Supporting Information for

Encapsulation and Controlled Release of L-Leuprolide from Poly(β-hydroxyalkanoate)s: Impact of Microstructure and Chemical Functionalities

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Table S1. Homo- and copolymerization of β-butyrolactone and *rac*-allyl-butyrolactone.[a]

Entry	$[BL^R]$	(co)polymer $[BL^R]$[b] in copolymer (mol%)	$M_{n\ exp}$[c] ($\times 10^3$ g/mol)	M_w/M_n[c]	P_r/P_m[d]
1	*rac*	*s*-P(HB-*co*-HB^{allyl}) 11	9.2	1.24	84/16
2	*rac*	*s*-P(HB-*co*-HB^{diOH}) 11	11.2	1.28	82/18
3	*rac*	*s*-P(HB-*co*-HB^{allyl}) 11	33.5	1.50	84/16
4	*rac*	*s*-P(HB-*co*-HB^{diOH}) 11	38.4	1.68	nd
5	*rac*	*s*-P(HB-*co*-HB^{allyl}) 11	61.2	1.62	82/18
6	*rac*	*s*-P(HB-*co*-HB^{diOH}) 11	69.6	1.76	nd
7	*rac*	*a*-P(HB-*co*-HB^{allyl}) 7	25.4	1.45	55/45
8	*rac*	*a*-P(HB-*co*-HB^{diOH}) 7	21.0	1.52	53/47
9	*R*	*i*-P(HB-*co*-HB^{allyl}) 11	30.1	1.30	nd
10	*R*	*i*-P(HB-*co*-HB^{diOH}) 11	35.1	1.41	nd
11	*R*	*i*-P(HB) 0	4.2	1.06	03/97
12	*R*	*i*-P(HB) 0	8.5	1.13	04/96
13	*R*	*i*-P(HB) 0	15.9	1.11	04/96
14	*R*	*i*-P(HB) 0	28.0	1.13	05/95

[a] $[BL^R]$ = 2.44 mol/L; polymerization carried out at 20 °C; the results shown for each entry are representative of at least two reproducible (± 5%) runs. [b] Comonomer content determined by ^{1}H NMR in $CDCl_3$. [c] Average-number molecular weight in g.mol^{-1} (uncorrected) determined by GPC vs. PS standards. [d] P_r is the probability of racemic linkages between monomer units and is determined by $^{13}C\{^1H\}$ NMR spectroscopy.

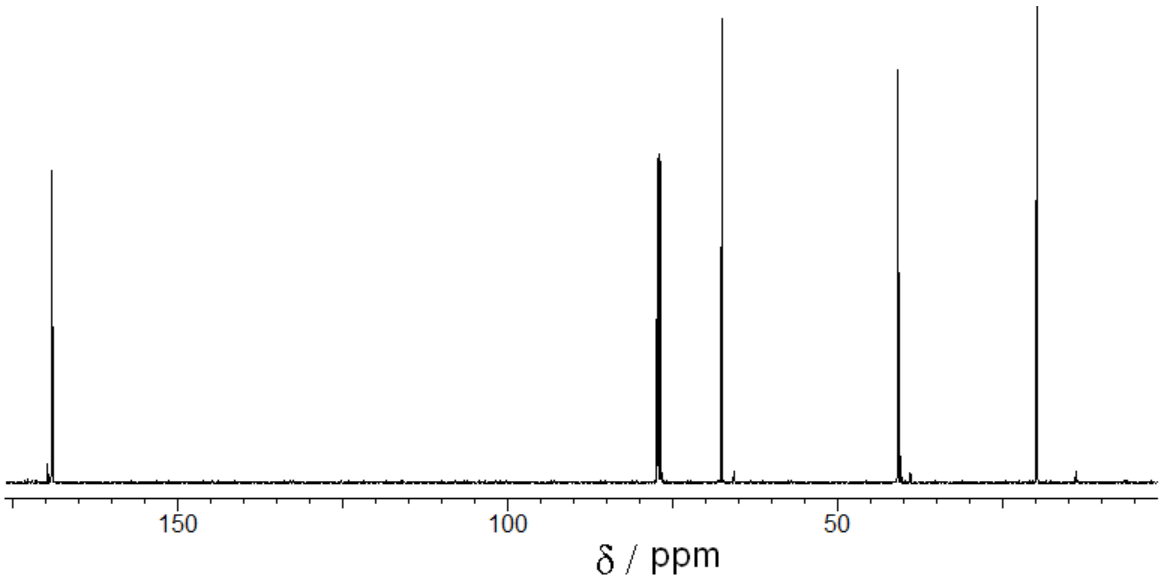

Figure S1. $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz, $CDCl_3$, 40 °C) of a highly isotactic PHB (P_m = 0.95) sample prepared by ROP of *R*-BL^{Me} with complex **1**.

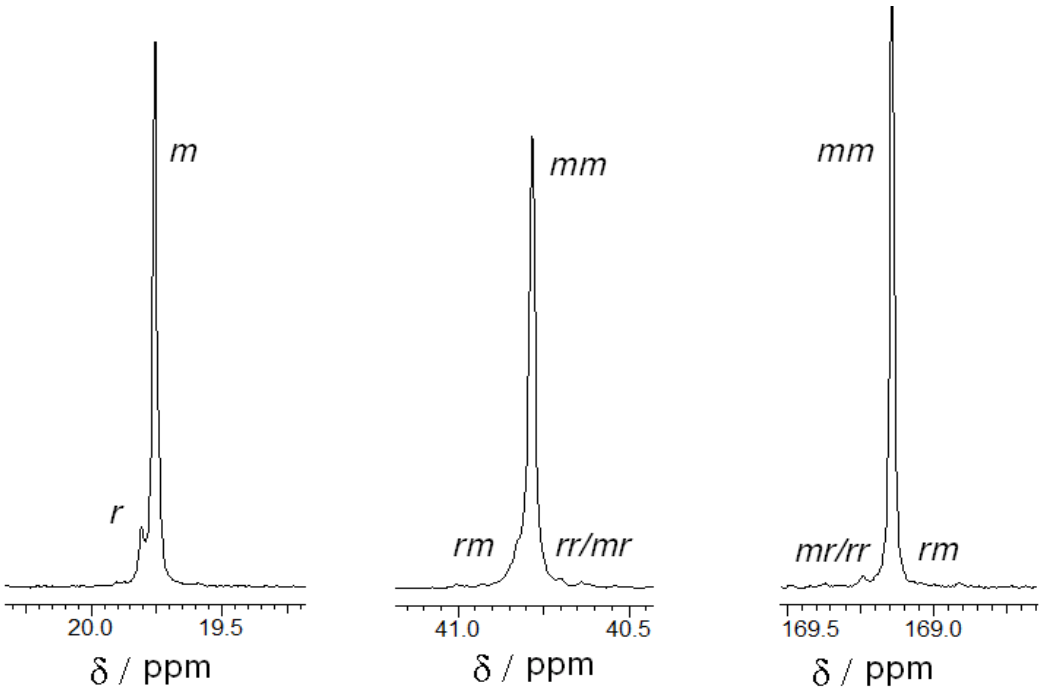

Figure S2. Methyl, Methylene, and carbonyl regions of the $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz, $CDCl_3$, 40 °C) of a highly isotactic PHB (P_m = 0.95) sample prepared by ROP of *R*-BL^{Me} with complex **1**.

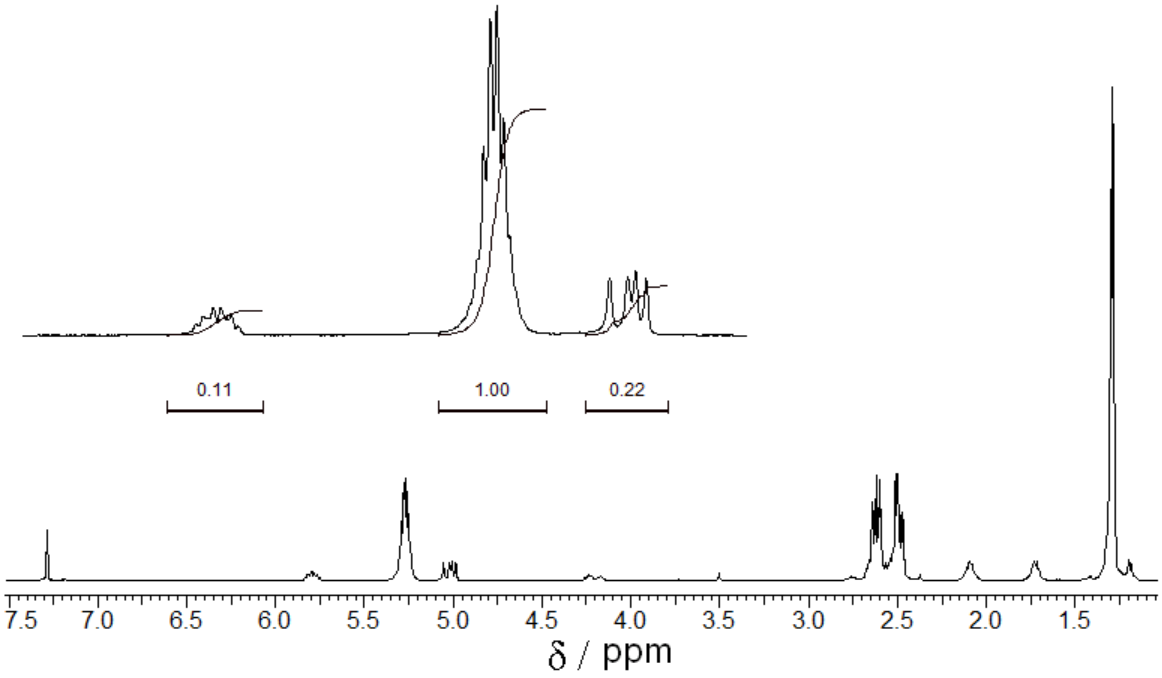

Figure S3. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 20 °C) of an isotactic-rich (P_m = 0.85) *i*-P(HB-*co*-HB^{allyl}, 11 mol%) sample prepared by ROP of *R*-BL^{Me} and *rac*-BL^{allyl} with complex **1** (Table S1, entry 9).

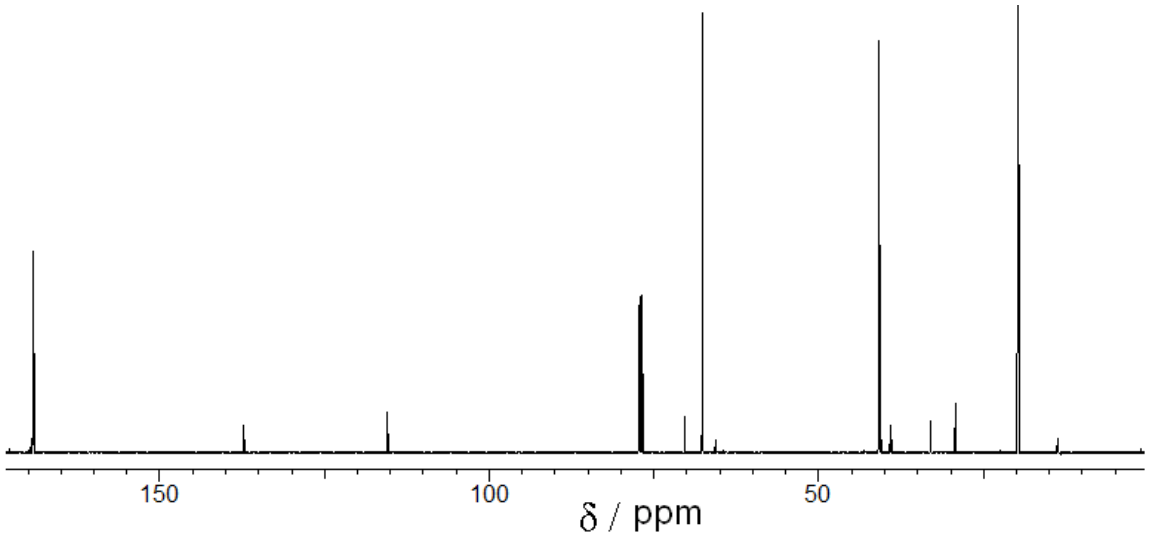

Figure S4. $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz, $CDCl_3$, 40 °C) of an isotactic-rich (P_m = 0.85) *i*-P(HB-*co*-HB^{allyl}, 11 mol%) sample prepared by ROP of *R*-BL^{Me} and *rac*-BL^{allyl} with complex **1** (Table S1, entry 9).

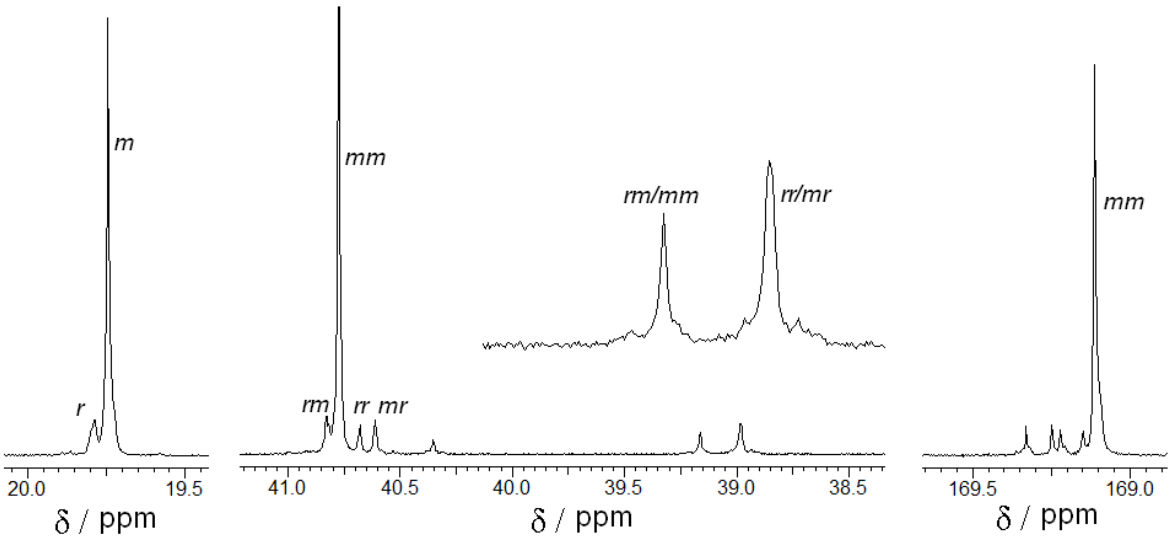

Figure S5. Methyl, Methylene, and carbonyl regions of the $^{13}C\{^{1}H\}$ NMR spectrum (125 MHz, $CDCl_3$, 40 °C) of an isotactic-rich (P_m = 0.85) *i*-P(HB-*co*-HB^{allyl}, 11 mol%) sample prepared by ROP of *R*-BL^{Me} and *rac*-BL^{allyl} with complex **1**(Table S1, entry 9).

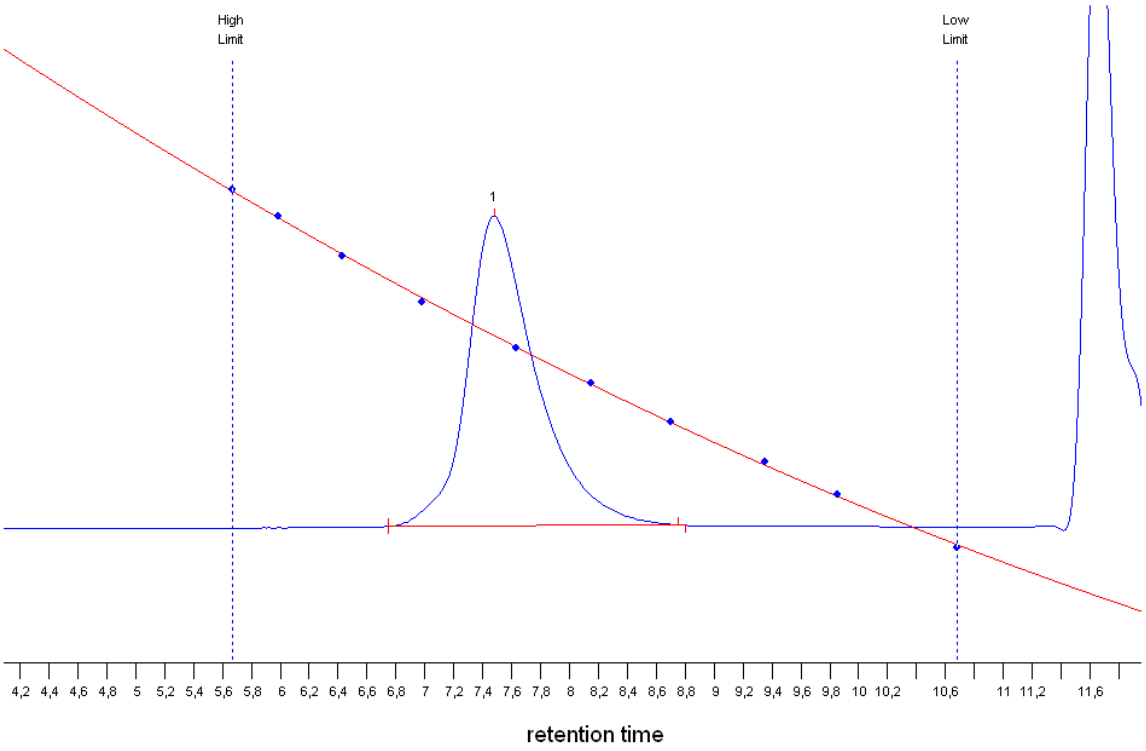

Figure S6. RI detector responses during Gel Permeation Chromotography (GPC) (THF, 25 °C) of an isotactic-rich (P_m = 0.85) *i*-P(HB-*co*-HB^{allyl}, 11 mol%) sample prepared by ROP of *R*-BL^{Me} and *rac*-BL^{allyl} with complex **1**(Table S1, entry 9).

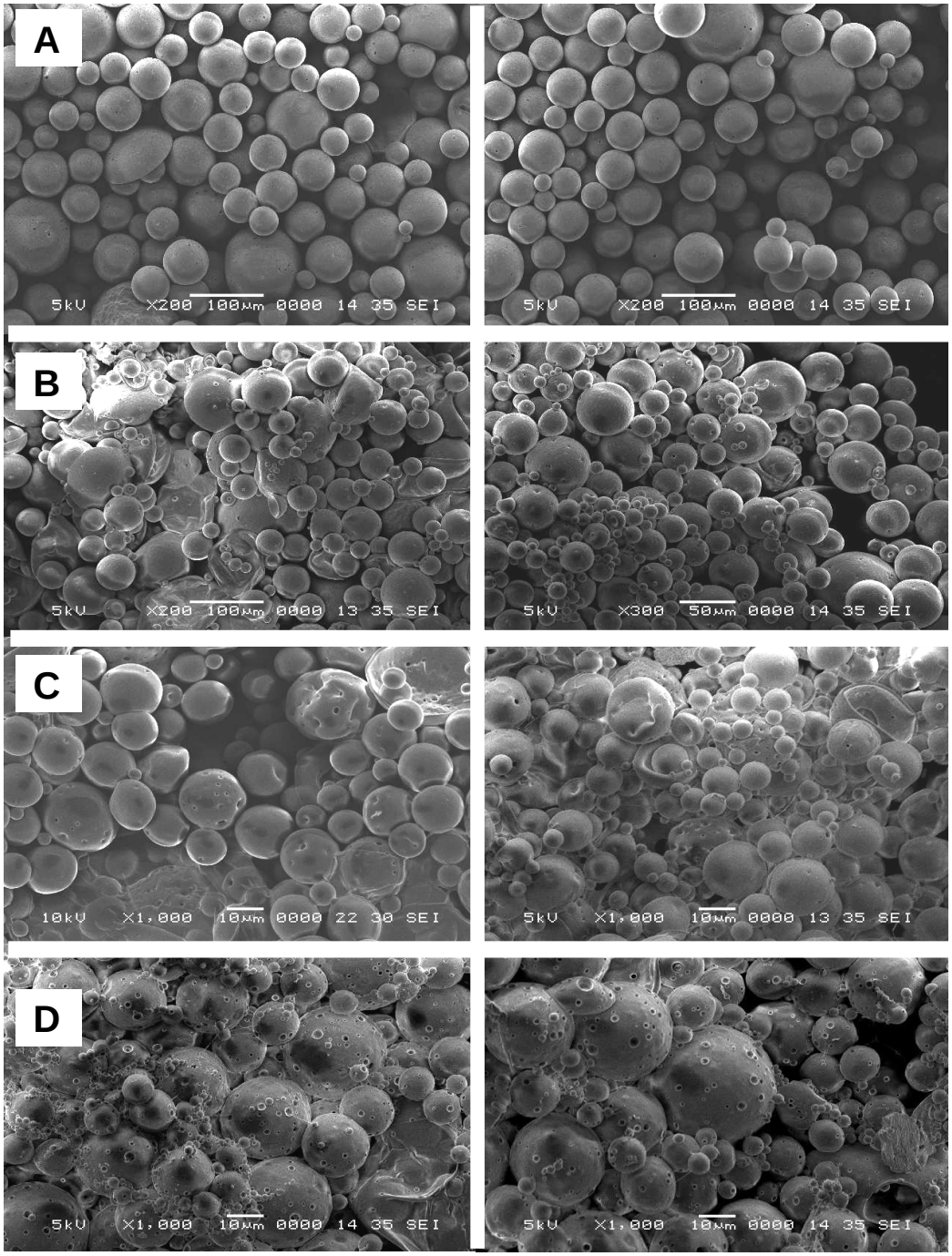

Figure S7. SEM images of microparticles prepared by the ”solvent evaporation” method, the size of the bar is 10-100 µm. **A**: *s*-P(HB-*co*-HB^{allyl}, 11 mol% allyl) (Table S1, entry 3). **B**: *s*-P(HB-*co*-HB^{allyl}, 11 mol% allyl) (Table S1, entry 3) containing 7 wt% of LeA. **C**: *s*-P(HB-*co*-HB^{diOH}, 11 mol% diOH) (Table S1, entry 4). **D**: *s*-P(HB-*co*-HB^{diOH}, 11 mol% diOH) (Table S1, entry 4) containing 7 wt% of LeA.

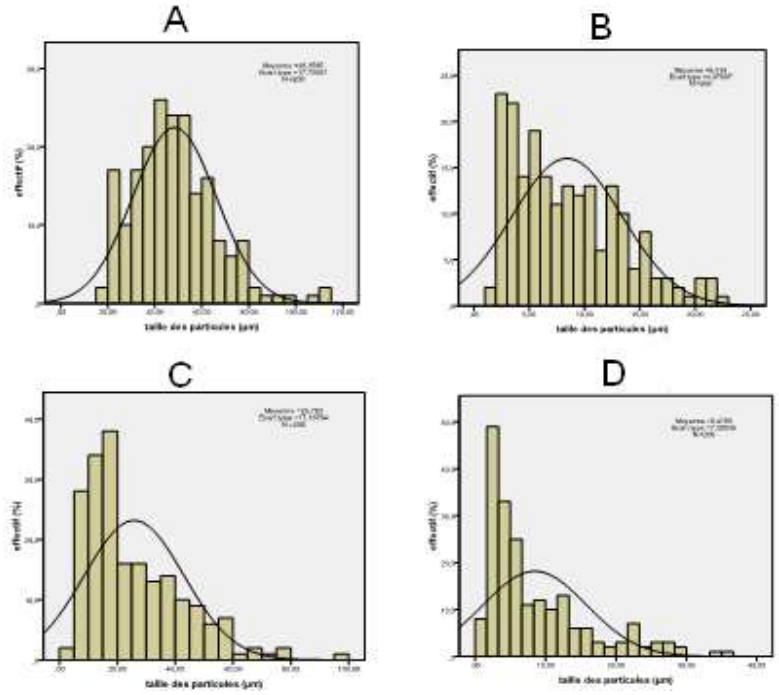

Figure S8. Gaussian distributions of microparticles size. **A**: *s*-P(HB-*co*-HB^{allyl}), **B**: *s*-P(HB-*co*-HB^{diOH}), **C**: *s*-P(HB-*co*-HB^{allyl})/LeA, **D**: *s*-P(HB-*co*-HB^{diOH})/LeA.

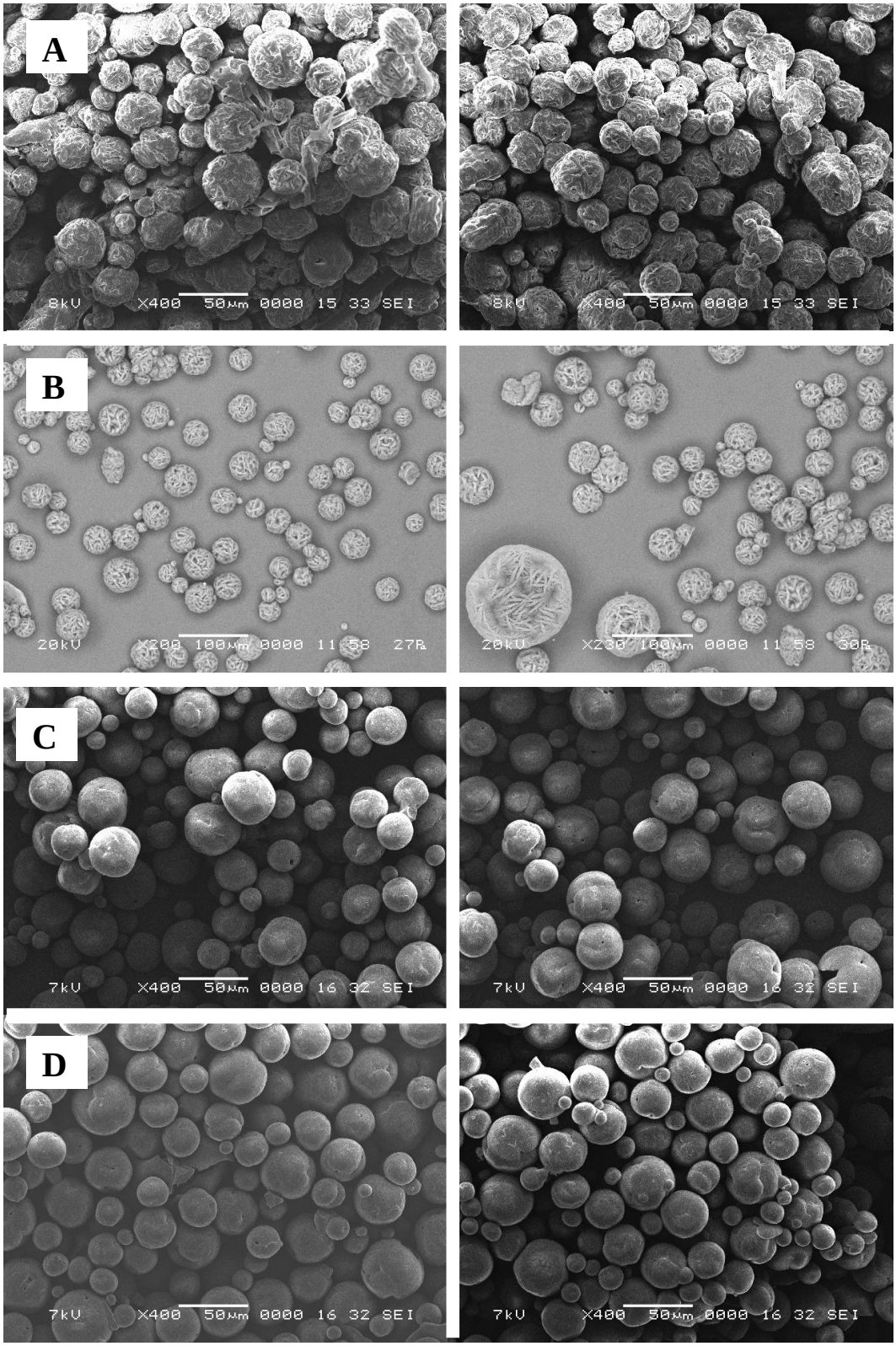

Figure S9. SEM images of polymer microparticles prepared by the "solvent evaporation" method, the size of the bar is 50-100 μm. **A**: *i*-PHB (Table S1, entry 14). **B**: *i*-PHB (Table S1, entry 14) containing 7 wt% of LeA. **C**: *i*-P(HB-*co*-HB^{allyl}, 11 mol% allyl) (Table S1, entry 9). **D**: *i*-P(HB-*co*-HB^{diOH}, 11 mol% diOH) (Table S1, entry 10).

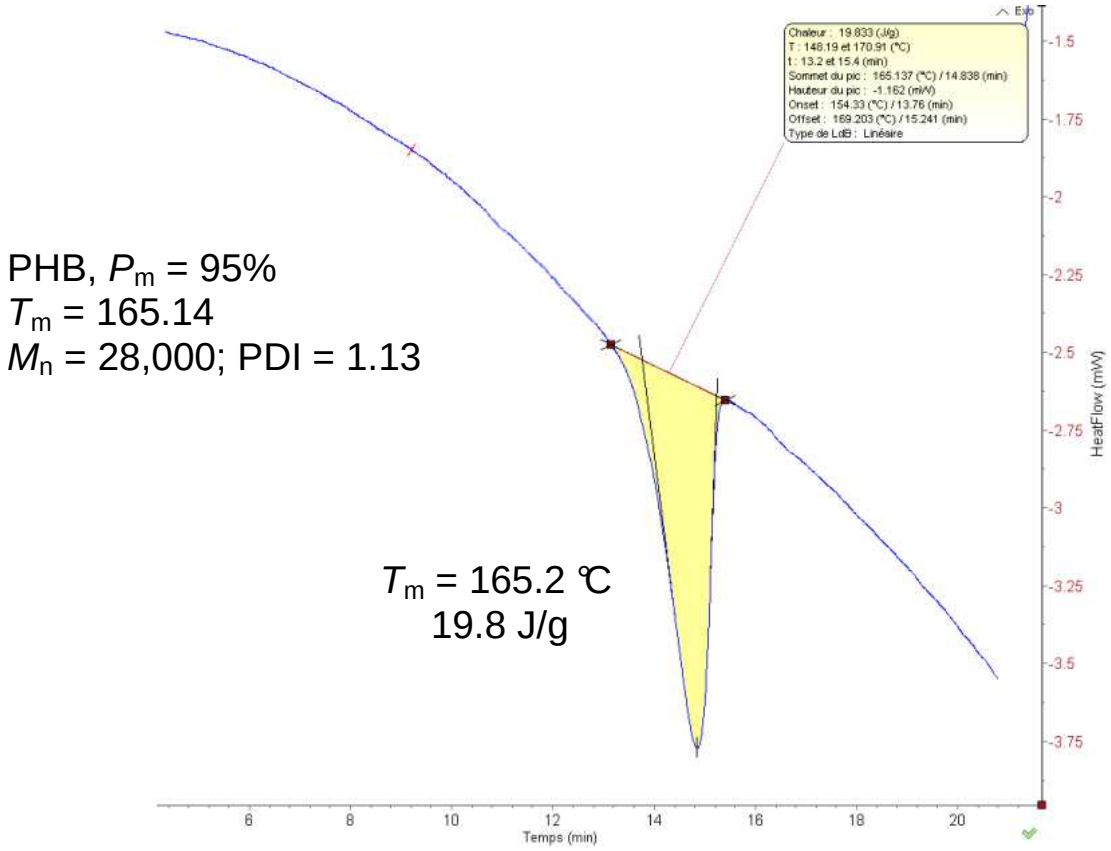

Figure S10. DSC trace (run from 23 °C to 200 °C at 10 °C/min) of *i*-PHB prepared by ROP of *R*-BL^{Me} with complex **1** (Table S1, entry 14).

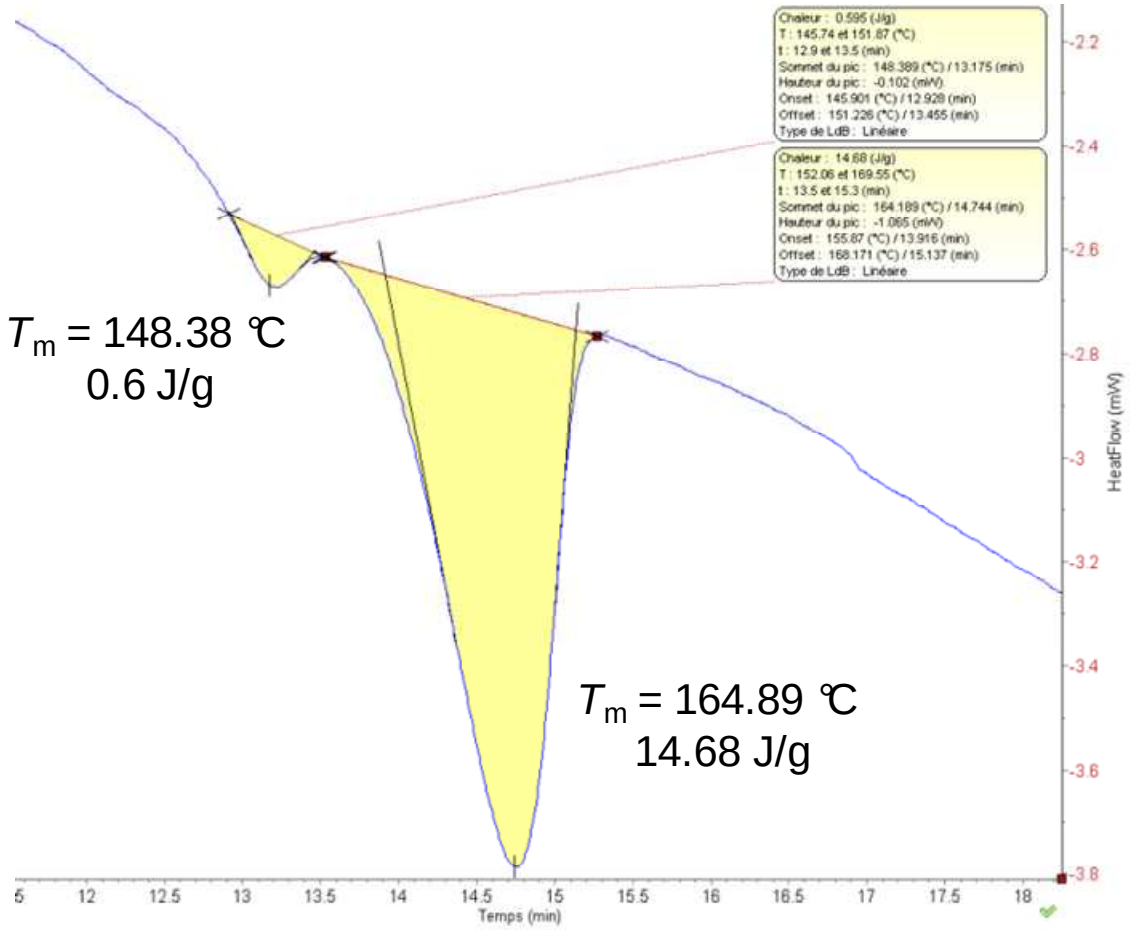

Figure S11. DSC trace (run from 23 °C to 200 °C at 10 °C/min) of *i*-PHB (Table S1, entry 14)/LeA microparticles.

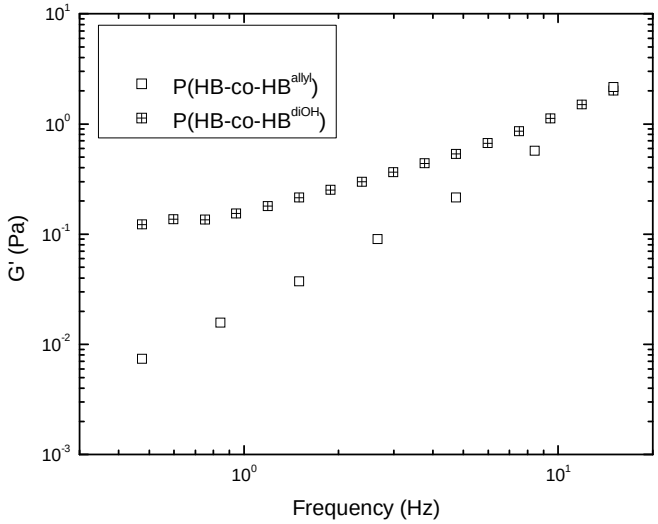

Figure S12. Storage modulus G' as a function of frequency of *s*-P(HB-*co*-HB^{allyl} (11 mol% allyl) and *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) in 10 wt% chloroform solutions

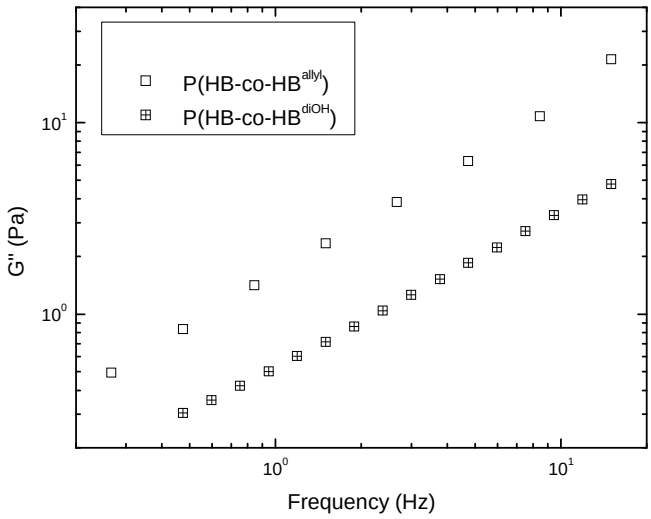

Figure S13. Loss modulus G" as a function of frequency of *s*-P(HB-*co*-HB^{allyl} (11 mol% allyl) and *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) in 10 wt% chloroform solutions.

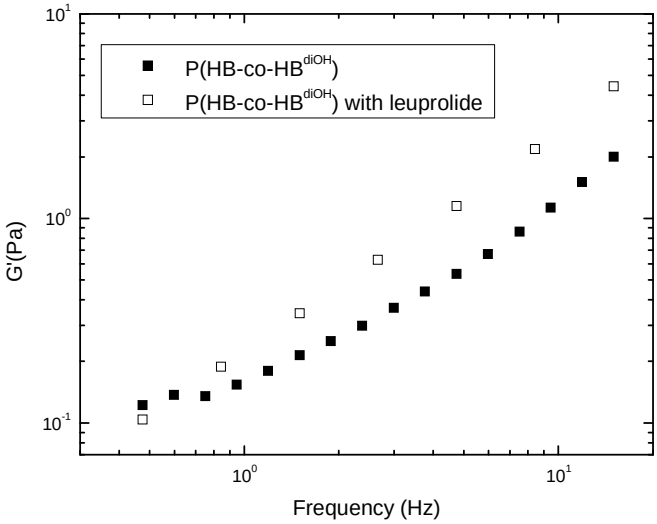

Figure S14. Storage modulus G' as a function of frequency of *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) and *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) encapsulated with LeA (7 wt%), in 10wt% chloroform solutions.

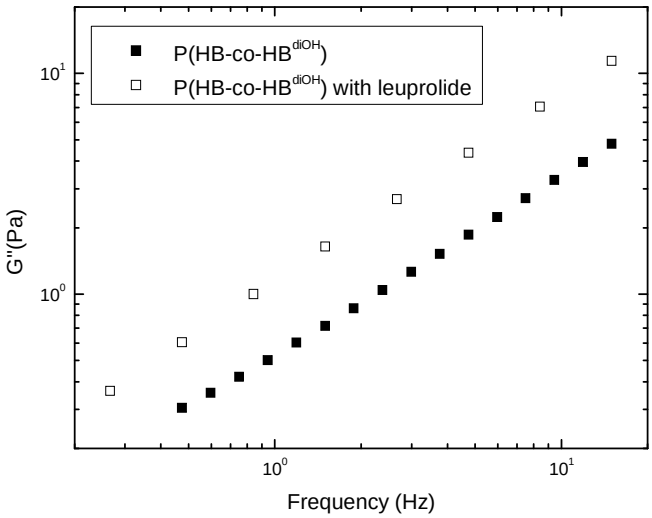

Figure S15. Loss modulus G'' as a function of frequency of *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) and *s*-P(HB-*co*-HB^{diOH} (11 mol% diOH) encapsulated with LeA (7 wt%) in 10 wt% chloroform solutions.

Supplementary Material (ESI) for New Journal of Chemistry

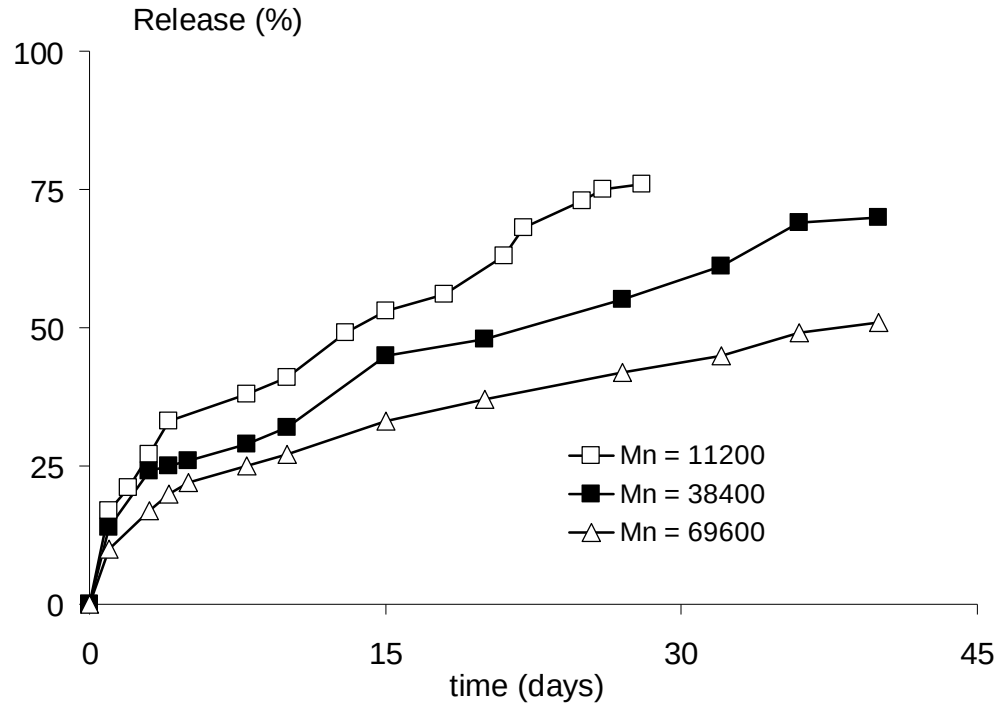

Figure S16. Effect of the molecular weight on the release profiles of LeA from LeA-loaded *s*-P(HB-*co*-HB^{diOH}, 11 mol% diOH) prepared by "co-precipitation" method,. Δ M_n = 11 200 g.mol^{-1}, (Table S1, entry 2); ■ M_n = 38 400 g.mol^{-1}, (Table S1, entry 4); □ M_n = 69 600 g.mol^{-1}, (Table S1, entry 6).