

Supplementary Materials

Antiproliferative Imidazo-Pyrazole-Based Hydrogel: A Promising Approach for the Development of New Treatments for PLX-Resistant Melanoma

Silvana Alfei ^{1,*}, Marco Milanese ¹, Chiara Brullo ², Giulia Elda Valenti ³, Cinzia Domenicotti ³, Eleonora Russo ², and Barbara Marengo ^{3,*}

¹ Section of Chemistry and Pharmaceutical and Food Technologies, Department of Pharmacy, University of Genoa, Viale Cembrano, 4, 16148 Genoa, Italy; marco.milanese@unige.it

² Section of Medicinal Chemistry and Cosmetic Product, Department of Pharmacy (DIFAR), University of Genoa, Viale Benedetto XV, 3, 16132 Genoa, Italy; chiara.brullo@unige.it (C.B.); eleonora.russo@unige.it (E.R.)

³ Department of Experimental Medicine (DIMES), University of Genova, Via Alberti L.B., 16132 Genoa, Italy; giuliaelda.valenti@edu.unige.it (G.E.V.); cinzia.domenicotti@unige.it (C.D.)

* Correspondence: alfei@difar.unige.it (S.A.); barbara.marengo@unige.it (B.M.); Tel.: +39-010-355-2296 (S.A.)

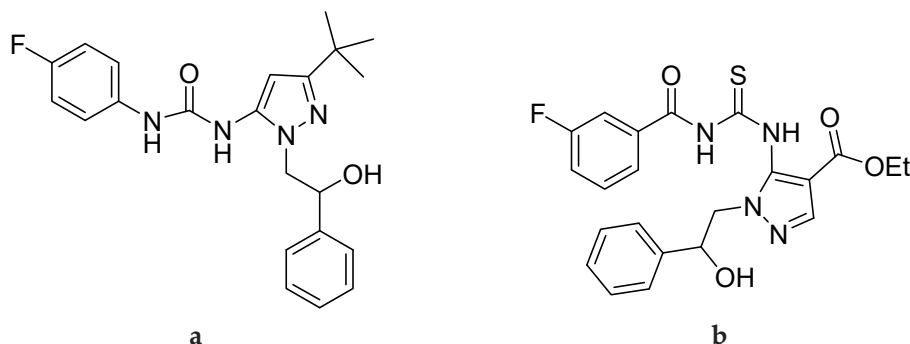


Figure S1. Chemical structure of previously reported anti-bacterial pyrazoles **3c** (a) and **4b** (b).

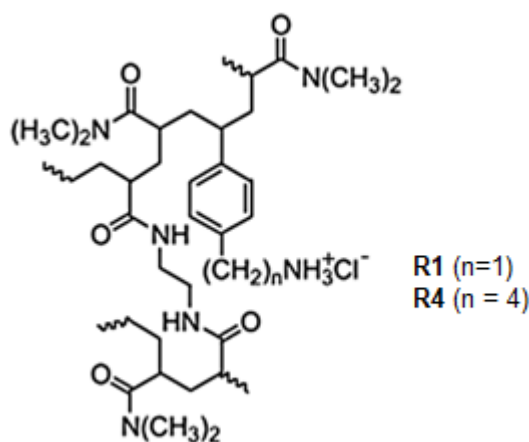


Figure S2. Chemical structure of previously reported resin **R1** ($n = 1$) and **R4** ($n = 4$).

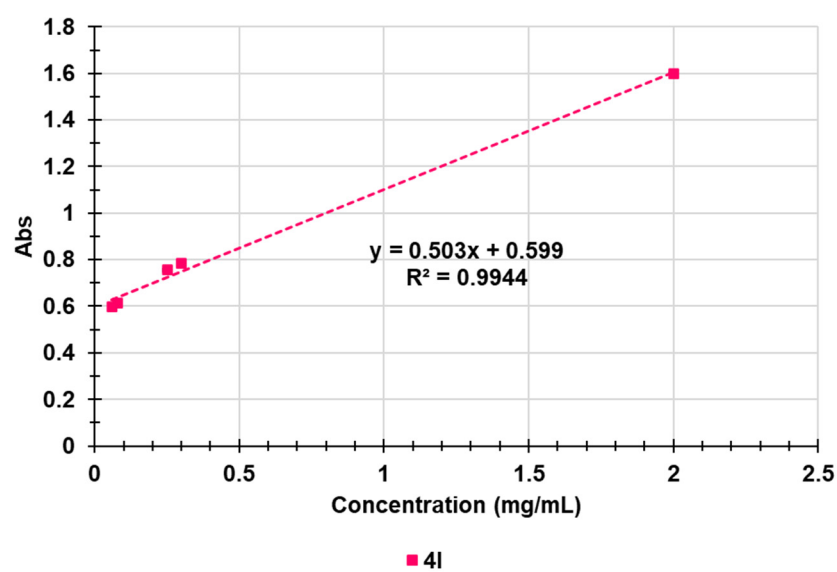


Figure S3. 4I calibration curve.

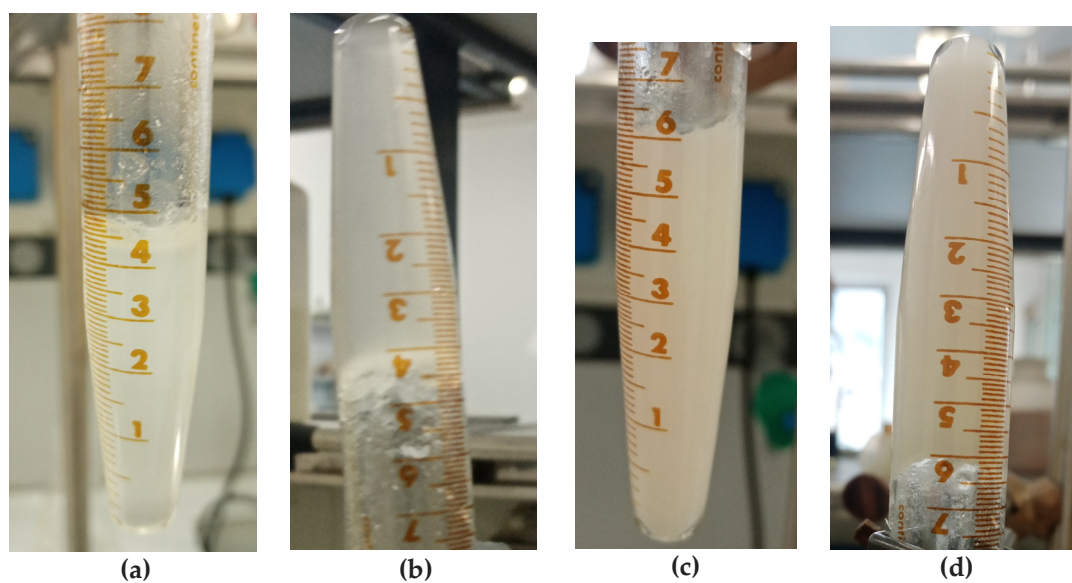


Figure S4. Appearance of R4HG (a,b) and R4HG-4I (c,d) at their equilibrium degree of swelling (EDS).

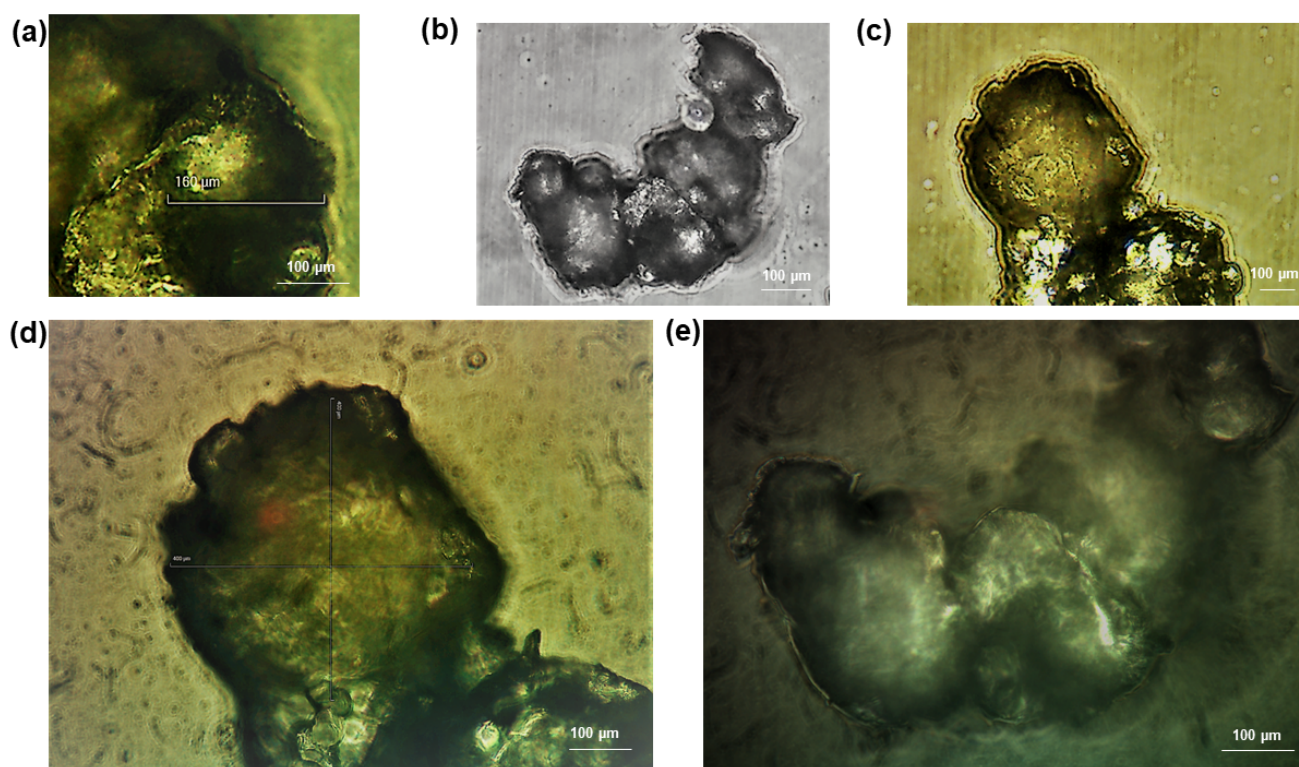


Figure S5. Representative optical microphotographs of R4HG after drying at 100°C until a constant weight equal to that before swelling was achieved (R4HG-D). Objective 40 × (a, d, e), 20 × (b, c).

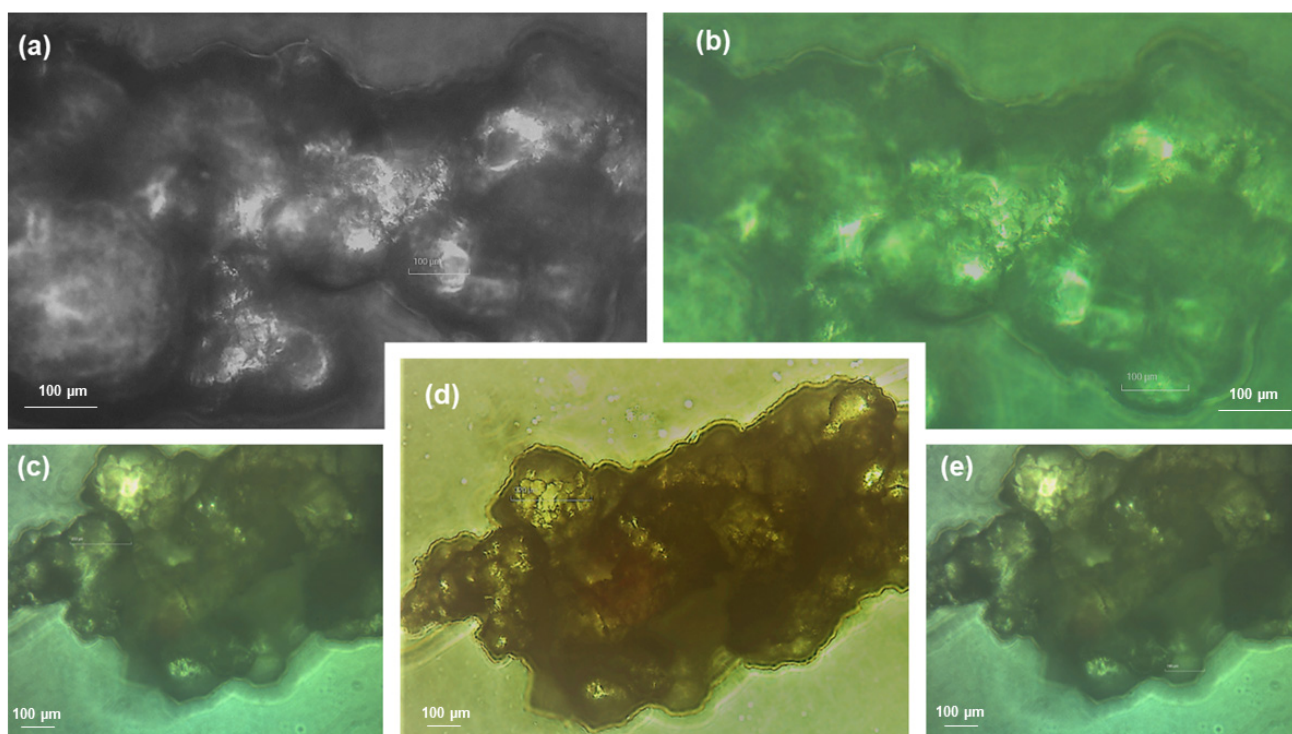


Figure S6. Representative optical microphotographs of R4HG-4I after drying at 100°C until a constant weight equal to that before swelling was achieved (R4HG-4I-D). Objective 40 × (a, b), 20 × (c, d, e).

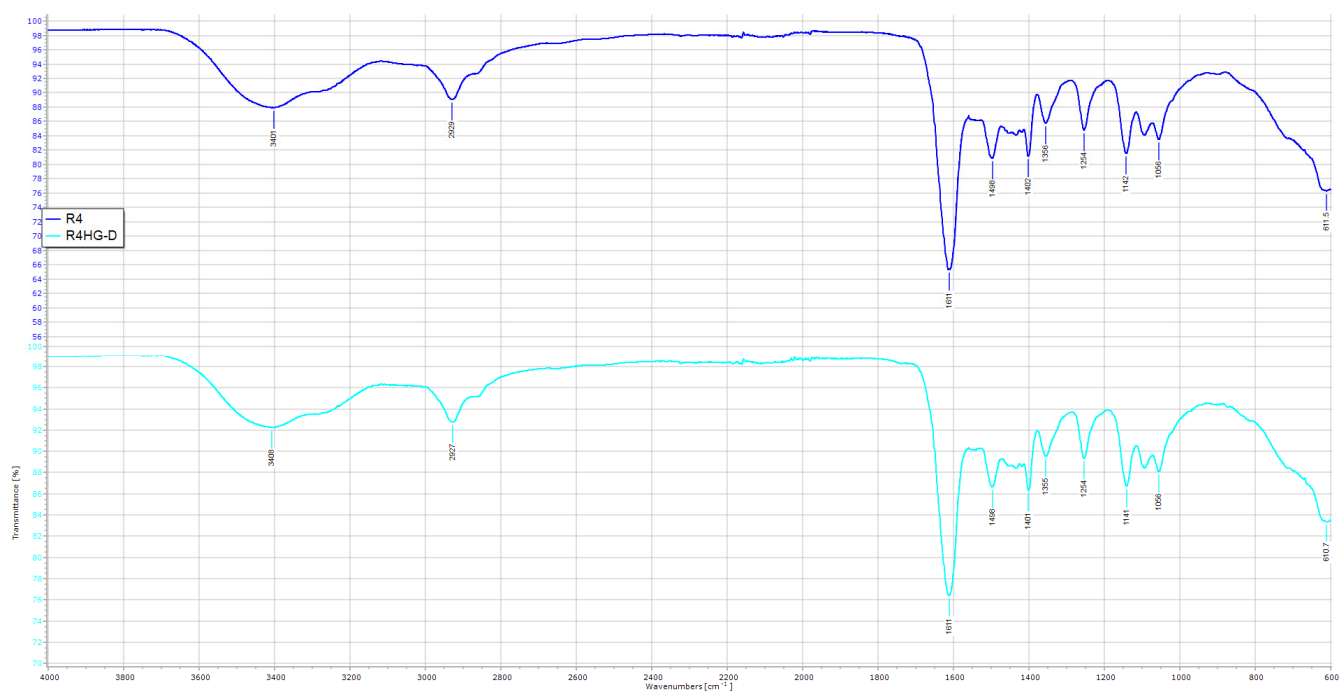


Figure S7. Representative ATR-FTIR spectra of resin R4 and fully dried hydrogel R4HG-D.

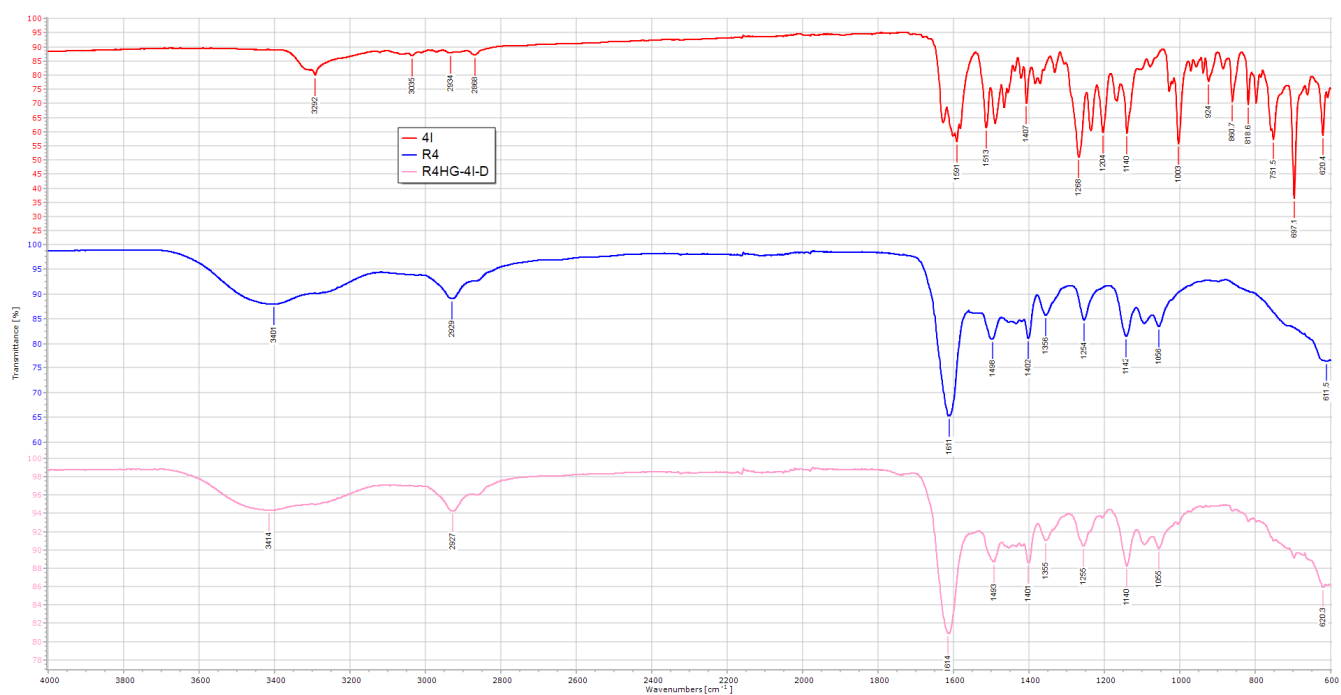


Figure S8. Representative ATR-FTIR spectra of resin R4, **4I** and fully dried hydrogel R4HG-4I-D.

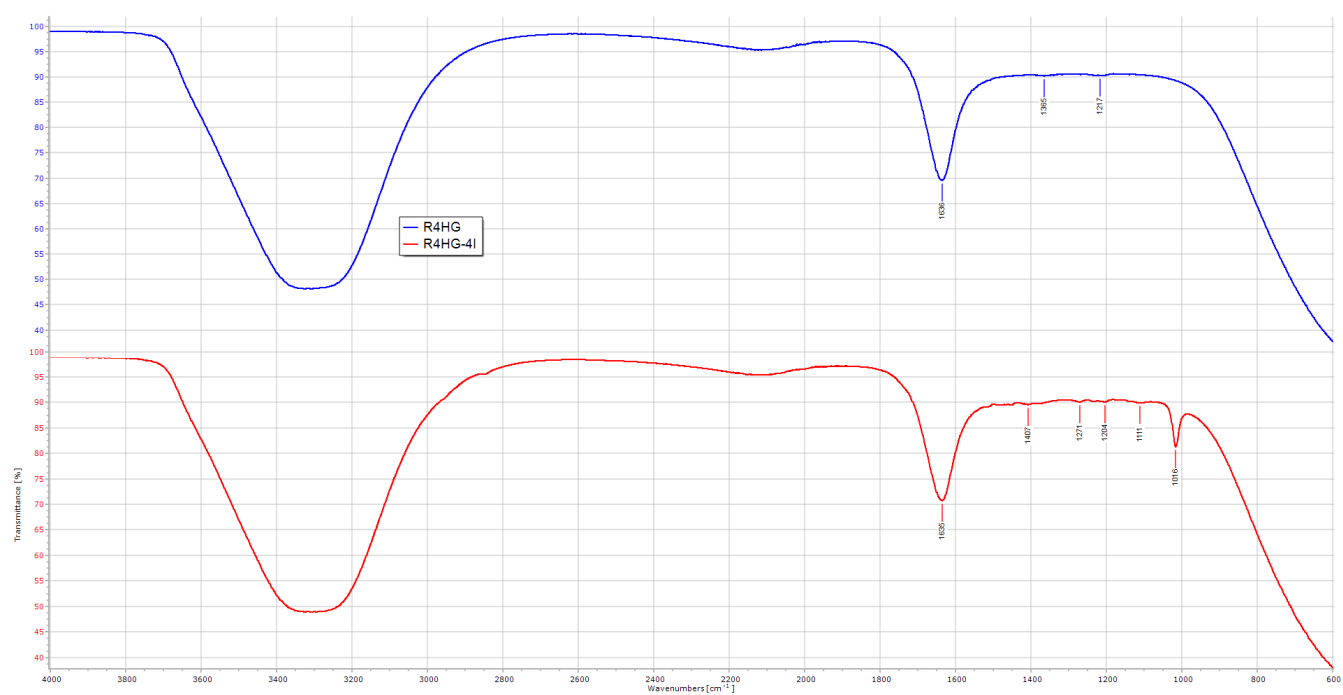


Figure S9. Representative ATR-FTIR spectra of swollen hydrogels R4HG and R4HG-4I.

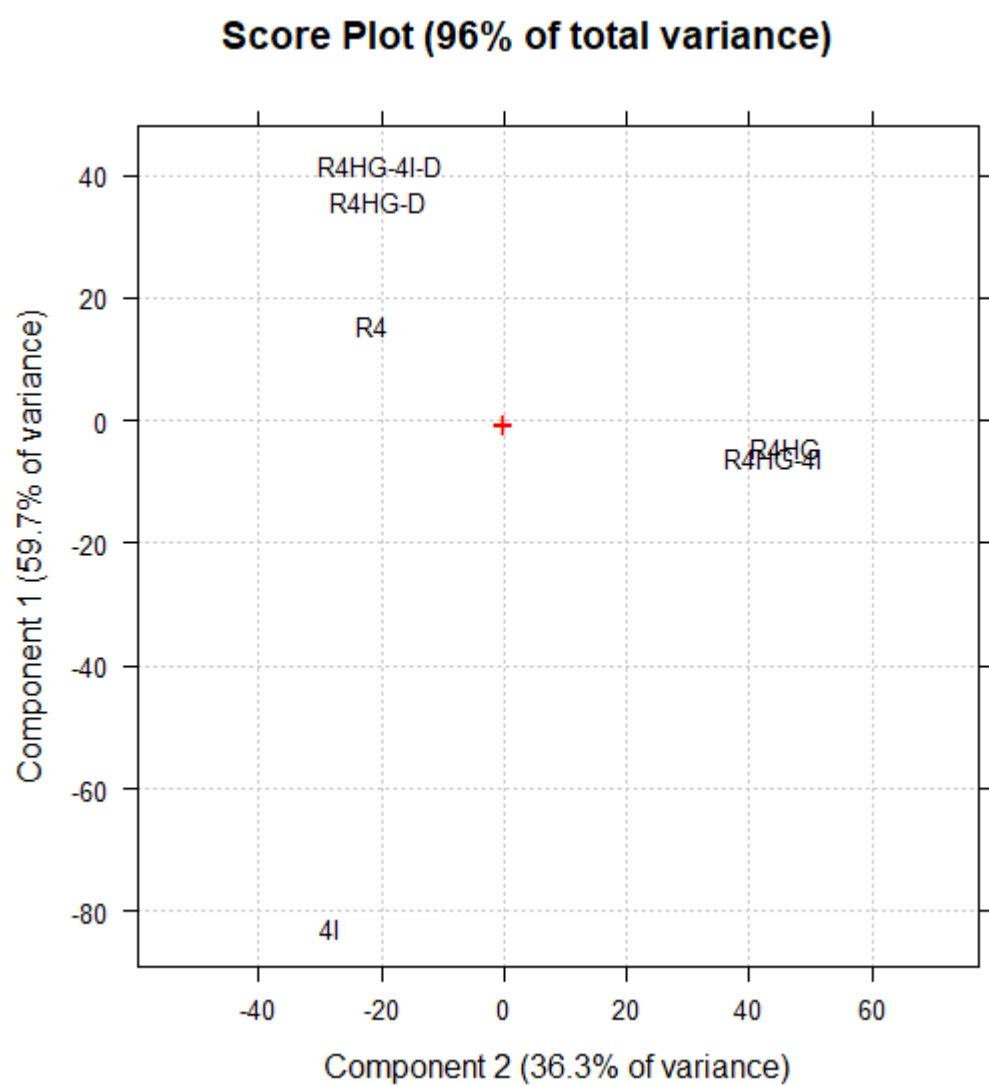


Figure S10. Score plot of PC1 (explaining the 59.7% of variance) vs. PC2 (explaining the 36.3% of variance).

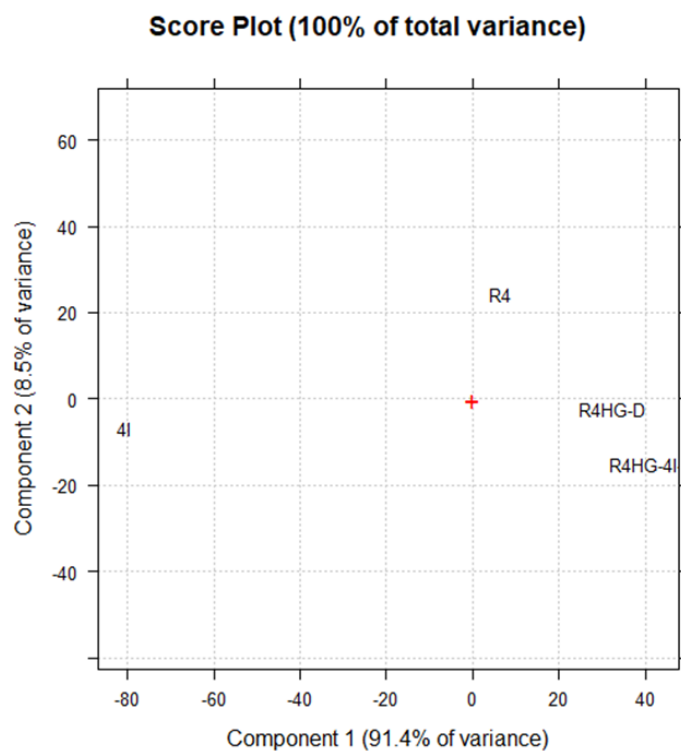


Figure S11. Score plot of PC1 (explaining the 91.4% of variance) vs. PC2 (explaining the 8.5% of variance).

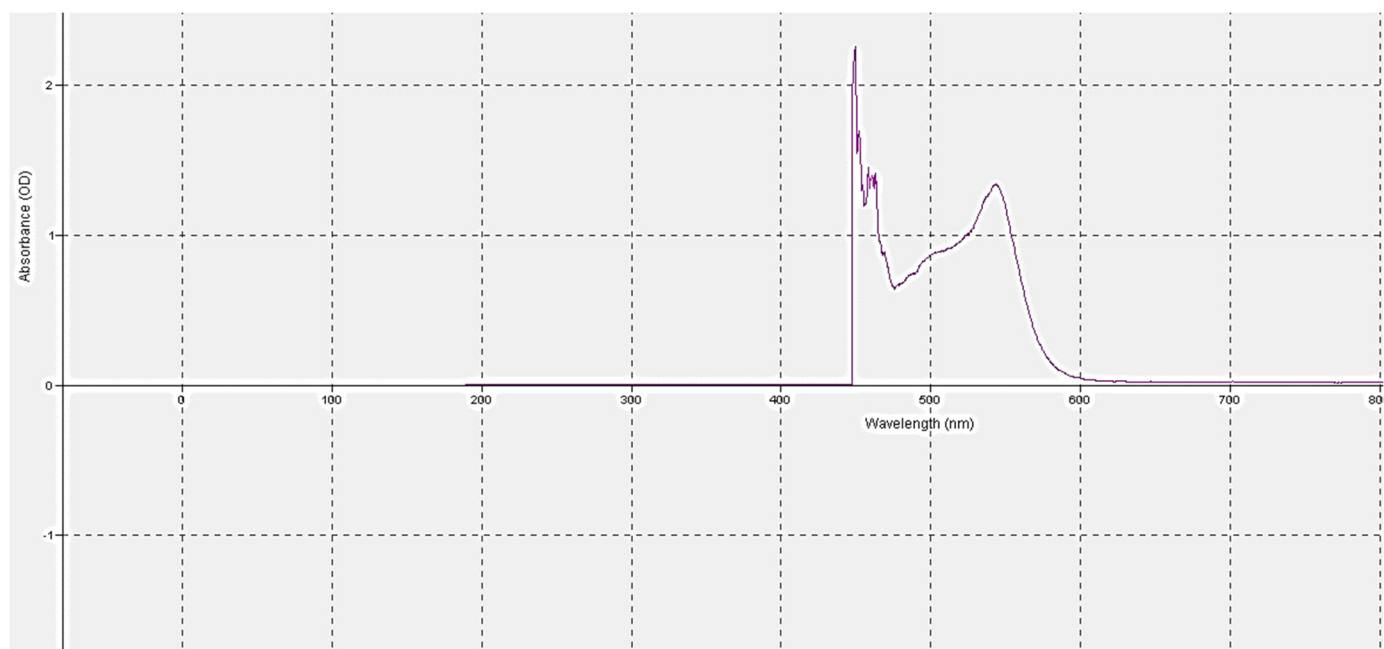


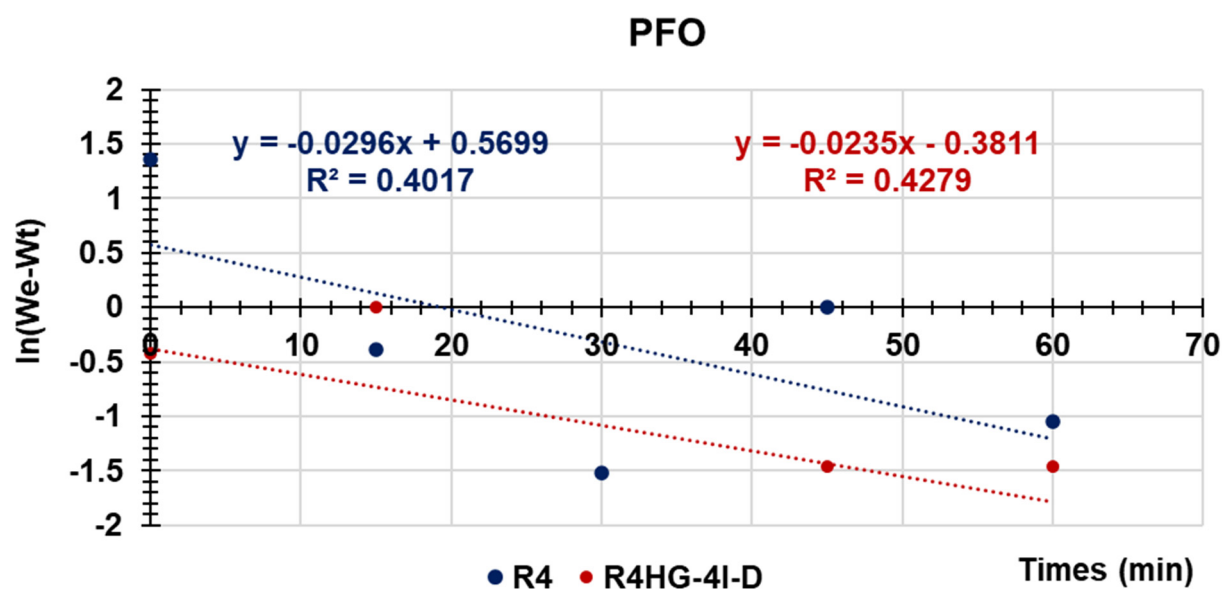
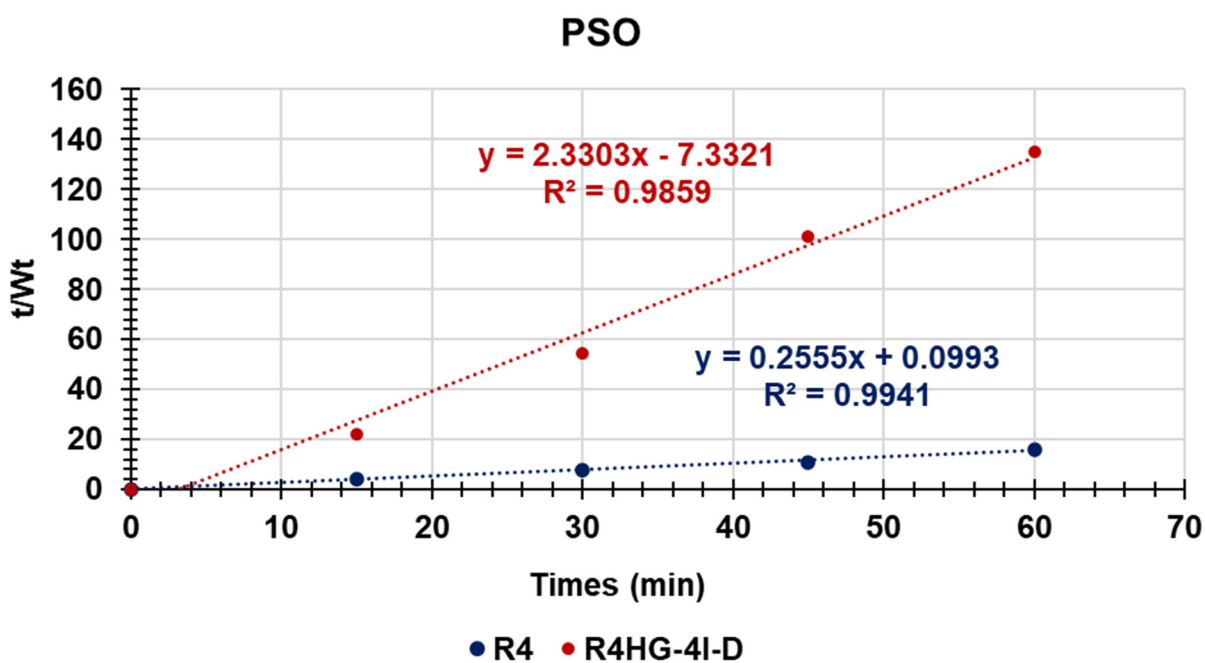
Figure S12. UV-Vis spectrum of 4I.

Video S1. <https://clipchamp.com/watch/LVAKVdP1F8f>.

Video S2. <https://clipchamp.com/watch/TtDuSbTIuWF>.

Table S1. Values of the coefficients of determination obtained for all the kinetic models used.

Kinetic Model	R ² of R4HG	R ² of R4HG-4I
Zero-order	0.8940	0.8451
First-order	0.9594	0.9422
Hixson–Crowel	0.8940	0.8451
Higuchi	0.9684	0.9580
Korsmeyer–Peppas	0.9828	0.9711

**Figure S13.** PFO kinetic model (We and Wt expressed as mg).**Figure S14.** PSO kinetic model (Wt expressed as mg; $t/Wt = \text{mg} \times \text{min}$).

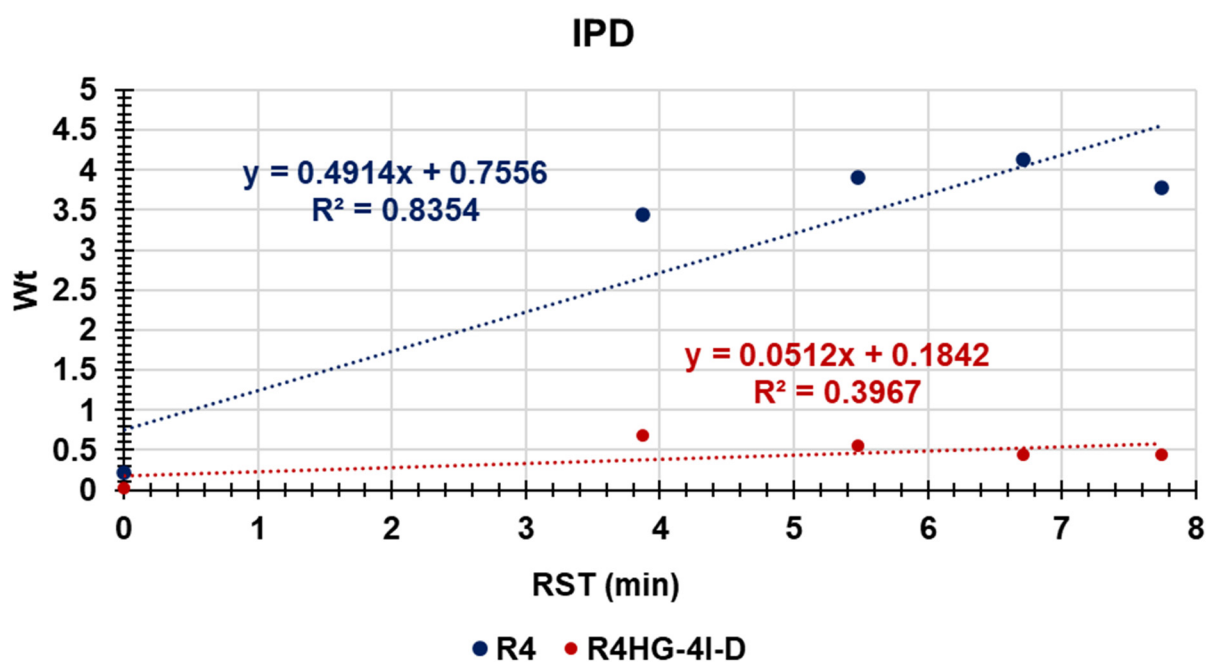


Figure S15. IPD kinetic model (Wt expressed as mg). RST = root square of times.

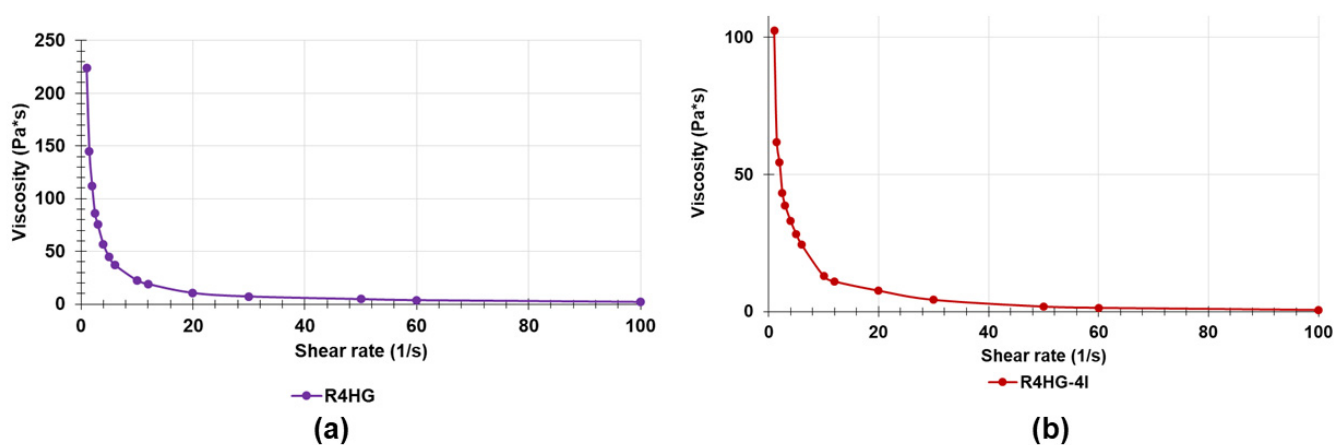


Figure S16. Curve of the viscosity vs. shear rate of R4HG (a) and R4HG-4I (b).

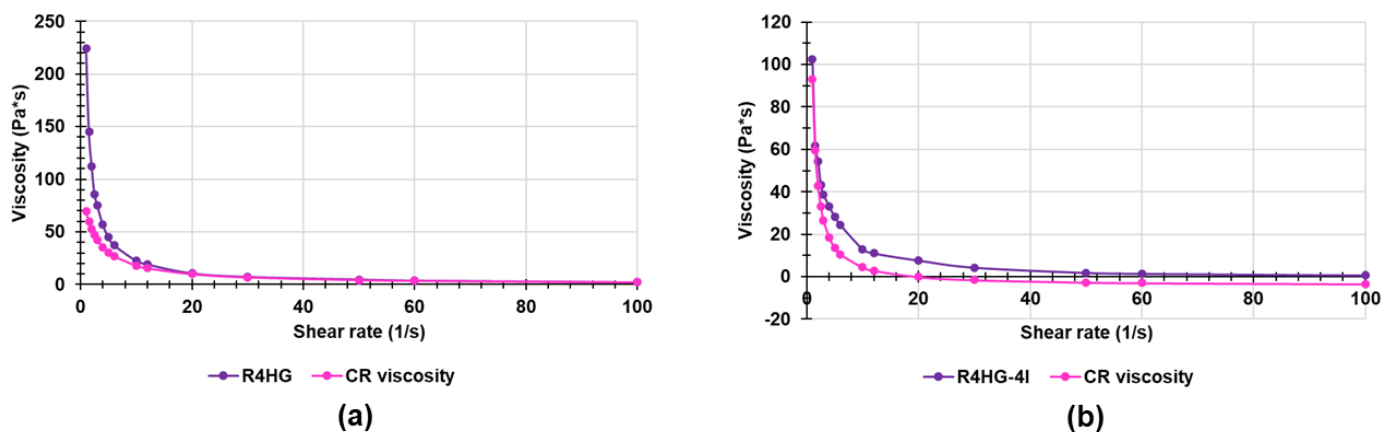


Figure S17. Relationships between the CR viscosity and γ for R4HG (a) and R4HG-4I (b) (fuchsia lines) and the experimental measurements (purple lines).

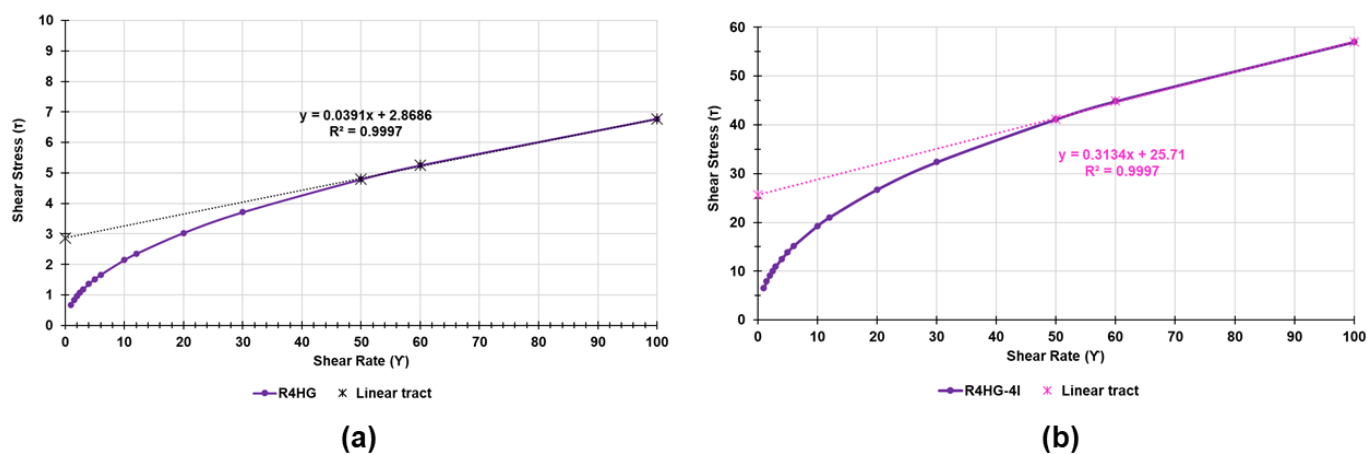


Figure S18. Plots of τ (Pa) vs. γ (s^{-1}) of R4HG (a) and R4HG-4I (b). The intercept of equations associated with the linear tract of the curves provides the values of the yield stress reported in Table 7 (main text).

Table S2. Values of coefficients of determinations (R^2) obtained for all kinetic models considered.

Kinetic Model	Coefficients of Determination (R^2)	
	R4HG	R4HG-4I
PFO	0.4017	0.4279
PSO	0.9944	0.9859
IPD	0.8354	0.3967

Zero Order

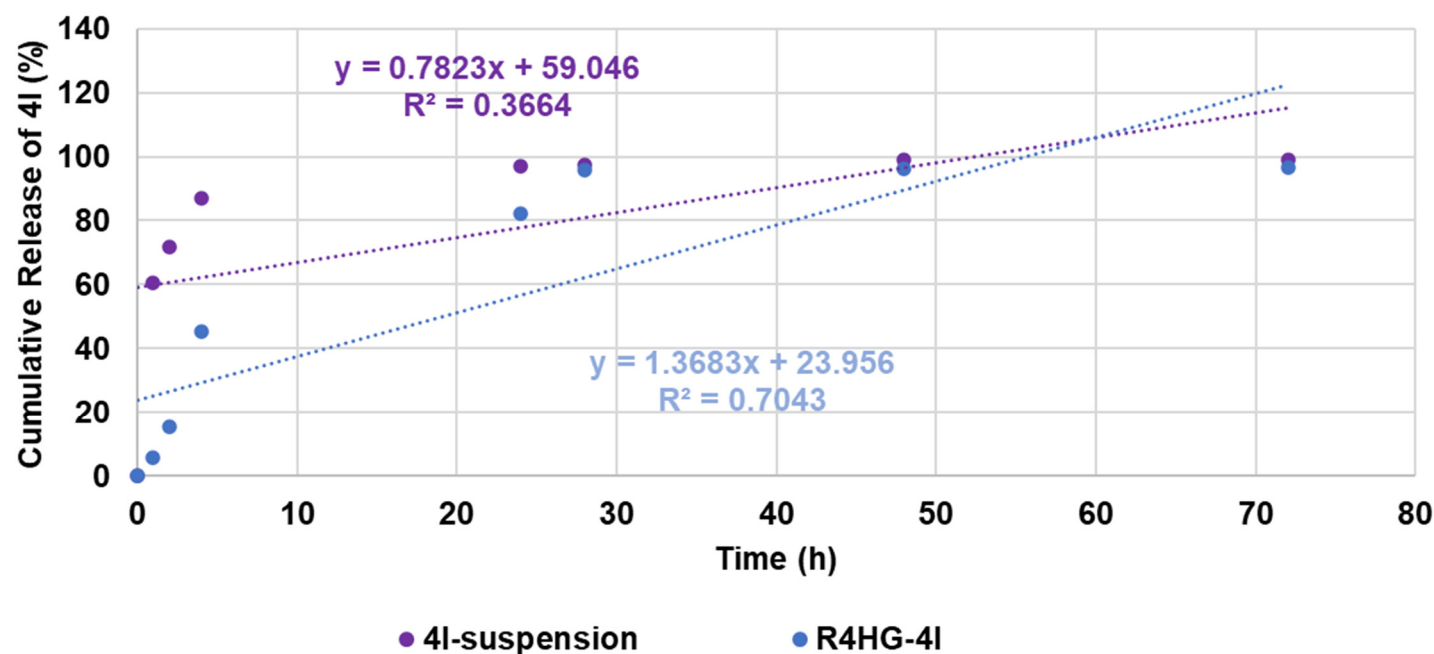


Figure S19. Zero order kinetic models.

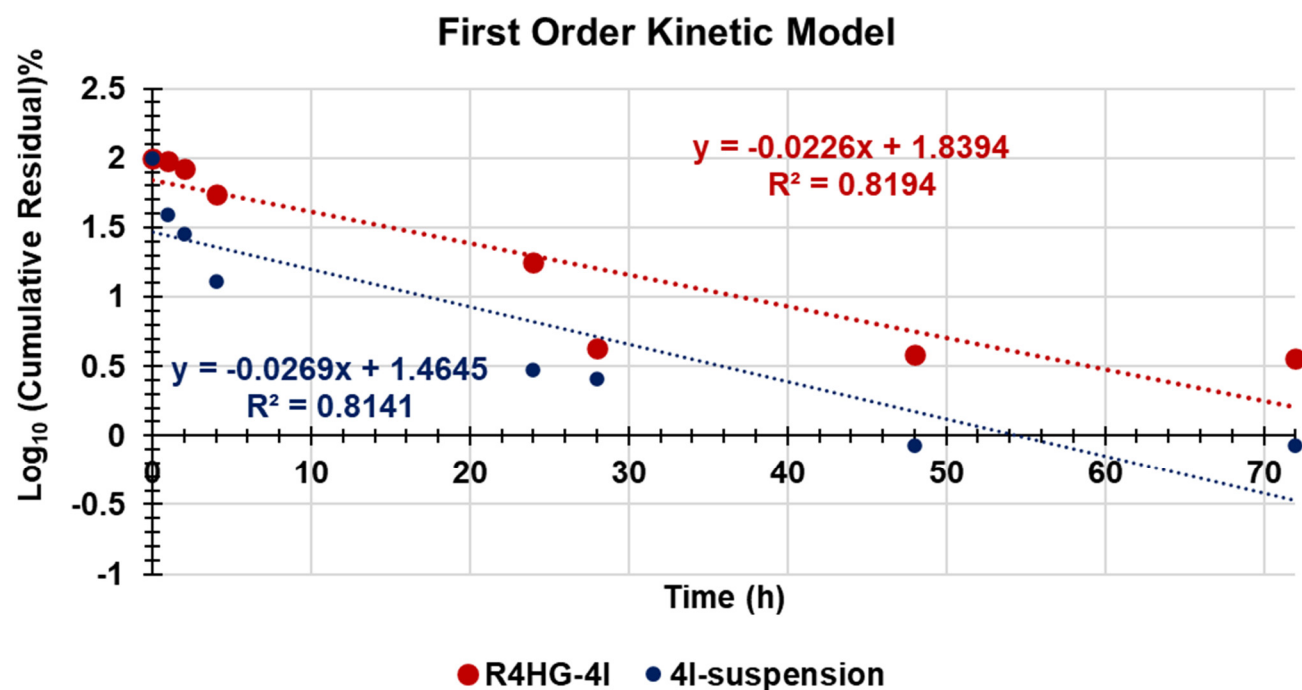


Figure S20. First order kinetic models.

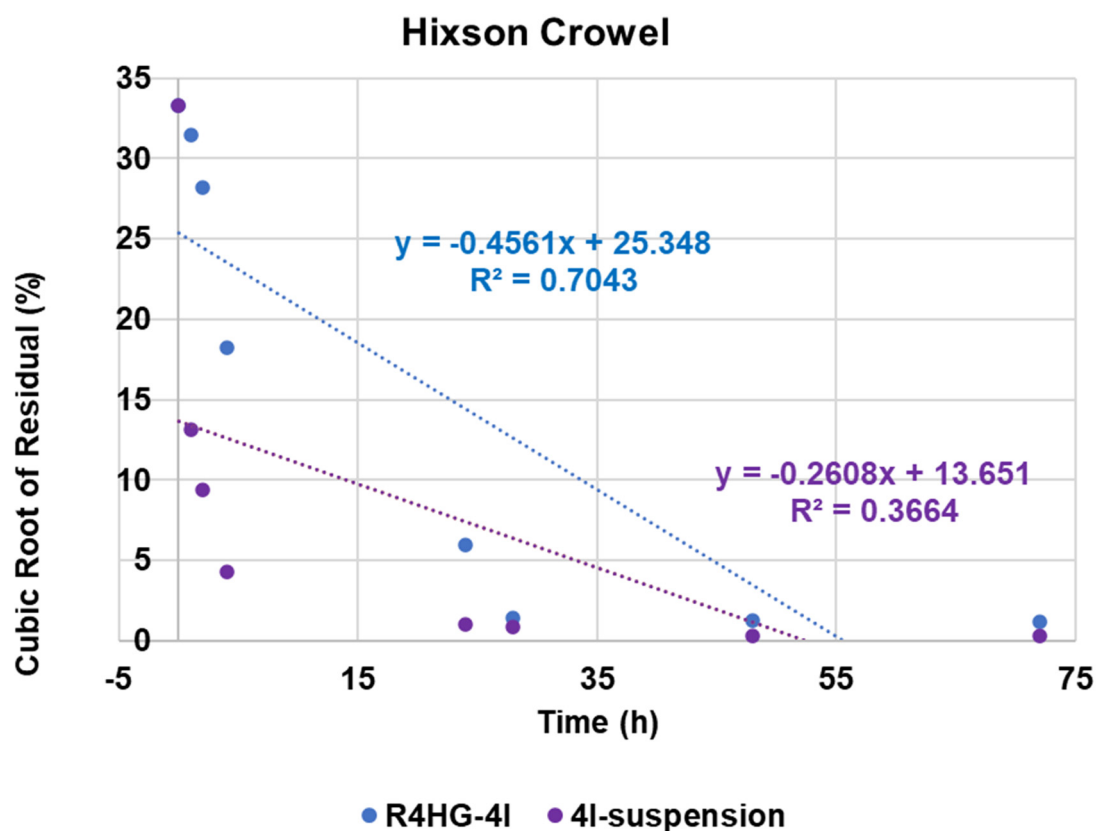


Figure S21. Hixson Crowel kinetic models.

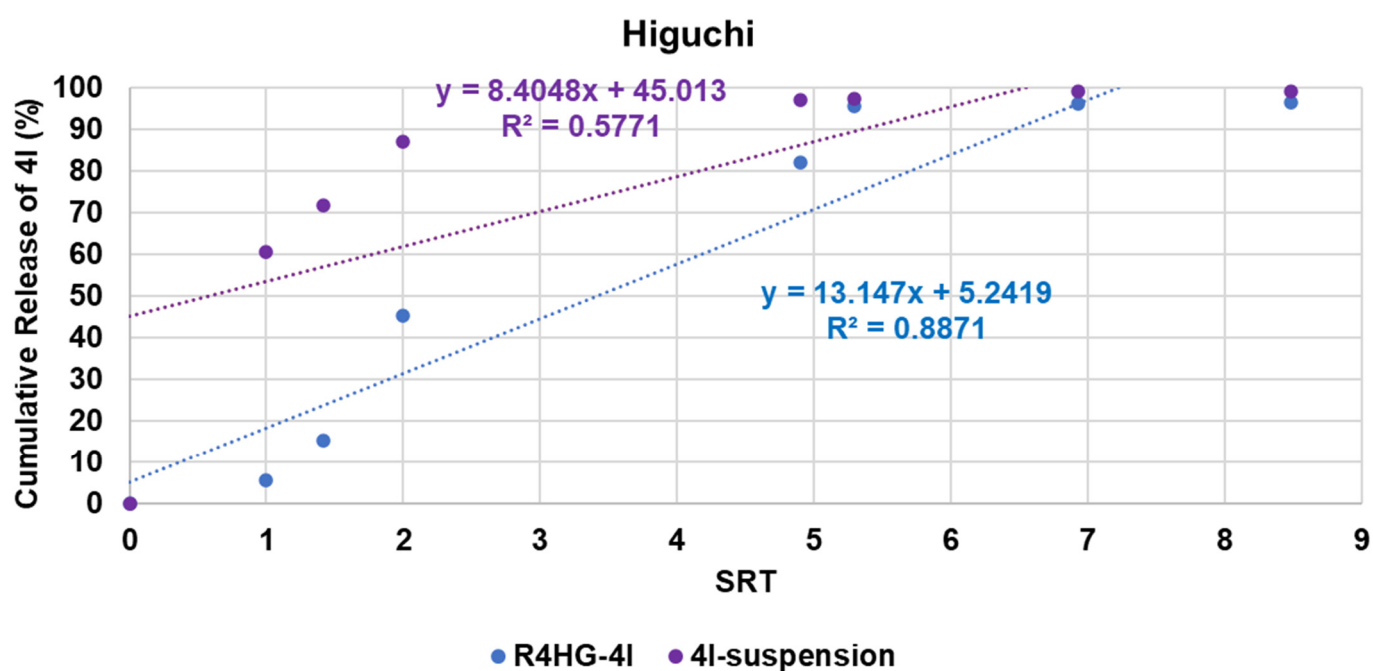


Figure S22. Higuchi kinetic models. SRT = square root of time.

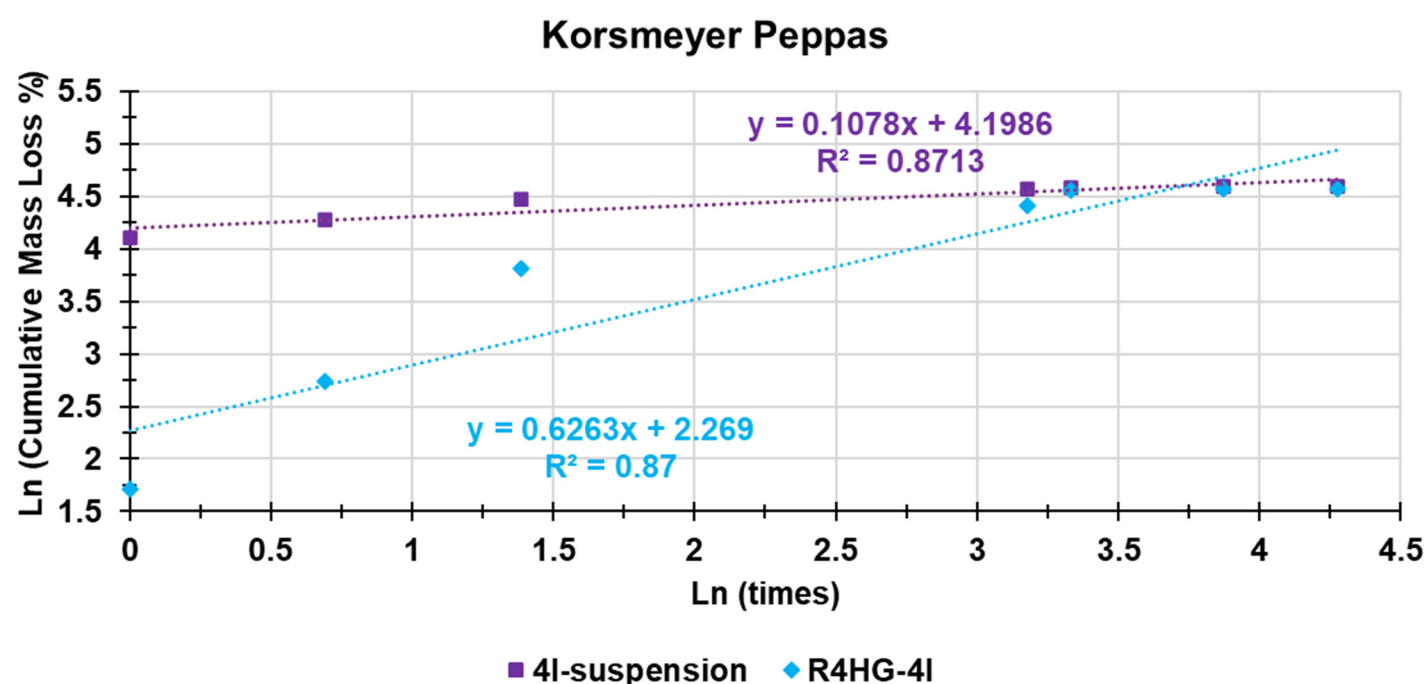


Figure S23. Korsmeyer Peppas kinetic models.

Table S3. Values of the coefficients of determination obtained for all the kinetic models used.

Kinetic Model	R ² of R4HG-4I	R ² of 4I-suspension
Zero-order	0.7043	0.3664
First-order	0.8194	0.8141
Hixson–Crowel	0.7043	0.3664
Higuchi	0.8871	0.5771
Korsmeyer–Peppas	0.8700	0.8713

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.