Supporting Information

Niosomes encapsulated in biohydrogels for tunable delivery of phytoalexin resveratrol

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1. Digital pictures of representative hydrogels

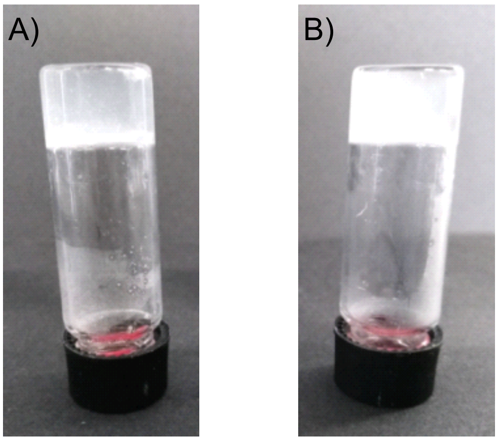


Figure S1. Representative hydrogel pictures: A) κ-C:gelatin (1:1 mass ratio, 4 % w/v). B) κ-C:gelatin (1:1 mass ratio, 4 % w/v) containing RSV-niosomes.

2. Additional rheological plots

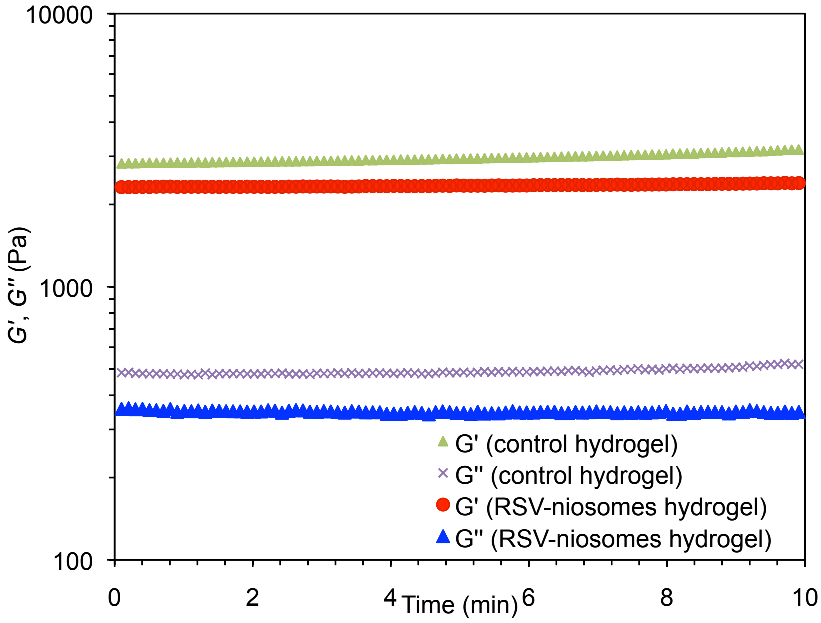


Figure S2. DTS measurements of native hydrogel (control hydrogel without niosomes) and hydrogel containing RSV-niosomes.

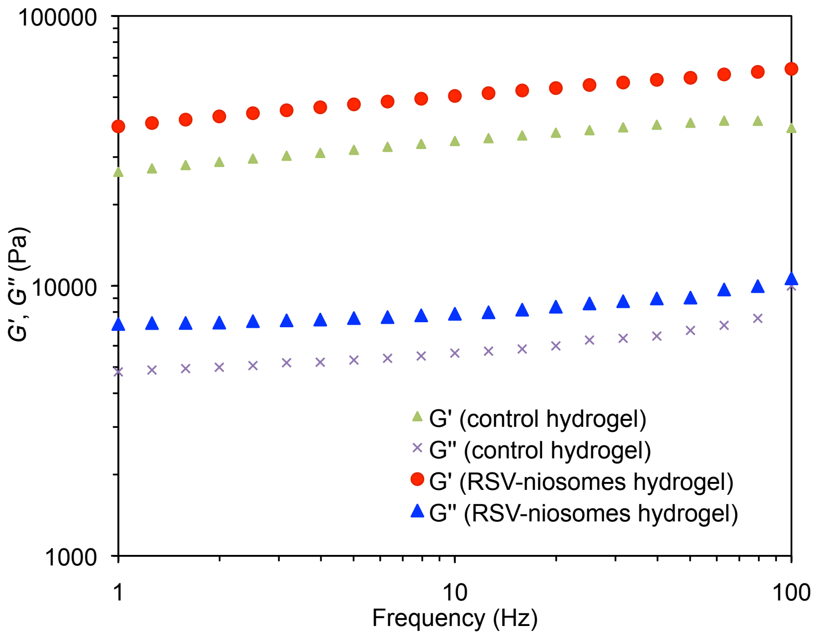


Figure S3. DFS measurements at pH 1.2 of native hydrogel (control hydrogel without niosomes) and hydrogel containing RSV-niosomes.

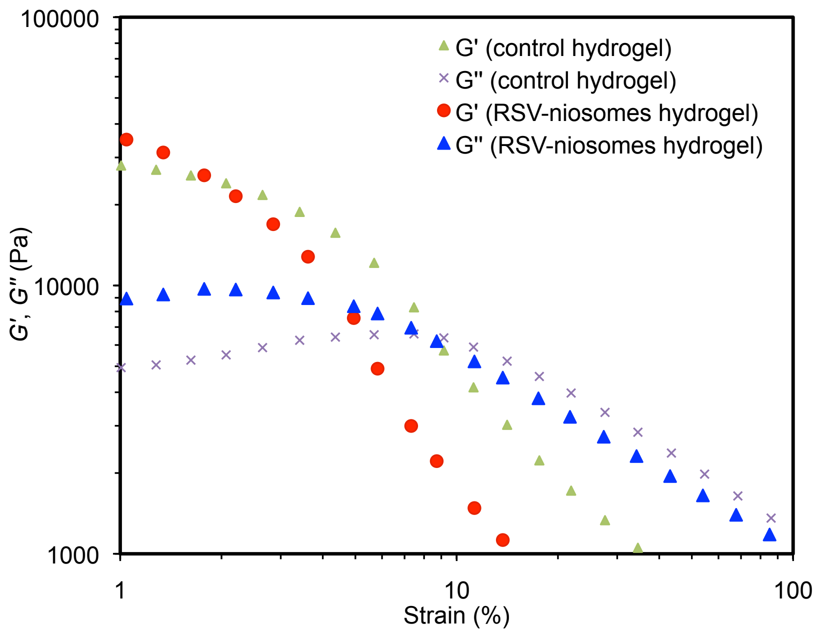


Figure S4. DSS measurements at pH 1.2 of native hydrogel (control hydrogel without niosomes) and hydrogel containing RSV-niosomes.

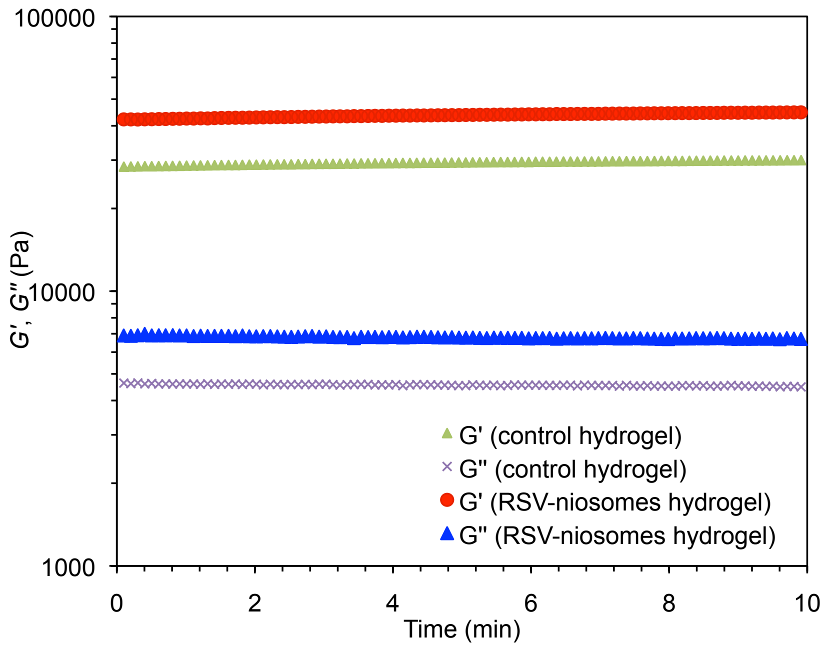
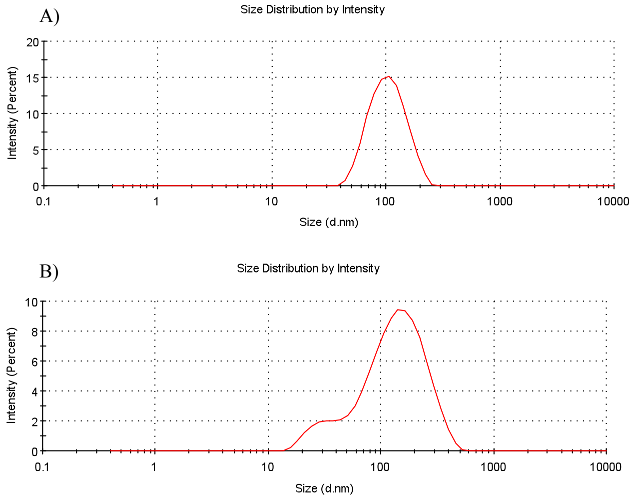


Figure S5. DTS measurements at pH 1.2 of native hydrogel (control hydrogel without niosomes) and hydrogel containing RSV-niosomes.

3. Stability of the niosomes in the hydrogels



Graph	Mean diamater (nm)	PDI
A	90.2 ± 0.4	0.15 ± 0.01
B	96.1 ± 0.9	0.434 ± 0.007

Figure S6. Mean diameter of RSV-niosomes A) incubated at 37 ºC for 24 h and B) after hydrogel degradation.

4. Standard curves for RSV

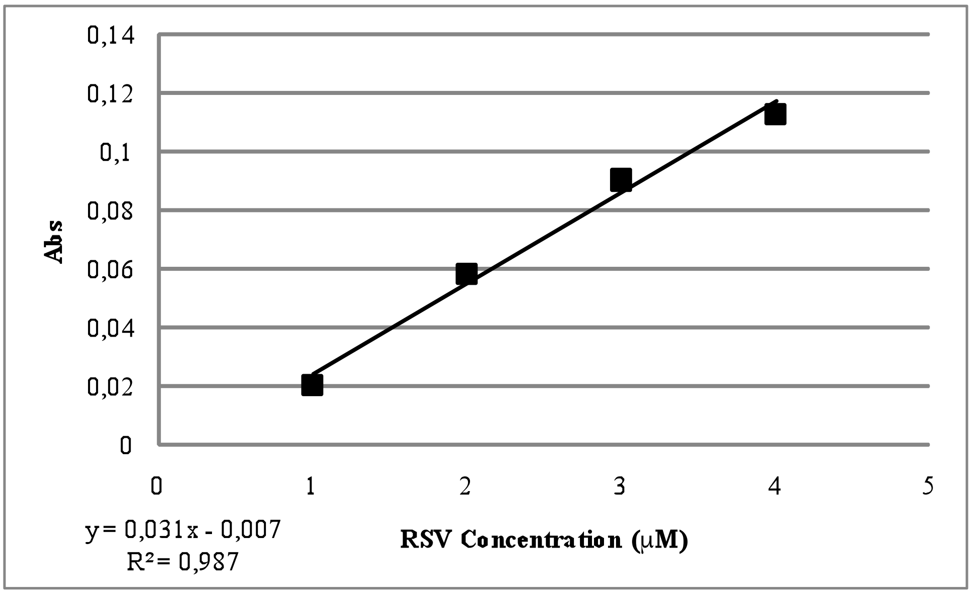


Figure S7. Standard curve of RSV in water using UV-visible spectrophotometry ($\lambda_{máx}$= 310 nm, cuvette path length 1 cm).

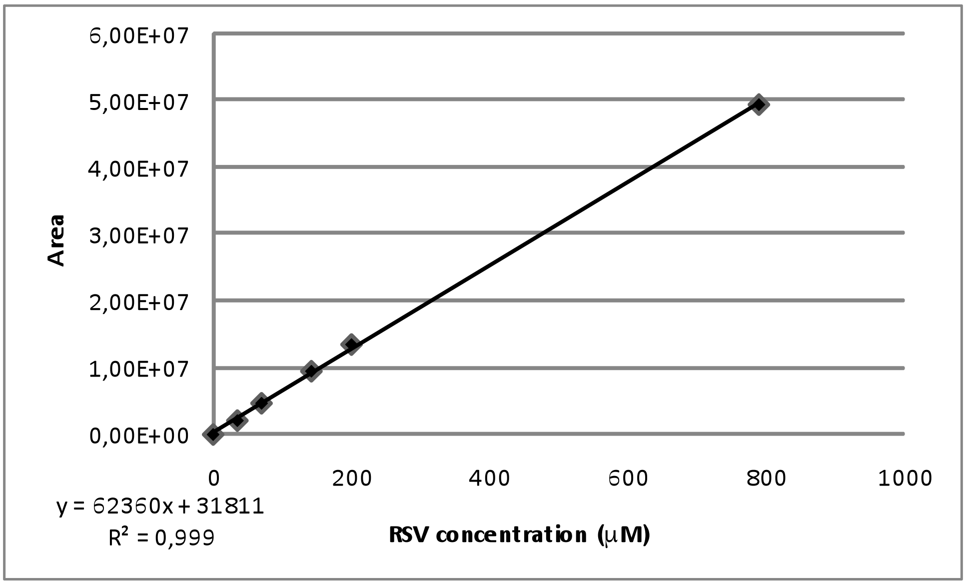


Figure S8. Standard curve of RSV using HPLC.

5. Model release parameters

Table S1. Model release parameters for *hydrogels* **κ-C:gelatin 4 % w/v** at pH 1.2, according to different mathematical models.

Mathematical model	*k*	r^2
First order	-0.0535	0.992
Higuchi	0.21	0.968
Korsmeyer-Peppas	2.85 (n= 0.7)	0.986
Weibull	-2.94× 10^{24} (a= 0.002, b= 0.05)	0.985

Table S2. Model release parameters for *hydrogels* **κ-C:gelatin 3 % w/v** at pH 1.2 according to different mathematical models.

Mathematical model	*k*	r^2
First order	-0.7189	0.997
Higuchi	0.28	0.989
Korsmeyer-Peppas	3.22 (n= 0.60)	0.993
Weibull	-2.94× 10^{24} (a= 0.005, b= 0.05)	0.994

Table S3. Model release parameters for *hydrogels* **κ-C:gelatin 2 % w/v** at pH 1.2 according to different mathematical models.

Mathematical model	*k*	r^2
First order	-1.070	0.998
Higuchi	0.38	0.992
Korsmeyer-Peppas	3.69 (n= 0.50)	0.985
Weibull	-2.94× 10^{24} (a= 0.013, b= 0.04)	0.988

Table S4. Model release parameters for *hydrogels* **κ-C:gelatin 4 % w/v** at pH 6.8, according to different mathematical models.

Mathematical model	*k*	r^2
First order	-0.1366	0.998
Higuchi	0.11	0.984
Korsmeyer-Peppas	1.06 (n= 0.65)	0.998
Weibull	-2.94× 10^{24} (a= -0.002, b= 0.05)	0.997

Table S5. Model release parameters for *hydrogels* **KC:gelatin 3 % w/v** at pH 6.8 according to different mathematical models.

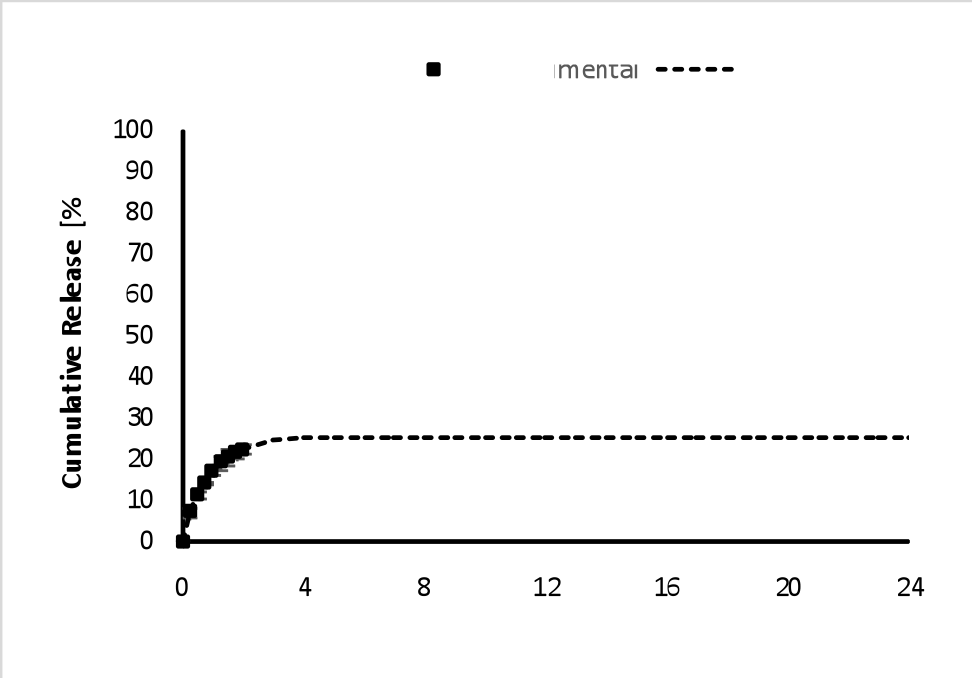
Mathematical model	*k*	r^2
First order	-0.1062	0.991
Higuchi	0.14	0.991
Korsmeyer-Peppas	2.14 (n= 0.61)	0.998
Weibull	-2.94× 10^{24} (a= -0.019, b= 0.05)	0.998

Table S6. Model release parameters for *hydrogels* **κ-C:gelatin 2 % w/v** at pH 6.8 according to different mathematical models.

Mathematical model	*k*	r^2
First order	-0.1110	0.990
Higuchi	0.18	0.970
Korsmeyer-Peppas	2.21 (n= 0.72)	0.986
Weibull	-2.94×10^{24} (a= 0.001, b= 0.05)	0.988

Table S7. Correlation coefficients obtained by fitting the experimental data with First Order, Higuchi, Korsmeyer-Peppas and Weibull models.

pH	Gel formulation κ-C:gelatin (1:1 mass ratio) w/v	Drug release mathematical models			
		First order	Higuchi	Korsmeyer-Peppas	Weibull
1.2	2 %	**0.998**	0.992	0.985	0.988
	3 %	**0.997**	0.989	0.993	0.994
	4 %	**0.992**	0.968	0.986	0.985
6.8	2 %	**0.990**	0.970	0.986	0.988
	3 %	0.991	0.911	**0.998**	**0.998**
	4 %	**0.998**	0.984	**0.998**	0.997



y = y0 + A * exp(R0 * x)	y0	A	R0
	25,27300464	-23,721708	-1,06978171

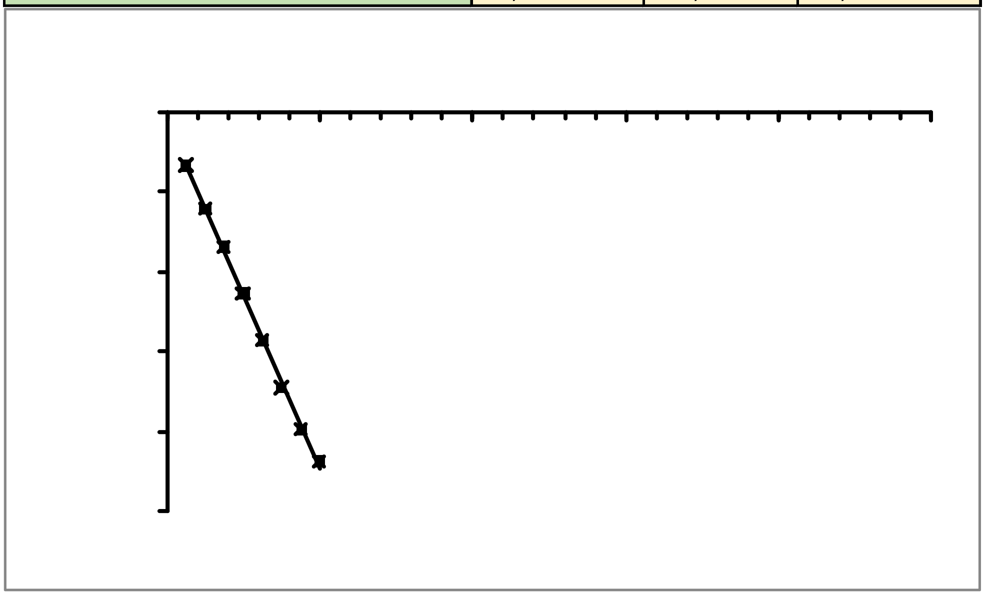
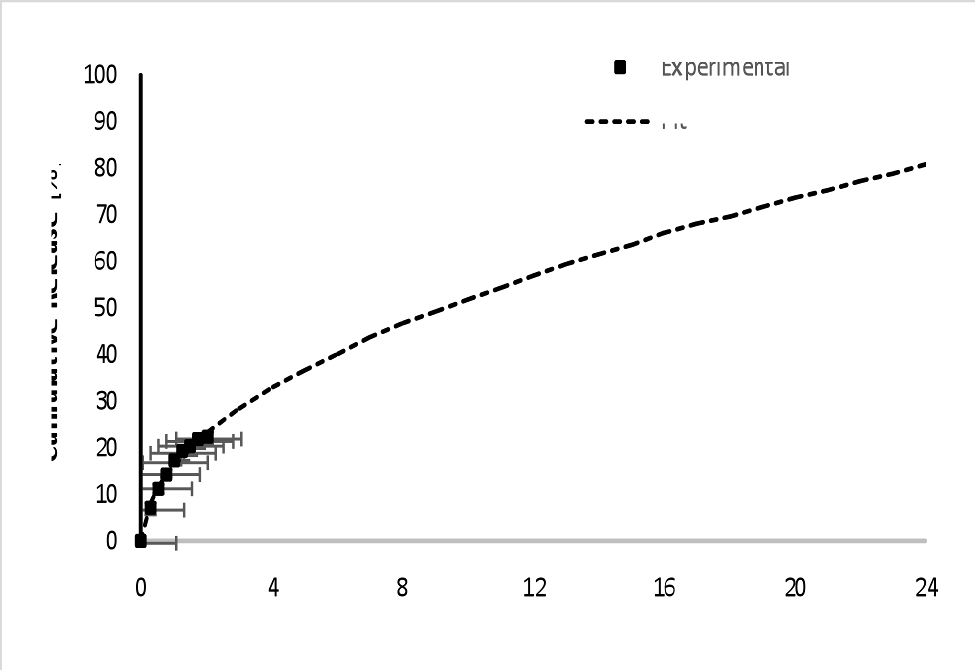


Figure S9. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. First order kinetic model at pH 1.2.



$y = y\infty * k * \sqrt{t}$	y∞	k
	43,0351502	0,38268156

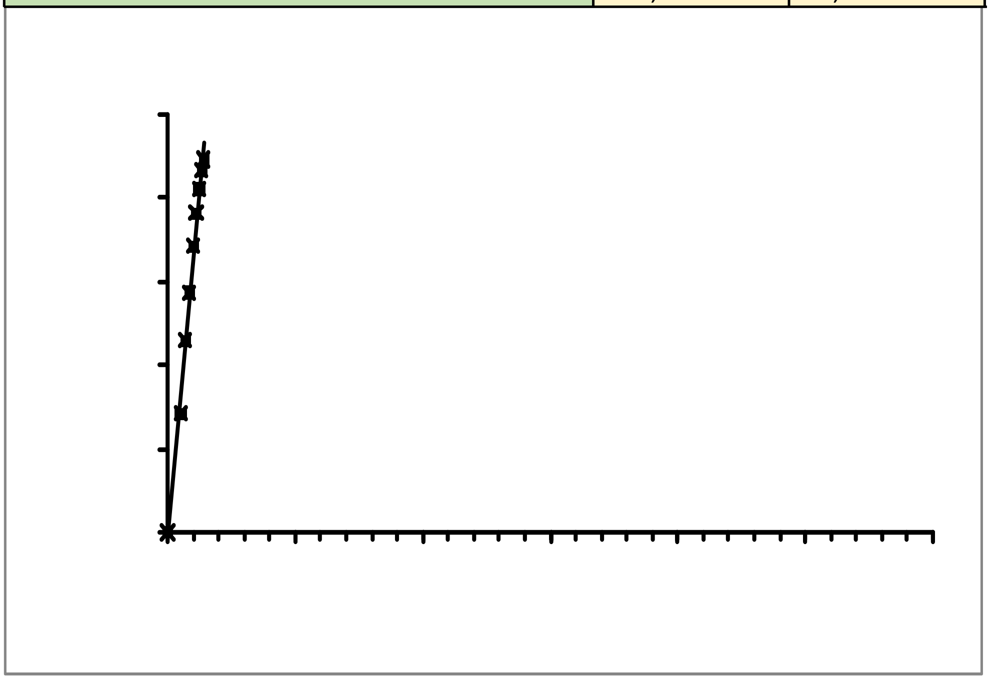
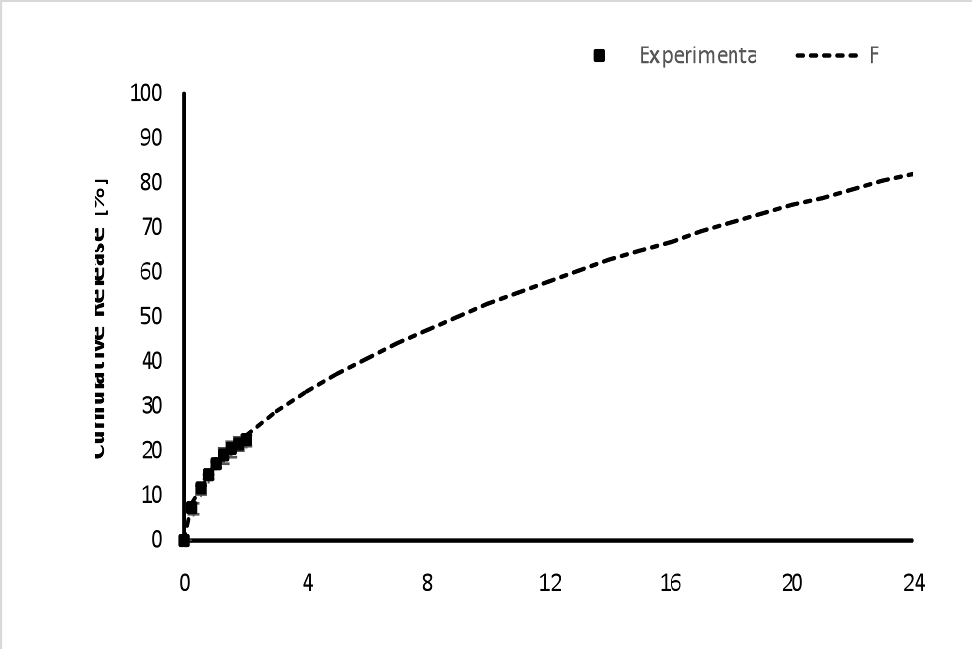


Figure S10. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Higuchi model at pH 1.2.



$y = y\infty * k * t^n$	y∞	k	n
	4,451031501	3,694046376	0,506153561

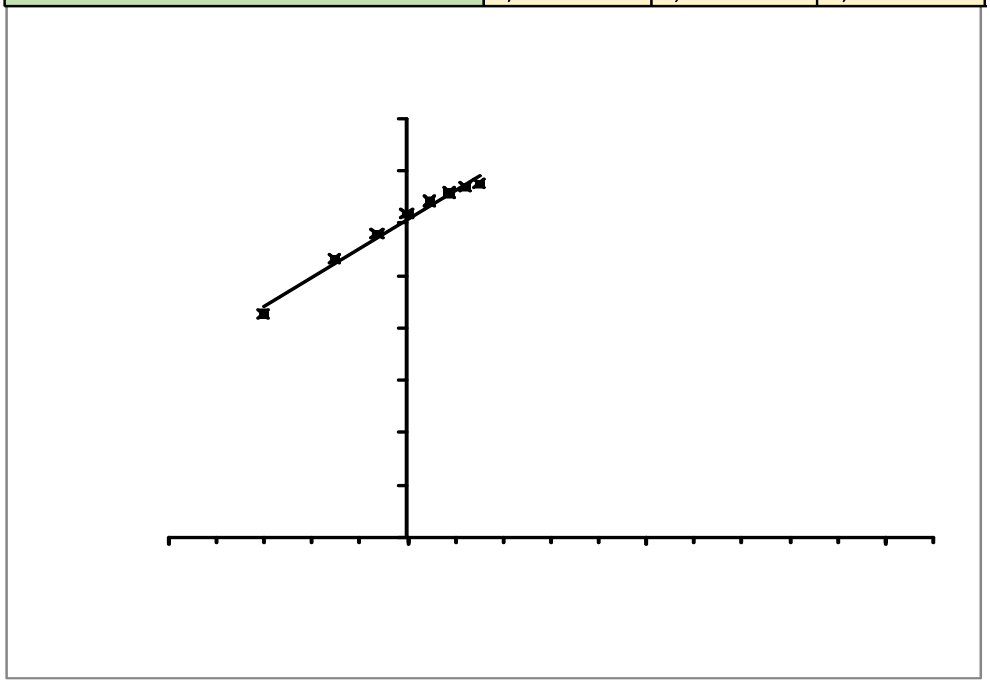
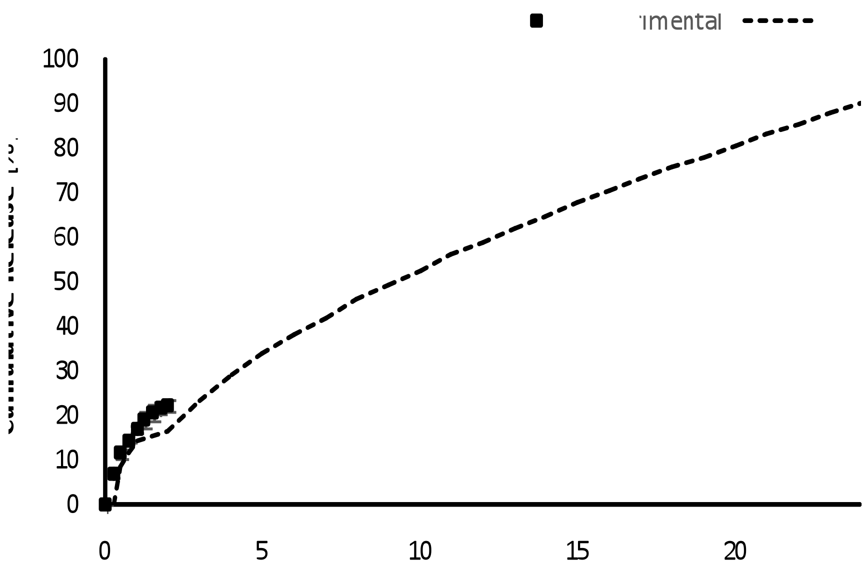
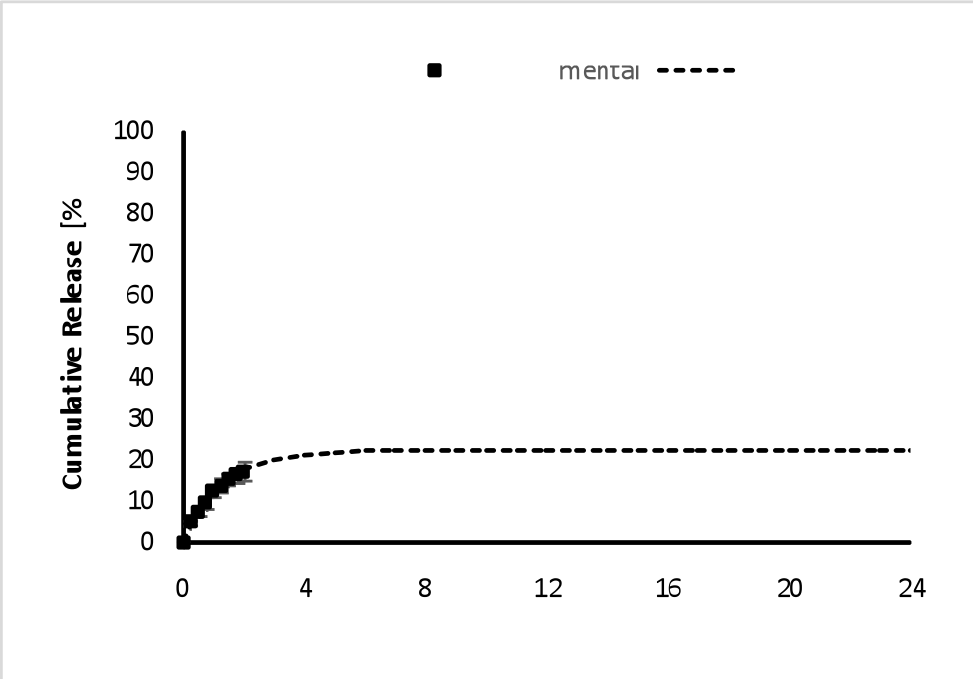


Figure S11. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Korsmeyer-Peppas model at pH 1.2.



$y = y_\infty * a * (1-\exp(-(kt)^b))$	y∞	a	k	b
	-0,01126133	0,013	-2,94647E+24	0,04

Figure S12. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Weibull model at pH 1.2.



y = y0 + A * exp(R0 * x)	y0	A	R0
	22,52075146	-21,323002	-0,718924601

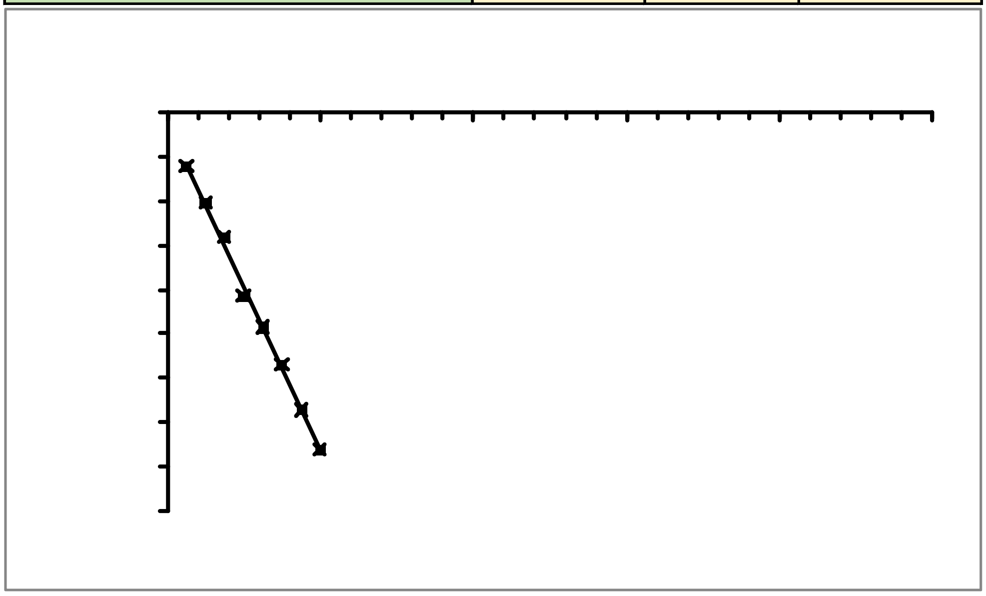
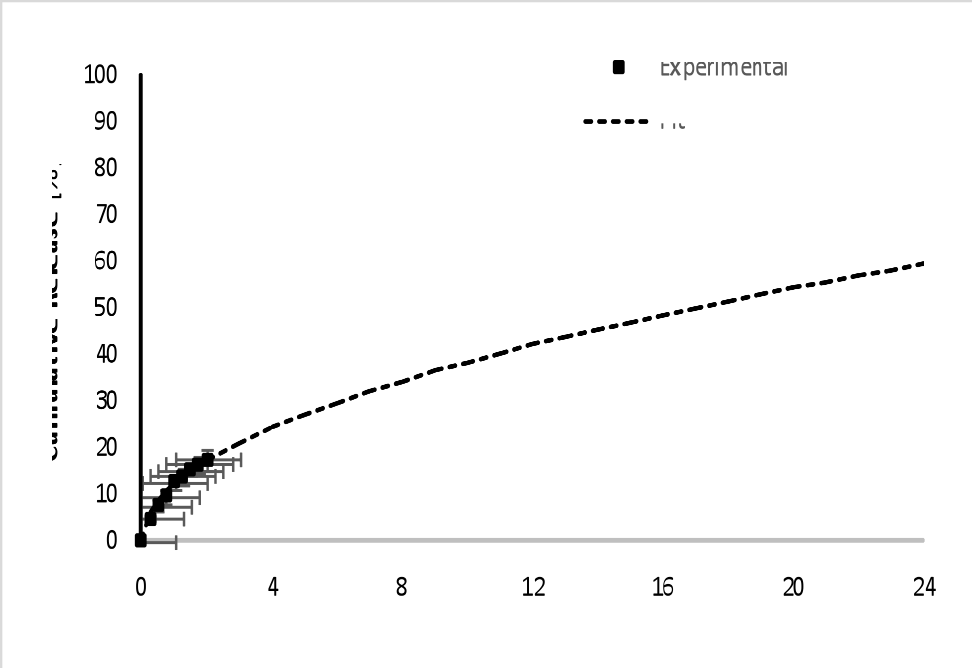


Figure S13. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . First order kinetic model at pH 1.2.



$y = y_{\infty} * k * \sqrt{t}$	y_{∞}	k
	43,0341866	0,2820662

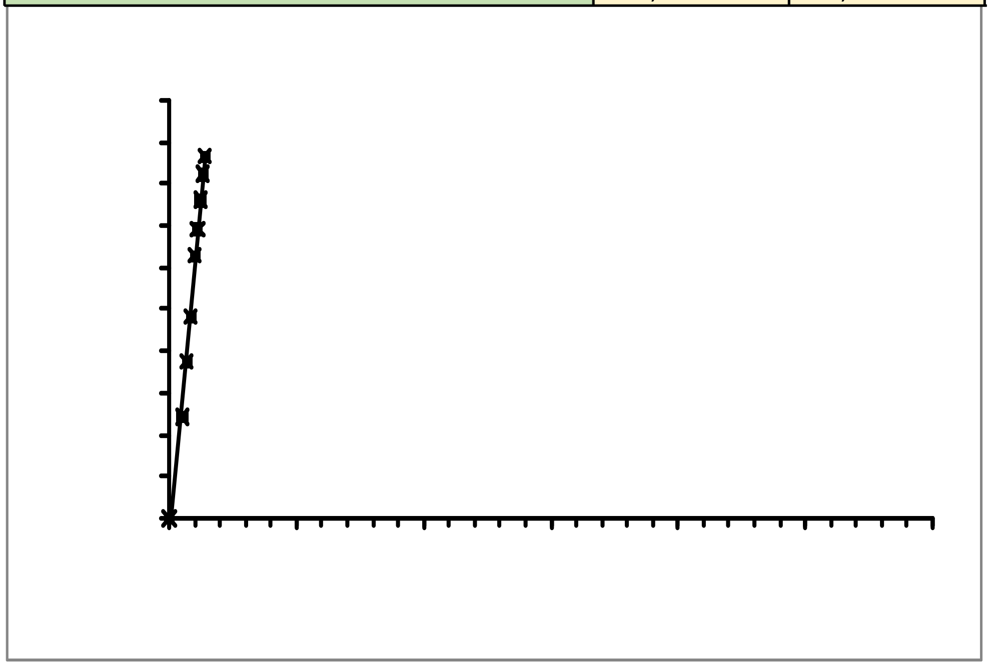
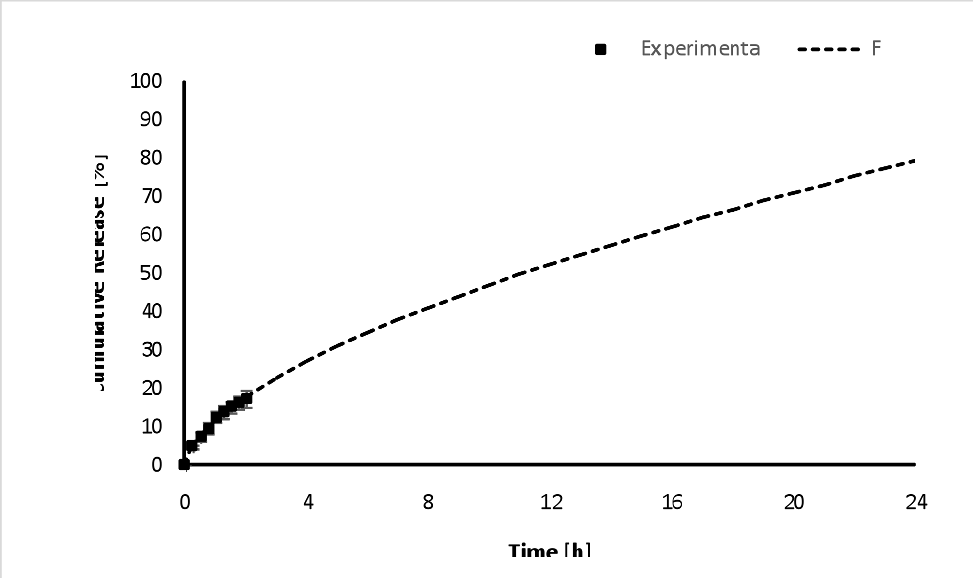


Figure S14. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Higuchi model at pH 1.2.



$y = y_\infty * k * t^n$	y∞	k	n
	3,666458912	3,22361686	0,598440286

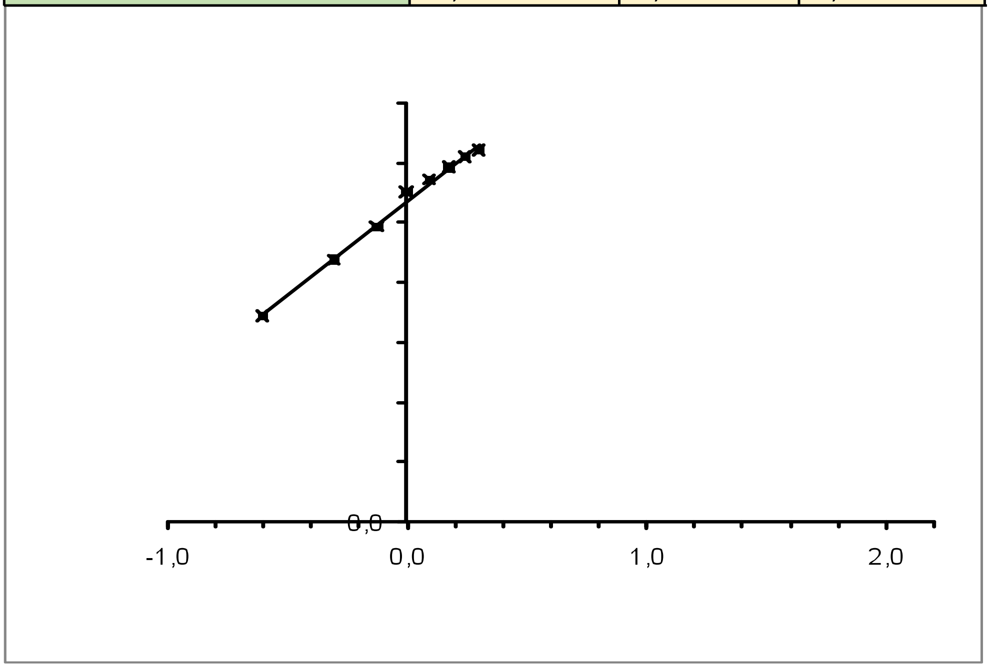
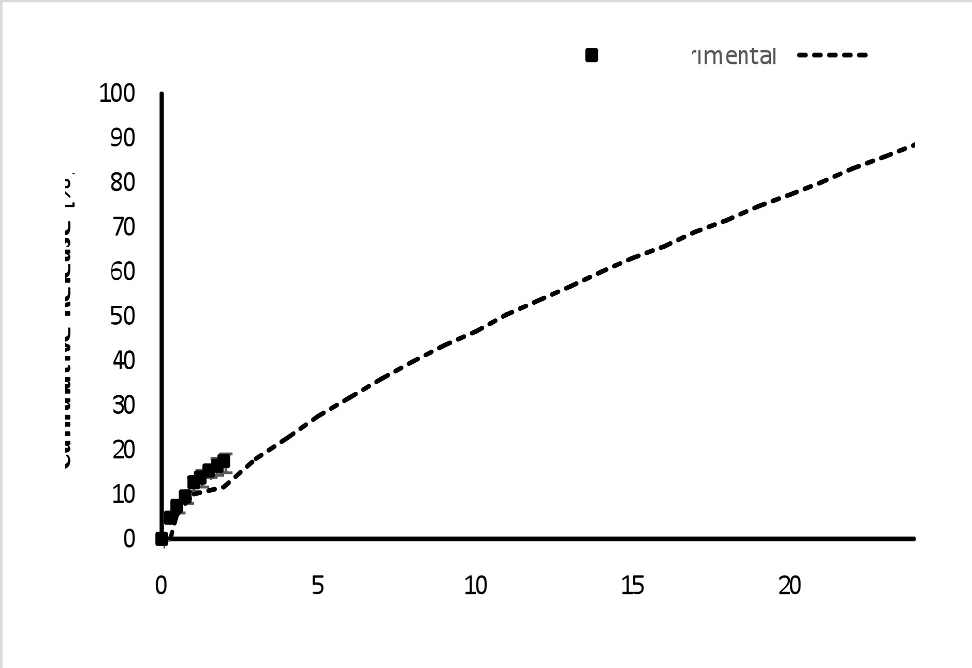


Figure S15. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Korsmeyer-Peppas model at pH 1.2.



y = y∞ * a * (1-exp(-(kt)^b))	y∞	a	k	b
	-0,00471097	0,005	-2,94647E+24	0,05

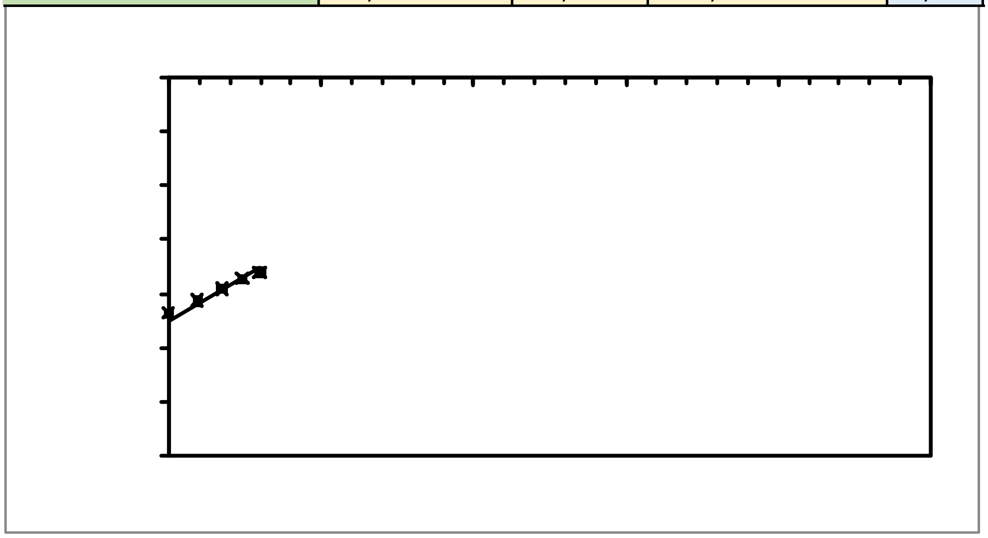
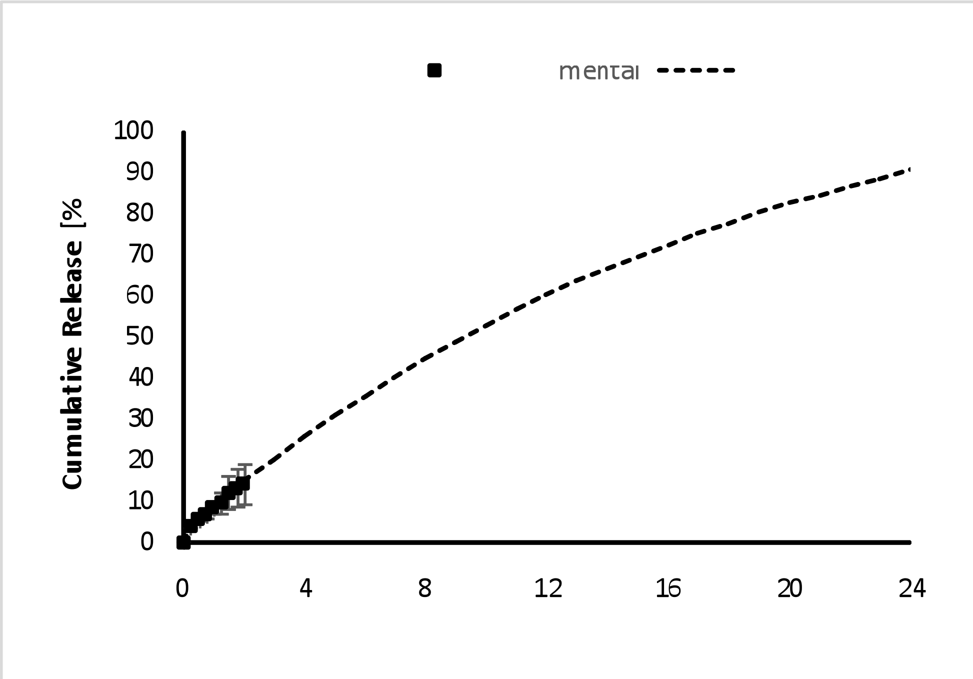


Figure S16. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Webull model at pH 1.2.



y = y0 + A * exp(R0 * x)	y0	A	R0
	124,2026331	-122,07231	-0,053555867

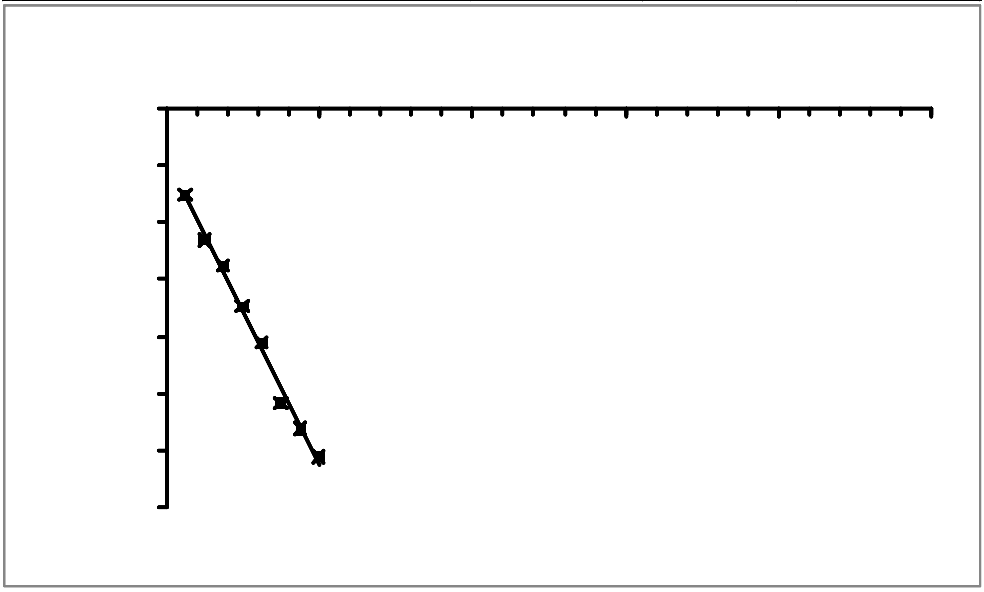
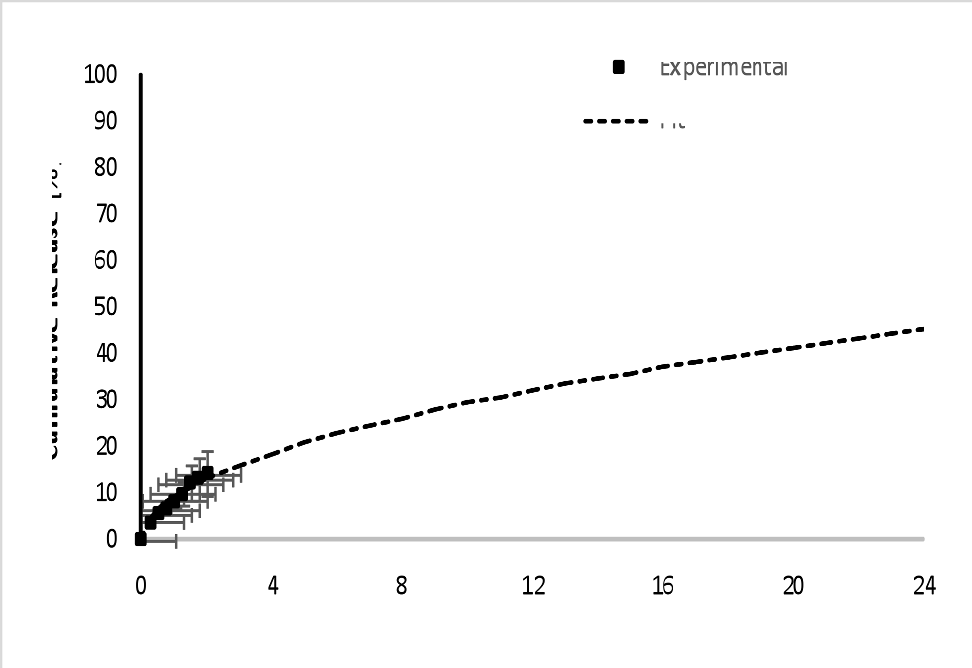


Figure S17. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . First order kinetic model at pH 1.2.



$y = y_\infty * k * \sqrt{t}$	y_∞	k
	43,0342093	0,21519152

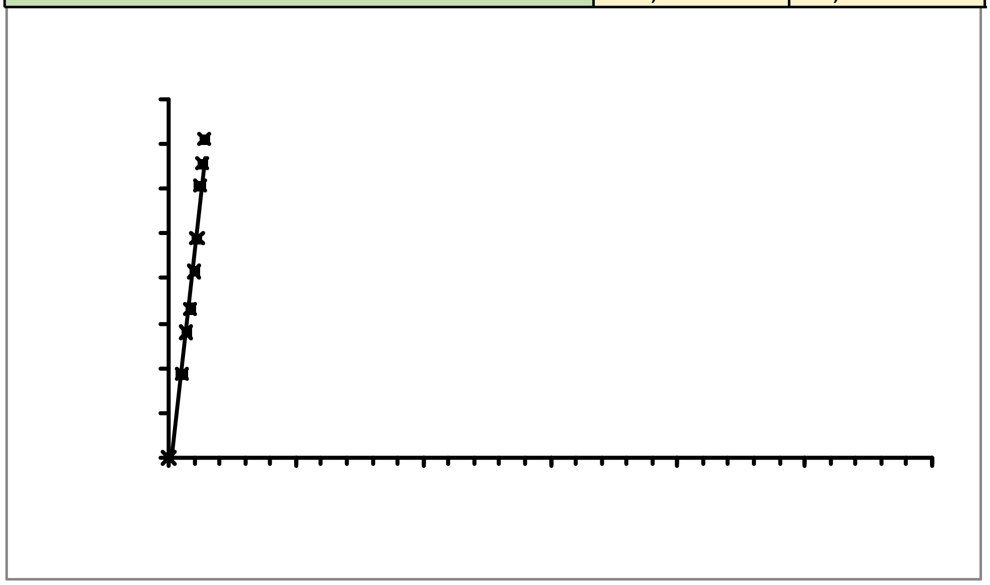
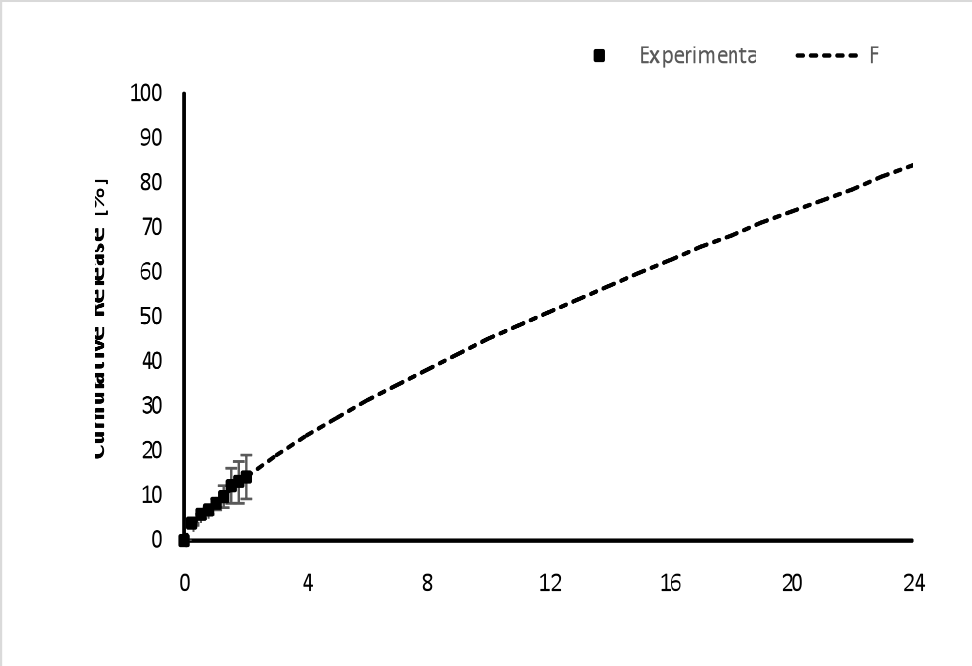


Figure S18. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Higuchi model at pH 1.2.



$y = y\infty * k * t^n$	y∞	k	n
	3,059859444	2,850225979	0,711737189

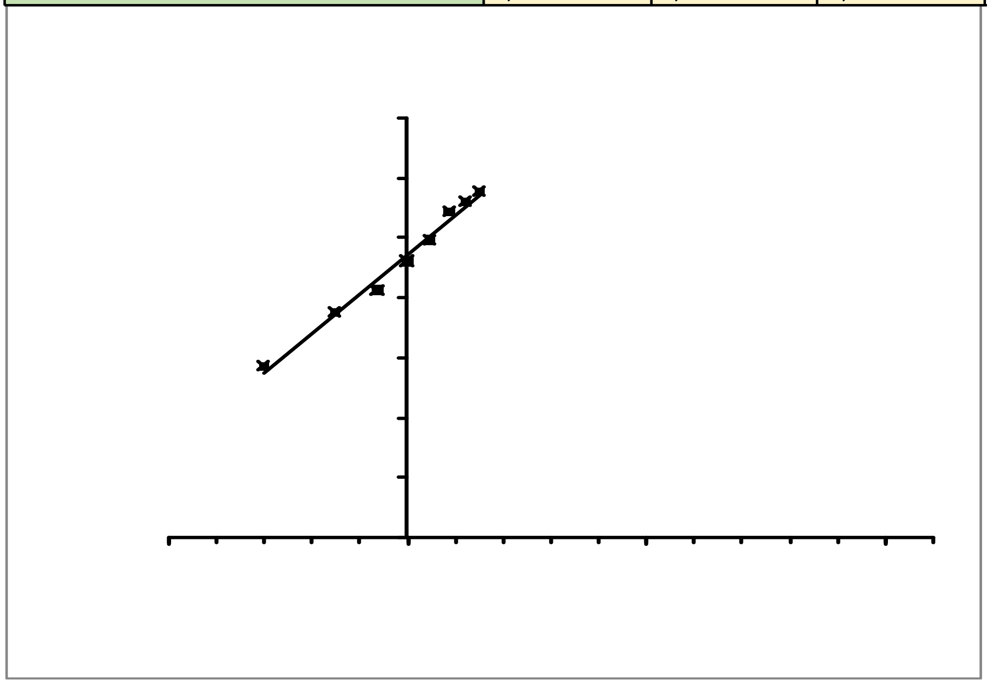
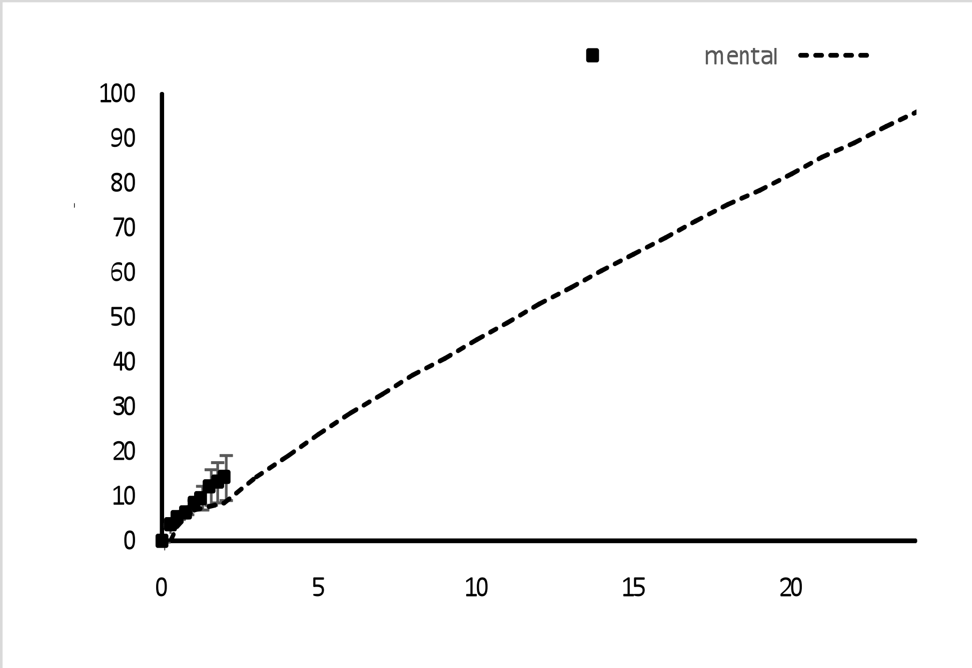


Figure S19. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Korsmeyer-Peppas model at pH 1.2.



$y = y\infty * a * (1-\exp(-(kt)^b)$	y∞	a	k	b
	-0,00163361	0,002	-2,94647E+24	0,05

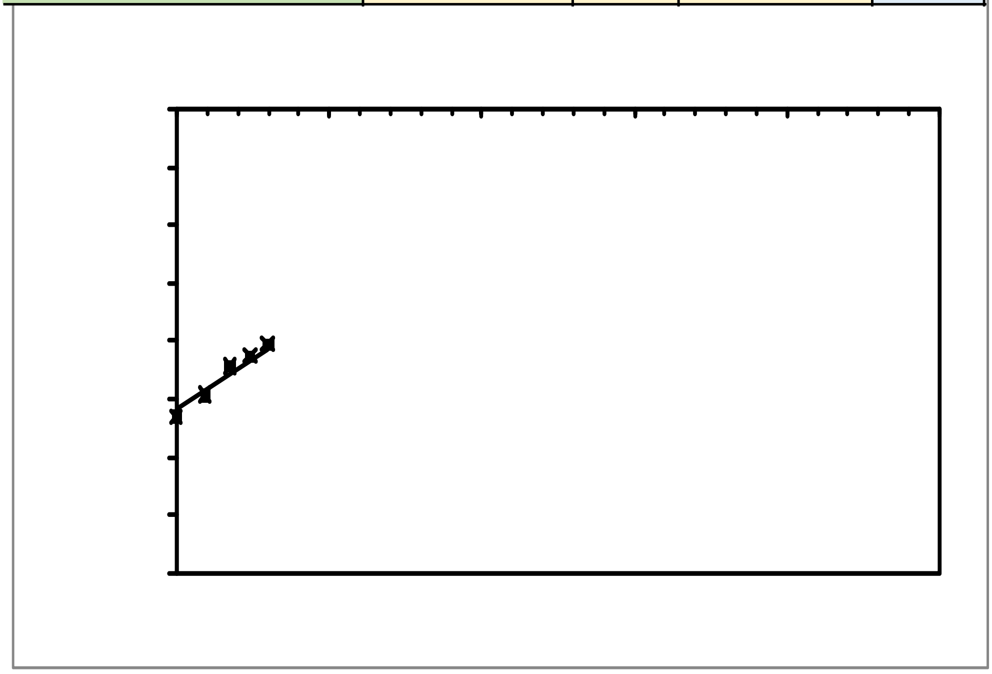
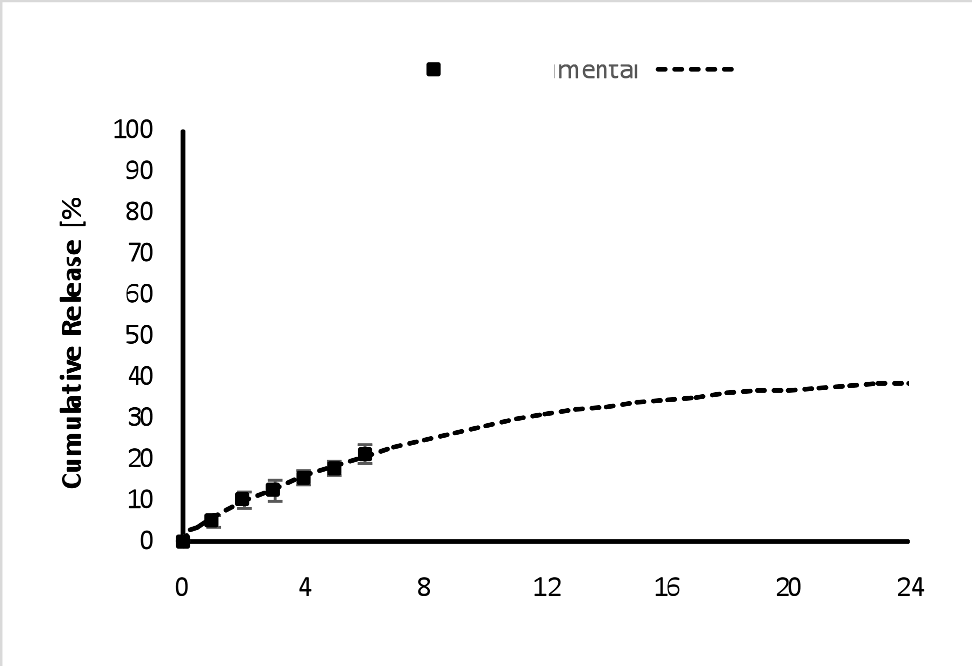


Figure S20. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Weibull model at pH 1.2.



y = y0 + A * exp(R0 * x)	y0	A	R0
	41,17113248	-39,719648	-0,1110271

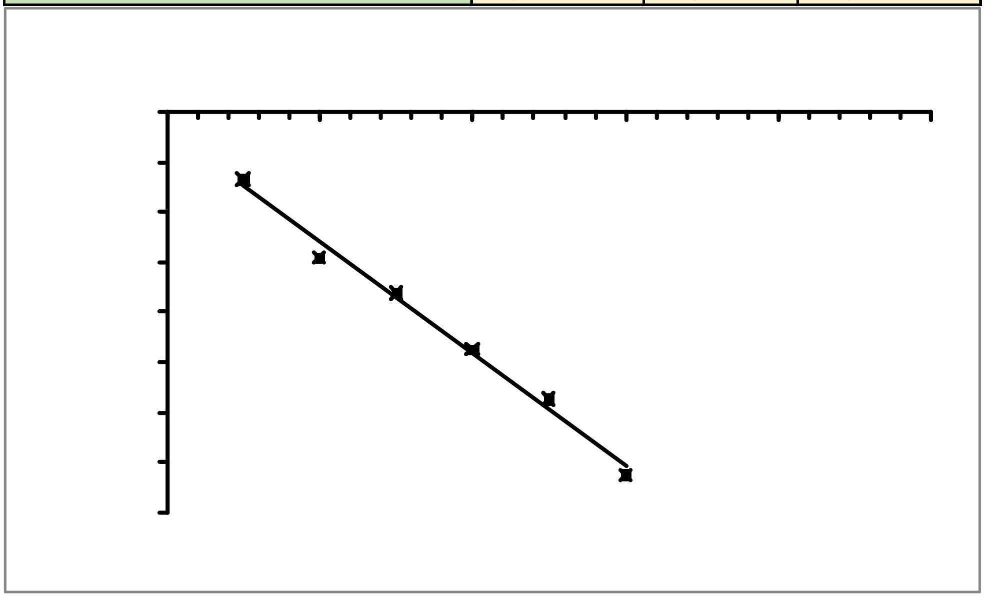
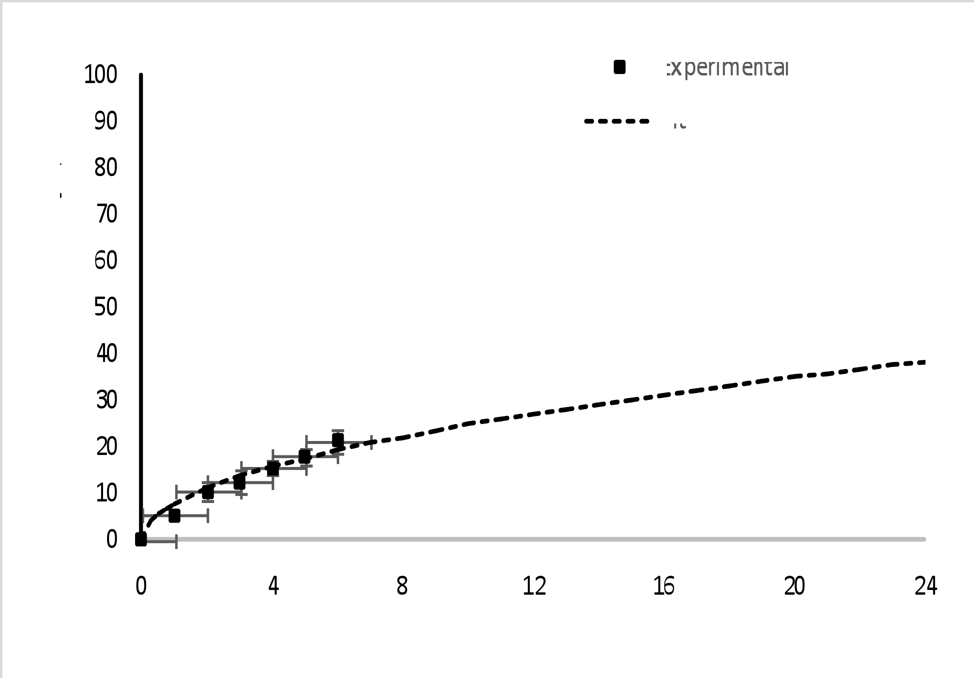


Figure S21. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. First order kinetic model at pH 6.8.



y = y∞ * k * √t	y∞	k
	43,0326545	0,18174104

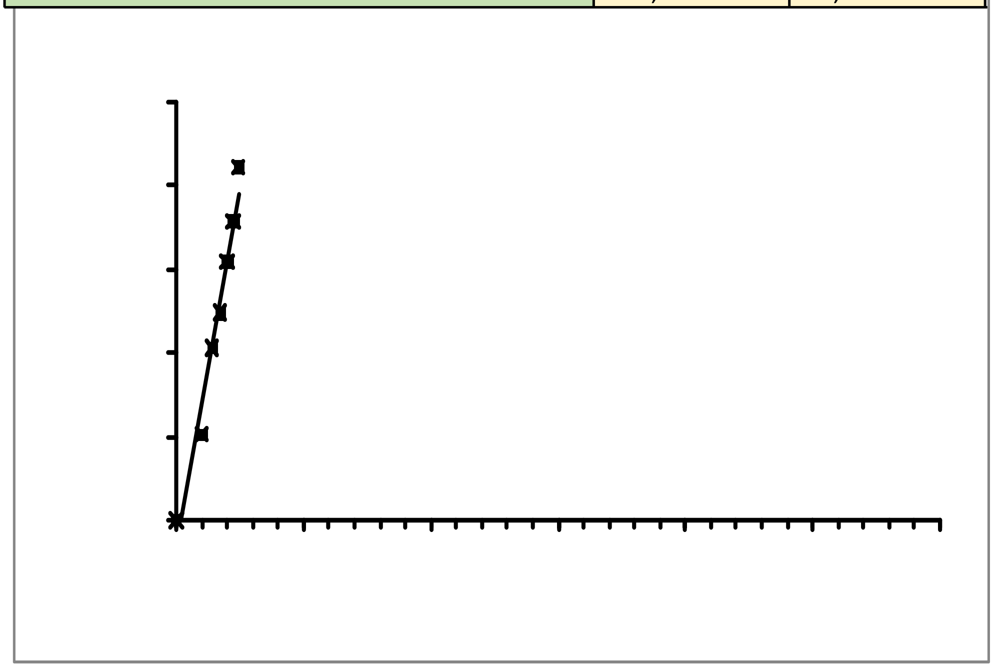
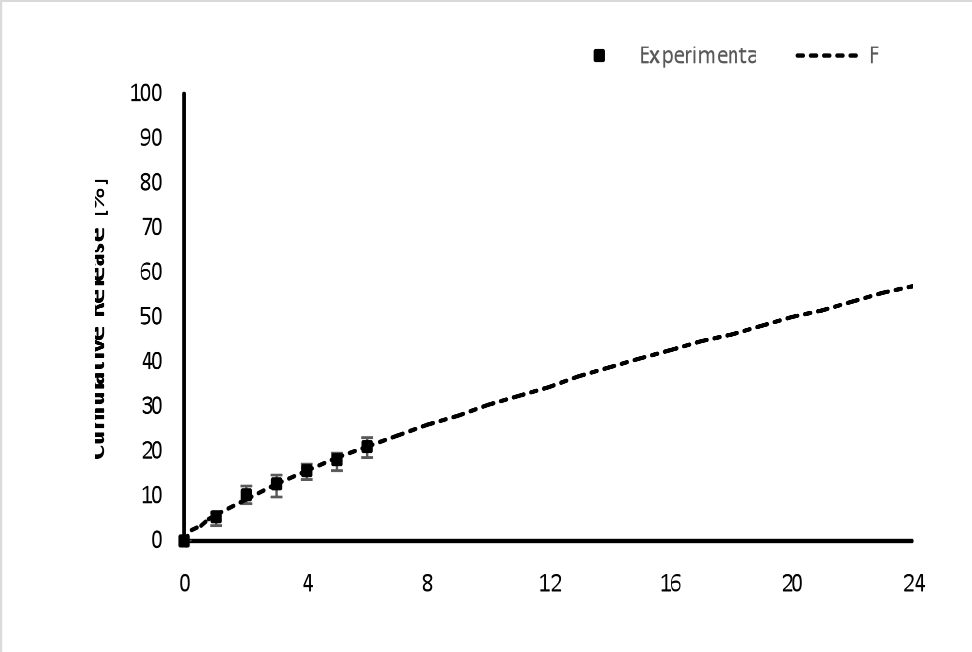


Figure S22. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Higuchi model at pH 6.8.



$y = y\infty * k * t^{n}$	y∞	k	n
	2,590177178	2,207520646	0,723063491

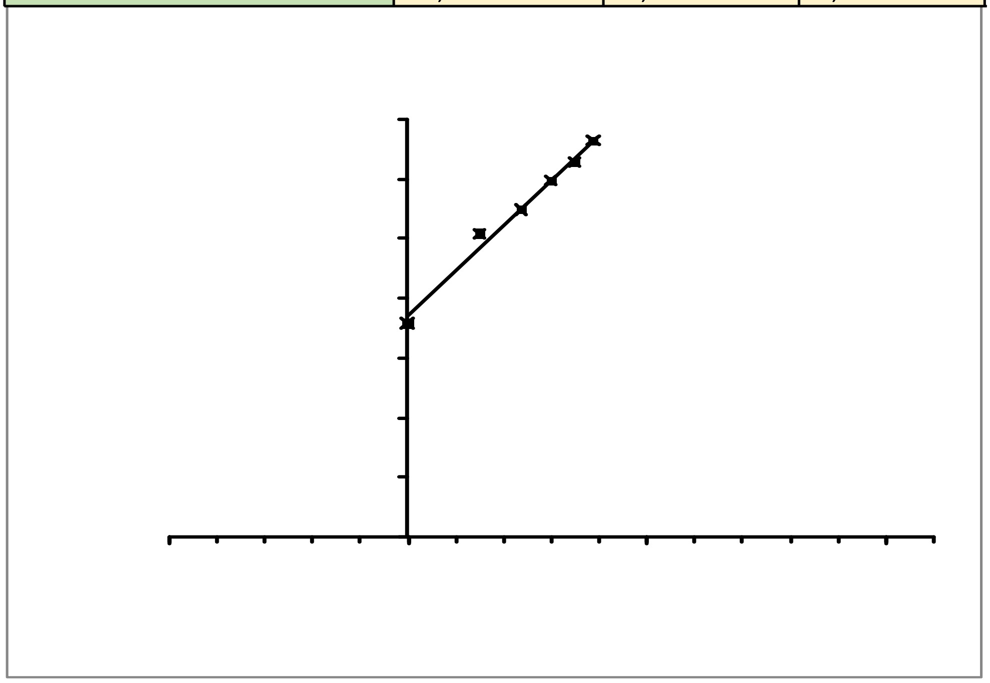
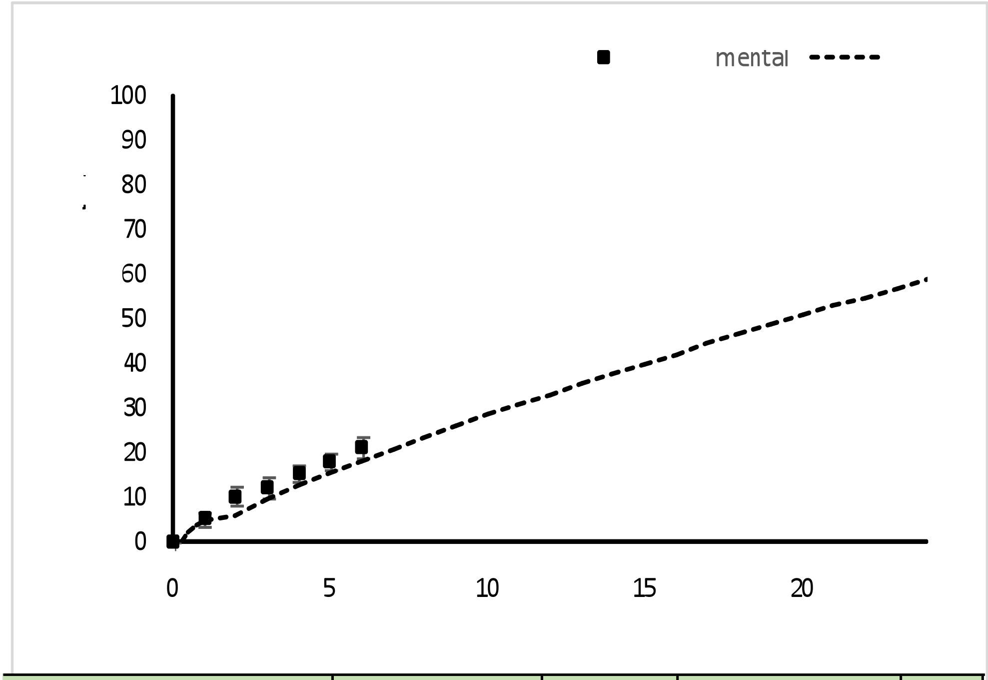


Figure S23. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Korsmeyer-Peppas model at pH 6.8.



$y = y\infty * a * (1-\exp(-(kt)^b)$	y∞	a	k	b
	-0,00312707	0,001	-2,94647E+24	0,05

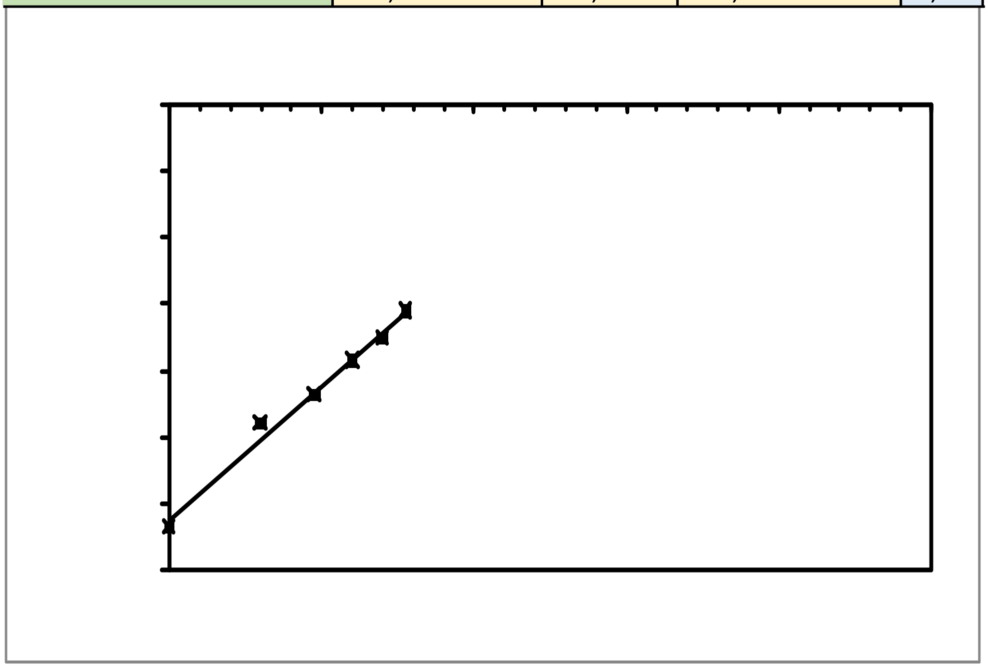
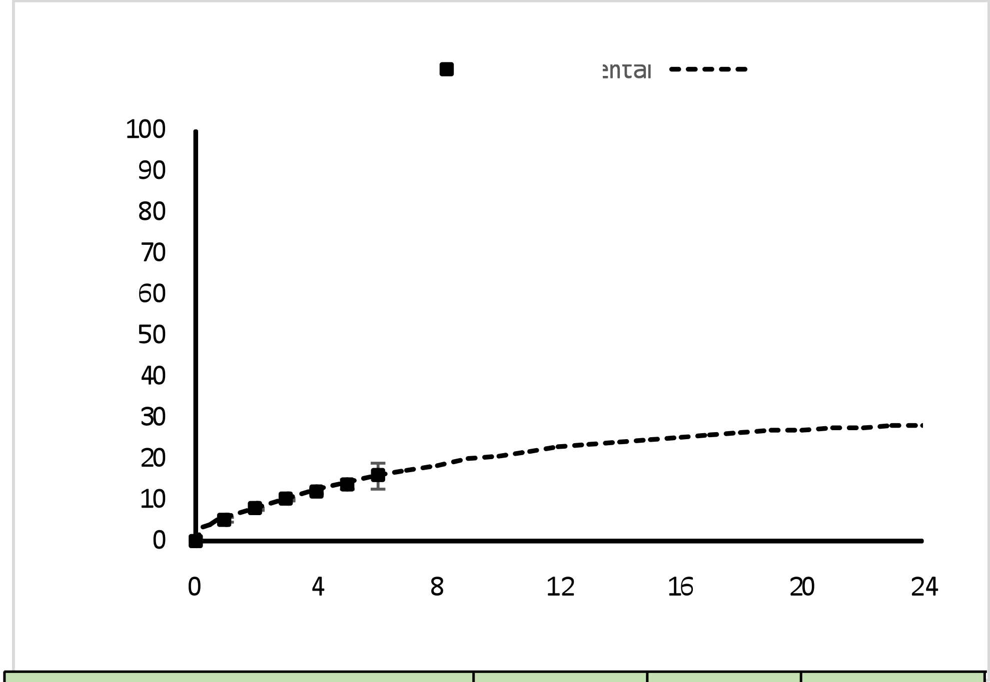


Figure S24. 2 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Weibull model at pH 6.8.



$y = y0 + A * \exp(R0 * x)$	y0	A	R0
	30,41499475	-27,764555	-0,106231109

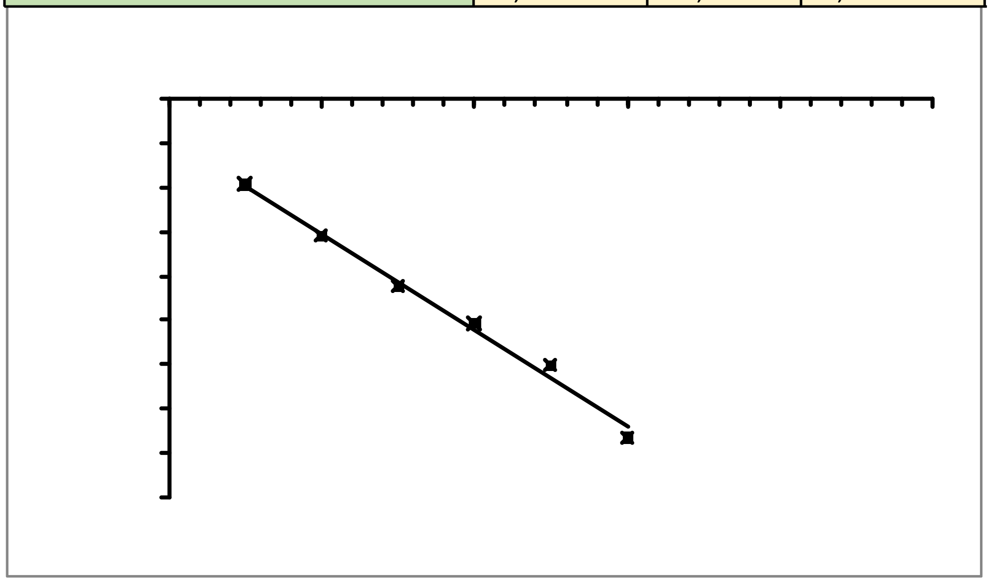
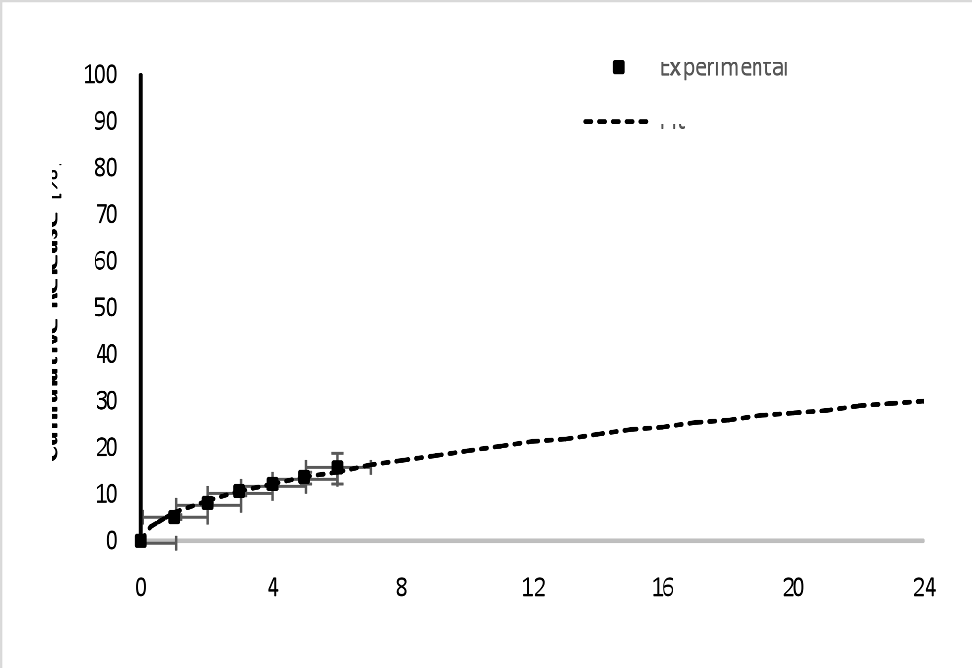


Figure S25. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . First order kinetic model at pH 6.8.



y = y∞ * k * √t	y∞	k
	43,0331782	0,1427619

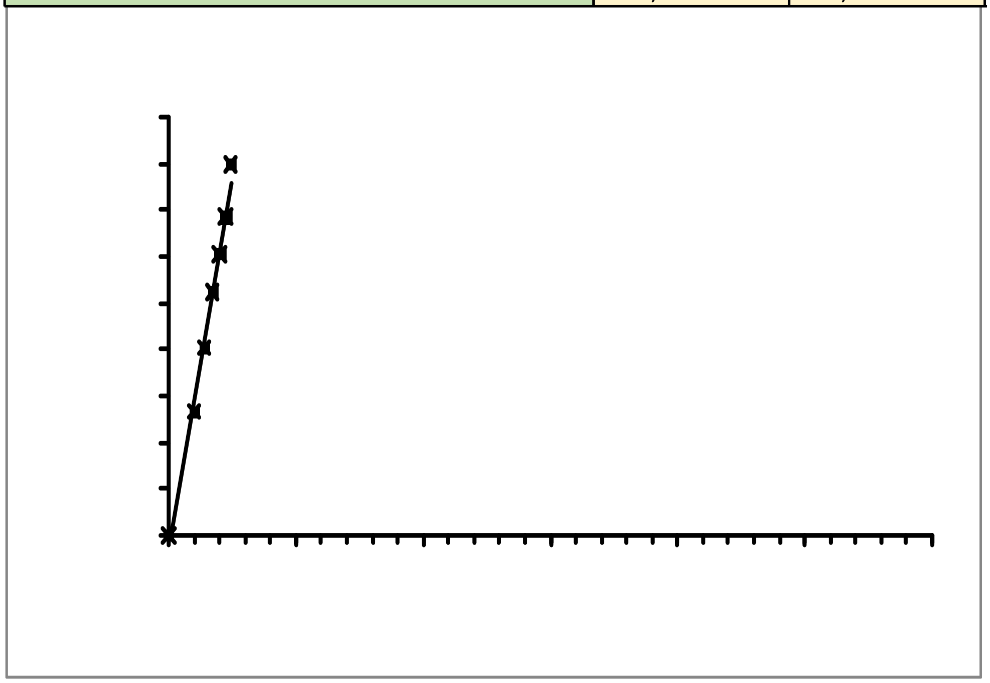
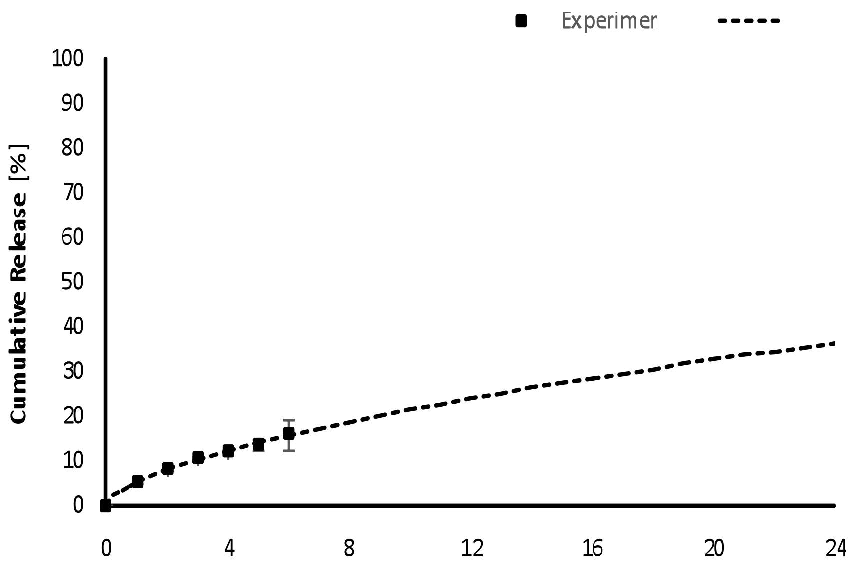


Figure S26. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Higuchi model at pH 6.8.



$y = y\infty * k * t^n$	$y\infty$	k	n
	2,470690501	2,144964828	0,606084034

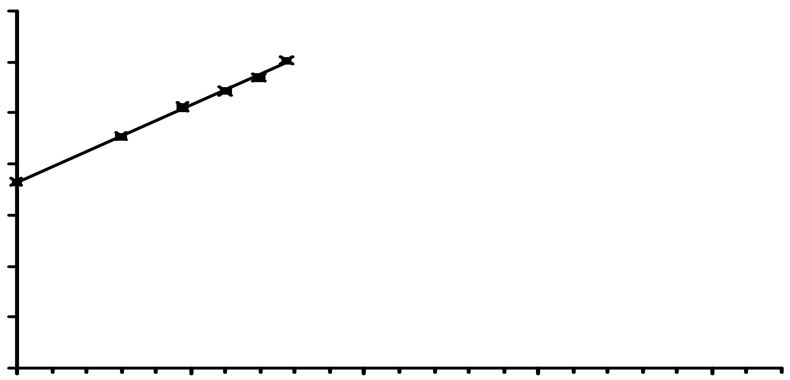
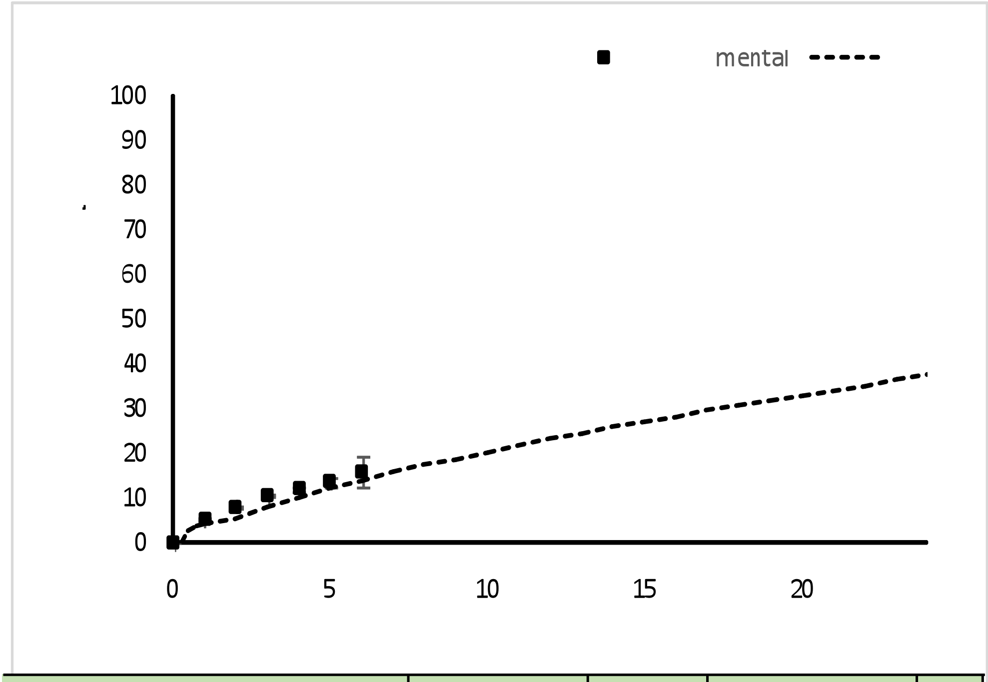


Figure S27. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Korsmeyer-Peppas model at pH 6.8.



$y = y\infty * a * (1\text{-}exp(-(kt)^b)$	$y\infty$	a	k	b
	0,000802502	-0,019	-2,94647E+24	0,05

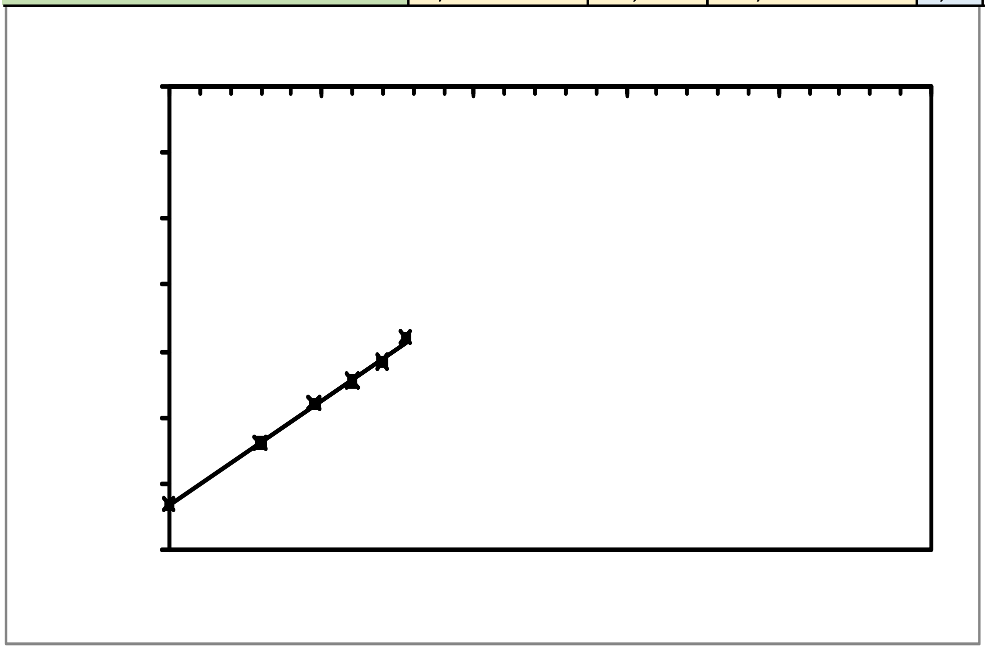
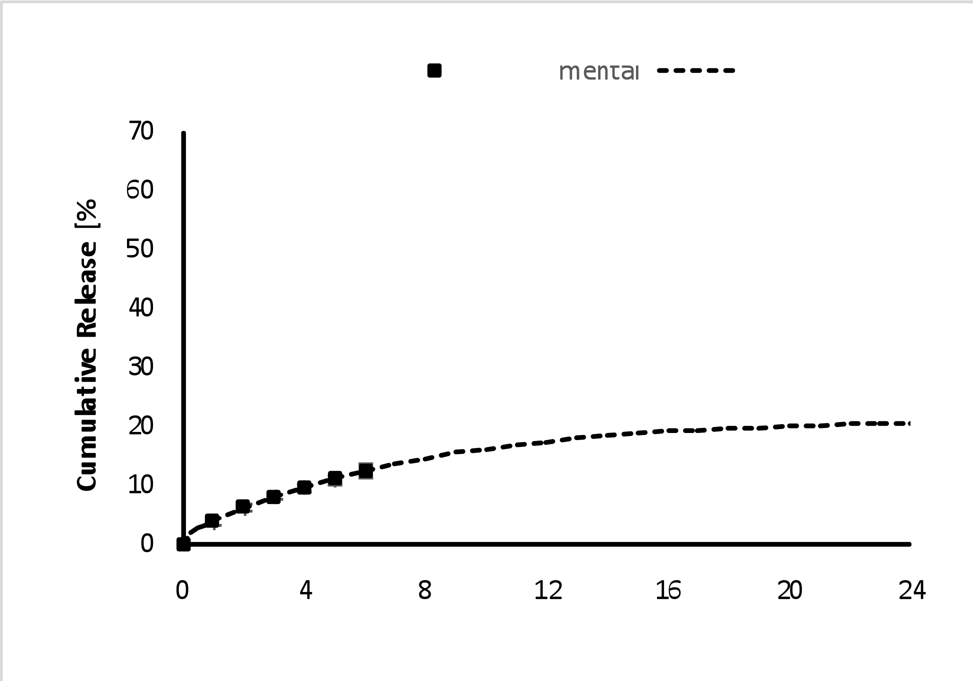


Figure S28. 3 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels . Weibull model at pH 6.8.



y = y0 + A * exp(R0 * x)	y0	A	R0
	21,2557884	-19,938854	-0,136578669

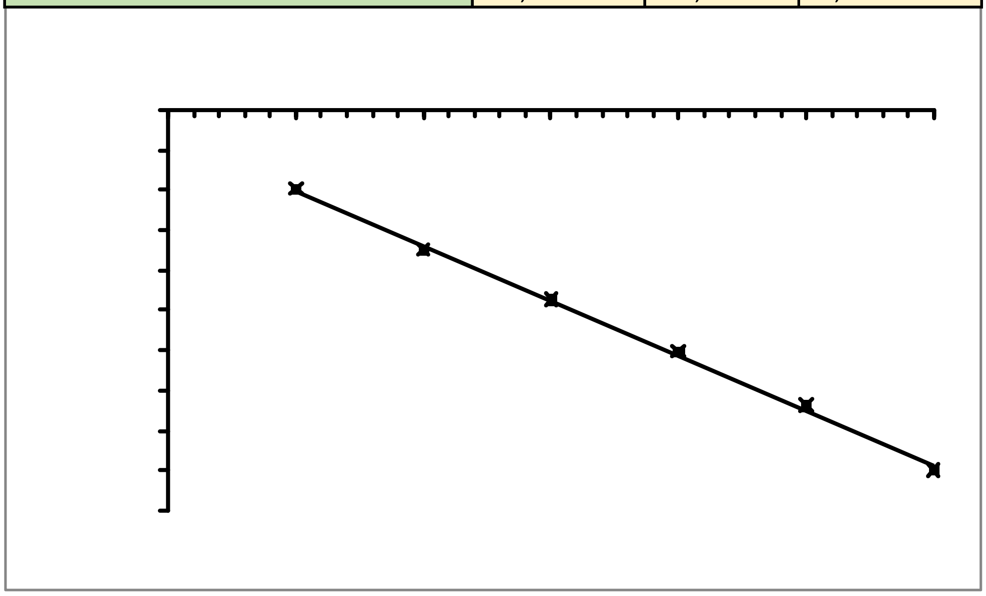
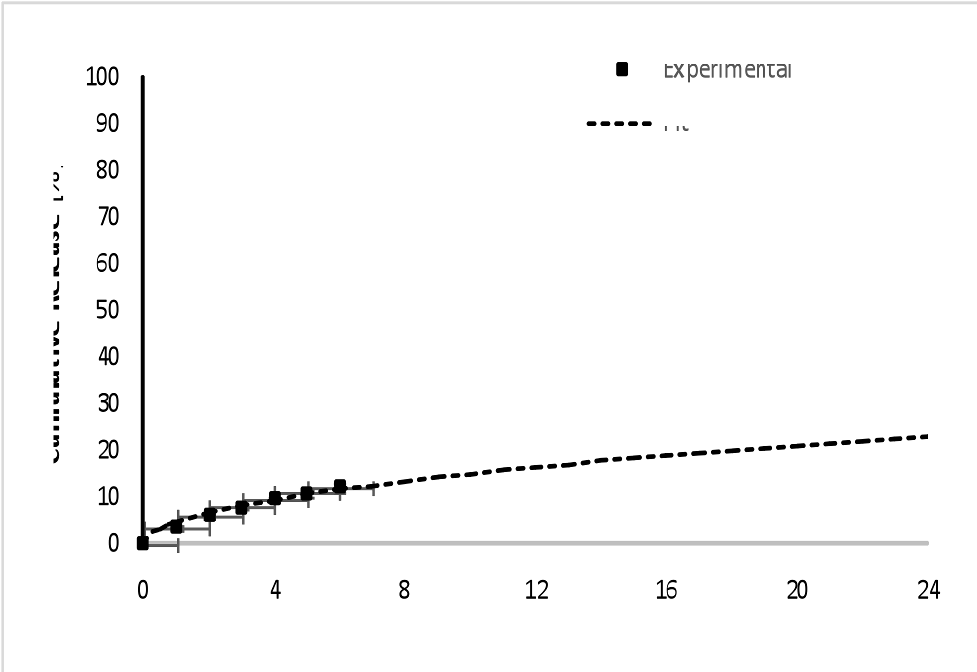


Figure S29. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. First order kinetic model at pH 6.8.



$y = y_\infty * k * \sqrt{t}$	y_∞	k
	43,0338816	0,10942306

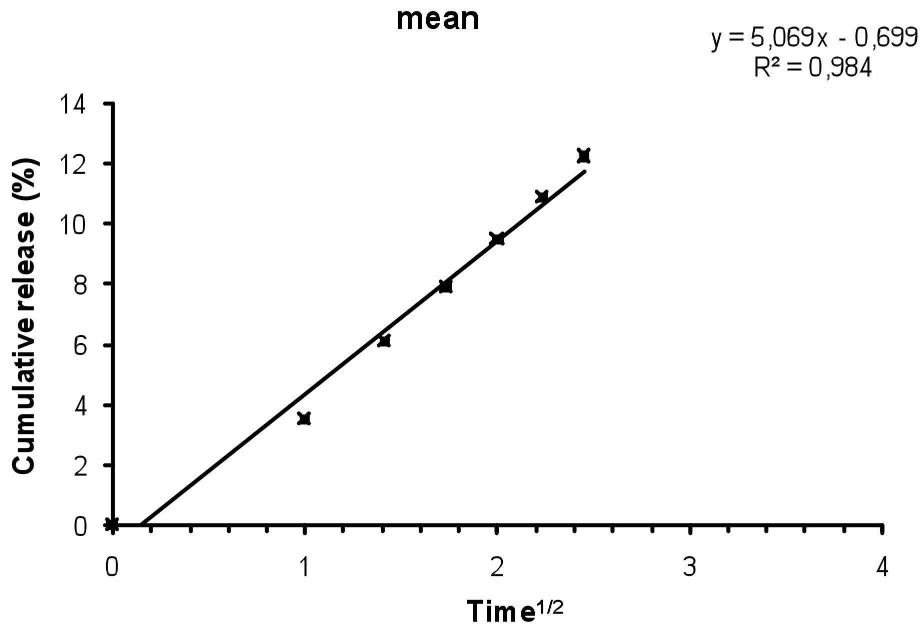
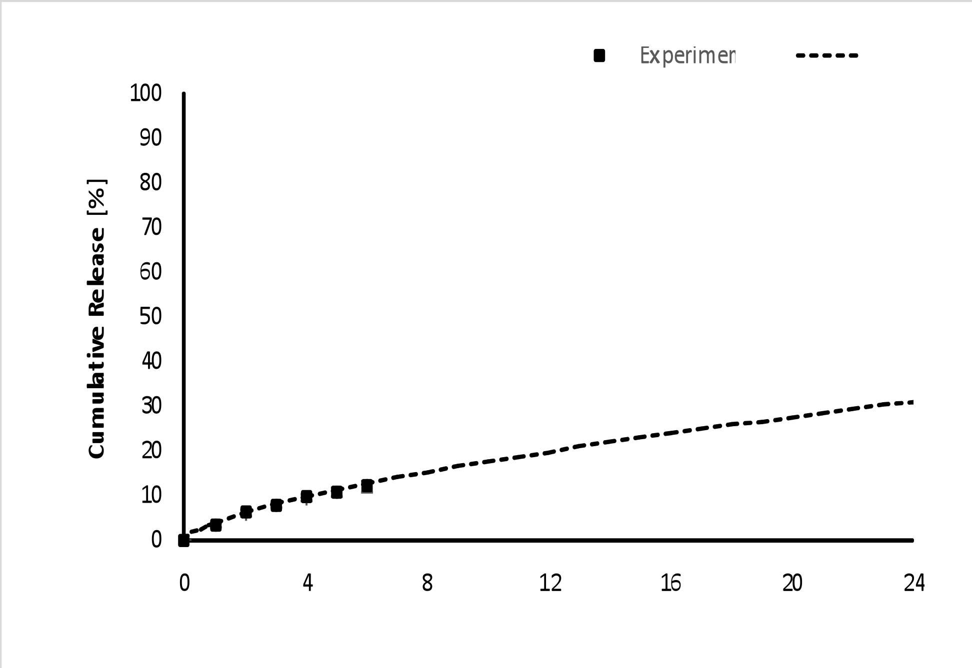


Figure S30. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Higuchi model at pH 6.8.



$y = y\infty * k * t^n$	y∞	k	n
	3,67380291	1,062078706	0,652022313

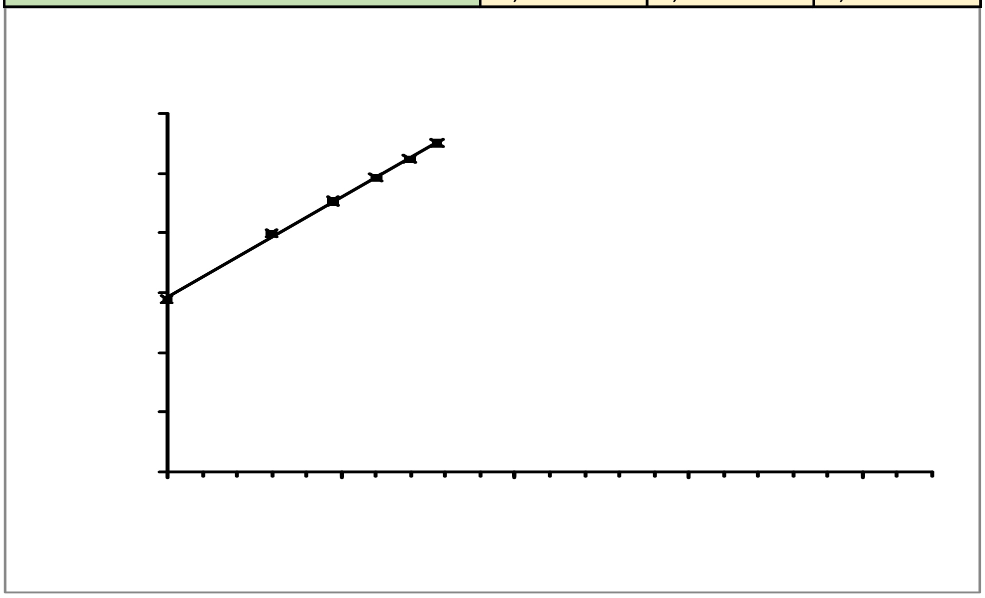
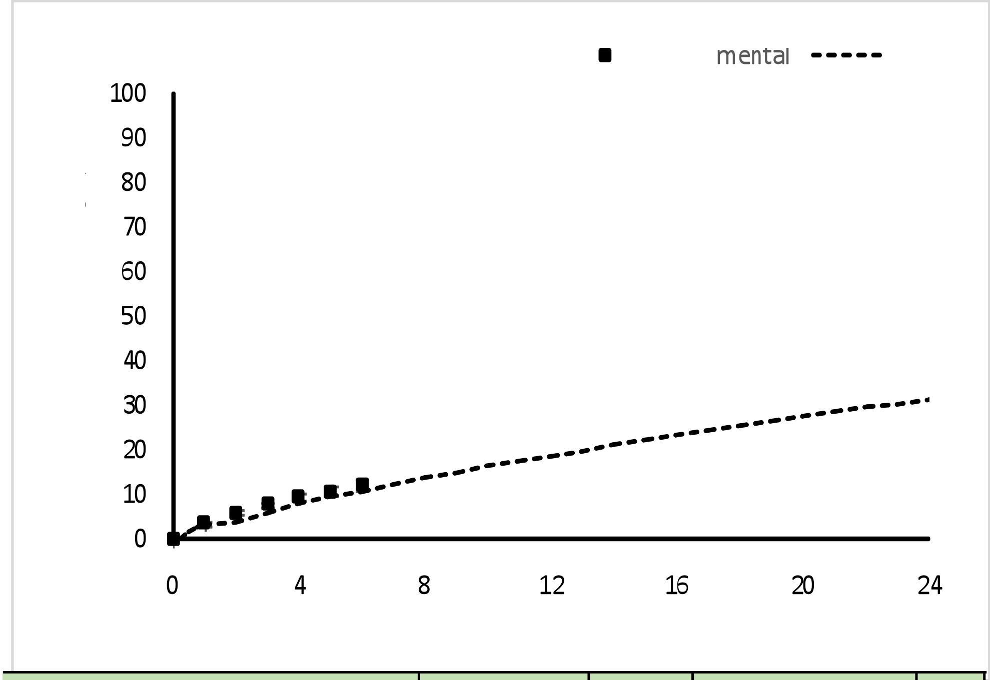


Figure S31. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Korsmeyer-Peppas model at pH 6.8.



$y = y\infty * a * (1\text{-}exp(-(kt)^b)$	y∞	a	k	b
	0,00261181	-0,002	-2,94647E+24	0,05

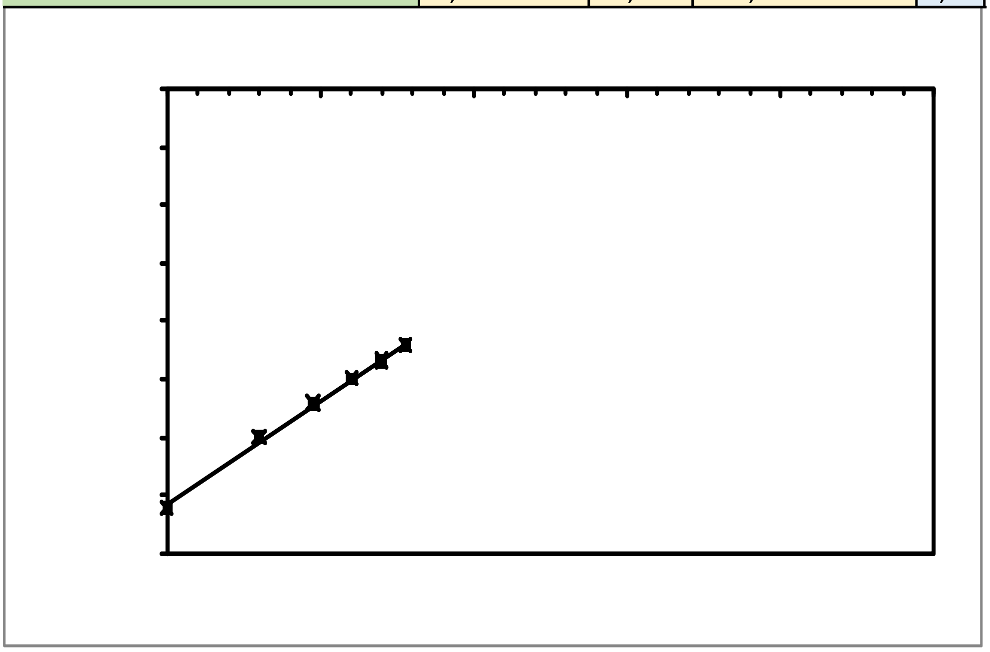


Figure S32. 4 % w/v κ-C:gelatin (1:1 mass ratio) hydrogels. Weibull model at pH 6.8.

6. Photoisomerization experiments

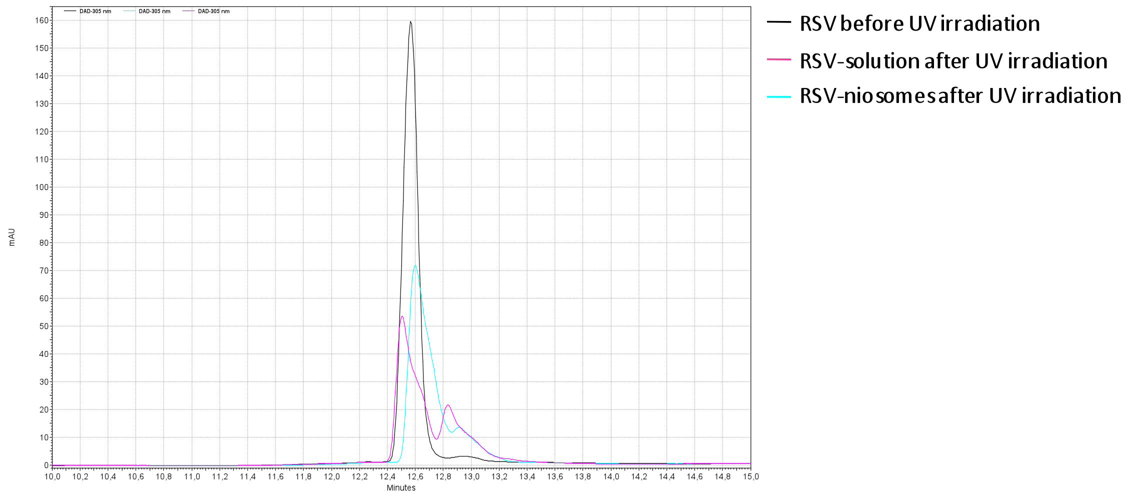


Figure S33. Chromatograms of RSV before (black line) and after UV irradiation (pink and light blue lines for RSV ethanolic control solution and RSV in niosomes, respectively).

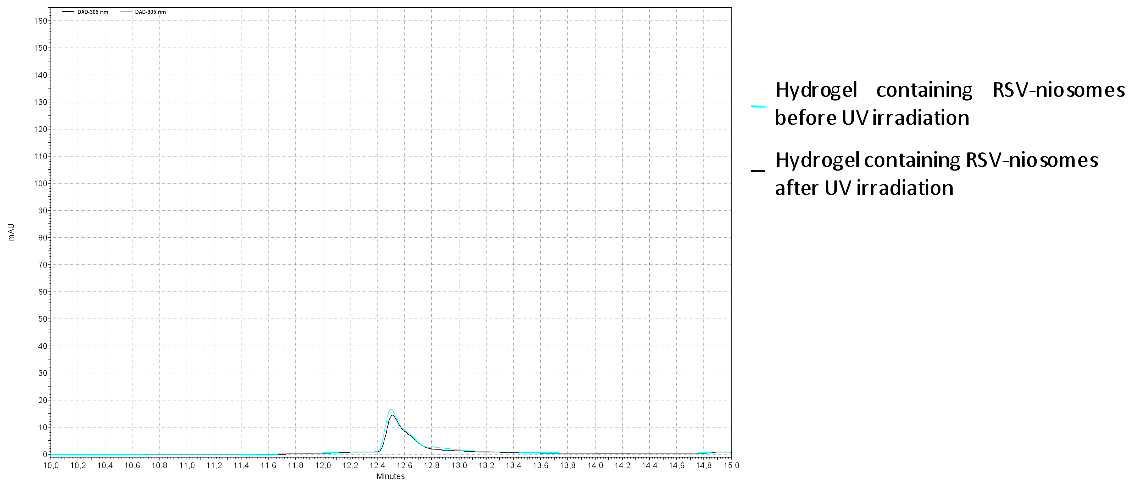


Figure S34. Chromatograms of RSV in niosomes encapsulated in hydrogel before and after UV-irradiation (light blue and black lines, respectively).

Table S8. Molar ratio of *trans*-RSV remaining in the sample after UV irradiation.

Sample	*trans*-RSV remaining
Ethanolic control solution	0,26 ± 0,03
Niosomes	0,70 ± 0,07
Niosomes entrapped hydrogel	0,89 ± 0,03