8	0.8
1.6	0.8	1.2	1.3	1.2	1.1	1.2	0.8	1.1	1.1	1.2
1.0	1.2	1.6	1.4	1.5	1.2	1.4	0.5	1.3	1.3	1.3
0.6	1.6	1.9	1.4	1.7	1.6	1.7	1.1	1.6	1.4	1.6
0.4	2.1	2.4	1.9	1.8	2.0	2.2	2.5	1.9	1.8	1.9
0.3	2.4	3.1	2.6	2.4	2.9	2.8	2.2	2.2	2.1	2.5
0.2	3.4	4.1	2.5	3.0	1.8	3.5	2.4	3.1	2.6	2.9
0.1	4.1	3.6	6.1	5.1	2	4.8	3.4	4.1	3.0	2.4

Abbreviations

P407	Poloxamer 407
EtOH	Ethanol
$T_{sol-gel}$	Solution-gel transition temperature
MLS	Multiple Light Scattering
ΔBS	Delta Back-scattering
ΔT	Delta Transmission
TSI	Turbiscan stability index
MS-DWS	Multi-speckle diffusing wave spectroscopy
MSD	Mean square displacement
SLB	Solid-liquid balance
EI	Elasticity index
LVR	Linear viscoelastic region
MW	Molecular weight